

Conference Proceedings

**Abstract**

The Center for Global Health and the Office of Cancer Complementary and Alternative Medicine

of the National Cancer Institute of the U.S. National Institutes of Health (NCI/NIH) hosted the Trans-NCI-NIH Conference on International Perspectives on Integrative Medicine for

Cancer Prevention and Cancer Patient Management. The main aims of the conference were to

(1) discuss the integration of traditional, complementary, and alternative medicine with

conventional cancer prevention and treatment approaches in global health, thus forming new

approaches to integrative oncology, and (2) discuss methods for strengthening integrative

oncology research in low- and middle-income countries. The virtual conference was held

October 27–30, 2020. Approximately 700 people registered for the conference around the

world, and approximately 350 people joined each day.

**Day 1: October 27, 2020**

**Location:**Zoom Webinar

**Time:**8:30 p.m. – 12:00 p.m, EST

**Date:**October 27, 2020

**Attendance Report:** 273

**Welcome Remarks**

**Dr. Alejandro Salicrup,**

**Senior Advisor for Global Health Research, Center for Global Health and the Office of Cancer Complementary and Alternative Medicine (OCCAM), Division of Cancer Treatment and Diagnosis (DCTD), National Cancer Institute (NCI), National Institutes of Health (NIH)**

Dr. Salicrup welcomed 700 registrants from 20 countries to the Conference on International Perspectives on Integrative Medicine for Cancer Prevention and Cancer Patient Management.

**Dr. Norman E. Sharpless**

**Director, NCI/NIH**

Dr. Sharpless discussed the importance of having this conference during a pandemic and a period of telework. He stated that these virtual engagements can still be useful and looks forward to a lively discussion. Dr. Sharpless mentioned that this is an essential area for the NCI. There are tremendous cancer research opportunities that will benefit cancer care for all patients, regardless of where they live or their income.

**Dr. Satish Gopal**

**Director,** **Center for Global Health, Office of the Director, NCI/NIH**

Dr. Gopal has spent some of his career in Africa and is aware of integrative medicine in international settings. He mentioned that the conference reflects a vibrant collaboration between NCI and international partners, and he looks forward to learning from this conference.

**Dr. James H. Doroshow**

**Director, DCTD, NCI/NIH**

Dr. Doroshow wished everyone a wonderful meeting. His division is committed to the program and integrative medicine. There are many highlights in the program, particularly for his division; the pharmacology of these agents and the clinical utility are of great interest.

**Dr. Robert T. Croyle**

**Director, Division of Cancer Control and Population Sciences (DCCPS), NCI/NIH**

DCCPS, as a co-sponsor of the conference, recognized the organizers of the conference and welcomed the national and international participants. Shared that the DCCPS funds research, epidemiology, surveillance, behavioral science, health services, outcomes research, cancer survivorship, and work in cancer disparities. He also introduced Dr. Paige Greene, a division branch chief, and informed attendees that she would provide a comprehensive overview of funding opportunities during a different conference session. DCCPS is interested in integrative medicine, implementation, and practical issues in LMICs and other international settings. Dr. Greene is also interested in applying rigorous scientific methods to answer what works and what does not work. The division is committed to growing the evidence-based research to empower patients to collaborate with their practitioners.

**Dr. Jeffrey D. White**

**Director, OCCAM-DCTD, NCI/NIH**

Dr. White thanked the planning committee and recognized the participants and the international organizations (e.g., World Health Organization [WHO], International Agency for Research on Cancer [IARC]). He stated that he is looking forward to building collaborations to solve shared problems and build alliances.

**Charge of the Conference by Dr. Alejandro Salicrup**

**Senior Advisor for Global Health Research, Center for Global Health and OCCAM-DCTD, NCI/NIH**

Dr. Salicrup welcomed participants from around the world and communicated the goals of the conference. They are to understand the interface between Western biomedicine and traditional medical systems, as well as to explore the type of collaborations that are happening. Also, to learn the gaps and challenges, particularly in low and middle-income countries (LMICs).

Cancer is recognized as a leading cause of premature death in LMICs. The rate of cancer is rising; there are share inequities and health inequities, affecting cancer survival rates worldwide. Most Western therapeutics are developed for high-income countries and are not affordable, compatible, or accessible by LMICs. Traditional, complementary, and alternative medicine (TCAM) plays a significant role in LMICs by practitioners and patients. Research on this can advance the field of oncology.

Dr. Salicrup shared the results of a portfolio analysis and reviewed the number of NIH competitive awards for ten years. He found that this particular area of complementary and alternative medicine (CAM) and cancer had very few international awards. The majority were awarded to high-income countries. Canada received the most, followed by European (EU) countries.

This conference is the first international forum to bring together diverse integrative cancer medicine researchers and clinicians. Hearing from various countries will allow a dialogue to understand better the integration of allopathic, traditional, and complementary medicine in different countries—particularly in LMICs. The conference shared examples what is and isn’t working. Participants will learn about the research gaps, challenges, and opportunities. Also, the need to work in collaboration and with teamwork.

Three NCI divisions helped organize the conference:

* OCCAM-DCTD, Center for Global Health Office of the Director, and DCCPS
* Two centers from NIH
	+ National Center for Complementary
	+ Integrative Health [NCCIH] and the Fogarty International Center
* Outside partners
	+ WHO
	+ IARC
	+ Brazilian Academic Consortium for Integrative Health
	+ National Cancer Institute (Brazil)
	+ China Academy of Chinese Medical Sciences
	+ Central Council for Research in Ayurvedic Sciences – Indian Ministry of AYUSH
	+ The Society for Integrative Oncology

**Keynote Presentation: Challenges of Cancer Prevention, Therapy, and Survivorship in Low and Middle-Income Countries (LMICs) and Gaps That Integrative Oncology Research Could Address**

**Dr. Partha Basu**

**Head, Screening Group, International Agency for Research on Cancer (IARC), WHO, Lyon, France**

Dr. Basu discussed how cancer is a disease that highlights the inequities around the world. Men and women are diagnosed with cancer at a late stage and do not have access to good-quality treatment. The incidence of cancer is lower in LMICs, but account for almost 80% of the global cancer burden in terms of years of life lost to cancer1.

Dr. Basu defined traditional and complementary medicine (TCM) and shared that it is the same as CAM—it refers to a broad set of health practices that are not part of conventional medicine and are not fully integrated into our dominant healthcare system. Integrative medicine makes sure that there is a good marriage between TCM and allopathic medicine. Integrative oncology should be patient-centered and involve holistic care.

Pillars of traditional and complementary medicine include:

* Lifestyle modifications
	+ Dietary alterations
	+ Exercise
	+ Maintaining sleep
	+ Hygiene
	+ Managing stress
	+ Avoiding addictions
* Mind-body practices
	+ Mind therapies
	+ Movement-based practices
	+ Manipulative and body-based therapies
	+ Use of natural products.

The cancer care continuum is divided into four areas:

* Prevention
* Early detection
* Treatment and survivorship
* End-of-life care

Dr. Basu believes that, at each stage, there is a role for TCM where it can improve the process of care by improving access, minimizing disparities, and making quality care affordable.

Dr. Basu presented a few examples of where we stand on an integrative approach. First, obesity and a sedentary lifestyle are rising in LMICs. Obesity is no longer just a problem of Western countries; countries in the southern hemisphere are increasingly becoming obese. In high-income countries, the proportion of men and women going for physical exercise is quite high; some countries have 80% who are active. Low-income countries have much less physical activity. Traditional interventions to encourage physical activity may not be suitable for LMICs. There is a disconnect in public health recommendations. A photograph in Afghanistan was shared that depicted sugar-sweetened beverages being sold directly in front of a high school.

Dr. Basu looked at systematic reviews of mind-body practices and found that yoga significantly reduces body mass index in obese persons compared with the usual care2. Practitioners of body-mind practices tend to choose better lifestyle practices. Practicing meditation, tai chi, and yoga could significantly improve quality of life and reduce the severity of insomnia. Yoga does improve obesity, but there is no hard-core evidence that yoga reduces cancer risk.

Concerning the relationship between stress and cancer, TCM can play a role in reducing stress. The Finnish Twin cohort study showed that women with one major stressful life event had a 35% higher risk of breast cancer than those who did not. Other studies show that chronic stress increases the risk of cancer. In one randomized control trial (RCT), acupuncture significantly impacted perceived stress compared with the control. The stress level was reduced over time.

Concerning natural compounds and cancer prevention, the studies show mixed outcomes. In one study, Japanese women who consumed high-soy diets reported lower breast cancer risk. A meta-analysis of 18 epidemiological studies did not observe any preventive effect on breast cancer. There is an oxidative effect that can increase cell proliferation and induce tumor promotion. The evidence is not concrete in terms of cancer prevention.

Regarding the early detection of cancer, we have not taken advantage of the workforce available in LMICs. We should learn from the HIV experience. Traditional healers are right at the doorstep and have excellent communication skills. These healers can send messages across the community. There are very few studies that have used traditional healers for the early diagnosis of cancer. In one qualitative study in South Africa, 40 traditional healers were randomly selected from a group of 117 traditional healers. The community was more willing to listen to the healer, even over a religious minister. Healers can encourage self-respect and self-discipline, especially among youth. Traditional healers are well connected in the community, and we need to find out how best to integrate them into early diagnosis and care of patients.

There are three aspects to think about in terms of management of care:

* Reducing the symptoms
* Improving the quality of life
* Improving survival.

A meta-analysis study found that there was a significant reduction of pain intensity with the use of acupuncture3. This is important because access to morphine is limited in LMICs.

Cancer diagnosis and treatment are associated with profound stress. A systematic review of RCTs showed significant results but poor methodological quality. There is a gap in blinding in the studies. Quality of life can be improved, but the quality of evidence needs to be better.

One RCT study looked at extracts of Viscum album—a mistletoe species—and found a significant benefit concerning overall survival improvement.

Cancer survivorship is an important and neglected area in LMICs. Evidence from RCTs looked at yoga and survivorship care—outcome measures were physical and psychological. The trials had low sample sizes. The evidence was mixed; physical outcomes did not improve overall. Except for breast cancer patients, patients had fewer hot flashes and joint pain during hormone therapy. There were significant benefits in reducing depression, anxiety, fatigue, sleep, and increasing quality of life for psychosocial outcomes.

The advantages of integrating TCM with oncology care in LMICs are:

* It does not require much investment
* Practitioners are close to home and available 24 hours and seven days a week
* It is affordable, adapted to local cultural values and traditions, and well trusted by the local populations

The challenges are:

* Myths and misconceptions surrounding cancer often drive patients to TCM
* The practice is still faith-based
* There is a disconnect in bringing practitioners into mainstream practices
* Doctors are apprehensive about being criticized for legitimizing inappropriate practices.

Lack of research data is the number one challenge in implementing and regulating TCM. There is not enough evidence to convince patients and organizations to implement TCM. It is challenging to get eligible patients to participate in the trials.

The way forward at this present moment is:

* Team building and getting people from diverse backgrounds involved.
* The focus on a specific target in terms of disease and intervention
* Design studies on integrative approaches with specific objectives and endpoints.
* Having a clear plan for knowledge translation, including effective communication. Outcomes for efficacy and safety are essential.

We also need to look at cost-effectiveness, resource and service utilization, need efficacy, training needs, and how we implement practices into the entire health care system to ensure they have the care that men and women need.

1. Knaul, Felicia Marie, and Farmer, Paul. Overview. In Knaul, Felicia Marie, Frenk, Julio and Shulman, Lawrence for the Global Task Force on Expanded Access to Cancer Care and Control in Developing Countries. Closing the Cancer Divide: A Blueprint to Expand Access in Low and Middle-Income Countries. Harvard Global Equity Initiative, Boston, MA, November 2011.
2. Lauche, Romy, et al. "A systematic review and meta-analysis on the effects of yoga on weight-related outcomes." Preventive medicine 87 (2016): 213-232.
3. He Y, Guo X, May BH, et al. Clinical Evidence for Association of Acupuncture and Acupressure With Improved Cancer Pain: A Systematic Review and Meta-Analysis. JAMA Oncol. 2020;6(2):271–278. doi:10.1001/JAMA Oncol.2019.5233

**Question & Answer Session**

**Question:** What are the major opportunities for integrative oncology research?

**Answer:** The primary focus should be on the evidence that is already there. For example, utilizing the traditional healers for relaying the message in terms of changing the health setting of the population. It has shown great results in HIV care in some African countries. Screening is very complex and requires resources in terms of diagnostic care. Looking at cancer prevention, we need appropriately designed research that shows if you follow this, then there will be less risk of cancer. This kind of research is needed, and the data is lacking. There are several opportunities.

**Question:** Are there global data on other types of exercise and cancer survivorship?

**Answer:** No, the data is still inadequate. Survival can be improved by doing traditional medicine in any of these practices, but there are indications that it does reduce stress, and stress is one factor that reduces survival. There is indirect evidence, and we need to put all of this evidence together. It is not always focusing on RCTs as good observational studies are as good as some RCT data. We should focus on more observational data trials.

**Question:** Given that there is literature showing that patients diagnosed with cancer tend to have poorer sleep and increased fatigue when compared to healthy controls, what are your thoughts on targeting sleep and cancer-related fatigue as a primary intervention, especially since insomnia and fatigue may be related to both poorer quality of life and compromised immune functioning?

**Answer:** The systematic review shows that, yes, there is a trend toward a better quality of life for patients that are practicing traditional medicine. The studies are weak because they do not have adequate power because of small sample sizes. There are problems with randomization. It is very difficult to come to a conclusive message. The trend is definitely there to improve quality of life.

**Question:** Is the WHO or IACR plan to set up a research council or regulatory body like institutes in each of major continents to represent the traditional medicinal practices?

**Answer:** NeitherIACR nor WHO has a role in regulating practices or implementing things in countries. We are more of a recommending body based on our synthesis of information. At IACR, we synthesize research for policymakers so that they may make a decision. We can have dialogue in terms of sharing the evidence.

**Question:** Many of the practices are NOT affordable to patients in the United States. Acupuncture and even yoga are expensive and often not covered by insurance.

**Answer:** Exactly, that is the gap. Where is the good evidence to show it is cost-effective? To convince insurance companies that it is more affordable to invest in encouraging people to participate in these practices, they will actually save money in terms of treating cancer.

**Question:** The interface is supposed, among others, to seek discussion and cooperation with countries, including low- and middle-income countries. How will this interface be gauged?

**Answer One:** Increased funding to these countries, increased cooperation among researchers/clinicians, increased interaction in terms of understanding diagnosis, prognosis, treatment options, or looking at all avenues to create a database in some or all enumerated among others. Clarity is needed here!

**Answer Two:** Interventions need to be locally contextualized. We cannot have a one-size-fits-all. We need to look at what is practiced, what is accepted, what is the gap, and what is the opportunity. Cancer control is always about taking the opportunities and building from there, rather than reinventing the wheel. We work better with collaboration, with people thinking of understanding the local situation.

**Question:** If oncology centers are not open to TCM, such as acupuncture treatment, how do you overcome that in LMICs.

**Answer:** I have practiced for more than 35 years; the common practice is to recommend a patient for TCM if they are considered too advanced (this has to change). There is no point in patient care that we cannot do something. The systematic review of acupuncture and pain shows that acupuncture reduces the need for morphine. This type of evidence has to be shared with the cancer centers, policymakers, and the national system. In India, TCM and allopathic systems are different. They are managed differently and have different regulations. There needs to be more cohesion between these two practices.

**The Role of Integrative Cancer Therapy, Cancer Prevention, and Management in Global Health**

**Moderators:**

**Dr. Paul Jacobsen**

**Associate Director, Healthcare Delivery Research Program, DCCPS, NCI/NIH**

It is important to note that this conference is taking place during the pandemic and a growing global burden of cancer. The American Association of Cancer Research predicts that the number of cancer cases is expected to increase from 17 million to 27.5 million in 2040. This increase comes from the rise of cancer in less developed countries and will create worldwide cancer care challenges. This impending crisis has created several questions:

How do we increase evidence-based screening in less developed countries so that cancer can be detected at an earlier and more treatable stage?

How can we increase access to and accept effective conventional treatments that may be rejected in some cultures or traditions?

What is the best strategy for helping cancer survivors by increasing the availability and use of supportive and palliative care services?

Improvements in early diagnosis and earlier access to treatment mean that more people will be experiencing shorter-term side effects from traditional cancer treatments. To the extent that those treatments are successful, we will have a growing number of survivors who may be experiencing persistent side effects and toxicities for decades, and some may develop late effects. How do we address quality-of-life issues at scale to improve population health outcomes worldwide?

**Dr. Jun Mao**

**Chief, Integrative Medicine Service, Memorial Sloan Kettering Cancer Center, New York, New York, USA**

Integrative oncology emerged about 20 years ago in large academic NCI Cancer Centers, such as Memorial Sloan Kettering Cancer Center and MD Anderson Cancer Center. Over the years, the field has matured and received a cohesive definition of integrative oncology. This approach is a patient-centered, evidence-informed cancer care field that utilizes mind-body practices, natural products, and/or lifestyle modifications from different traditions alongside conventional cancer treatments.

Integrative oncology aims to optimize health, quality of life, and clinical outcomes across the cancer care continuum. It seeks to empower people to prevent cancer and become active participants before, during, and beyond cancer treatment.

They have seen healthy growth in the provision of integrative strategies for symptom control in NCI-designated Cancer Centers. In a 2017 paper, the recommendation of acupuncture, massage, meditation, and yoga in controlling symptoms in cancer patients has risen from about 60% to 90%.

However, our work is not entirely done.

There are inequalities in the distribution of services between NCI-designated Comprehensive Cancer Centers and community hospitals. For example—in the provision of acupuncture, meditation, and music therapy—NCI Cancer Centers have a higher percentage of provisional services than community hospitals. The pandemic highlighted the importance of the determinants of health.

In communities that provide care for lower-income populations, essential integrated strategies—such as acupuncture, meditation, and yoga—are utilized less than for communities serving middle-income populations. This is just in the United States. How do we take these sorts of challenges globally? How do we recognize the need for integrative oncology to have a cohesive strategy, not only for the United States but for the world? The Society for Integrative Oncology has expanded our work of building our membership globally. In 2019, they had 420 members in 29 countries. That has grown to 599 members in 44 countries, despite the pandemic's challenges, including several from Africa for the first time. To combat the global cancer burden's challenges, we have to take a global approach and recognize regional differences. The rest of the session discusses how we graduate to a more cohesive vision despite cultural, political, and regulatory differences.

**Speakers:**

**Dr. Lorenzo Cohen**

**Professor in Clinical Cancer Prevention and Director of the Integrative Medicine Program, University of Texas, MD Anderson Cancer Center, Houston, Texas, USA**

Dr. Cohen has been researching with China and India for 20 years, specifically in integrative medicine in China with traditional Chinese medicine, and examining aspects of the benefits and role of yoga in cancer care with colleagues in India.

Dr. Cohen provided a financial disclosure regarding product royalties and licensing fees for the book, *Anticancer Living: Transform Your Life and Health with the Mix of Six*. The talk discusses the book and how it applies to cancer prevention and control. More broadly discussing integrative medicine—looking at individual modalities, adding on to Dr. Mao’s definition of integrative oncology, is the broader definition of integrative medicine and health.

It is essential to use the term "health." We are not looking at the absence of disease as is WHO's definition. It has to do with overall health and wellbeing. This has to do with focusing on the whole person while using evidence-based practices. We must be making use of all of the appropriate therapeutic approaches and lifestyle approaches.

A paper published in Nature in 2015 looked at extrinsic vs. intrinsic factors as they relate to cancer development4. This was a mechanism study looking at the drivers of cancer. Although a portion of cancer is hereditary, it only accounts for 5% to 10% of cancers. There is, of course, random chance or bad luck. This paper concluded that environmental and lifestyle factors count for 70% to 90% of the gene mutations that are critical for allowing cancer to grow and thrive in the body. Tobacco use is an additional lifestyle factor, and it accounts for 35% of cancers. If you combine obesity, being overweight, and its link with physical activity and diet, and other factors, it accounts for over 20% of cancers. HPV accounts for 100% of cervical cancers; there is a vaccine for this. Even in developed countries like the United States, only about 50% of individuals are receiving the vaccine, and it helps prevent penile cancer, head and neck cancer, anal cancer, and others. Cervical cancer could be wiped off the planet if everyone were to be vaccinated.

Alcohol has been a known carcinogen for decades now. New guidelines state to avoid alcohol, but state that if you do drink, do so minimally, which is still an excessive amount of alcohol, considering it is a known carcinogen. This language is not used with smoking or the issue of obesity in high-income countries. A recent issue of The Lancet discusses the double burden of malnutrition (undernutrition and overweight/obesity). Several factors contribute to this—diet/nutrition, food environments, and socioeconomic factors. These are things that need to be intervened. The New York Times highlighted Nestlé, the largest food producer globally, and countries like Brazil have a high percentage of overweight/obesity, at the same time being malnourished, because the quality of food is devoid of nutrition. There is a direct link between obesity and the risk of more than a dozen cancers.

Physical activity affects mortality, similar to smoking and obesity. In Dr. Cohen's book, *Anticancer Living: Transform Your Life and Health with the Mix of Six,* he discusses the mix of six:

* No tobacco
* Improve nutrition, including moderate alcohol use
* Reduce sedentary behaviors to reduce obesity
* Decrease environmental toxins
* Reduce stress, increase social support
* Improve sleep quality.

The last three areas are critical in modifying lifestyle factors to prevent cancer. They are directly related to obesity; they have indirect and direct effects. Sleep deprivation changes the way our body metabolizes food. These six lifestyle factors activate one or more of the cancer hallmarks. Exercise deactivates all of the cancer hallmarks. Something that is ignored is getting people to eat more plants, and exercise more is not a lucrative way to run a business. Cancer kills millions of people because of bad policies. We must take a systematic approach.

The integrative medicine model is used at MD Anderson, including mind-body, physical health, and social wellbeing practices. There is tremendous evidence-based in those areas. MD Anderson uses the National Comprehensive Cancer Network guidelines for symptom control. The guidelines recommend:

* Massage
* Acupuncture
* Cognitive modalities
	+ Mindfulness-based stress reduction
	+ Imagery/hypnosis
	+ Distraction training
	+ Relaxation training
	+ Yoga

The world should follow these evidence-based techniques for controlling pain, fatigue, etc. The insurance companies should reimburse these activities; and this needs to be done globally. It is not happening in high-income countries.

In a systematic review, yoga was shown to improve physical wellbeing during and post-treatment. Meditation has been shown to change the way our brain functions and increases regional brain gray matter density. The challenge of studying traditional medical systems is that a fixed approach is used, yet it is more of an individualized approach when looking at traditional systems.

This is something that is not being studied. In closing, we need to start exploring this using a systematic approach. Synergy is not studied, each area should be looked at individually, and cohesively. Interventions should look at the "mix of six."

1. Wu, Song, et al. "Substantial contribution of extrinsic risk factors to cancer development." *Nature* 529.7584 (2016): 43-47.

**Dr. Geetha Gopalakrishna Pillai**

**Technical Officer, Traditional, Complementary and Integrative Medicine Unit, Service Delivery and Safety Department, WHO, Geneva, Switzerland**

The global cancer burden is significantly increasing, growing to 30 million in 20 years. One in six deaths is due to cancer. According to the United Nations Sustainable Development Goals (SDGs), there should be enough mechanisms to reduce incidence rates. The trend shows that high-income countries will reach the target of reducing premature death due to cancer. LMICs are not on target and are way beyond where they should be and should be looked at to reduce future cancer deaths.

Looking at different integrative kinds of cancer therapeutics is inclusive of traditional medicine. It defines integrated cancer therapy or integrative oncology as mutually supportive medical systems working for a common objective. The characteristics of traditional, complementary, and alternative medicine (TCAM) that make it attractive in cancer care are the approach, how patients perceive it, and how society benefits from it. TCAM is holistic and humane. They give you a different way to look at cancer, approaching and managing it from another perspective.

Traditional medicine looks at cancer independently, gives you different clinical goals to achieve. What we measure is different. We offer multiple intervention opportunities, such as managing inflammation, epigenetics, and nutrition.

For patients, it delivers:

* Better compliance with cancer therapy
* Improved follow-up
* Rehabilitation support
* Occupational health
* Social integration
* Mental health support
* Improved quality of life

For society, it delivers:

* Improved expectations
* Economic benefits
* Improved community engagement
* inherent cultural acceptance
* Simplified delivery and follow-up
* Increased technology and infrastructure independence
* A simplified delivery and follow-up

Integrative oncology can offer LMICs improved:

* Primary prevention
* Early detection and screening
* Education
* Quality of life
* Mental health
* Survivorship
* Cancer management
* Prevention

The essential components for delivering integrative cancer therapy services are policy, availability, and implementation. It would be best if you had policy and regulation to support cancer care in LMICs. If traditional medicine is not available, then no amount of policies will help you. You need models or frameworks for delivering integrative cancer therapies. One is clinical practice, and the other is public health.

It is essential to have person-centric delivery, having multiskilled practitioners, teamwork, and be referral based. The public health framework is community health-centric delivery; independent streams are one way, and the other is integrated streams where teams work together.

There should be an apparent strategy and plan to make integrative cancer therapies viable in LMICs. There should be strategic investments, practical implementation, and decisive policies. It is teamwork and has to work together to reach the goals of integrative oncology.

**Question & Answer Session**

**Comment:** To Dr. Cohen, issues of obesity should be treated carefully as traditional diets that could be fattening do not necessarily lead to cancer. Each area has its own set of traditional practices; in much of Asia, acupuncture, yoga, etc., have been established and exported elsewhere. In Africa and a few areas, medicinal herbs and traditional spiritual practices hold sway!

**Response:** That is one of the great things about this kind of meeting and us needing to learn from each other. At the end of the day, it comes down to the evidence. In China, acupuncture, to some degree, is a part of the standard of care. The majority of allopathic hospitals in cancer acupuncture are not always utilized (the same for the United States). In African countries, acupuncture would not be used as much. Ideally, we learn from other cultures what works for symptom control and cancer prevention, and we figure out ways to implement it across countries.

**Comment:** Some herbal medicines can also help with nausea and stress management. Ghana has excellent ones for those symptoms.

**Response:** Absolutely, ginger, for example, is helpful for nausea. We know that St. John's Wort is helpful with depression, notwithstanding some concerns about drug group interaction. MD Anderson does not treat herbs differently than conventional medicines. We all need to learn from each other to see what is successful in countries around the world.

**Question:** Does WHO have data on the country or regional level on the availability of cancer screening and cancer treatment, and the availability of complementary and alternative medicine practices? Do we know the data of practice in LMICs, i.e., who provides traditional care versus providing integrative services? Without that knowledge, it is hard to strategize or move forward.

**Answer:** We do not have it; we are in the process of collecting it. We recently did a global survey, and it was not specific to cancer. It was on the general use of traditional medicine.

**Question:** Is it a concern (and valid) that some traditional approaches show adverse drug interactions with allopathic medicine, especially in the context of cancer?

**Answer:** It is a concern, but we do not need to pick on natural or herbal medicine more than we pick on allopathic medicine. Chemotherapy and hormonal therapy interactions can also occur. We know that natural medicines play a critical role in the allopathic arsenal that we have today. These are all drugs, whether it comes from a plant or a laboratory.

**Question:** I am an integrative pediatric oncologist at a pediatric cancer center and developing our intramural program for pediatric hematology/oncology patients. Many of the “lifestyle” modifications, while *critical*, aren’t causative factors (at least directly) for childhood cancer. I am seeing *many* patients who want to substitute supplements (*many* of them) for changes in behavior. I see this as trading pills for pills. How do I help to dissuade the use of unstudied products while introducing things like TCM, massage, mind-body practices, etc., for people who are super supplement/herb focused?

**Answer One:** It is hard, of course, with pediatrics; you are trying to convince understandably desperate parents who want to set up their kids for success. Part is trying to impart the evidence. We undervalue lifestyle changes. The harms of stress, the benefits of exercise, good sleep, and good hygiene, and the aging process are directly linked with these lifestyle factors.

**Answer Two:** As a physician, it is important to understand some of the fears and health beliefs of patients. Provide them with the evidence of what we know and what we do not know. A lot of patients are motivated by the belief that this other supplement will cure their cancer, and oftentimes they do come from a more desperate approach. They were told that they will die. Our goal is to provide evidence-based care and find a way to validate some of the patients’ concerns. To make sure that the risks do not outweigh the benefits. In this circumstance, there are really no good answers. The way is to work with the patient’s belief system and outline where the evidence is, especially if there is a chance of harm. Some natural products can cause toxicity.

**Challenges and Clashes of Worldviews and Circles of Influence of Western Medicine and Traditional Medical Systems**

**Moderators:**

**Prof. Vd. K.S. Dhiman**

**Director, Central Council for Research in Ayurvedic Sciences, New Delhi, India**

Dr. Dhiman discussed the challenges and problems of adopting modern research methodology for traditional medicine. The first problem mentioned was that traditional medicine has a diverse and complex approach, considering that various factors of a one-size-fits-all approach cannot be used, neither in diagnosis nor in treatment. The second problem is a gap in understanding the functional, fundamental parameters based on measurable parameters in conventional medicine's current scenario. This gap still exists despite thousands of years' worth of clinical- and practice-based documentation is deficient in traditional medicine to support treatment-based knowledge.

The third problem, T.M. and CM (contemporary medicine), run parallel. They lack an interface to cater to the needs of a system that has entirely different principles. The fourth problem is a knowledge gap at various levels: academic, scientific, and practice.

Additionally, there is a lack of epidemiological studies to document the incidence and prevalence of diseases using traditional nomenclature, making it challenging to calculate the sample size.

The next problem discussed, there is not a fixed universal dosage that suits all, and no single medicine/therapy that gives an equivalent result in all stages and all categories of a single disease. Also, different responses to therapy by patients, depending on the various factors; the extent of disease, cause of disease, etc. Inability to interpret the pharmacodynamics of T.M. in contemporary terms.

Lastly, “absence of evidence is not the evidence of absence." T.M. is practice-based, and lack of proper assessment tools does not imply that formulation/therapy is ineffective, but CM implies no evidence and absence of efficacy.

**Dr. Jeffrey White,**

**Director, OCCAM-DCTD, NCI/NIH**

Clashes can stand in the way of collaboration, both for groups in a given country and between different countries. The challenges are multifaceted and can arise from differences between traditional and adoptive cultures. Different worldviews are at the heart of various systems and may lead to great difficulty in communication, agreement, and trust. Bridge builders and people with the capacity, the credentials, and authority to facilitate safe and productive dialogue between groups with different worldviews are essential. We need those people, and many are participating in this meeting. There are also power differentials between individuals and systems of practice and institutions. This can affect both the magnitude and the influence of a set of ideas. The speakers will present potential solutions for these identified challenges.

**Speakers:**

**Dr. Geetha Gopalakrishna Pillai**

**Technical Officer, Traditional, Complementary, and Integrative Medicine Unit, Service Delivery and Safety Department, WHO, Geneva, Switzerland**

This is an important session as we understand worldviews and how they relate to integrative medicine. Existing challenges and clashes of worldviews make integrative medicine is hard to try. The logical understanding of the disease's cause and effect has diverse worldviews of traditional medicine and conventional medicine.

Conventional medicine is a bottom-up approach. Traditional medicine is a top-down approach. Modern medicine goes to the molecular level and tries to find out the systematic effect an intervention or medicine will have. Traditional medicine looks at it from the other point of view. It asks which kind of systematic effect is causing this problem and sees whether it is a single organism in the body or multiple organs working together in the body. Then they try to find a solution for it.

Traditional medicine goes from macro to micro and accepts multiple possibilities for a given set of causes. Conventional is micro to macro and expects the cause to lead to one of the two possible outcomes.

Discussed a poster, *The Complex World of Systems of Biology of Ayurveda*, depicts the Ayurveda system and provides 300 different factors within the human system that will lead to a disease or a healthy system5. All interact with each other. The concept of health is different among systems.

WHO says health is a state of complete physical, mental, and social wellbeing and not merely the absence of disease or infirmity. Ayurveda says health is a state of optimal physical functional response and mental and spiritual wellbeing. This health is maintained by a resilient person—who, while continually interacting with the environment, society, and other living beings—carries on with daily life activities. In modern medicine, health is a state of set parameters of the system.

At a point in time, the individual is a passive spectator there. Whereas in traditional medicine, the system can maintain a set of parameters. It is a continuum in time, and it's more holistic, considers the variables faced while living. It involves active effort from the individual. This kind of difference can be seen in the understanding of disease also.

For example, conventional medicine looks at effective molecular targets to define outcomes. At the same time, traditional medicine looks at efforts on the system to define the outcomes. This is also the case for clinical choices, for a patient in end-of-life care. Conventional, hospital-based care usually sees the person as a passive subject with a set parameter of life that needs to be maintained. In contrast, traditional medicine approaches to end-of-life care involve interventions to improve and strengthen the individual system and its active effort to regain health while being observant and sensitive to the active decision of the system itself not to do so.

Regarding nutrition as an intervention for cancer: conventional medicine views it as a problem of calories needed per day, and to prepare the diet plan to ensure the required calorie intake. In comparison, traditional medicine approaches this as an issue of the ability to digest and absorb. This approach holistically views the requirement of nutrition, the patient's health, the medication, and the patient's digestive and absorptive capability.

This circle of influence on the scientific worldview happens because of several factors that we cannot delineate from our lives. It is part of our history. Sometimes it is remnants of subjugation that lead us to circles of influence. Culture, individual rights, the concept of suffering, and the extent of suffering are very different from community to community. Social structures are defined by existing policies, like mechanisms or structure of social interaction, and functioning perceptions of the influences. These are all social structures that lead to circles of influence and a so-called scientific view.

Of course, education was already mentioned, and education sometimes makes us believe what constitutes science. Sometimes traditional medicine—even if it is scientifically based—is not considered a science at all. Economics is another major factor in our present to our future gains of the individual or the community. And sometimes unnecessary medicalization leading to economic benefits are also part of circles of influence. This leads to scientific decisions, which probably are not all scientific.

We need to consider all these things when we are looking at circles of influence. To overcome this, we have to define evidence in integrative oncology. In LMICs and high-income countries, we have to base the research on practice-based evidence being created first.

We should utilize tools like the International Classification of Diseases (ICD) 11 Traditional Medicine chapter, where dual coding is possible and an internationally acceptable understanding of oncology terms and traditional medicine terms when they could be understood together. Defining evidence is cultural-based and personal expectations in our community. This structure changes with personal expectations and outcomes and is firmly based on culture. What we consider evidence in one culture might not be evident in another culture. We cannot look at bench to bed evidence. I think we need to look beyond that.

Dr. Gopalakrishna presented a diagram on the essential components for establishing integrative oncology (i.e., decisive policies, strategic investments, and effective implementation). These components can help establish integrative oncology to overcome clashes of understanding.

Decisive policies need to be established to create acceptability, accessibility, and affordability. These changes can happen only through policy, especially in a low- and middle-income country setting. Then we have to look at strategic investment—such as capacity building in human resources, institutions, and mechanisms—especially institutions where co-location is a possibility, and of course research, which will support all this with evidence.

Then we also have to look at the effective implementation. Do we have enough finances to compare the data between integrative oncology and otherwise simple oncology interventions or regular conventional quality interventions? We need to have the finances for that. What are the outcomes that we are going to look at? What are the data, analysis, and impact? What kind of tools are we going to use?

These are all set requirements for making sure that integrative oncology is a possibility. We will be able to transcend the problems of this clash of cultures and a considerable clash of understanding regarding science. Of course, there needs to be a robust translation mechanism that will evolve through practice-based evidence. This will lead to that evidence-based research, and then again, leading to research-based practice. This is my suggestion.

For integrative oncology to be effective and successful, we require:

* Collocation in infrastructure
* Communication among the practitioners
* Collaboration between the practitioners and the community and the patients

All of us should be ready to change our perspectives and way of working. Because without these three requirements, integration is not going to happen. We will always see silos of integration where people will be working together. But if you want to see integration generally across the systems and effectively available within the community, co-location, communication, collaboration, and change are the words we need to embrace.

1. Patwardhan, Bhushan. (, 2012). Evidence-based Ayurveda. Current science. 102. 1406-1417.

**Dr. Carlos Jose Andrade**

**Coordinator, Integrative Oncology, Brazilian National Cancer Institute, Rio de Janeiro, Brazil**

Dr. Andrade believes that the discussion of integrative care goes far beyond medicine and health. You're living in a health care system crisis, and based on this crisis, we need to create a new model. Each country has its own problems, challenges, and proposals for a solution. We are leading a global ecological challenge, and that puts all of us at risk. That is why we need real change.

Dr. Andrade shared a well-known image that may represent our limitations in the perception of the whole. This image shows how our opinion can be conditioned to our interpretation. He highlighted the need for openness when we are talking about worldviews. It has never been so necessary to have an inclusive attitude, where differences are respected. We need to overcome racism, prejudice, and any other attitude that creates distinctions based on gender, color, religion, or social class.

Dr. Andrade's talk was split into three parts:

* Challenges
* Clashes of worldviews
* Circles of influence of Western medicine and traditional medical systems

A common challenge for Western medicine—and all traditional medical systems—is the need to collaborate with the sustainable development goals of the United Nations. Good health, wellbeing, and difference in worldviews cannot be seen as a barrier for the Western and traditional medical systems.

We need to collaborate for health promotion, disease prevention, and cancer control by offering access to a continuum of care, including:

* Early detection
* Prevention
* Palliative and end-of-life care

The dialogue should try to establish a common language that can attest to the level of evidence of the techniques used in the traditional system and investigate more deeply to understand the knowledge base from which these techniques come.

These are the challenges of cancer control that are asked at the same time—especially in developing countries:

* Expand access to care
* Carefully evaluate and incorporate new technologies
* Wholeheartedly act to avoid cancer fractions, which relate to a lifestyle present in traditional systems

By recognizing the attributes of an ideal health care system that is preventive, predictive, personalized, and proximate, we open an avenue of collaborative dialogue between East and West. We seek to bring together the best vision, impact of signs to reduce human suffering sustainably.

Dr. Andrade mentioned some WHO data:

90% of the morphine supply is consumed by North America, Europe, and Australia, which leaves only 10% or more to address the rest of the world's pain.

70% of cancers were cured in LMICs in 2008.

An effective national response for prevention and control requires multiple stakeholders and engagement, including:

* Individuals
* Families and communities
* intergovernmental organizations and religious institutions
* civil society
* academia and the media
* policymakers
* voluntary associations
* the private sector
* Industry
* Traditional medical practitioners where appropriate.

To start to work together, we need a kind of integration, a kind of evidence-based cooperation. An organized plan could increase the chance of succeeding in some way. It has been done before. In Finland, they did an amazing transformation of health outcomes with education and reduced risk factors. This resulted in an impressive change in mortality by cardiovascular and cancer cause6.

This is our challenge. We need to make a plan to support a broad behavior change program. This is not just a health issue; it's a political, social, and economic issue. We can say that the 19th century solved health programs by fixing issues with water and sewage. The 20th century was known as the medicine century, with drugs, vaccines, and devices. But now we are in the 21st century, which should be the behavior century. We need to reshape our behaviors on a large scale.

A clash of views in health care was always present in the human journey; people have always cared for those in need. A human group's worldviews are conditioned by a future that interferes in the physical existence of human beings, operates within its own logic, and remains denied. As a result, the configuration of the future elements—sometimes functional, other times not so functional—is complex.

From H.L. Mencken: “For every complex problem, there is an answer that is clear, simple, and wrong.”

Dealing with worldviews is a delicate and complex issue. Dr. Andrade allegorically described the differences between Western and Eastern cultures. He shared illustrations by Yang Liu, an artist born in China and moved to Germany at 13 years old.

Liu’s art compares Westerners' individualistic behaviors and Easterners' collectivistic behaviors, for example, differences in waiting in a queue, way of life, punctuality, and restaurant behavior. Dr. Andrade read a phrase by Lao Tzu, “Life is a series of natural and spontaneous changes. Don’t resist them, that only creates sorrow. Let reality be reality. Let things flow naturally forward in whatever way they like.”

If we look to the West from the East, we see the treatment starts at the last month of life. These are patients with malignant disease progressing, dying in intensive care units, and too high treatment costs in the last months. Dr. Andrade thinks that we need a merge of two worldviews to improve the actual situation. We need integration. We need evidence-based cooperation.

Finally, Dr. Andrade provided his opinion about Western medicine's circles of influence and the traditional medical system. We should overlap these fields of knowledge s; that the interceptions are based in science. He provided examples in Western and Ayurveda medicine. The first example of a promising research line is the correlation between the phenotype and people's genotype. As we know, Ayurveda has refined an ability to individualize people based on physical examination. I congratulate the study of Dr. Bhushan. His study demonstrated statistically super expression of a human leukocyte antigen7. Likewise, we know that some of these markers are more prevalent in specific diagnoses. This example reinforces that it is possible to access genotype markers through phenotype.

Another example involving cancer treatment with immunotherapy, obese patients respond at a higher rate than non-obese patients8. There is no clear explanation for this phenomenon in Western medicine, but we know that people with Ayurveda have a greater immunity, which we call Ojas. These are just two examples of many possibilities of how those circles of influence overlap to better understand health and disease.

We have never been so close to transforming health care into integrative care. This transformation depends on the whole of society, not only on health care workers. Different worldviews can converge to construct this new reality. Dr. Andrade closed with a quote from Rudolf Virchow, "Medicine is a social science, and politics is nothing more than medicine on a grand scale."

1. Puska P. From Framingham to North Karelia: from descriptive epidemiology to public health action. Prog Cardiovasc Dis. 2010 Jul-Aug;53(1):15-20. doi: 10.1016/j.pcad.2010.01.003. PMID: 20620421.
2. Bhushan P, Kalpana J, Arvind C. Classification of human population based on HLA gene polymorphism and the concept of Prakriti in Ayurveda. J Altern Complement Med. 2005 Apr;11(2):349-53. doi: 10.1089/acm.2005.11.349. PMID: 15865503.
3. Cheng, Monica, and Richard B Gunderman. "Is obesity a disease?-the evolving concepts, cancer paradox, and association with improved cancer immunotherapy efficacy." Hepatobiliary surgery and nutrition vol. 9,2 (2020): 247-249. doi:10.21037/hbsn.2019.11.35

**Dr. Bhushan Patwardhan**

**Vice-Chairman, University Grants Commission, New Delhi, India**

Dr. Patwardhan designed a talk on clashes in convergence and discussed a real-life experience involving what we are actually facing in India. In a case study format, he discussed how to expand our current view to move from our current system to person-centered holistic health care. Dr. Patwardhan discussed the challenges, why there are clashes, and who influences them.

The first challenge before us is because of the present pandemic—all of us are facing COVID-19, and these adversities are actually opening up an opportunity to reform health care systems.

Currently, he believes that health care systems are based too much on curative practices and market forces. Allowing affordability, accessibility, and availability to be a significant challenge—we are actually converting society into some kind of medicalization society. On the other hand—because of the higher level of scientific research—the commercialization levels are going up, and value systems are going down. This is a conflict.

The root cause of these clashes is coming from need and greed conflict. For sustainable development—people, planet, partnerships, peace—all of these are important components. Now many societies are actually moving to minimalism. We see greed when we look at the prices of cancer drugs in the market. These prices are absolutely unaffordable for people in poorer countries, but it is not affordable even for rich people. So global greed for profit is one of the significant points of clashes.

Clashes are also between traditional and modern outlooks, whether food or medicine, is a clash. Nutrition or supplements, because many times we are trying to take an easier route or because nutritional supplements are easier to put in the market. So that is maybe replacing many pharmaceutical products. The family chats are getting replaced with mobile apps, and our living rooms are getting converted to home theaters.

These challenges lead to clashes, and we have to choose between consumerism or minimalism; there could be some more options. The clashes are also based on whether we are really giving health care.

Are we really understanding health?

Are we converting health care into a health cure?

Are we scaring our patients?

These are the questions that have become part of the discussion. If you take India's example, and I can see that in many other countries, the same challenges will be there. What kind of budget is available to traditional systems, and what kind of budget is available to mainstream medicine? In terms of service proportion, AYUSH is a large portion; however, only a small portion of the budget is allocated to it.

There are about two million medical doctors in India, and about 1.1 million of them are from allopathy. Half of our doctors in India are allopathy, and half are from traditional systems of medicine. These doctors give services, but they are not considered doctors because they are not counted in the doctor population ratio. Therefore, India's ratio falls behind in terms of the global average of one doctor to 1,000. But when we combine these two doctors, the Indian average is much more impressive, not considering this service is one of the clash points of a local challenge in traditional medicine.

If you look at medical doctors actually in India, you know doctors are considered as guards. They are considered as guardians of health and not merely drug prescribers. But today, most of the time, doctors have become drug prescribers, and the role of the guardians of health seems to be missing.

Diagnosis precision, emergency medicine, acute and palliative care are important. However, management of mental health and non-communicable diseases is also important. None of these systems can meet all the needs together, so there is obviously a need for integration. The guardians' health role has to adopt circles. The first circle—how many of our doctors are trained to look at the fundamental determinants of health? How many medical curricula address genetics, nutrition, lifestyle, and environment? These are four pillars of health, and if one of the pillars becomes weak, we would require some kind of support system. That support system is our medical care—which is considered health care—and that has become the central pillar. Basic medical education can address patient vulnerabilities in a system where health and medical care compete against each other. This system creates conflicts for patients between diagnostic labs, insurance companies, doctors, hospitals, and drug companies. The issue of medical education, integrating both the Western and traditional systems, may be the best way forward.

Our health is actually in our hands, and this kind of approach we should promote. We should not ignore the mind’s capacity to heal ourselves. People need simple ways to achieve health other than primary care, for example, a healthy lifestyle, peace, and relaxation. People need health assurance, not necessarily health insurance. We need to transition to preventive care.

Dr. Patwardhan closed with how to move from clashes to convergence, emphasizing a need for evidence-based practice and practice-based evidence. Biomedical evidence, experimental evidence is important. At the same time, experiential evidence is also important, which comes from practice. It is important, or else evidence-based medicine is going to be the way forward.

Integration is the answer, and many agencies have given policies on this. Finally, clashes to convergence are possible if we move from a practice-based system based on silos, which is based on more actors—to people-centered holistic health care. We hope this kind of transition will address the clashes and the challenges with this vital topic.

**Question & Answer Session**

**Question:** I think nurses have much knowledge on moving toward the holistic area. How does the convergence of medicine types plan to leverage nursing practice for holistic health care?

**Answer One:** I’m sorry, I focused only on doctors, but nurses, the entire paramedical staff, they play a vital role, and without nurses, I don’t think this transition is possible. This question is should we move from a practice-based approach to a people-centered holistic approach, or holistic health care. In the interest of the patient, should we move toward this?

**Answer Two:** This question about the nurses is extremely important because two years ago, the European Society of Medical Oncology was talking about the importance of nurses in cancer control, not just for the implementation of lifestyle changes, but also in care and survivorship. Dr. Andrade thinks that it's extremely important that the measures of health promotions are not exclusive to M.D.s. It is important to have nurses collaborate.

**Answer Three:** The Ayurveda system says that the health care system revolves around four things—first is the physician, second is the drug, third is the care provider, and fourth is the patient. All have a very important role in the health care system, so the nursing staff, the care providers, are most important in providing the health care.

**Question:** If there is one single factor or one single process that you will take up to overcome these clashes and challenges, what is it that you will do?

**Answer One:** From my point of view, it is to create the best communication between the systems, it could be like a video among practitioners, the science, and the system. That is what we’ll need for integration, and that is what will lead to the ability to overcome these challenges, which are assumed by a culture and belief system.

**Answer Two:** Education will be the starting point because, in education, we are cultivating minds, and allowing integration or synergy.

**Answer Three:** I would like to reinforce education, but I think that we should put more value on the way that we expose the evidence. We need to improve our capacity to expose the evidence of all these benefits, which I think that is a point that is very important to decrease this clash that we are looking at today.

**Answer Four:** I think that’s critical, particularly when we talk about traditional systems in medicine for which the evidence is often not in English, or traditional Chinese medicine. There’s so much literature that is not easily accessible to people who don’t speak Chinese or don’t read Chinese.

**Question:** How do you make the economic argument that a person-based model of health care is better in the long run for our society compared with an allopathy-based model?

**Answer:** No, when I said a transition from allopathy-based, and I’m not really undermining any allopathy, I’m saying that every part has some good things that we can draw from and use in the best interests of patients. I hope that you will be optimal and economically viable in the system to create synergy. There is no straight answer because economy is not that easy to give a straight answer to. But I think that we will slowly move in that direction so that, today, you use a prescription-based approach, but maybe it will turn into a more holistic-based approach where mind management also welcomes exercise, or physical, or other management approaches also will come, and a lot of cost will be brought down.

**Question:** The pharmacological companies dominate the scene in health care worldwide. What can be done to balance their influence?

**Answer One:** To stress the question that we are spending money in a bad way, if we put in the society perspective and we look to the avoidable fraction of cancer, we could use this money to offer better treatment for the patients who really have diagnoses that are not related to lifestyle. I think that it’s just a different way to spend our money with better utilization.

**Answer Two:** And I also think that a greater degree of what Carlos said is right. I think, at the highest level, that there is a realization that of any business, which is based on the agonies of the people, cannot be sustainable, so we have to find out better ways of keeping people healthy and still make money, and there are ways and means of doing that, for example, addressing immunity.

**Answer Three:** The concept of prevention has been, of course, discussed in countries that have medicine available for all. I won’t use the term “socialized medicine” because somehow socialized medicine is being viewed negatively in this country, but medicine is a human right for everyone, and in societies where the government foots the bill for this, you shouldn’t have to do a cost-benefit analysis for getting people to quit smoking and get to a healthy weight. We know what the financial ramifications are going to be.

Yet prevention is not part of the model, so I think it's hard to know exactly what it is, but it's a part of the medical model, it's not taught in medical school. It's not compensated. Can I get reimbursed for providing patients with behavioral counseling, diet advice, exercise advice? And the answer was essentially "no." Even though we know that cancer patients who are obese, sedentary, and eat a low-fiber, low plant-based diet will not respond to their treatment as well and will die of their disease at a higher rate than people who follow the guidelines.

So changing the system isn't as simple as, How do we compete against big pharma, and how do we prove that what we do saves money? I think part of it is culture and changing the culture, and this comes back to that article I read in The Economist a few years ago, which has to do with policy and needing more of a systems-based approach to tackling this issue. It's not just the evidence; it's not just about the policy; it's not just about educating the public and the medical community. We all need to be in this together and doing demonstration projects and, ideally, again, in countries where there is a vast interest in getting this right because it'll save them a tremendous amount of money.

If there’s a vaccination system, in which HPV vaccination, I assume, is relatively cheap. What are the financial implications? There needs to be more of a systemic level, and part of it is the culture of the physician, and I think the patient. We want the magic bullet, we want a simple answer, we want a pill, and that’s often not the answer, particularly when it comes to preventing cancer.

**Question from the Moderator:** Some of the speakers discussedthe over-medicalization of health and the issue about health promotion versus medicine, and I think it plays into a lot of what we’re talking about, and I wonder if we could get the speakers to make some comments along the lines of this. We’ve been talking about integration across medical systems. What can be said about the way in which pushing forward the idea of health promotion over the disease-focused approach?

**Answer:** I think that the modern understanding of nutrition that the research has given us is fantastic. The Ayurveda system is sophisticated, and it should be researched further. So nutrition, if we look at it in a mechanical way of nutrition, protein, minerals, and calories, it is not the way that is important, and I’m not saying that it’s not important, but that is not enough. We should look at nutrition from a personal point of view, to determine what is good for an individual. It must be there in Chinese medicine, so it must be there in other systems also, so such concepts we must bring forward and bring about the overlap of science and bring them together.

**Question:** Can you elaborate on your statement about the 21st century being about behavior? This seems to be key to the path forward for the integration of TCM and conventional medicine, and at the root of many of the current global challenges. How do we include food, tobacco, or alcohol and industrial companies in this discussion?

**Answer One:** That is a challenge for both traditional and Weston systems. But I think that if you look to the fraction of avoidable cancer that we have today, we see that lifestyle is responsible for almost all of this fraction. This is why we need to move in this direction, and depending on the country, these numbers are up to 60% of the cancer diagnoses. It's too much related to lifestyle; that's why we need to add more attention or more decisions because it's not just an individual question; it's a society perspective also. And more than that, it's a political question that we need to deal with. If we use the example of Finland, the situation, the environment, and condition that they had in that time, to make those changes and decrease the mortality, not just from cancer cost, but also cardiovascular cost, you would see the importance of this movement. It's not easy, but we need to keep on talking about that. I think that, individually, if you educate, people will move in this direction. We can see the bankruptcy of individual families because of this cancer diagnosis, and we need to talk about this. But if you look to society and a political perspective, we create an environment that's trying to put this question at the top of importance.

**Answer Two:** One of the things that we have to be very thoughtful about is how to make this behavior change. How to make sure that people change their behavior, and there should be a way of approaching that, and it usually comes from a good policy and angulation for that. Let us look at the preventive aspect of it. For example, we tell people not to take in too much sugar; we say not to use tobacco and to reduce alcohol. There's something that you take away from people, and we tax them if they use it more in some way or other, and that's how we prevent many of these people from going through this.

Look at it from the other point of view: If you start supporting or giving tax benefits for going with positive cited aspects of life that can prevent diseases, physical exercise or yoga, following a particular kind of diet plan based on a particular kind of phenotype that can be identified through traditional medicine, making sure that people do go to sleep, this is not what I’m talking about. This is not possible, because nowadays, I’m sure that your organization and most of the organizations in the world would ask their employees to do so.

**Chat:**

**BHUSHAN PATWARDHAN:** Dear Participants, you may like to read JAIM Editorial that elaborates few points from my presentation, <https://www.sciencedirect.com/science/article/pii/S0975947620300887>

**Day 2: October 28, 2020**

**Location:**Zoom Webinar

**Time:**8:30 p.m. – 12:00 p.m., EST

**Date:**October 28, 2020

**Attendance Report:** 232

**Research and Evidence-Based Integrative Oncology for Cancer Prevention and Treatment**

**Opening Remarks:**

**Dr. Alejandro Salicrup**

**Senior Advisor for Global Health Research, Center for Global Health and OCCAM-DCTD, NCI/NIH**

The conference goals are to clearly understand the interface with Western biomedicine and traditional medical systems in different countries. You will hear perspectives and experiences from many hospitals, universities, and research centers worldwide through these four days. We would like to explore what types of collaborations are happening and some of the gaps and challenges in research. We would also like to explore these opportunities, particularly in low- and middle-income countries.

Yesterday was a very productive day, and attendees from 24 different countries joined the conference. We focused on the role of integrative oncology in prevention, treatment, and patient management globally. There was also a discussion about the challenges and clashes of worldviews and circles of influence into integrative oncology between conventional Western medicine and complementary, integrative medicine. In today’s sessions, we will go over:

* Research and evidence-based integrative oncology
* Aspects of cancer biology
* The pharmacology of traditional medicine
* Integrative oncology and related research by our colleagues from China

**Moderators:**

**Dr. Jun Mao, Lawrence S. Rockefeller Chair in Integrative Medicine, Chief, Integrative Medicine Service, Memorial Sloan Kettering Cancer Center, New York, New York, USA**

Dr. Mao shared that today’s sessions will focus on research evidence-based medicine. His first teaching job at the University of Pennsylvania, more than 17 years ago, was to work with first-year medical students on evidence-based medicine. Here, you're challenged every session by super-bright, articulate, and often critical medical students. You're trying to learn the game. Evidence-based medicine integrates the best available research evidence with our clinical expertise and our patients' values and circumstances.

There's a long history of use for complementary integrated medicine, so there's tremendous clinical wisdom in different regions of the world. Patients often have belief systems that make them want to use it. If you want to be part of standard cancer treatment or medical education, we need research evidence. Many of you may know that my research focus is acupuncture. Twenty years ago, I started this journey as a fourth-year medical student, reflecting on the literature on acupuncture in oncology. It has grown over the years, beginning in 2000.

In recent years, there are 50 articles per year in the PubMed English language database on average. Certainly, there could be a lot more papers in other languages. Dr. Mao presented a selection of seminal acupuncture articles in oncology.

In 2000, Judy Shen from UCLA studied acupuncture for chemotherapy-induced nausea and vomiting. In the next decade, research began to tap into pain and fatigue. In 2015 and 2016, published articles studied hot flashes and fatigue. Most recently, there was a large JAMA meta-analysis conducted on pain and acupuncture. This body of literature has strengthened the evidence base of oncology acupuncture.

As a result, five of the 11 National Comprehensive Cancer Networks’ clinical guidelines have supported the use of acupuncture for:

* Managing pain
* Palliative care settings
* Survivorship for cancer-related fatigue
* Nausea
* Vomiting

Our conventional oncology colleagues' guideline work, together with our supportive care specialists, starts the process of integration. Cancer Centers are leading cancer programs with basic research, clinical research, and population science. They are providing the most comprehensive array of clinical services for our patients. Cancer Centers' support for the use of acupuncture and other integrated approaches has increased in recent years. This would not be possible without the research evidence.

1. Hyeongjun Yun, Lingyun Sun, Jun J. Mao, Growth of Integrative Medicine at Leading Cancer Centers Between 2009 and 2016: A Systematic Analysis of NCI-Designated Comprehensive Cancer Center Websites, JNCI Monographs, Volume 2017, Issue 52, November 2017, lgx004, https://doi.org/10.1093/jncimonographs/lgx004

**Dr. Paige Green**

**Chief, Basic Biobehavioral and Psychological Sciences Branch, Behavioral Research Program, DCCPS, NCI/NIH**

Reflecting on the values that Dr. Mao articulated, what this session will do is grapple with how we integrate those values to conduct effective and respectful research. We must research traditional, complementary, and alternative medicine and integrative medicine therapies. The research will be conducted in patients, individuals, and communities in low- and middle-income countries. We will focus on the cancer control continuum—from primary prevention to survivorship, palliative care, and end of life. We do this. We will conduct rigorous research that leads to evidence that will guide clinical practice and the implementation of those research findings into the care delivery setting.

**Speakers:**

**Dr. Jennifer A. Ligibel, Director**

**Leonard P. Zakim Center for Integrative Therapies and Healthy Living, Dana-Farber Cancer Institute; Associate Professor of Medicine, Harvard Medical School, Cambridge, Massachusetts, USA**

Dr. Ligibel discussed what makes this research challenging. The large number of attendees today speaks to the growing base of evidence. This demonstrates that integrative therapies provide quality of life and many other benefits for patients during and after their cancer treatment.

As we see this body of evidence grow, we see the uptake of these therapies through the oncology community increase with increased awareness of patients and acceptance on the part of the oncology community. Nevertheless, this research continues to be challenging, and there continue to be skeptical individuals about the value of these types of approaches. That underscores the importance of continuing to conduct high-quality research in this area.

There are difficulties related to choosing an appropriate control condition, recognizing that it can be difficult to blind people to whether they’re exercising or not, or getting a massage, even acupuncture at therapy. There are sham conditions, and it can be hard to fully blind people to whether they're receiving these therapies are not. That's often a central part of the way that we design randomized trials.

One of the other challenges for this type of research is that many times we’re trying to help people feel better. Those are subjective outcomes, and patients may be particularly susceptible to placebo effects and bias. One of the other challenges is that unlike a pill, something like exercise or massage may be widely available. So preventing contamination from your control group can also be a real challenge.

Dr. Ligibel also discussed the challenges of standardization for integrative therapy research. When thinking about integrated therapies, one of the real strengths of this treatment approach is that the patient's services are individualized. They are often not prescribed purely by the condition that they're trying to treat and the patient's characteristics. So how do you think about standardizing an intervention like that?

There are also very different cultural contexts into which these integrative therapies are applied. Suppose you want to conduct a large-scale trial to look at the effects of these therapies across populations, which creates many challenges in the intervention you're delivering. Is it the same in North America and China, and other places?

To illustrate these points, Dr. Ligibel talked about some of the research that has been conducted at Dana-Farber. In the Preoperative Health and Body Study, a lot of research focuses on exploring the biological mechanisms underlying the connections among:

* Physical activity
* Bodyweight
* The risk of developing and dying from malignancy

They were interested in looking at the direct effects of exercise on breast cancer in humans. There are many fascinating studies on animals, but these trials are a lot harder to do in people. The goal was to look at whether exercise impacted tumor proliferation and gene expression.

They used a window of opportunity model to do this. We enrolled women in this study shortly after being diagnosed with breast cancer, and before they had undergone their definitive surgery. The goal was to see if you expose a woman to an exercise intervention in the time between her breast cancer diagnosis and our surgery, whether that would induce any changes in proliferation or gene expression in the tumors. This was as previously seen in animal models, but not in people.

Dr. Ligibel and colleagues encountered many challenges as we were thinking about how you design the study. First, it's a relatively short period. If you tell people that exercise is beneficial, everybody, regardless of which group they are assigned to will exercise during this time. This would make it harder to see whether exercise had any benefit.

Dr. Ligibel recognizes that this is a challenging time in people's lives, and many of our studies were with breast cancer advocates. They didn't feel like that was something fair to the patients who enjoyed the study. They also pointed out that a study with many biopsies might not be very appealing if you might not get anything for your participation.

Therefore, they thought a lot about appropriate control for this study, and we decided that we would incorporate two different, potentially active interventions in this space. They chose our second intervention thinking about secondary outcomes—recognizing that this was a time in many women's lives associated with very high degrees of stress and anxiety.

Rather than randomizing women to exercise versus usual care, we randomize them to exercise or a mind-body visualization intervention. Making sure that this intervention would not impact the primary outcome, looking at proliferation and gene expression. They did a fair amount of research looking at the physiologic changes of this type of intervention.

Dr. Ligibel found that there were not many, at least in the limited studies, so they moved forward with this design. Our two interventions were an exercise intervention. This was a supervised, moderate-intensity exercise intervention, very similar to the work that we typically do that involves strength training and aerobic exercise.

The teams’ mind-body intervention was based on a commercial program called Prepare for Surgery, Heal Faster. Many of our patients were using this intervention at that time. It involved listening to a relaxation CD.It started a few years ago, clearly, and also involved using a book. This was more of a self-directed program, so it wasn’t a contact time-matched control, but it was of potential interest to our patients.

The study was successful in enrolling about 50 women over 3.5 years. They did see that having these two active interventions did effectively separate the behavior of the group. At baseline, individuals in both groups were exercising about 50 minutes a week at the end of the intervention. This was an average about a month after they enrolled. Women who had been randomized to the exercise intervention were exercising around 250 minutes a week. There had been only a minimal increase in exercise in the mind-body group.

Conversely, the women assigned to the mind-body group had very high engagement levels with the mind-body program. For 69% of the days between enrollment and the time of surgery, they engaged with these materials in some way, mainly listening to the audio files.

They were able to separate the physiologic effects of these two interventions, looking at gene expression, and found that the women randomized to the exercise intervention experienced significant up-regulation of many different pathways. This was not seen in women randomized to the mind-body group.

They found this very interesting and thought that they could separate the effects of these two groups again. They also saw that the mind-body intervention had different but also positive effects on patients who recorded greater than moderate anxiety at baseline and surgery time.

After the intervention, there was a much more significant decrease in anxiety in the mind-body group, with relatively similar effects on stress. This is one way when you’re thinking about designing a study. Rather than comparing patients to usual care, when you're looking at an integrative type of intervention, trying to find something else that may have value for the patients, but potentially a different set of potential benefits.

Now, shifting to standardizing interventions—especially across cultures.

In a currently ongoing study at Dana-Farber, the multi-national hot flash study led by my colleague. This study was designed to develop a multi-national project evaluating the potential for acupuncture to reduce hot flashes, which are a prevalent side effect of breast cancer treatment in breast cancer patients treated in the United States, South Korea, and China.

This study's schema, so it's a relatively straightforward trial, randomized individuals to immediate participation in an acupuncture intervention versus a waitlist control. The goal was to enroll 160 women who were currently experiencing hot flashes from their breast cancer treatment and randomize them to one of these two conditions.

The goal was to enroll half of the patients from the United States, and then the other half of the patients would be divided equally between China and South Korea. The study objective was to determine the impact of the intervention on hot flash frequency and severity. Another object was to look at the various elements of quality of life in these patients. Generally, quality of life, breast cancer, the specific quality of life, menopausal symptoms, and sleep are unfortunately often disrupted by hot flashes in this patient population. They spent about a year and a half talking about the design of this study and working through the details, and several different elements arose as we were trying to put this together.

With any multi-center study, it is crucial to have good communication between investigators and a shared understanding of the research protocol's goals and implementation. They found many different areas where they needed to spend significant efforts to ensure that there was consistency. These focused on our eligibility criteria, the delivery of the acupuncture treatment, and our outcome measures in data collection.

Any study has these challenges, but they found this to be especially challenging with integrative therapy research across countries. One of the first challenges that we needed to overcome was standardizing the intervention. They felt that if we were going to be administering this intervention across three different countries, we needed to be a standardized approach for treating hot flashes.

Initially, a group at Dana-Farber put together a reasonably comprehensive acupuncture protocol based on how we often treat our patients at Dana-Farber based on previous acupuncture studies for hot flashes. These selecting points were utilized in those studies.

The goal was to have about 19 points using a two-phase treatment approach with manual needling and add electro-stimulation. I will never forget the initial meeting where we propose this intervention, and our colleagues in South Korea and China looked at us and said, we use about five points to treat this. What ensued was an excellent discussion about differences in philosophy and how acupuncture was delivered for this condition across these three countries. Ultimately, through a collaborative effort led by Dr. Liu, we developed a combined hybrid approach where they had a smaller subset of acupuncture points that we would administer to all patients. We would still use the two-phase approach, but they give sites the ability to use a subset of those and the other 19 points—keeping meticulous track of what acupuncture points were used for each patient.

All of the different sites were in agreement that they would use these same core points with the option of adding additional points that were part of that 19-point system. This took a bit of deliberation, but all acupuncture providers across all sites were comfortable with this. We've been able to see that there's been very high fidelity to the intervention's delivery after these discussions.

One of the other challenges faced was the selection of study measures. They found that in the United States—if they were conducting this study just to English-speaking patients—there was sort of the best measure for hot flashes that we had planned to use. This was not a measure that had been validated in South Korea or China, which led us to think about the appropriate primary outcome for a study being collected worldwide.

Dr. Ligibel recommends finding a measure that has been validated to be an accurate indication of your measure across all of the populations included. They also spent a lot of time thinking about uniform data collection, creating a common case report form. They included multiple training sessions for study staff.

They found that things such as the dates are recorded differently in different countries. To have had very close degrees of attention to this, we also had a real-time viewing of data from the first five patients enrolled at each site to make sure that we were troubleshooting any issues that arose early.

Lastly, a group can help when you're thinking about scaling, whether it be an integrative medicine trial or other types of trials across different countries. This is especially important with low- and middle-income countries where there may not be the infrastructure to conduct high-quality clinical research that’s already existing.

The MRCT, the Multi-Regional Clinical Trial Center at Brigham and Women's Hospital, and the Harvard Research and Policy Center are focused on oversight, ethics, and regulatory environment for clinical trials. Their goal is to increase standards around the world for global research. The different domains work to develop standards, establish best practices, improve transparency, and identify improvement opportunities. We worked with the center very closely on our study. They were able to create checklists for the study's regulatory aspects for other sites and helped with some standardization of the data forms. This might be a resource for other groups that are interested in conducting this type of research.

There are some final thoughts about integrative oncology research; Dr. Ligibel thinks that careful study design is essential to these trials' success. Choosing an appropriate control group is going to strengthen research findings also can help with enrollment. Patients are very excited about these types of interventions. Multi-national research is critical, but it also has its inherent challenges. It's essential to be aware of the resources that are emerging to help support this work.

**Dr. Karen M. Mustian**

**Professor, Wilmot Cancer Institute, Department of Surgery, University of Rochester Medical Center, Rochester, New York, USA**

Dr. Mustian discussed lessons learned as part of her research and journey. Working with integrative medicine, and reflecting on her work early on, her interest in what was then called alternative medicine back in the mid-90s. This inspired her to leave her position, go back to school, and completed a Ph.D. in order to research with cancer patients. She was introduced to yoga and tai chi in the United States when it was considered alternative, not integrative. Dr. Mustian began to see some potential value for the cancer survivors I was working with within my community.

Dr. Mustian has conducted two large nationwide clinical trials in the United States, examined the effect of yoga in cancer survivors, and, most recently, just completed a large Phase III trial. This trial involved 740 cancer survivors, comparing our intervention to a very rigorous behavioral placebo condition, survivorship health education. Moreover, it compares head-on with the gold-standard behavioral treatment for insomnia, which is cognitive-behavioral therapy.

The trial was recently presented at ASCO 2020, the American Society of Clinical Oncology meeting back in June. You can find that information, and there's an oral presentation that you can watch that will tell you all about the data and our findings. We are currently focusing more on the study design and some of the lessons we learned. This trial was a basic randomized control trial; we consented patients, we screened for eligibility and consent; they completed a series of study forms, as well as physiological assessments. They were blinded to our study hypotheses and randomized to our yoga condition or survivorship health education—which was our behavioral placebo or cognitive behavioral therapy for insomnia.

Dr. Mustian and colleagues did their assessments immediately post-intervention, and then again at 3 and 6 months to look at the maintenance of our outcomes. What were some of the significant challenges we faced in conducting this clinical trial and getting reliable data in this trial? They face differences in ideological paradigms, meaning challenges, and clashes between worldviews in traditional and integrative medicine.

When they began to talk about doing yoga intervention for cancer survivors, and they were working with our colleagues from India, as well as colleagues here in the United States and providers across the country. They began to realize that there were very different worldviews on yoga's value, precisely what yoga is, and whether it was or was not worth pursuing as an effective option for cancer survivors to manage their side effects. That was very challenging. One of the ways they overcame that is through a lot of communication and a lot of education. One of the things they face in their trial is defining the clinical problem they were treating. In this particular trial, they were treating insomnia, specifically clinical insomnia.

To ensure that they were getting patients with that clinical condition, they had to clearly define our eligibility criteria. This meant screening out many potential patients who may have wanted to participate in the yoga trial, but they would not have been diagnosed with clinical insomnia. This is important historically. When they first started doing this work and integrative medicine, you might think, “Let’s give yoga to cancer patients and see what it does. Let’s see if it actually helps them with a wide variety of things, or see what it actually treats.” That is like saying to a cancer patient, “Let’s give you some chemotherapy and see what it does.”

They defined a particular clinical problem for patients when we’re doing a treatment trial regarding cancer. What they are trying to treat is usually associated with the disease itself. In integrative medicine and oncology, they need to do the same things when we're developing trials. Studying these modalities requires a clear clinical problem to treat.

They had to define the modality very clearly. Yoga can mean lots of different things to lots of different people. Moreover, there's lots of different forms and systems of yoga. For example, we had to make sure that people knew we were not doing yoga in a heated room; we also had to make sure that people knew that we were not doing a Tongan, a very rigorous form of yoga. Clearly defining our modality of yoga and what that meant, whether we were just doing postures and movements or whether we were actually including the mindfulness components of yoga, was vital. Making sure that we standardized our intervention and that it was reproducible was also important.

We did this by developing a manual with very explicit components that were included. We also worked with a yoga instructor who was also a cancer survivor—a very experienced instructor who helped us use yoga therapy components that have historically been known to improve sleep.

It’s also important in these clinical trials to ensure quality, fidelity, and lack of drift in our intervention. Making sure that the intervention you're delivering is of high quality and that the practitioners are maintained doing the intervention that you want and not something slightly different. When you do sizeable definitive Phase III trials, they often last for many years. Therefore, to make sure that what goes on with the first person who gets your intervention is the same as what goes on with the last person who gets your intervention three years later. Moreover, if you have an instructor working with you, what they do in the first six months of your trial, they do the same thing three years later in the last six months.

You also want to think about how you can characterize your yoga intervention's explicit dosing or integrative medicine intervention. That was an interesting challenge with yoga because historically, we haven't always thought about a dose of yoga that way. We want people to integrate yoga into their lives and become part of their everyday life. In a clinical trial, how do you quantify that? How do you get specific parameters around the minimal amount of yoga that we want you to do to benefit? So for us in yoga, we started to borrow from our friends in exercise, and we began to talk about frequency, intensity, the time, and the type of yoga as a way of characterizing those prescriptions.

Monitor adherence to your intervention, work with licensed, qualified practitioners, which are not always easy to find. When you find those practitioners, you want to train your integrative oncology colleagues to work with you on research trials. Although they may be very qualified practitioners, they may not know some of the things that need to be standardized and done in specific ways as part of the research.

For example, we had to train our yoga instructors that even if they had different Asanas, they would like to do or thought would be beneficial for these patients, we could not have them include that Asana in our class sessions. They were not used because it was not part of the standardized yoga prescription that we were providing.

This large randomized trial worked with more than 50 different practices and oncology practices across the country to do this Phase III trial. We did also have a placebo control when that was our survivorship education intervention. One of the things to think about in terms of blinding and placebo controls in these trials is that you want to think about an intervention with a couple of characteristics.

First, you want it to be potentially believable to your participants, that it might help with the thing you're trying to treat—in our case, insomnia. Second, you want it to be similar in terms of what they call non-specific characteristics. It should be a similar amount of time, whether they meet in a group or meet with an instructor. However, you wanted to leave out some of your modality's specific characteristics that you think are effective.

In our case, mindfulness, the physical Asanas were not part of our behavioral condition. You want to compare it, don't be afraid to compare your intervention head-on with an effective gold standard treatment. In our case, we did that with cognitive behavioral therapy. It’s best to use measures and approaches that are valid culturally and linguistically, and also, it's essential to think about studying mechanisms of action.

Dr. Mustian believes that there is a need for more Level 1 randomized controlled trials. For example, if you have 50 trials that have recruited 50 people and all of them see positive effects, that still will not necessarily rise to the level we would call Level 1 evidence. That is definitive evidence. When you look at evidence-based treatment guidelines in oncology, you need at least two, sometimes more than two, Phase III randomized clinical trials to get that Level 1 evidence. Do not be afraid to report null results. This kind of results will teach us many ways that our interventions don't work, and knowing what doesn't work is just as important.

In this day and age, public and social media use to disseminate results is important because it's wide, fast, and gets to people who do not necessarily comb through research journals and read research papers. There is also two other types of research that we need to integrate modalities into standard care. One is that we need to begin to think about system-level care delivery research. This means, once you know that an intervention is sufficient and that it works, we need to research how best to use the system. You need to organize the system and coordinate care to access the providers and these types of interventions.

Obviously, cost-benefit analysis and research are important, but at the patient's level, the practice, and the payers. Work with and train our community partners to be able to make effective referrals. Engage, engage, engage, engage, engage.

There is no way that they could have defined an important problem that needed to be treated among these survivors without engagement. There is no way to have thought about all the practical problems that we would face implementing this intervention without engagement. Working with clinical practices, yoga practitioners, and working with our yoga partners across the country, and then obviously community partners and our international colleagues was incredibly helpful in all of this.

**Question & Answer Session**

**Question:** Dr. Ligibel, what is the role of patient family support during diagnosis, prognosis, and treatment/management of cancer? Is it factored into integrative oncology? What parameters in family and other nonclinical care are significant, and how is it weighted?

**Answer One:** I think that is very important, obviously, and is often managed by the psychosocial faculty of the staff of an organization. I think that integrative oncology interventions often involve the caregiver, as well as the patient. I know our center provides available programming, not just to the patient but also for families or other caregivers. Just recognizing that the stress of cancer and cancer treatment are not only affecting the person who's getting the treatment but their broader support system. There are absolutely studies that focus on caregivers with integrative oncology. We have not conducted those at Dana-Farber, but several other trials have looked at the value of different types of integrative therapies on caregivers' stress and anxiety. A critical aspect of the care that people receive is also supporting the people who are caring for them.

**Answer Two:** I'll speak to family members and caregivers, we are extending our yoga intervention, and we developed a partnered version of it, where the caregiver and the patient or survivor can do it together. When I think about integrated medicine and what I've learned from my colleagues internationally, one of the most important things is that—and Jennifer alluded to this—they don't necessarily prescribe something that just treats a disease and characteristics of a disease. They look at patient characteristics. As part of looking at that, they also look at family characteristics and the dynamics of some of what goes on in that system. We're finding in our work with cancer that it's very important to consider doing that with the yoga intervention. I'm excited to see what our data is going to say. I think we need to take that into account and do more of that work and research.

**Answer Three:** We published a paper about two years ago in support of cancer caregivers. When the family is supportive, we found out the expectation from the individual cancer patients for CAM increased for all outcomes, whether symptom control or for case cure. Clinically, it does present both benefits and challenges. I think the benefit is engaging the patient to family, as caches of unity can promote passive health behavior change, such as fines or yoga if you have the whole army unit on board. Nevertheless, sometimes the families have a strong belief in the pursuit of alternative medicine, and the patient is kind of ambivalent. So then I think that many jobs as the integrative medicine physician are often trying to present the evidence, again, addressing the health beliefs, trying to make sure family cohesiveness remains intact. However, patients can adhere to conventional treatment and incorporate alternate treatment as part of the cancer treatment rather than the alternative role.

**Question:** Did exercise or mind-body intervention affect Ki-67? The gene expression results that you obtained were from tumor tissue, or were they from plasma or blood?

**Answer:** We talked mostly about the methodological aspects of that study versus the results. The results were published last year in clinical cancer research for people who want more information. The gene expression was in tumor tissue. So paired between the initial biopsy at the time of surgery or a core that we had taken at surgery, we did not see changes in Ki-67, just in gene expression and in some immune infiltrates that are all kind of detailed more fully in the paper.

**Question:** Are there any studies addressing the role of yoga, acupuncture, or exercise to improve symptoms for GI cancer patients, particularly diarrhea, etc.?

**Answer One:** Many exercise studies that do focus on GI cancer populations, some of them focus on hospitalized patients, looking at gut motility after surgery. There are also nutritional interventions that focus on diarrhea, specifically in GI cancer patients. I'm not as aware of acupuncture or other interventions.

**Answer Two:** In terms of yoga, I'm not aware of any yoga trial that has mentioned diarrhea as a primary outcome of interest for that trial in cancer patients. Now, there are yoga trials that may have looked at a series of side effects among patients or survivors, and diarrhea may have been one of them. However, as far as I know, really thinking about yoga's actual effects on diarrhea in GI cancer patients, has there been a trial focused on that kind of design and answering that question? Not that I'm aware of, but I don't claim to know every single study that's published out there all the time.

**Answer Three:** I collaborate with a colleague who ran a hospital in China, and she just recently published a paper on a pilot study of irregular acupuncture for anorexia patients with advanced colorectal cancer. We found some potential benefits in reduced anorexia score and maintaining weight for patients with GI cancer. We're currently collaborating with several centers in China on acupuncture for patients with stomach cancer, following surgical resection, and undergoing chemotherapy to see whether it improves life quality and reduces stomach cancer symptoms. Right now, we mostly focus on breast cancer because I think there's a large survivorship population. This field is just beginning to move into more active treatment for patients with advanced cancer. I feel like, overall, GI cancer patients, especially, in say, pancreatic cancer, definitely need more research.

**Question:** The effects of integrative medicine are very likely to be idiosyncratic and personal. Have you thought about designing N01 trials instead of randomized controlled trials?

**Answer:** I think one of the main challenges in this type of research is really thinking about what is the most appropriate design for interventions that are meant to be not just focused on the particular symptom but also on the characteristics of the patient, and it makes it very difficult. I think that when I design these trials, I often think about how do we broaden acceptance of these types of practices in the oncology community, how can we start to think about third-party reimbursement to make these types of services more available to people more broadly?

I think what’s hard is that the end of the trials, at least with our current ways of evaluating evidence, is unlikely to lead to that. It doesn’t mean that it will provide value for an individual patient, but I think in terms of globally thinking about how do we advance this field, I think there needs to be some trade-off. And that was honestly why we had this discussion with the three centers that were participating in this hot flash study in terms of how do we design this intervention in a way that there’s enough standardization that we feel like what we’re offering is the same thing, so that if we find that it doesn’t work in China, then we don’t ask whether it was the same program versus whether there are differences in those patients. I think that these are the sorts of questions that we are always thinking about when designing these studies.

**Understanding the Pharmacology of Traditional Medicine**

**Moderators:**

**Dr. Emmeline Edwards**

**Director, Division of Extramural Research, National Center for Complementary and Integrative Health, NCCIH, NIH**

This session on traditional medicine's pharmacology includes a wonderful panel that’s geographically diverse—from Brazil to South Africa to Colombia to the United States. The panel discusses the National Center for Complementary and Integrative Health efforts to understand natural products' pharmacology better. So essentially, at NCCIH, we have a fairly extensive portfolio of natural products. Under that umbrella, we come with botanical herbs, special probiotic diet, but the focus of this session, in particular, is on natural products.

Over the years, the natural products' field was somewhat stymied by the infusion of new methodology and technology. So, it has been a focus for us to introduce, apply, and integrate new methodology to natural product research—the number of opportunities funded through NCCIH supports innovative approaches that address current limitations in natural products.

Three examples:

In July 2020, they funded The Natural Products Nuclear Magnetic Resonance (NMR) Open Data Exchange et. This is an advantageous resource for the field. Investigators would be able to deposit their data, providing the ability to use an existing data set to do more pharmacology research.

They also have a Center for Natural Product Technology, Methodology, and Productivity Optimization. In this center, the focus is primarily unused in informatics and big data to help in characterization and the determination of the mechanism of natural products' action.

Lastly, they have botanical centers. This is the current focus for these centers and is very appropriate for this conference because these centers are primarily looking at natural products and their potential impact on resilience with several different conditions.

**Dr. Ikhlas Khan**

**Director, National Center for Natural Products Research, University of Mississippi, Jackson, Mississippi, USA**

This session is critical because most attendees are on the clinical side; this session will highlight the basic sciences' significant need. It is apparent that we don't need any more convincing than traditional knowledge and complementary medicine are worth using.

The bottom line is it’s not up to people to believe or not believe; it's a different thing. That question does not exist anymore, which used to be 20 or 30 years ago, whether yoga, acupuncture, or traditional medicine helps or not. We have seen enough evidence; it had been tested over centuries. This is more than enough evidence.

Dr. Khan believes what is missing in the whole picture is that we still have, for a long time, not defined the product that we will be looking at it. First of all, it is not the same as what is traditionally used. On the other hand, everybody makes their own standardized for the compound with no pharmacological activity, and it does not have any impact. I just use it as a chemical marker. Traditional practitioners don't believe in these markers because what is the purpose of it?

Dr. Khan agrees with this. Randomly choosing some marker doesn't make sense. This action actually will highlight that basic science needs to be done and how important it is. It needs to be connected when we are discussing clinical outcomes. This is important because this is where the real product is going to come. One of our presentations would be from just talking about growing plant material consistently. Because that’s where the lab is, where the product is, and it has been ignored. Standardization and consistency are essential in order to move into the future.

All the centers are funded to make sure that research is being done and is fully characterized. It is important that the research can be reproduced after the clinical study.

**Speakers:**

**Dr. Carla Holandino Quaresma,**

**Professor of Pharmacology, Federal University of Rio de Janeiro, Rio de Janeiro, Brazil**

Dr. Holandino provided some input about the new technologies and innovations currently in use with natural products for cancer treatment and the importance of research and scientists to support natural products as anti-tumor agents. There are 29 integrative and complementary health practices in Brazil since 2006 (e.g., herbal medicine, music therapy, hypnotherapy).

Dr. Holandino reinforced why it is important to conduct cancer research—since cancer is responsible for a significant number of deaths globally, and herbal medicine has the potential to prevent those deaths. We discussed the findings of 30 systematic reviews that showed that medicinal plants could minimize the side effects of chemotherapy.

The primary plant was Curcuma longa, and there is a long history of using this plant for medicinal use. In Brazil, it is estimated that 1% or 2% of the Brazilian native plant species have been successfully studied10, 11. There is a great need to study the native plant species in Brazil further. One plant of interest is theorbignya speciosa, which is known as babassu in Brazil.

This plant is vital to the economy as it is possible to use or extract the oil from the coconuts to use as food or other products. Also, it's very important to note that many people are involved with the extraction of this oil because it is done through a handmade process. This process employs over 300 thousand families.

Dr. Holandino and colleagues were the first group to describe the potential of ethanol extracted from babassu12. They tested this using four different cell lines, including a drug-resistant cell line, and compared it with normal ones. Dr. Holandino presented Table 1. from the article, using the *ID*50, the non-tumoral cell lines are less sensitive than the tumor ones.

It is interesting to think about this kind of selection of the tumoral cells to normal cells. Another approach discussed was the possibility of combining nanotechnology and natural products. This helps diminish the amount of extraction needed.

This theory was tested using oil from babassu. Additionally, different polymers in this conjugate process were also tested in order to treat benign prostatic hyperplasia.

The second paper discussed highlighted the high potential of this nanotechnology combined with plant extracts (citation unknown). Using a very similar strategy and rationality, the group also developed a mini-emulsion using piper cabralanum extract and tested it against K562 cells13. The group also evaluated a different quality of polymers. Both of them are very effective in inducing a high phytotoxicity effect. When comparing this to the extract, they detected more than a 20-fold effect compared to the other extract. The nanotechnology parameters were also evaluated and showed good potential due to size and other aspects.

In another approach, using European plants, the group collaborated with colleagues in Switzerland. The research team explored the anti-tumoral potential of the Viscum album. Europe has over 100 years of history using traditional medicine. Also, extensive literature about using Viscum album for cancer treatment and its relationship to aqueous fermentative preparation. It is well known that when you use different quality solvency distractions, you can also have a different chemical composition with this preparation.

In this project, ethanolic preparation was compared with aqueous fermentative preparation. The first paper published on this research detected that phenolic compounds are the major important substances and tested this against melanoma cancer cells.

The result showed that the normal cells are less sensitive than the two tumoral cells that we tested. When the cells were incubated, several blebs in the cell membranes of the tumor cells were detected14. They also tested the different species of the plant.

In conclusion, phytochemical sources trigger different tumor cell death (apoptosis, necrosis, cell growth arrest) with low side effects. The research and development of new strategies, including nanotechnology, increase the anti-tumoral potential with a low amount of herbal material, improving this source's sustainability. It is crucial to elucidate the phytochemical profile of herbal medicines to increase the pharmacologic uses of natural substances. The use of sensitive methodology, as well as an adequate statistical approach, are fundamental to guarantee the quality control of herbal sources.

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**Dr. Chrisna Gouws**

**Associate Professor of Pharmacology, Centre of Excellence for Pharmaceutical Sciences, North-West University, Potchefstroom Campus, South Africa**

Dr. Gouws is from South Africa and talked about traditional African medicine and the need for innovative research to move this further. South Africa and Africa as a whole are very biodiverse. South Africa has more than nine biomes already identified. Although South Africa represents only 2% of the world’s land surface area, we have approximately 10% of the world’s plant species, which shows you the rich possibilities of potential treatments that we have around here.

More than 5000 species, plant species, are traditionally used as medicine in Southern Africa, but it's a very old and diverse medicinal system. African traditional medicine is very poorly recorded and studied and moved into a new phase of application for these types of medicines. There's a real need for research to discover new drugs and validate the traditional use of these automated teller machines.

To have phytomedicines as potential treatment sources, we must still follow the same drug development pipeline for any other new chemical compound. However, currently, there's quite a problem in this pipeline because most pre-clinical screening happens in in vitro models that lack physiological relevance. This is part of the problem and leads to only approximately 3.4% of new cancer drug candidates having the possibility of success in clinical trials. That is almost negligible, so this highlights the need for new models that we can use to increase successful treatment and screening.

In our search for better models, we came across dynamic 3D cell culture models to increase the success rate. We specifically chose clinostat-based rotating bioreactor spheroids. It is basically a cell chamber with a humidifier chamber at the back, which is constantly protected by a drive unit. This allows omni-gravitational forces to be present, which lets the cells conglomerate and form the spheroid. This creates a very stable growth environment for the cells.

With this system, we have very constant yields and consistent sizes of the spheroids. These spheroids are very compact and uniform with very active diffusion. This system allows cells to maintain cell-to-cell contact and the formation of an intercellular matrix—which is essential for more complex structures and processes to be present as it would be in tissues. In normal flat cultures, we continuously break all communication between the cells.

This is important because when we allow cells to communicate, they can mature, and these dynamic spheroids then undergo what we call metabolic reprogramming. They get a chance to recover from interventions, and this maturation or reprogramming completely affects all processes in the cell. This changes the cell behavior and allows them to behave more as they would in vivo. Using the spheroids, we have a much higher physiological relevance than a tumor in vivo.

Regarding two of our models, our liver cancer model is based on the HepG2/C3A cell. This cell would culture on the bond drive unit from CelVivo. They are matured for 18 to 21 days before we start experiments to undergo metabolic programming. This model is tough to characterize, and there are quite a few publications on it already.

In the second model, we took a bit of a different approach. Not all cells behave as we would want them. LS180 colorectal cancer cells were not very happy with making their aggregate. We kind of had to enforce them by encapsulating them in sodium alginate. There are different ways to get to where you want to go with these models. In this model, we also cultured by constant rotation. We are also busy with quite a few other cells that we are creating models for. Currently, validating them, characterizing them to have them published soon.

These include several small cell lung cancer models, a melanoma model, and some breast cancer lines, and so forth. We are looking at quite a few indigenous plants or traditional medicines in our research, but I just wanted to highlight two today because they are quite different in approaching this.

The first being Sutherlandia frutescens (Cancer bush). You may have heard of it before because it's been well-known and well-studied in the past to treat cancer. Mostly because it has been used for centuries by traditional healers for this purpose, therefore its indigenous name, cancer bush. Furthermore, although you will find many publications concerning the plant in cancer research from all over the world, there is no commercial product available yet for the treatment of cancer from this plant.

That brought us to the question of why there is not a commercial product available for this plant. The one potential reason is that the focus shifted in the research. It became apparent that many traditional doctors prescribed this plant to boost the immune systems of HIV patients, which became the new focus of the plants. Causing the cancer treatment to fall behind a bit. The other question is if the preparations were excellent. We went back to basics and looked at the traditional preparations used by healers in practice, which is usually prescribed as a tea or an infusion. We then prepared a grid aqueous extract, and we treated our colorectal cancer model with this extract for 96 hours with treatment every 24 hours.

As we compare this with the untreated control, which is the solid black line, we also compared the activity with what we could find when treating the model with the chemotherapeutic drug paclitaxel. What was very interesting for us to see is that in little as 24 hours of exposure, we could see a significant decrease in cell viability and activity in the groups treated with the different concentrations of this extract. This decreasing activity was significantly more pronounced than that of the chemotherapy drug paclitaxel.

We also did some other studies. We could see an effect in as little as 4 hours after exposure of these spheroids to Sutherland's extract. We also treated one of our small lung cancer models with this extract, and we saw pretty much the same level of activity in that model as well. The other plant we were looking at was Xysmalobium undulatum (uzar); it’s one of the most widely used phytomedicines in South Africa.

We initially started working on the plant because some people had questions about toxicity potential and things like that. It became apparent this plant contains quite a lot of cardenolides, which has emerged as a promising new agent in treating diseases such as cancer, which brought us to the question of whether there's some potential here.

In our initial studies, we treated our liver cancer model with this extract. Again, we use the whole extract of fractions or single compounds. Again, we used Xysmalobium undulatum. We saw some decrease in activity and viability, or they're not that pronounced, while we did see a decrease in cell growth.

We also treated our colorectal cancer model with the same extract, and once again, we compared it to the chemotherapeutic drug paclitaxel. Once again, you could see that there was quite a marked response in this model relative to the untreated control and the paclitaxel. However, it was not quite as dramatic as what we saw with Sutherland.

Whether this effect is cancer-specific is still a question we need to answer, or if it’s just general toxicity, but that’s ongoing work now. We can say that all models are highly reactive. These models give us a lot of potential work options to study new plants and even chemical compounds. We have some options now to maybe get more clinically relevant data already in vitro. When we look at the plants, Sutherland appears to be very highly active in colorectal cancer. What is important to note is that there have been several in-future in vivo and clinical studies on southernlandia. These are not toxic in general, which implies that we should have quite a reasonable specificity against cancer with this extract. It appears to induce necrosis in this specific cancer line within as little as 4 hours of exposure.

Xysmalobium undulatum seems to not necessarily be toxic to the liver cancer model, but possibly sadistic, which we want in this COBIT. It also is active against colorectal cancer, although it was pronounced uzar. Again, as I mentioned, there are some toxicity issues with the specific extract. Even though traditional healers widely use it, we have some concerns, so that's also ongoing research to study these questions.

The big question we have is whether we can go from these crude extracts to specific active compounds or the synergistic activity of these extracts. To answer that question, we will need to use the whole extract. That's a question that frequently pops up when working with these traditional medicines because everybody wants that golden compound, a miracle cure. It's not that easy with plants—getting to that one single compound because it is not necessarily as simple as that. So that’s the question we’re asking and what we’re investigating, and we’re using these models to do it.

I would like to acknowledge our funders, which helps with this quite a lot. Then I would like to thank all of my collaborators (i.e., National Research Foundation, Advancing life – South African Medical Research Council, and CELVIVO Stress-Free 3D). I would also like to thank my research team.

**Dr. Susana Fiorentino**

**Professor of Immunology and Director, Immunobiology Group, Biomedical Sciences Research Unit, Pontificia Universidad Javeriana, Bogotá, Colombia**

Dr. Fiorentino discussed her research on discovering new medicines found in natural products, and her focus is on anti-tumor immune responses. The control of the tumor is mediated by different conditioning factors that play an important role in tumor growth, and these factors need to be studied.

The first is the tumor metabolism. Second is the quality of the immune response induced by the chemotherapy — how the tumor dies. The third conditioning factor is the tumor micro-environment, which is important to understand and study to know the signals given to the tumor cells.

Dr. Fiorentino shared that the system of pharmacology can be used to understand the appropriate steps of tumor control and the complexity of the plants. Systems or network pharmacology for the study of botanical drugs involves:

* The identification of metabolites present in plants
* The screening of biological activity
* The identification and validation of molecular targets and
* The analysis of the networks of compounds present

Dr. Fiorentino’s research team has a project looking at elements from Colombian plants. The project consists of 250 researchers with financial support totaling $6 million from the World Bank and additional support from different collaborators. The team is currently studying at least 40 different species.

There are some national universities, companies, and international universities and colleagues who are working on the same subject, as well. Their research goes from the beginning of the plants' productive chain, working on the ethnobotanical knowledge of the plants included in the project.

The team is also working on the cell and molecular research of these plants' interaction with tumor cells with three-dimensional models and human beings. They combine ethnobotanical knowledge, cell, and molecular research — tumor cells from human beings — data from animal models to validate the in vitro activities.

They then use the data to construct the network pharmacology to understand the relationship between the plants and the biological system. Next, they make the scaling, quality control, and traceability of the extract to do the regulatory pre-clinical studies. This allows them to make the clinical trials with the normative of the FDA and the Columbia normative. This is all done to register and commercialize natural products as phytomedicines.

Some of the tests are used to study biological activity. For example, the high throughput screening with saccharomyces cerevisiaeis is used to look for the intracellular signals working or as a target of the plant extracts. They have 10,000 cells with different mutations to identify the intercellular targets.

Also, in this platform, they study the metabolic alteration of the different extracts of the plants they are obtaining and studying the mitochondrial functions that can be targets of the natural products. They are using 3-D cultures to study the dimension and interaction.

They have tumoral cells coming from primary tumor cells from the patient, close to the physiological system. All of the data they obtain from this work are introduced in a platform constructed in collaboration with supporters and other universities.

For the clinical trials, they are working with the National Hospital University and different institutions and companies. The development of phytotherapy products started by studying two products obtained from two Columbian plants: petiveria alliacea and Caesalpinia Spinosa. They are also distributed in some countries of Latin America.

For these plants, they have the chromatographic profile already, and the extracts are already standardized. The compounds are isolated to use them as a normal compound. The anamu extract identified that it induces death by different dependent and independent mechanisms of the mitochondria.

They induce some alteration in the cytoskeletal and the G2 phase of the cell cycle arrest19, 20, 21. They also induce alteration of glycolysis and the decrease of mitochondrial respiration. The research team used primary tumor cells from leukemia patients to show that anamu extract has more activity on the resistance cells, normally more glycolytic cells. Anamu models led us to show the anamu fraction reduced the induction of in vivo tumor cells in mice models.

The second extract — named P2Et — is commonly used for the treatment of diseases. The research team showed that it also induced apoptosis and can have synergistic activity in some tumoral cells. The extract also induced immunogenic cell death with signals that are commonly known in immunology, the expression of calreticulin, and the secretion of adenosine triphosphate 22, 23, 24. Also, the anti-tumoral activity in vivo reduces the metastases. It also induces CD8 T cells' activation producing lFN when the cells are activated with tumor antigens25.

Dr. Fiorentino also discussed that this extract — when it is used as a therapy — significantly diminished the tumor growth. However, when used before the tumor was implanted in the mice, the mice's treatment can induce death. The treatment of prophylactic vs. therapeutic treatment with P2Et extract is dependent on the stage of the mice or the stage of the patients.

The team’s vision for the development of phytotherapy comes from the necessity of the country to develop its therapies and to develop a bioeconomy based on biodiversity knowledge. The team began the development of botanical drugs some years ago and has progressed through registering a drug.

To date, they have scaled the extract, obtained certification, and quantified the molecules used with the extract's normalization. They also made the biological traceability of each of the loads produced, learned the natural and accelerated stability to make the drug development, and conducted pre-clinical studies to go into a clinical trial. A Phase I clinical trial has already been completed in normal patients scheduled for completion in January 2021.

Their research found that the phytomedicine is safe, and some secondary effects were found (e.g., epigastric pain, myalgia, retching). Further, they found that some immunological populations are increased in normal patients, and they are studying that in cancer patients in a Phase II clinical trial.

They began a Phase II clinical trial in COVID patients more recently because their extract has a very important antioxidant activity and diminished important T cells. This is implied in the destruction of the lung when the patient is infected with COVID-19. They are currently conducting a clinical trial with five patients, which is set to end in December of 2020.

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**Dr. Pamela Weathers**

**Professor, Biology and Biotechnology, Worcester Polytechnic Institute, Worcester, Massachusetts, USA**

Dr. Weathers discussed Artemisia annua. Artemisinin is the active principle that’s known to be produced in Artemisia annua. She shared a picture of it in its native state and described how it is isolated from the plant. It also has a very active and endoperoxide ring, which is also present in all the semi-synthetic derivatives that exist and is mainly used to treat malaria.

These were developed because the native compound has poor solubility, low bioavailability, and a short half-life. The picture shared was of the plant in a pot, which can reach 2 meters, or more, in height.

Dr. Weathers’ team is looking at some effects against non-small cell lung cancer in particular. However, there are a lot of studies that have shown efficacy against many types of cancer with the use of artemisinin derivatives. The compounds are not toxic to healthy cells from the same tissue of origin.

She discussed one of their published lung cancer models (NSCLC)26, 27. The goal of the research was to validate that — indeed — this is non-toxic in healthy cells. The research team took human dermal fibroblasts with increasing concentration of artesunate. They found a slight decrease in cell viability.

The same was seen in the healthy cells with a DLAe (dry leaf Artemisia extract). Further, with the increasing concentration, they found quite a bit of increase in these healthy cells' viability. The research team found this interesting and positive effect.

Dr. Weathers also talked about the effect of DLAe on non-small cell lung cancer, which — of course — is nasty, very resilient, and drug-resistant. There are a series of treatment options. She discussed three cell lines:

* A549
* H1299
* PC9/PC14

These artemisinin derivatives can affect cancers in inhibiting angiogenesis, tumor growth, migration of the cells, cell growth, the cell cycle, and enhance apoptosis. These are all good modes of action that seem to occur29, 30, 31.

When conducting this research, it is important to learn how the extract works in these different cell lines and ultimately in tumors. They looked specifically at the mixture and how it compared to pure drugs. Most of these studies used Artemisia because it was very commonly used in many of the other studies.

Artemisia is generally recognized as a safe plant by several different agencies, including FDA, for food purposes. There is a lot of evidence on how and where dried leaf Artemisia can work. The team believes that using the whole plant versus a pure drug or an extract is advantageous.

Their research began with in vitro studies with extract or DLA, and the dried leaves were ground into a fine powder then extracted. They used methylene chloride and then validated the content of artemisinin because that is the tracking molecule and GC-MS aspect. This work was published in 201932.

The material used had about 1% Artemisinin in the dried leaf Artemisia extract. The extract was a concentrated form, and everything done was based on the amount of Artemisia that was actually in the extract. They found that both artesunate and DLAe inhibit the proliferation of non-small cell cancer cells, which was an MTT assay.

They analyzed the three lines, PC9, H1299, and A549, and calculated the IC 50s for both artesunate and DLA so that the results helped guide future studies. The research team also looked at cell cycle arrest using flow cytometry and found that the PC9, H cells, and A cells responded somewhat differently based on the phases — whether it is the zero to G1 phases.

However, what’s interesting in every single set of these cells, they saw that DLAe seemed to have a rather pronounced effect. The team looked at this further, looked at phospho-H3-SER10, and found that artesunate or DLAe, the extract, altered the phosphorylated H-3 proteins, which indicate a mitotic arrest. This was true for PC9 and the H cells.

In another case, they asked whether anti-proliferative effects the result of DNA damage, and there is evidence of double-strand breaks. The results showed effects on the Western blots for the H2AX and other housekeeping genes. Further, they saw some effects on all three cell lines, for both artesunate — in most cases — and DLA.

There was evidence of DNA damage in the form of double-stranded breaks. They also found stimulation of cell death, which occurred in the cells in the different lines. The question was: was it through the intrinsic or extrinsic pathway? When analyzing different caspases: caspase 9, 8, and 3, they found differential effects in the different cell lines among the different treatments.

The research team was interested in how cells might migrate because they do not want these cancer cells to spread throughout the body. In this case, they used a wound/scratch monolayer of cells and tested all three of them again with these differential concentrations of artesunate or DLA. They found the PC 9 and the A cells responded quite effectively with DLAe — less so with artesunate. For the H cells, they saw slight changes, but they were not statistically significant.

Next, Dr. Weathers discussed their in vivo research. In one study, they used female mice treated with DLA (not the extract form). DLA is a thick slurry of dried leaf Artemisinin leaves. The leaves are powdered into a fine mesh size, and then they are mixed with water. You must then gavage into the animal, which already has tumor induction, allowing the tumors to develop first.

They gavage quickly, and the process is tricky. It is required to gavage within 20 minutes of making that slurry, allowing the animal to be injected. If the process is not done quickly, it then turns into cement.

The analysis of the A549 cells was used to generate these xenografted tumors, and this was work that another group had previously published. Dr. Weathers’ team was interested in replicating this work; however, the other research team had only used artesunate.

They wanted to see if we got the same results and DLA (the direct leaf consumption). The comparison did not show a big difference. They reduced tumor size, but they are not different from one another — at least not significantly.

They only did the A and P cells because it is an extensive amount of work, and they felt as though these cells showed the most promise. In a separate analysis, DLA substantially and significantly reduced the tumor, and it was better than the treatment with artesunate and better than the untreated controls. The in vivo data suggested that one could get a tumor reduction after 14 days of treatment. This was a daily gavage of equal amounts of Artemisia on a molar basis of Artemisia content of either the plant material or the pure drug.

Dr. Weathers summarized that extracts:

* Exert cytotoxic effects
* Slow proliferation
* Stimulate cell cycle arrest
* Include DNA damage
* Include apoptosis
* Inhibit migration

Their in vivo studies delivery of DLA-artemisinin accommodated complex interactions within the body that could not be replicated in vitro.

Dr. Weathers discussed plausible explanations for different responses between the NSCLC cell line, such as:

* Differences in amount
* Location
* Metabolic rate of iron
* Differences in heme biosynthesis
* Different antioxidative profiles
* Expression of antioxidant enzymes
* Adaptive mechanisms to ROS,
* Reactions to other compounds in the plant.

Further, DLA provides significant benefits as a cancer therapeutic. It may be a way to enhance recovery between chemo treatments; other potential benefits are for patients who refuse chemotherapy, who are willing to take a natural product. She knows of one case right now where an individual being treated for melanoma is taking this plant material. They are in the beginning stages of treatment. Dr. Weathers ended on the note that there is still a lot more work to do.

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**Question & Answer Session**

**Question:** How does a person with cancer become a subject in a natural drug trial?

**Answer:** At the hospitals in Columbia, the recruitment of the cancer patients takes into account the condition of the patient. It is the decision of the clinician group to invite the patient to be part of the cancer trial. For example, one of the clinical trials that we are writing now, and that will be in February. I think it will be done on the care of breast cancer patients that receive chemotherapy. This study has two arms. One arm receives normal chemotherapy, one arm receives phytotherapy, and the third arm receives both. The patients are in stage 2 or 3 of the disease. The study is double-blinded. For example, we receive the COVID patients that arrive at the hospital, and that meets hospitalization. And for that, we do the same thing. So we asked them, they signed the form, and they were going to the study in two arms and is the same and also blinded.

**Question:** Dr. Gouws, can you elaborate on the use of traditional medicinal plants in the African setting? I would like your comments on casual treatment, use which is a huge patchwork—in food, burned and inhaled as smoke, continuous boiling and patient inhaling vapor, bathing with crude extracts, more semi-refined taken orally or as a patch applied to cuts on the body to cure diseases and ailments. Where do you really start? The rotating culture to establish a 3D in vitro model is good, but won’t it deprive the cells of their basic property of anchorage-dependence (especially for the epithelial cells), a the majority of solid cancers are of an epithelial nature?

**Answer:** Yes, African traditional medicine, I think as most traditional medicine is, is a very complex thing, it’s not just herbal medicine, it’s not just spiritual, this is a very complex interaction between different approaches, especially if you look at the way the traditional healers approach it. As a scientist, how do you measure the spiritual effects? We focus mainly on the plants, the herbal medicines, and then we try to look at the most standard way of treatment, how it is prescribed. This is not as easy as it sounds, because the traditional healers are very secretive, they are not very trusting of scientists. Because there has been issues in the past of stealing the knowledge and things like that, so there’s now protection of the indigenous knowledge that must be taken into account. So it’s a very complex thing that must be considered, but I think, as scientists, we always look at what facts we have and what we can measure. This article gives a very nice overview about the different aspects of traditional African medicine and how the herbal medicine fits into the bigger picture (E.J. Ozioma and O.A. Nwamaka Chinwe. Herbal Medicines in African Traditional Medicine. DOI: 10.5772/intechopen.80348). This might give some answers or some perspective, but I would say the way to start is with what you can measure. That’s where we usually start. With regard to the technical questions about the rotating cultures, what is important to know is that it’s not an anti-gravity situation. It’s just moving of the gravitational force, so they still experience a gravity of one. So it’s not the anti-gravity, it’s not like in space, it’s just the gravitational forces, or physics. And the thing is that the cells are not in suspension as much, they are grown on each other, so they are attached; they’ll just attach to each other, and they give the time to excrete extracellular matrix. So that’s why we say it’s more like in vivo. Where instead of being attached, they are attached to a plastic flat surface that’s not very natural, it’s not the way it happens in the body. Allowing them to interact with each other and interact with intracellular in a matrix is what gives them the opportunity to focus on their original function. That is why it’s actually more closely related to what you would see in a solid tumor because what we see is that the doubling time of these cells decrease dramatically over time. Instead of 24 hours, or something, for doubling time, it becomes weeks for doubling time, which is more representative of what the cell behavior would be in a solid tumor. Metastases can be tricky. We have seen cells escaping the spheroid structures. So that’s something we’re still looking into if that’s something we can measure, but metastatic cells will still be dispersed from this solid tumor type environment. You can see as the blood supply would be for the solid tumor.

**Question:** Dr. Weathers, I interpret that when you say the effects of Artemisia are benign, are you referring only to what you found in cell studies? I am aware of at least one patient who had hepatotoxic effects from Artemisia (prescribed by an integrative medicine physician). Are you aware of this toxicity occurring more broadly in the clinical setting?

**Answer:** We have never seen any adverse effects in any of our animal studies. We have not specifically looked for a powder toxicity, but the animals were thriving. In the human studies we know of that have taken Artemisia, there are actually measurements of toxicity, and they were not seen. It could be a one-off. I’m not sure which one you’re talking about. I know some people have combined it with rapeseed extract, and when you add a lot of essential oils to something, that’s not wise because essential oils can be very toxic, so we’re talking about straight DLA, just dried leaf Artemisia.

I was asked about extracts—would they perform better? And again, I’m going like, well, I’m not sure that could be toxic. Extracts and dried leaf material are two very different things. We have not seen any evidence. I’ve personally taken dried leaf Artemisia at 1 or 2 grams a day for months and had absolutely no bad effects, but it did get rid of the problem I had, which was Lyme disease.

**Regional Approaches to Integrative Oncology and Related Research (Part 1)**

**Integration of Traditional Chinese Medicine (TCM) with Western Medicine for Cancer Treatment and Prevention and Related Research**

**Moderators:**

**Dr. Libin Jia**

**Program Director, OCCAM-DCTD, NCI/NIH**

Chinese medicine (CM) has been used in China for cancer treatment and symptom management and conjunction with Western medicine, known as integrative Western and CM. CM is also known to alleviate cancer symptoms and enhance the patient’s quality of life. In this panel, three distinguished scholars and physicians from China were invited to talk. The panelist discussed the current status of cancer treatment, prevention, and research with CM, along with Western Medicine. They also discussed the challenges and new questions pertaining to integration in cancer care during the pandemic.

**Dr. Lixing Lao**

**Professor of Integrative Medicine and President of the Virginia University of Integrative Medicine, Fairfax, Virginia, USA**

Dr. Lao introduced Dr. Feng as a famous oncology expert of Chinese medicine and integrative medicine.

**Speakers:**

**Dr. Li Feng**

**Senior Researcher at the Chinese Medicine Department, Chinese National Cancer Center, Beijing, China**

De Feng discussed the National Cancer Center of China, a comprehensive cancer center that integrates clinical practice with the basic research and fieldwork: The hospital emphasizes cancer prevention, diagnosis, and treatment. Their hospital has a lot of international collaboration with many hospitals all over the world and is in charge of releasing national incidence and mortality rates.

The data show that the Eastern areas have higher incidences than the Western areas. The top four cancers are lung cancer, stomach, colorectal, and liver cancer, which accounts for more than half of the cancer incidence in the country. In recent years, the relative survival rate has increased.

The research team receives inquiries from resident doctors and patients on learning when Chinese medicine can become a part of the treatment. However, Chinese medicine can participate in the whole treatment of cancer patients. Chinese medicine can prevent the disease prior to onset and can also be used as the treatment for the disease. Chinese medicine and acupuncture can be combined with Western medicine such as surgery, radiotherapy, chemotherapy, or immunotherapy because it can reduce the recovery time after surgery.

In fact, Chinese medicine can effectively improve the gastric intestine function. Also, together with chemotherapy or radiotherapy, Chinese medicine can reduce toxicity and increase their efficiency.

In a meta-analysis, the results showed that integrative Chinese medicine, together with Western medicine, can relieve cancer pain33. The researchers knew that a lot of people love exercising in Western countries. They wondered, what a kind of exercise and how much exercise can bring benefits for the cancer patients. Therefore, they finished this meta-analysis and the results show that the short-term exercise can slightly improve the quality of life of cancer patients.

A sub-analysis found that mind-body exercise can benefit and can provide better benefit to the patients than aerobic exercise. Yoga is an example of a mind-body exercise. Chinese medicine can provide improvement on the quality of life. A retrospective study on advanced ovarian cancer with a sample of 236 patients results showed at 3-years follow-up, patients who received Chinese medicine had a prolonged survival time34.

The cox analysis showed that the syndrome differentiation decoction is an independent protective factor for advanced ovarian cancer. The risk of death could be reduced by 17% every 3 months of treatment with Chinese medicine.

To find out the mechanism of Chinese medicine, the team also established the cancer-induced pain and the bone metastasis model on rats and mice. The results show that Chinese medicine can reduce cancer-induced pain, and also protect the bone.

Dr. Feng and colleagues wanted to learn the mechanism of gutong paste for relieving cancer pain. One prescription can have hundreds of ingredients. They used pharmacology to try to find the target compound that treats cancer pain. They found that there are more than 200 targets in this one prescription and more targets related with cancer pain. Further, they found the top four most important acting compounds that can stably combine with cancer-related targets. It is harder to find the active one.

Another project discussed was is a collaboration with Yale University (YIV 906). Phase III clinical trial that started in September 2020. The results are not available yet.

Also mentioned was a successful drug discovery conducted by their colleague, Dr. Yan Sun, who is studying the Chinese herb target medicine, Icaritin. This drug is extracted from herb epimedii35.

A few problems were reported; some Western doctors gave a Chinese over-the-counter medicine prescription without following accurate syndrome-differentiation and an invalid effect can be predicted, which affects the positive evaluation of Chinese medicine. Some Chinese medicine practitioners take radiotherapy and chemotherapy as the main treatment, with low chance of utilization of Chinese medicine and acupuncture.

The goals of Chinese medicine are to improve a cancer patient’s quality of life and gather overall survival benefits. Difficulties and challenges do exist such as, Chinese medicine’s multiple functions, multi-targets, and multi-pathways.

It is quite difficult to find active target compounds, but at the same time, a cancer tumor is also regulated by a lot of pathways. Chinese medicine is the syndrome-differentiation; therefore, it is hard to copy and to evaluate. Dr. Feng and colleagues also believe this is a kind of individual treatment, but it meets the needs of the patient standard comprehensive management.

It is better to find a more appropriate evaluation system and to establish a large database. I use the modern research masters to standardize and internationalize this. Chinese medicine can be combined with the modern research, experimental measures, and many great original findings can be expected.

Dr. Feng and colleagues highlighted another successful drug discovery that was originated from the ancient Chinese medicine books. Further, Professor Tu Youyou won a Nobel Prize in 2015 for obtaining an effective Artemisia annua extract.

1. Li Feng et al., Chin J Integr Med. 2020
2. Qinglin Zhang. Beijing University of Chinese medicine. 2020
3. Feng S, et al., Carcinogenesis, 2015

**Dr. Yang Yufei**

**Researcher, Department of Cancer, Xiyuan Hospital, China Academy of Chinese Medical Sciences, Beijing, China**

Dr. Yang discussed inequality for colorectal rectum cancer in China, evidence-based research and the clinic practice. Introduced to you from the full aspect.

First, evidence-based evaluation of TCM of treating colorectal cancer. Second integration of Chinese and Western medicine, and whole phases of colorectal cancer treatment. Third, utilization of a survivorship care model in colorectal cancer. Last, integration practice during COVID-19 pandemic in China.

In China, colorectal cancer has been a major cancer in the Chinese population for over a decade. We started to focus on colorectal cancer research and the clinical practice 25 years ago. Her department was named the top colorectal cancer center in China.

In China, TCM oncologists like me can use both conventional cancer treatments, such as chemo or radiotherapy, and TCM such as acupuncture and herbal medicine to help cancer patients.

After 20 years of effort, do we have enough evidence to show TCM effectiveness in treating colorectal cancer now? TCM’s role in increasing recoveries in stage 2 or 3 colorectal cancer? The result shows that more than one year of herbal medicine treatment was associated with longer overall survival and disease-free survival. This paper was published in the Journal of the National Cancer Institute in 2017.

We conducted an RCT study to evaluate effort of Quxie capsule. The Quxie capsule was developed by my team and it contains 20 different herbs. The results show that — compared with standard treatment —the Quxie capsule could have significantly prolonged overall survival, and the progress-free survival for colorectal patients. The two studies show that TCM treatment may prolong the outcome of colorectal patients, but we still need to highlight our evidence to stress this effect.

In 2017, we received funding to study evidence-based evaluation of TCM regimens for secondary prevention, synergy in chemotherapy, and reducing the recurrence or metastasis of gastrointestinal malignancies. This research contains six RCT clinical trials to evaluate TCM’s role in three different disease phases, including precancerous lesions, adjuvant chemotherapy, and cancer recurrence and metastasis for gastric and colorectal cancer.

The sample size is over 2,000 and includes more than 100 cancer research centers. During COVID-19, we have finished 50% of enrollment, and hopefully we will get our final result in 2022.

Another national program of which I am in charge is in collaboration with Beijing Cancer Hospital. We are working to establish integrative TCM and Western medicine oncology guidelines for the whole period of colorectal cancer treatment through systematic review and clinical studies. These integrative guidelines of TCM and Western medicine could be affected by both TCM and the Western medicine experts, and applied to clinic practice in China.

Meanwhile, we will also promote international communication on this proposal and hope to provide new ideas and a possibility for the global oncology integrative field.

In China, we are trying to establish a new multidisciplinary cancer survivorship care model in colorectal cancer. This model integrates TCM and Western medicine, the oncologist, nutrition, psychotherapy, diet, music therapy, education, surgery, acupuncture, etc.

The model, used since 1971 for cancer patients at our hospital, is welcome by the patients and their families.

As an example: Mr. Wang, 80 years old, 6 months post-radical surgery, chemotherapy, and adjuvant chemotherapy. Resident of Shanxi Province, middle school teacher, retired. Children in Beijing. Cardiac function level 2, despaired renal function, seeking cancer survivorship care (nutrition, medication, and lifestyle guidance).

In the past, he had to take a train for 2 days to Beijing for survey surveillance every 3 months. He was very tired, and the cost was large. After visiting the collaboration clinic, he can see an oncologist, nutritionist, pharmacist, cardiologist, and rehabilitation doctor. He can fix all these problem at one time. Such a model is less stress, less tiring. It can give the patient more comprehensive care.

A part of the integrative practice covers COVID-19 patients. TCM has played a very important role. More than 19% are treated with TCM, reducing the need for antibiotics and reducing complications.

We never stopped helping cancer patients and providing TCM services. At this same time, we are also doing research on the impact of COVID-19 on cancer patients in China. By analyzing the enrolment and progress of the multi-clinic care, we found that nearly half of the patients had a delay in chemotherapy.

The main reasons for delay or modification of chemotherapy regimens were due to hospitalization policies and transportation blocks. This article was published in Current Oncology.

The challenges of the integrative oncology field in China:

1. More communication and further education between the PCM and Western medicine oncologist that is necessary,
2. The need to establish integrative TCM and Western medicine guidelines that work for Chinese people, and
3. The need to establish a multidisciplinary cancer survivorship care team to treat cancer patients as a whole person not as a disease. We’re going to hold the first annual meeting in integrative oncology November 28–29 in Beijing, China.

**Dr. Wei Hou,**

**Director of Oncology, Department of Guang’anmen Hospital, China Academy of Chinese Medical Sciences, Beijing, China**

Dr. Hou discussed the history of the oncology department. It was created in 1963 and is one of most respected cancer centers focusing on research, education, and prevention. With basic science research starting in 1993, by 2003, we have become a National Administration of Traditional Chinese Medicine-designated National Key Disciplines and Laboratory of Tumor Cell Biology II.

In 2008, we started to collaborate with NCI, and in 2015 the International Consortium for Chinese Medicine and Cancer started. There are now 130 members from six countries. Recent years have seen the formation of a Cancer Project Group and the construction of a TCM regional medical center.

From 1963 to present, research has advanced from chemoradiotherapy enhancing efficacy and reducing toxicity to the formation and popularization of treatment guidelines. The department is also the creator of the Chinese Association of Integrative Medicine Specialty Committee of Oncology, and plays a major role in TCM oncology in China.

Since then, more than 2 million people have turned to the hospital for cancer care in the form of Chinese medicine, chemotherapy, radiotherapy, immunotherapy, or a combination. This multidisciplinary approach to the treatment of cancer was also pioneered in China. We have four major centers:

* Ward Medical Treatment Center
* Endoscopy and Diagnostic Center
* Experimental Research Center
* Radiotherapy Center

Our department has carried out a number of TCM treatment techniques in clinical practice, achieving good effects. For example, topical TCM cream for cancer pain, TCM soak/electromagnetic therapy, acupuncture to relieve nausea and pain. Especially in the latest stage of cancer, Chinese medicine can help to relieve symptoms, which leads to a better quality of life.

Our research focuses on lung cancer as it is the leading cause of cancer deaths in the world. TCM can prolong the survival time, reduce metastasis and recurrence, reduce adverse reactions, and decrease the cost of treatment.

The basic idea of the TCM treatment for lung cancer can be divided by different stages

* Post-operation
* During chemotherapy
* Late-stage cancer patient

At each stage, different strategies are used to treat the patient. Currently data show that – after the post-operative stage – we can see 2-year recurrence and metastasis is decreased by 6%.

I do ask you a question: Does the TCM prolong the survival time of late-stage patients?

A national project which compared TCM combined chemotherapy to a single chemotherapy group found that a combination treatment of TCM prolonged the median survival time for 3.47–3.57 months.

Chemotherapy has adverse reactions (e.g., fatigue, gastrointestinal reaction). TCM, however, when combined with chemotherapy, reduced loss of appetite, nausea, and vomiting. They were concerned whether the patients had a good quality of life. TCM can significantly improve the quality of life of a patient in the postoperative or advanced stage. TCM maintenance treatment was found to decrease relapse and metastasis, chemotherapy adverse effects, prolong survival time, and improve quality of life.

The research team closed by discussing what is and what is not working. Things that are working:

* Use of modern science and technology to reveal the mechanism of TCM
* Evidence-based medicine has verified the efficacy of TCM in some diseases
* Acupuncture and moxibustion in the world is increasing yearly

Things that are not working:

* Modern research methods cannot explain the whole picture of TCM
* There is an incompatibility between evidence-based medicine and TCM
* Restrictions of policies and regulations on the internationalization of TCM

**Question & Answer Session**

**Question:** Do you have anycomments on most medical oncologists’ concerns about concurrent administration of Chinese medicine custom formula herbal treatment with allopathic medical oncology treatments? This is due to concerns of toxicity and reduced efficacy of oncology treatments when given concurrently with Chinese medicine herbal treatments.

**Answer One:** Herbal medicine is divided into two parts: (1) promoting strong body chi, and (2) anti-tumor. We treat the patient with chemotherapy; we only use safe herbs.Some patients get both. We often tell patients that it is okay to use the herbs.

**Answer Two:** In over 30 years, Dr. Feng hasn’t seen a case of a patient who took Chinese medicine together with chemotherapy who reported negative side effects. Patients who use TCM report that their symptoms are improved and they can benefit from Chinese medicine. Also the product of our department, the studies were completed by Yale, prove that the Chinese prescription herbs, they effectively prolonged the OS or PFS of the patients and also reduce the side effects of chemotherapy, such as diarrhea. We need more clinical trials to prove this, but it’s harder to find the standard, the evaluation system, and also it’s harder to establish a large database and to collect this valuable practice.

**Question:** To Li, what exactly does the body-mind exercise do in improving the quality of life of patients? Is it mental alertness, physical activity, or both?

**Answer:** Meta-analysis found that the body-mind exercise can improve depression, fatigue, and the symptoms of lymphoma in patients.

**Day 3: October 29, 2020**

**Location:**Zoom Webinar

**Time:**8:30 p.m. – 12:30 p.m., EST

**Date:**October 29, 2020

**Attendance Report:** 170

**Continuation of Regional Approaches to Integrative Oncology and Related Research (Part 2: India, Brazil, Argentina, and Latin America)**

**Integration of Ayurveda with Western Medicine for Cancer Treatment and Prevention and Related Research**

**Moderators:**

**Prof. Vd. K.S. Dhiman**

**Director, Central Council for Research in Ayurvedic Sciences, New Delhi, India**

Prof. Dhiman introduced the session panelist who are experienced with integrative oncology and modern medicine. Currently, there is a multicenter trial on breast cancer and lung cancer, as well as cervical cancer being conducted in India. Ayurveda is integrated in the main care system and quality of life, as well as life expectancy, have shown positive results within this trial.

This session provides opportunities s for NCI and NIH to learn of future research perspectives and for colleagues to see the potential of that traditional medicine and Ayurveda science. Having a holistic approach can play a role in integrative oncology. The approach is probably different. It has to be from bed to bench, and one has to think of the whole-system approach for this traditional system.

**Dr. Ram Manohar**

**Research Director (Ayurveda), Amrita Vishwa Vidyapeetham University, Kollam Campus, Kerala, India**

This session focused on integrative oncology in India and alternative systems of medicine, known by the acronym AYUSH, which stands for Ayurveda, Yoga and Naturopathy, Unani, Siddha, and Homeopathy. India has a pluralistic health care system. India is perhaps one of the few countries in the world where people have free access to different medical systems to deal with health problems.

Different practitioners are able to treat patients independently, and this is also true in the case of cancer. However, we have to say that our systems have not been formally integrated in the management of cancer and integrative oncology, which is still in the very early stages of development. On the other hand, they are seeing that cancer patients are seeking care from AYUSH practitioners, and there are some cancer hospitals where Ayurveda is integrated in cancer care in a limited way.

There are also Ayurveda practitioners specializing in cancer care as well as trained oncologists using AYUSH interventions in cancer care. This is true with other complementary alternative systems also coming under the purview of AYUSH. Additionally, some other trained oncologists are also incorporating AYUSH interventions in cancer care.

The most prevalent uses of traditional medicine are for individuals who have incurable or refractory conditions; non-life-threatening conditions that may be chronic neurological disorders, etc. The second largest group of users are those who are struggling with chronic, potentially life-threatening diseases, such as cancer and HIV/AIDS.

In India, although there is a lot of health-seeking behavior from the general public accessing AYUSH systems, it’s still not formally integrated. We do not really have a well-organized integrative oncology framework in the context of India.

Now, all these groups that we discussed earlier turn to AYUSH systems for a variety of reasons, such as an alternative or to complement conventional medical care. These behaviors are actually influenced by faith or a belief in the advantages of CAM family, traditional culture, emotional support, or expectation of a better quality of life. Also, to boost the immune system, prevent recurrence, or obtain a synergistic effect with conventional therapy. Sometimes there is dissatisfaction with conventional therapy.

Through collaborations with conventional medicine, AYUSH and other Ayurveda systems we could potentially make contributions for the development of integrative oncology. This needs to be actually facilitated and we — at this point in time — are still in the beginning. The ideal symbiosis would be one in which Ayurveda and AYUSH systems do not lose their own core fundamentals, but still integrate with modern medicine at a pragmatic level.

That will probably give the best outcomes. And, in this context, this new initiative by the policy thinktank of India (NITI Aayog) — which has just recently issued a One Nation, One Health System policy — is planned to be rolled out by 2030.

For the first time, the special focus is on integrating modern and traditional systems of healing — such as Ayurveda — because in India there is an independent model. There are different systems where they are independent of each other.

This initiative from NITI Aayog is bringing — for the first time — an effort to put these systems on one common platform. As part of this working group, especially to develop the integrative health policy, Dr. Manohar sees this as an opportune moment that has emerged in India for the development of integrative approaches in oncology.

**Speakers:**

**Dr. Ram Manohar**

**Research Director (Ayurveda), Amrita Vishwa Vidyapeetham University, Kollam Campus, Kerala, India**

Dr. Manohar’s presentationfocused on Ayurveda for cancer care in India. India reports the world’s highest incidences of cancer — the world’s highest incidences of:

* Lower pharyngeal and tongue cancers in men
* Gall bladder cancer in women
* Mouth cancer, mouth and tongue cancers in men
* Nasopharyngeal cancer

India has its own unique problems in dealing with cancer. For example, late diagnosis and higher mortality, so 75% to 80% of patients have advanced disease at the time of diagnosis. Some of the reasons are late presentation due to:

* Low levels of awareness in the population and among community physicians
* Lack of attrition screening programs and diagnostic facilities
* Vast distances that people have to travel to reach a major tertiary cancer center
* Financial constraints and stigma associated with the diagnosis

Dr. Manohar shared that these are all the different challenges that India is facing when dealing with cancer. It is alarming to notice that the number of cancer-related deaths in India has more than doubled between the years 1990 and 2016.

Dr. Manohar summarized the cancer care challenges in India as being:

* Early detection and prevention of cancer
* Compliance with conventional treatment protocols for cancer care
* Prevalence of the use of traditional complements and alternative medicine interventions (AYUSH)
* Underreporting of the use of TCAM interventions
* Lack of systematic efforts to integrate effective TCAM therapies with mainstream oncology

Things are in a preliminary stage of development when it comes to integrative oncology in India. Cancer patients do receive care from TCAM practitioners (AYUSH) regarding the fear of conventional treatments, the idea of side effects, how to minimize it for added benefits to improve the quality of life, or sometimes even with the hope of a magical cure, patients continue to seek care from TCAM practitioners.

The indigenous health care system of India is also used by cancer patients at different stages and different types, so it is quite widespread. These interventions are administered either as standalone or adjuvant medications concomitant to Western medicine treatment. There are various kinds of prevalent practices, but they all have not been equally documented or studied.

Dr. Manohar shared three studies and reported that studies reporting prevalence of TCAM in India is scarce. The number of good studies reporting actual numbers are quite limited and — with India being quite diverse in different cultural backgrounds — a widespread survey to get a real picture of the ground realities is needed.

The first study discussed, found that the prevalence of use is 23.5%37. Another study showed 34.3%38. In yet another study, it was 38.7%39. In a recent study that Dr. Manohar and colleagues did out at their institute, TCAM use was found to be used by 34.4%. About 30% of people are actively using traditional, complementary, and alternative medicine for the management of cancer.

Further, one study reported that the most common TCAM that have been used was found to be Ayurvedic treatment, but the trends are different throughout India. In South India, there is another system called Siddha medicine — which is widely used in one region — so there is a need to do more systematic surveys and studies to really understand what is going on at the ground level.

There are some interesting findings amongst those who were aware of traditional, complementary, and alternative medicine, only 40% were actually using them39. Sixty percent of people knew that traditional systems are available and are an option, and they did not opt for these medicines.

In Dr. Manohar’s recent study at the Amrita Institute of Medical Sciences, they found that home remedies were used most. There are a couple of plants in Kerala that are very commonly used by people, and they do not fall under the organized systems of medicine like Ayurveda. In a different study, the results demonstrated that there was a significant relationship between the use of traditional, complementary, and alternative medicine and reported delays in seeking help from clinical medicine40.

This is a matter of concern, but the study was small. There is a need to look at the possibility of accessing traditional medicine becoming a hindrance in a timely diagnosis. So, some studies do indicate that possibility. Now, underreporting of practices is a real challenge. The outcomes of such usage are underreported or not published, and the lack of information regarding drug-herb interactions or rigorous reporting of treatment outcomes is what really keeps integrative oncology from developing in a full-fledged way.

There is concern about safety and efficacy, especially due to drug-herb interactions. One study reported that 68.75% of the users were simultaneously receiving conventional anti-cancer therapy37. This concomitant use of traditional medicine and modern oncological treatments and non-reporting of such practices could lead to undesirable outcomes. The benefits of TCAM may go unnoticed.

Both are important. It is not that they always create problems or side effects. There are also reports of benefits, but those, too, go unnoticed because of this situation. Because 53% of the patients who have received some form of traditional, complementary, and alternative medicine have claimed to have experienced symptomatic benefits37. In another study, Ayurveda was found to be very useful for the patients39. More studies are needed, as these are all scattered and don’t really represent the entire population.

Sanjoy Kumar Pal, is a gastroenterologist from Sanjay Gandhi Postgraduate Institute of Medical Sciences, he points out that unless there is a dramatic improvement in cancer mortality using conventional treatments, complementary and alternative medicine will continue to attract many cancer patients.

Considering the fact that 50% of the world’s cancer burden is carried by developing countries, which have access to 5% of the resources available to fight the disease41, Dr. Manohar believes that complementary and alternative medicine will continue to be an important component of modern oncology, and therefore we really need to integrate, even in the context of countries like India.

The need for cooperation between Ayurveda and conventional medicine is recognized, and there are cross-talks between the systems, and some programs have also been initiated in India. The CCRAS, Ministry of AYUSH, and government of India has initiated major programs such as:

* Documentation validation
* Analysis of unpublished data of Ayurvedic interventions
* Analysis of unpublished data of practitioners

However, they still need to make up a lot of ground before they can bring integrative oncology in and transform it into a very systematic discipline.

Currently, there are Ayurvedic physicians caring for cancer patients. And — in rare instances — we also see modern oncologists treating cancer patients with Ayurvedic medicines or supporting the use of such interventions for cancer management; both in individual practice and institutional settings.

Dr. Manohar provided a quick overview of Ayurveda Cancer Centers in India. He discussed a unique center in Pune, which is an Ayurveda Integrative Center. This is unique in the sense that it is an Ayurvedic institution that is integrating modern oncology into the care for cancer. Usually, it’s the other way around—modern oncology hospitals have a department for Ayurveda.

In this integrated cancer treatment and research center in Pune, there are modern oncologists working. They come there and they also implement radiation, as well as chemotherapy. This is a unique experiment that is happening in integrating modern oncology with our Ayurveda. The Tata Memorial Center, is the more common type of system, where the hospital explores integration of Ayurveda, yoga, and such other systems.

He discussed another hospital in Kerala — called the Amala Hospital and Research Center — which has also been exploring the integration of Ayurveda into cancer care for many decades. The CCRAS has itself a very dedicated center focusing exclusively on cancer research and Ayurveda, which is situated in Mumbai. There are all kinds of efforts are happening to bring Ayurveda and modern medicine together, and to promote the use of traditional medicine in the management of cancer.

Dr. Manohar discussed a case study of a medical oncologist in Kerala, Dr. CP Mathew. He is the first medical oncologist of Kerala, and has been integrating Ayurveda in Siddha interventions into his clinical practice. He is retired as the head of medical oncology and when he encountered some of his patients who were in terminal stages, he found that they had remarkable improvement with traditional medicine.

Ever since, he has started integrating Ayurveda into his clinical practice. He has experience of about 30 years, and Dr. Manohar reported that the CCRAS has recently taken on an initiative to do a detailed documentation of the clinical experience of this physician. This is a unique instance where — since a modern oncologist is involved in integration — he is able to work more freely, and has explored a lot of the possibilities of how traditional Ayurveda could be integrated with mainstream oncological care.

There are many other individual practitioners, making it difficult to track and discuss each of them, but this is activity that is happening in earnest in India. If you look at the scope of integration, that is where we are standing now. From anecdotal experiences and what has actually been happening at the point of care, Ayurveda can be administered as an add-on to conventional treatment, keeping two objectives in mind:

* Enhancing the activity of conventional treatment, namely chemotherapy and radiation therapy, where synergism has been established by research studies like enhancing radio-sensitivity, enhancing the activity of chemotherapy, even through diet, because recently some studies have shown that fasting before chemotherapy optimizes the activity of chemotherapeutic agents
* Enhancing the quality of life, reducing morbidity of the treatment, radiation-induced mucositis, and xerostomia. A lot of research work has already been initiated in these areas. Further, Ayurveda can help reduce chemotherapy-induced nausea, vomiting, neutropenia, fatigue, peripheral neuropathy, and such other complications, so hepatotoxicity, sleep disturbances, cachexia, and lymphedema. Ayurveda as an add-on or stand-alone therapy in palliative care, such as pain, constipation, wounds, and for improving nutrition in advanced stages of diseases.

Dr. Manohar has personally witnessed and experienced very good results in the end-of-life, terminal stage of cancer, and Ayurveda as a stand-alone therapy for:

* Relapsed and stable cancer where no active conventional treatment is suggested
* Inoperable presentations of malignancy
* Unsuitable cases for chemotherapy or radiotherapy

Dr. Manohar discussed recommendations to moving the research forward. Some ideas shared were generating evidence of the benefits of Ayurvedic interventions through:

* Rigorous clinical documentation
* Well-conducted studies
* Targeting independent practitioners
* Targeting researchers
* Targeting institutions

Additionally, a network needs to be created, and a society for integrative oncology in the Indian context. Bringing together these diverse practitioners is very important, and this looks to be the opportune moment. Publishing systematic reviews, ensuring clinical documentation systems as point of care — especially where Ayurveda is administered as a stand-alone treatment — is important.

This kind of basic documentation should inspire, and develop into well-conducted clinical trials that especially look at a whole-system approach and Ayurveda. Further, herb-drug interaction studies, chemo-sensitivity studies, both laboratory research and real-time clinical should be conducted. Dr. Manohar is actively involved in this area and it is an important area of focus, because they are trying to bring Ayurveda into our own allopathic hospital.

Another recommendation discussed was the need to establish a database of medicinal plants and natural compounds, especially the formulations that are used in systems in India. Creating a transdisciplinary team of experts from different health care systems. Additional considerations are medical, legal, and ethical issues. It’s very difficult sometimes for Ayurveda physicians to plan clinical trials.

Ethical committee clearances are very difficult, which is a big hindrance in conducting clinical trials, and making available insurance coverage for integrative oncology care. These are going to be very important steps, followed by networking with global research and the clinical community.

In closing, India should perform self-organization within the country because — at this point of time — things are quite scattered. There is momentum, but a need to get it organized, and then connect with the global community. Currently, with India’s health initiative — One Nation, One Health — this may be the opportune time to nurture integrative oncology in India.

He quoted S.K. Pal: “With the high propensity for late stage diagnosis, many treatments offer little more than palliative care, and it is possible that CAM approaches will play an important role in those situations when cure is no longer a realistic objective.”

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**Dr. Narendra Bhatt**

**Consultant, Ayurveda Medicine and Integrative Oncology, Mumbai, India**

Dr. Bhatt shared that there are two major dimensions that he has observed to be important. He believes while trying to integrate, we are not able to recognize the symptomatology and the clinical richness of the traditional systems of medicine that are there, as well as the possibilities, the potentials of product interdevelopment. His area has been in product development and drug discovery as a part of industry research and he has always been a practitioner. His presentation was from the perspective of a practitioner.

In India, the Ayurvedic system is not officially recognized as medicine. Some cancer patients seek Ayurvedic treatment because they have no other treatment options. For some patients, Ayurvedic treatment is complimentary to ongoing cancer treatment. Others seek treatment pre-cancerous or while having an uncertain diagnosis.

Dr. Bhatt discussed the causative factors of cancer, to include:

* Addictions
* Genetic predistortion
* Aging
* Trauma
* Surgeries
* Obesity
* Excessive use of conventional medicinal drugs
* Invasive root canal
* Occupational chemical exposure
* Diet
* Frequent radiology exposure

Dr. Bhatt shared several clinical examples from his practice. In the first example, the patient had palate cancer, which was a very simple case. Dr. Bhatt started seeing him post cancer treatment and the patient experienced several clinical benefits (e.g., weight increase) and is leading a normal life for the last nine years.

In a second case, the patient had terminal bone sarcoma in an acute phase, however, with Ayurveda medicine complimentary to cancer treatment Dr. Bhatt was able to increase the survival time to more than 1.4 years. In the cases presented, the prognosis was not more than 4 to 6 months.

Another interesting case was a chronic lymphocytic leukemia where the patient already had opted not to undergo an Ayurvedic treatment, but she continued with other treatment and she came to Dr. Bhatt at a much later period. However, she remained with him for 2.1 years after a prognosis of only 4 months.

In a pre-cancer example, a lady had a possible diagnosis of ovarian cancer and she was now with Dr. Bhatt for more than 5 years. Similarly, a patient with colon cancer is now surviving for more than 2 years, whereas the prognosis was very poor.

The case example shared was of a patient who had buccal mucosa. He has already lived for more than 10 years and he had a speech problem, but with Ayurvedic treatment, they have been able to bring it back to normalcy.

When Dr. Bhatt has a new patient, he places them into one of two categories, a part of the Ayurvedic investigative process. He tries to determine the cause (i.e., exogenous, endogenous) of the cancer prior to starting a treatment approach. He will ask if there are any exogenous causes such as alcohol, something ectopic, or something that chemical X was, or not?

Then he looks at the endogenous causes. This is a very simple way of Ayurvedic investigation, as well as categorization. Once it goes into the endogenous category, he will determine if the case is age related, if the individual has a genetic predisposition, and determine disease process variance.

The disease processes have four categories that a patient can fall into

* Inflammatory
* Angiogenetic
* Obstructive
* Proliferate

Following this simple system of establishing the cause is an important step in order to decide the best treatment approach.

The Ayurveda system is based on “functional balance,” which is actually health, and health itself is defined in the form of clinical symptomatology, which is known as the constitution types. The two constitution types in Ayurveda assume that there is metabolic predominance and they are divided into eight types.

There are seven types of constitutional variances and eight types of metabolic predominance. The Ayurvedic knowledge includes more than 7,500 signs and symptoms — a large knowledge base. This knowledge provides a great idea of approaches that lead to diagnosis. There are three main parameters:

* Observation
* Inspection/tough
* Interrogation/inference

These are the methods and they are highly symptomatology-based.

The diagnostic methods include five categories:

* Causative factors
* Prodromal symptoms
* Signs and symptoms
* Prognostic
* Diseases processes.

In prognosis, Ayurveda defines all diseases by four categories:

* Easy to cure
* Difficult to cure (surgical intervention is needed)
* Those that are incurable
* One which led to death

The process allows one to be able to identify the types at what stage and what kind of therapeutic intervention is required for that particular stage of a disease.

Now there are eight kinds of diseases which are identified as similar to cancer, or that can lead to cancer. Most of them are falling into the easy to cure disease, but they have a subtype when it becomes incurable.

Each of these diseases may be five types, or seven types, or eight types, or even 11 types, but there is always a subset when it becomes incurable. Now, this is where the disease development from curable to incurable becomes of significance. There may be a round mass. It may be an abscess. It may be a cold abscess. It may be an ulcer.

The common feature is necrosis. Necrosis of tissues is a very common feature in all those eight diseases. In other words, when the inflammation takes a severe form and when it gets into the proliferative status, that becomes the most meaningful, targeted point from a research point of view, and the metastasis actually takes place. This is what we can look at from the research point of view. Whereas in modern science, we are looking at the cellular and biological phenomena to evolve a cancer therapy or cancer treatments.

Similarly, in Ayurvedic, there is the concept of what known as dysfunction. Dr. Bhatt shared a pentagon shaped chart, which is indicative of the five-element theory of Ayurveda. The diagram also includes a depiction of modern systems, of biological systems, or system biology. A translational approach is possible by integrating these two systems.

Dr. Bhatt described the challenges of a translational approach. A translational approach is looking at how a disease is from how it spreads and what are the causes. The Ayurvedic points, one point of view, the homeopathic system’s, the role of liver and spleen, the role of bone marrow and several others component becomes vital.

Now, how does this process develop into tumors, knotty hard masses, glandular enlargements, or deep longitudinal masses and proliferating abscesses? That becomes an issue of interest. By bringing modern senses of system biology and cell biology, genetics, and biological pathways together — and based on the products that we are using, pharmacological and toxic approaches — we are able to establish a translational approach. A good translational approach will give us a therapeutic intervention where the therapy and the therapeutics are already co-linked with the possible activity.

Clinical Ayurveda is targeted toward a clinical manifest. We can create a confirmation of the hypothesis, and then we can evolve towards newer and newer interpretations. Dr. Bhatt proposed that we use the words “transformational” and “plasmolytic.” Whereas plasmolytic, the plasmatic part is a very important part, concept of Ayurveda.

In Ayurveda, we do not believe in blood circulation, but we believe in what we call the plasmolytic circulation, which is nourishing each and every cell and molecule of the body. In other words, we can target the cancer process in a very, very specific manner based on comparing the two systems, begin together at the therapeutic interventions, targeting the things and thereby getting into a new immunotherapy.

There are more than a thousand ingredients and plants described in Ayurveda, and more than 80,000 formulations. The formulations could be in the form of dosage forms. They could be the form of liposomal production. Perhaps in the form of the hepatoprotective product. It could be in the form of an alkaline approach. Each one has got its own therapeutic approach.

If you bring the clinical business and the therapeutic relevance, we can create unique, effective, and standardized products that could be complementary to chemotherapy. They could be complementary to radiation. They could be a precancerous treatment addressing precancerous situations.

Specifically, Dr. Bhatt emphasized that protection with all the chemotherapies that we can evolve specific chemotherapeutic hepatoprotective drugs out of this. The whole plethora of Ayurvedic products and ingredients can be utilized for product development and drug discovery.

Dr. Bhatt is involved with two major projects. One is on the hepatocellular carcinoma. They are trying to evaluate an Ayurvedic product, but he would like to expand it more to a specific combination of drugs, which could be taken for further research. One is the marine product, which we know the colors are used in inflammation, and a coral-based product could be developed into biological biomolecules. Those molecules could reduce intermediary processes or the inflammatory processes in the cancer situations.

Dr. Bhatt summarized that Ayurveda’s potential to provide a clinical contribution to prevention and early diagnosis in clinical oncology, we can undertake therapeutic research in terms of product development and drug discovery.

And what are the benefits? We can have benefits in terms of multi-target and multiple possibilities. We will have reduced costs. It will be about one-tenth or one-fifth of the cost of what we use, and it will help also reduce time because of parallel developments. In summary, he proposed that Ayurveda has huge potential and there is the need for an integrated approach. People must come together for translation research.

**Question & Answer Session**

**Question:** Are there funding mechanisms in India to support Ayurveda interventions in oncology care?

**Answer:** There is a funding opportunity. Both the collaborators have to contribute in some other way, in a financial way, or in another way. This is one of the opportunities. The other opportunity is in the form of extramural research, but that has a limited scope of up to 70 lakhs of rupees. But if some such international proposal is there, the ministry can think, or that can be put to the ministry for their consideration, if it can be. So that way, this biotechnology mission of India has also the funding program for these studies. This is up to my knowledge. This is there.

**Question:** How can we develop a new platform where all Ayurvedic physicians can come together to learn and practice integrative oncology, especially what are the prospects for Ayurvedic students to think of working in this direction?

**Answer:** I think this has been a long-standing demand of the young, upcoming Ayurvedic scholars, and also the new scientists. I think we need to create one initiative and I think today’s platform is the right platform to take that step. And Dr. Dhiman, we can also chip in together; I hope you recollect that we had conducted one consultation to meet, which was there. This desire is a long-standing desire. I also want to give one more comment, that we must create a methodology within this country, where the oncologists and the Ayurvedic physicians are, we need some mechanism to bring them together. Not only from the institution, which is central government-based, but also local-based. If we can provide some sort of a mechanism so that they can come together, I think that will be a great, great help for the whole, all oncology and Ayurveda to come together. I think we can create one initiative by forming a group or a society, and which could be actually involved with government machinery also. That is what we should do.

**Answer:** Some of us are already working on setting up a society in India of oncologists working together. And so, we are hoping to formalize, making it into a formal mechanism. And I think as I was mentioning, the integrative oncology initiative for integrative health systems, as a policy, seems to create a more favorable environment to work in this direction.

**Question:** Are there NCI collaborative funds available to partner with our colleagues trained in Ayurvedic medicine?

**Answer:** I say that the system of NCI/NIH is always through competition and awards. But I think it’s important to mention, and Dr. Dhiman will talk more about that tomorrow, that we just signed an agreement with the Central Council for Research in Ayurvedic Sciences, and this is essentially to enhance collaborations and short trainings as changes and so on. So, I think that would be a pivotal road for enhancing more collaborations.

**Question:** Where does the addition of Ayurvedic medicine become most effective in the management of cancer patients? Side effect management, or quality of life, or synergism with modern oncology therapies? This is a progression. Where you think there is much promise?

**Answer:** If I were to choose a sequence, if there is no choice, then first is hepatoprotection. That is the chemotherapy toxicity, which we can target, number one. Number two will be related to the disease processes and specific kinds of cancers. There can be complementary treatment in a very successful manner; for at least three or four kinds of cancer, we can play an important role. When it comes to these specific kinds of diseases, like leukemias, then maybe we really have to look at some new, innovative drugs. As we know, there are one or two examples since that is also being involved in some of the drug research. And I think we should explore those possibilities of homeopathic compounds, which could be utilized for specific targeted biologicals, or we can do the biological studies on one end. I think these are the opportunities of which we have so many. I think this is the reach to move forward. This is how I look at it. I will not be really, you know, the quantity of life is a very complex thing to interpret. I think we should take these certain situations head-on and we should look at very specific solutions, therapeutic solutions, in some cases.

**Answer:** Mucositis and xerostomia in oral cancer post-radiation can be very well managed by an Ayurveda approach. And secondly, the dermal injury by radiation, we did this preclinical study on this one Ayurvedic traditional product for reducing the dermal toxicity of the radiation. These are the other areas where this system can give, is giving, very good results. In the end, the outcomes are mitigable.

**Brazilian and Latin American Approaches to Integrative Oncology and Related Research**

**Moderators:**

**Dr. Alejandro Salicrup**

**Senior Advisor for Global Health Research, Center for Global Health and OCCAM-DCTD, NCI/NIH**

Dr. Salicrup discussed examples of what is working in terms of practices in integrative oncology. He shared that we would like to see what is not working and why, according to the speakers, and what are some of the challenges and opportunities to enhance integrative oncology. Latin America, is a vast and huge, and very complex region. That spans from Mexico, the Caribbean, and then all the countries of South America, from Venezuela to Patagonia. So, it’s a very, a huge region, and it’s complex in many ways. There are several languages, including not only that they have Spanish and Portuguese and English in some of the countries, but also, French; there also are hundreds of indigenous languages that are there. Related to that, there are also many diverse ethnic groups and races, and some of the ethnic groups, you know, they do not have contact with what we call civilization. As in other places, it is a region with a lot of inequities and disparities. Latin America, the region has the most inequities in the world. The region is not the poorest or the richest, but it is where the gap between rich and poor is the largest. This reflects on disparities related to health. Then you have the Amazon. When you talk about the Amazon forest basin, not only that it’s huge, it’s the lungs of the world. There are about nine countries here.

Some people that are very far apart, yet they are not necessarily close to different health services. But at the same time, they have their own traditional medicine and system, and a system to attend to health. At the same time, the biodiversity, just the bit that we spoke about national products, the biodiversity in Latin America is among the largest in the world. It is essentially between two countries, Brazil and Columbia, I believe they are the two most biodiverse countries in the world. For many years, these countries have received immigrants from many parts of the world. This is important in the context of this meeting because traditional Chinese medicine or Korean practices or Indian Ayurveda is not new there. They have been experimenting, depending on the country, because they have many people that had come from those different countries. Traditional, complementary, and integrative health is widely used and is well-accepted by the population and the patients in cancer care, too. And, importantly, particularly in some countries, particularly in Brazil, most recently, there have been very important current policies and norms that are important to discuss.

**Dr. Daniel Miele-Amado**

**National Coordination of Integrative and Complementary Practices, Department of Primary Health Care, Secretary of Health Care, Ministry of Health of Brazil, Brasilia, Brazil**

Dr. Miele-Amado discussed the health system in Brazil. The public health system is strong because traditional, complementary, and integrative medicine is a part of a national policy known as the Integrative and Complementary Practices. It is integrated throughout the public health system. Brazil has many experiences in different levels of the system — primary health care, hospitals, mid-level care.

The goals of this policy are to incorporate/implement Traditional Complementary and Integrative Medicine (TCIM) in the national public health system to increase the population’s access to those practices. It is integrated in conventional or Western medicine, and most of the professionals who offer this kind of practice are health professionals, provisional health care professionals, with additional formation in integrative care.

Brazil is a large country. Not so populous as India or China, but one of the most populous. They have 70,000 establishments that offer these kinds of practices with conventional medicine. 90% of those establishments are in primary health care — most parts of the country offer at least one type of this practice, and they have more than 4,000 municipalities that offer it.

In 2006, when this implementation became a national policy, they’d already had some experience. Traditional Chinese medicine, homeopathy, herbal medicine, anthroposophic medicine, and thermalism were practices that were already offered by physicians and other health professionals. These practices were already provided it in some municipalities, but the national policy allowed the practices spread throughout the country.

In 2017, we included 14 more practices, like Ayurveda, biodanza, meditation, yoga, and other practices. In 2018, the policy included 10 more practices, like apitherapy, aroma therapy, and other ones.

The Ministry of Health, has strategic planning with four axes:

* Qualification of the public health management to provide this kind of practices
* Integrate it in the national health system
* Provide the guidelines and protocols for health care
* Research focusing on systemization and evidence synthesis of what we already have in the TCIM

**Speakers:**

**Dr. Ricardo Ghelman**

**Chair, Brazilian Academic Consortium for Integrative Health and Integrative Oncology, University of São Paulo Hospital, São Paulo, Brazil**

Before implementation of the national policy of complementary integrative practice in 2006, there were two studies done about the belief and resistance of the clinical oncologists about TCIM. It was discovered that only 10% of oncologists support the prescription of at least one type of CAM42.

In 2005, a study from Dr. Giglio from São Paulo, and another group from Campinas University, researched the use of a complementary approach between the patients — the oncological patients — and found that was about 63%. It was realized that the disparity between the use and the research from the patients stemmed from big resistance from the oncologists based on the belief of lack of scientific proof of efficacy.

Then, as Dr. Daniel Amado discussed, the policy changed that situation, officially, in the three categories:

* Whole medical systems
* Natural products
* Non-pharmacological therapies

The traditional Chinese medicine that is used here in Brazil was studied in a clinical map of evidence together with phytotherapy, meditation, yoga, and reflexology.

Just this year, Dr. Ghelman published 12 evidence maps based on systematic reviews. They gathered about 900 systematic reviews from clinical trials for policy informed by evidence in a collaborative work together with the Minister of Health. They also searched the evidence for cancer therapy. From the 12 maps, the main benefits in the symptoms — general symptoms or chemotherapy symptoms — like fatigue-related cancer symptoms to breast cancer.

From the website of the Virtual Health Library, from TCIM that was developed in Brazil, you can search more than 1,000 clinical publications in the area of cancer. This is an example of how to foster the implementation of integrative oncology in the country. Given the example of research in the whole medical system that are non-traditional in Brazil (e.g., Chinese medicine and Ayurveda) it is important to keep the quality of the diagnostic and the physiopathology as was presented from Ayurvedic. There were two important studies in two large hospitals that show the benefits of acupuncture, and that level of implementation, is increasing quickly.

The main style of use of the integrative approach is the multimodal approach. Dr. Ghelman gave an example from the Northeast area in Brazil. The program was designed to revitalize patients. Several approaches were included such as yoga, biodanza, Reiki, singing circle, meditation, body therapy, Ayurvedic medicine, and use of traditional remedies from medicinal plants were also joined. The evaluation showed quality of life improvements in several functional levels, and also the reduction in the symptoms of fatigue, nausea, vomiting, and pain were found.

Also, the qualitative results showed that more than 150 patients experienced feelings of gratitude, solidarity, love, and acceptance, compared with the previous feelings of fear, doubts, and pain before the integrative approach being implemented in that university.

Dr. Ghelman discussed the challenges and opportunities for research related to integrative oncology in Brazil. First, the lack of surveys on services and experience in integration between services in the country. Lack of organized training. Lack of investment funding in research in the field of integrative oncology for pharmacological and non-pharmacological therapies. Further, the three main fields of TCIM, like natural products, non-pharmacological, complementary therapies, and the whole medical system need to be studied as a multimodal approach and how to integrate it in conventional oncology.

There are a lot of opportunities for research, in the area of the Amazon. Dr. Ghelman discussed some studies to evaluate the cytotoxic activity of some Brazilian medicinal plants, and what was shown was that more than 200 medicinal plants have a lot of evidence in preclinical studies. Some aren’t in clinical studies, but it is a huge amount of plants that need to be developed in the years43, 44.

Dr. Ghelman shared a specific integrated approach that was developed in Brazil in 2017. This advanced psychosocial intervention in groups approach is known as light and relational technology in mental health care. The program has low-cost, non-medical, and effective in relieving psychic suffering and it improves self-esteem in general. It also shows in that study the quantitative reduction of anxiety and depression scores. Nowadays, that approach had spread in 27 countries, but started in Brazil. That could be an interesting opportunity also for a non-pharmacological approach.

Dr. Ghelman and colleagues have the honor of being part of the international collaborative network on integrative oncology, gathering with NCI, NIH, NCI in Brazil, NCCIH, Brazilian academic consortium, the American network, Society of Integrative Oncology, the International Society for Complementary Medicine Research in that area, and the WHO. Since June 2018, when we visited the NCI in United States, and just after we started visiting in our country, then we saw the possibility of doing a larger survey.

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**Dr. Carlos Jose Andrade**

**Coordinator, Integrative Oncology, Brazilian National Cancer Institute, Rio de Janeiro, Brazil**

Dr. Andrade’s presentation specifically focused on the intramural initiative of the Brazilian National Cancer Institute. Dr. Andrade showed a picture of the Brazilian National Cancer Institute, which is an 83-year-old public institution, and is part of the Brazilian Unified Health System that we call SUS. It is responsible for the development of national projects and policies for cancer control, involving prevention, early detection, and cancer treatment, in addition to conducting basic and clinical research and training of professionals. It has four hospitals, in many buildings, at different points in the city of Rio de Janeiro.

Historically, the institute has initiatives in complementary practice since the 90s with the use of acupuncture in pain treatment. The institute also implements some local initiatives with an integrative approach, most of them regarding end-of-life care with auriculotherapy and acupuncture. We also have a group with a focus on spiritual support.

Since 2017, the institute has a start-up program with a focus on the practice of mindfulness for health care professionals and also parents of children who are hospitalized. Dr. Andrade shared an example involving a father who started to threaten the doctors who were providing end-of-life care of his son. The tension was so high in that occasion that some doctors applied to seek leave.

The beginning of the process that culminated in the Plenamente INCA program took place in 2014 with a series of lectures on evidence-based happiness. We were trying to include wellbeing and the perception of propose and happiness in the institutional agenda because, in my point of view, it’s a really important element in a health institution. The topic was introduced to doctors, nurses, volunteers, residents, researchers, and even in two inaugural lectures of the institutional academic year, where we discussed evidence-based happiness.

Within this team, the happiness and wellbeing meditation was presented as a practice with the potential to improve people’s perception of wellbeing. Additionally, a discussion about burnout and health care workers’ wellbeing. Data from last year’s institutional management report indicated alarming information on the main cause of sick leave: mental disorders. Thirty-seven percent of sick leave was related to international F-type disease codes, psychiatric codes. This is in line with international data pointing to increasing, rising burnout levels in health care workers around the world.

In addition, over the past few years, they have seen a progressive loss in the number of professionals in our institution due to retirement, a fact that increases the strain on the remaining staff. In the face of this scenario and understanding that our health is not just something related to ourselves, the program called Plenamente INCA was created (in English, something like Mindfully INCA). So, the beginning of integrative care at his institution has a focus on health care workers.

The rationale for defining the program was, first, they would like to be aligned with an official government policy. The National Policy for Integrative and Complementary Practice ensued. Second, the level of evidence available in scientific studies about mindfulness practice is scientifically robust. Third, the choice of a technique with a neuroscientific basis and not necessarily a philosophical or a religious belief, and also taking advantage of some scientific arguments presented by some societies, such as the American Heart Association and American Society of Clinical Oncology.

Initially, they began at the hospital, and started at the pediatric ward with adjustment in performance to take advantage of the hospital stay during children’s hospitalizations for treatments and complications. Then they included a hospice hospital that offered end-of-life care. Right after, we included prevention coordination. Each of these hospitals and units is located at different addresses around the city. That requires a shift to different addresses to take in the practice. There were also demands from a group of researchers, from volunteering and from the nursing continuing education program. They realized that people have an interest in this issue.

The format of the practice was, first, the presentation of a new topic each week that is repeated through the three sessions of the week. In some sessions, they reviewed the meditation technique. They encouraged the cultivation of a curious look that investigates and contemplates. Additionally, they chose some studies that are related to the real situation that we live in day by day.

After that, a practice of 20 minutes. They always simulate and look for replicators to continue the program all over the institution. Today, they are at around 160 weeks of practice. Dr. Andrade shared pictures of the practice.

Dr. Andrade shared some examples from the pediatric ward: The head of pediatrics supported the program. They were practicing in the playroom with parents and health care workers of the pediatric team. Although the practice, in the beginning, was aimed at the parents and pediatric professionals, children also followed their parents, and over time, they also became targets of the practice. The team received some touching feedback from people who practiced during this year.

This one is from a researcher:

“Usually, I did something thinking about what I had to do. I was always anxious to accomplish everything. Now I feel more peaceful.”

This one is from a pediatric doctor:

“It’s very good to start work after meditating. I feel lighter and less reactive. I have time to breathe and take a distance, less “mixed” with situations. In fact, I think we should do meditation every day before starting to work at INCA, as it improves the quality of care.”

Two more comments from parents:

The first one, a father, who when he arrived at the bedside, he noticed that his son was meditating with his eyes closed.

A mother that said, “After all these months, it was the first time that I didn’t think about my daughter.”

None of this would have been possible without the support from the doctor, Anna Christina Pino (she is the general director of the institute). And in the first day that she was director, she stated that we will support integrative care in that institution.

Dr. Andrade shared that having support of institutional communication was also a key factor in reaching people in need. There is wide support and dissemination of the program. For example, last year, a seminar was held and a newspaper printed a story on the program.

However, there are challenges:

* Difficulties implementing the program throughout the institution
* Challenges with hiring
* Issues with engagement of the staff
* Decentralized workforce: people work in many places

Dr. Andrade has learned that after 3 years, the institution is more sensitive to this issue. We have a Brazilian policy that assimilates initiatives like this, and they are planning to do more research with this topic. By increasing the target audience with mindfulness training programs to health care workers and residents, and students of INCA in all of the federal hospitals in Rio de Janeiro. They are increasing the target audience by including patients.

During the COVID pandemic sessions — now on a Zoom platform. Dr. Andrade wishes to interact with other institutions to implement the program in more settings. The CABSI, the Brazilian Academic Consortium for Integrative Health, will help them do this. Dr. Andrade believe that a program like this will not solve the burnout problem, but it could help a lot of people that start to practice meditation.

**Dr. Paulo Caceres Guido**

**Senior Researcher, Integrative Medicine Group, Garrahan Pediatric Hospital, Buenos Aires, Argentina, and the TCIM Americas Network**

Dr. Guido works at the Garrahan Pediatric Hospital, a very large tertiary pediatric health center in Buenos Aires, Argentina. He works in the Integrative Medicine Group, and also at the Clinical Pharmacokinetic Unit within the hospital. He shared that the U.S., French Guyana, Brazil, Uruguay, Chili, and Columbia have the highest incidence rates of cancer. Further, the main types of cancers are prostate, lung, breast, cervix, colorectal, and stomach, which are also the leading causes of cancer mortality in this region45.

Regarding the issue of the use of TCIM in cancer in Latin America and Argentina, there are very few reliable data. In Argentina, adult cancer patients use conventional medicines combined with unconventional therapies very often, probably about 90% of patients. In children with cancer in Argentina, the prevalence of use of TCIM is similar to the data reported in high-income countries. Around 47% of children use these practices. In Uruguay, use of TCIM is around 76% and is higher than that reported in low- and middle-income countries (66%)46.

Dr. Guido described the types of TCIM used in pediatric cancer patients in Argentina and Uruguay, which were special diets, medicinal plants, and touch therapies47. In an important survey covering Argentina — Buenos Aires specifically — in 2005, 90% of cancer patients had used TCIM through using a lot of different types of food, drinks, natural medicines, and also religious and some mind-body practices48.

Another survey — carried out in Argentina in 2019 — reported the main TCIM practices related to cancer patients. Some of them normally are not defined as TCIM, such as psychotherapy, but others are usually named in these surveys as yoga, homeopathy, massage, Reiki, fetal therapy, art therapy, and meditation, among others49.

Dr. Guido described two clinical practice examples of applying TCIM in cancer patients in different and sometimes limited ways. The first example, was implemented at the center FUNDALEU, meaning, Foundation Against Leukemia, a nonprofit private foundation created to serve the community in the investigation and diagnosis of oncological diseases. This center has an integrative medicine service that applies mainly acupuncture and electroacupuncture in a non-invasive way, mind-body therapies such as yoga and tai chi, medical massage, and also music therapy.

The second example was a public health angle — the Garrahan Pediatric Hospital in Buenos Aires City. With almost 700,000 annual consultations, Garrahan Hospital is one of the most important third-level pediatric centers in Argentina and the region, and the main pediatric cancer center in this country.

There are about 500 new cases per year. At this hospital, an integrative medicine group — an official group — works with patients, relatives, professionals, and other caregivers. Treated mainly with some therapies such as Reiki, singing bowls, guided imagery, mandalas, infant massage, horticulture therapy, mindfulness, and reflexology, more than 1,400 sessions were given to 5,000 persons during the last 10 years. 65% were given to patients or relatives, and the rest to hospital staff.

Dr. Guido shared some points related to TCIM and cancer research, including several issues that are not functioning.

* Hundreds of Spanish-American studies describe experiences of patients with cancer in relation to the use of TCIM
* In Spanish America, the most frequent studies consist of qualitative research, such as anthropological analysis using ethnographic methods, evaluating types of TCIM and disease in which it’s used, especially cancer
* Most of the papers are presented at congresses or theses that are published as full text only available on academic websites or in local journals, often not indexed in the classical databases, but in Google Scholar
* Many of these studies have notable methodological problems
* Overall, only very few studies are published in Pharma or Medline journals. If we took only papers on TCIMs that have been published in journals indexed in Medline, and that have been written in Argentina as an example of a neighboring country of this region, we have just 17 articles that were released in other studies over the last 30 years

Dr. Guido shared some plants that belong to several families, such as Lamiaceae, Loranthaceae, and Zygophyllaceae. You can see that two families, marked Lamiaceae and Malvaceae, are very important in general in the world with therapists and organic classes as key classes component in each family, respectively. Two-thirds of the plant studies belong to native species.

All these studies show different degrees of positive activities against a variety of cancer types. Anyway, there is probably a bias that hides a lot of negative or non-positive results of many experiments that test plants against many different types of cancer in many models. These types of studies and these negative results normally are presented at congresses or are not shown.

In closing, Dr. Guido discussed what is not working:

* University teaching on TCIM is very limited, which is why health professional often don’t supply them. The reasons are fear, ignorance, prejudice
* Formal research structures and national health and research policies of the Spanish-American countries don’t generate significant incentives to carry out long-term and high-impact studies in this field. So, based on the high frequency of the use of these practices in oncology, it seems necessary that their therapeutic and adverse effects be known more thoroughly through properly conducted research studies

Lastly, considering the concept of integrative medicine, it may be possible to improve cancer patients and optimize therapeutic results in cancer treatments. He ended by quoting a Nobel Laureates, Dr. Bernardo Houssay. “Latin America is too poor a region to allow itself the luxury of not investing in research.”

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**Question & Answer Session**

**Question:** How are services in integrative oncology reimbursed by the system?

**Answer:** We have a strong public health system so many of the systems are free of charge for the population, but we also have a private system were people can buy a health plan. And they buy this plan, and they have reimbursements from the government. And the states and municipalities have most of these services as a public health service. So, we don’t have this type of reimbursement for the main funding of our health provision. So, as an example, INCA is our National Institute of Cancer. People don’t pay to have the services of INCA. It’s a public health system, or it’s a public health service.

**Question:** Carlos, you said there has been a question about the Amazon people, the Amazon cultures. I know there’s some anthropological and sociological challenges there, and political, but is there any attempt to understand better the traditional medicine applied, in this case, to cancer?
 **Answer One:** We had some, maybe 40 years ago, some doctors who went to some regions with the native indigenous peoples from Brazil to do a study and understand better if there’s a different prevalence of cancer diagnosis, and to have some demiological studies about cancer in these native populations. But the question about the system of care that they have in trying to integrate this with the main, official mode of therapeutics, it’s not a very explorable issue.

So, personally, I went to Chingu to stay with native indigenous peoples to try to understand better the way that they deal with the cancer. I saw, for example, an old lady who was considered out of treatment, and

she returned to this tribe and was cared for by the Shamans of that region. But I think it is an attempt to explore because we have many plants and many ways to try to understand how there is a cure. And it’s an issue to be explored. Today it’s very understandable.

**Answer Two:** I go in the same direction as Carlos. Until now, as you know, there is a divorce, a big distance between that way of care from the traditional Brazilian medicine and from the oncological care. It’s a big issue of research because there are not big studies. Some surveys in hospitals show, since 10 years ago, the lack of prevalence of the traditional style of care compared with the other approaches, like meditation and yoga. There is a distance until now.

**Answer Three:** Yes, we have more than 200 ethnic group of indigenous people in Brazil. So one of these groups has this main system of care. So we are starting to study it. We have made many studies of this group, but not at the necessary level of care, to understand it. So, in the past 2 years, we are making efforts, the health ministry, to understand more. But we don’t have many studies until now.

**Answer Four:** As a medical oncologist, but also I have information in Ayurveda. And once in Chingu, I saw a native indigenous person doing a procedure that we know in Ayurveda as Vamana. And I asked him who taught him to do that procedure. And he told me that he always did like this, and his grandfather taught him doing it like this. This is very interesting because it’s very similar to a procedure of Ayurveda, and probably they do things like that.

**Question:** I know in Argentina you have a very structured system to promote science and technology, including health research, like the Science and Technology Council, CONICET. Has there been any attempt by CONICET or by the researchers to enhance or support these types of studies in integrative oncology also?

**Answer:** No, sadly I have to answer very simple. I know that many physicians or researchers don’t try to investigate in this field. I think so. But perhaps in the future, if we try to advance some very important points in research, multicenter research, perhaps it would be possible, but not exactly now, sadly.

**Question:** How do you envision ... It comes from Chile, the possibility of having multi-country collaborations related to integrative oncology? And that could be to all of you. And we have only a couple of minutes left.

**Answer One:** I would like to mention that you develop the mechanism of Latin American cooperation through the DCM American network that joins Chile and indeed 16 countries. And I believe that it’s a good example of how you can go further in the field of integrative oncology. If you connect this group more with the Society of Integrative Oncology that’s also doing efforts to be more international since the last conference, a wonderful conference last week, and together with the NCI/NIH, then the mechanism you have, you need just to organize to enjoin the hospitals and the clinicians and all the researchers in that field to really develop projects together for the Minister of Health.

**Answer Two:** I think that you are doing this, you are putting out all of those together and listening to the experiences of the other side of the world, inspire us to work in this direction. I think that we are in the, I don’t want to say it’s not the same page, but we are with the same problems, like training, organization, governmental funds, and we are living the kind of problem that is very similar around the world. So, it’s an opportunity to work together to improve this.

**Answer Three:** I’d like to try to give my personal perspective to this and I’ll speak more about it in the session. But my experience is that it’s so important to promote collaborative research by young investigators, across continents, and to really provide funds for young investigators to explore ideas and gain evidence that can then compete for greater funds. And I hope that all of us recognize that and promote that. That’s what I will be speaking to. And I know that in terms of reviews in the National Institutes of Health Extramural Grant funding system, evidence is so important, having preliminary evidence. And the only way to do that is really to promote the types of pilot experiments that occur between continents, between young investigators that are willing to take a risk.

**Examples of Partnerships to Enhance Integrative Oncology Research in LMICs**

**Moderators:**

**Dr. Alejandro Salicrup**

 **Senior Advisor for Global Health Research, Center for Global Health and OCCAM-DCTD, NCI/NIH**

Dr. Salicrup discussed examples of partnerships to enhance integrative oncology research in LMICs: This is not a comprehensive overview. This is only a few examples. For partnerships, in general, there is not an exact formula. There is no two plus two is four. It all depends on many things. He believes that it is important to consider the age of the partnership, why we need a partnership, what are the common goals.

Also, communication is essential and that you have to agree to a mutual understanding based on respect. Have clear expectations so then you don’t get any disappointments. On the contrary, you can enhance strengthening the partnership and get results that would be satisfactory for all those in the partnership. Partnerships are so important these days that even for the sustainable development goals developed by the United Nations system for these coming years, partnership is an essential key component of that.

**Dr. Daniel Gallego**

**Boston University, Boston, Massachusetts, USA**

During these 3 days, we have seen the relevance of integrative oncology, in general, and for LMICs, in particular. The speakers have highlighted the achievements thus far and the tremendous challenges to advance people-centered care, in general, and cancer care, in particular. We have seen fascinating examples of countries and institutions’ initiatives to advance integrative oncology research and practice.

And as Alejandro mentioned, this session focuses on partnerships and intends to portray some examples of collaborations to advance integrative oncology. Our speakers will tell us about national-level, bilateral, and multinational collaborative endeavors from different world regions. We will see examples of well-established collaborations and examples, also of the potential that represent developing networks for advancing multi-level partnerships that include integrative oncology.

This session then intends to show a range of collaborative initiatives with various characteristics. All the initiatives discussed, those we have heard about in these past 3 days, and those that because of time constraints were impossible to include in the program are driven by what we could call the spirit of collaboration. As seen during this event, collaboration for advancing research is critical. Collaboration is crucial in all contexts, and no organization today can think of itself in isolation. Collaboration is particularly relevant for advancing research in LMICs and, in particular, in integrative oncology.

To understand better the landscape of complementary and integrative approaches in these settings, this session will provide examples of partnerships with India, Africa, China and Latin American counterparts to advance understanding. There is a need to continue exploring the potential for therapeutic breakthroughs within the existing wisdom of the world’s healing traditions. Remember, that our approach to that traditional knowledge and healing wisdom should be with the utmost respect for the owners of that knowledge and a humanistic non-exploitative approach.

This session will also be an example of an original network for collaboration on traditional, complementary, and integrative medicine based in the Americas region as an example of the potential that exists when the wheel of a diverse set of stakeholders aligned. This session intends also to stimulate thought around the idea of potentially creating an international integrative oncology network consortium or collaborative.

**Partnerships and Speakers:**

**U.S. National Cancer Institute-China Collaborative Studies on Chinese Medicine and Cancer**

**Dr. Libin Jia**

**OCCAM-DCTD, NCI/NIH**

Dr. Jia discussed supportive research: The National Cancer Institute of the United States is very much interested in the pre-clinical and mechanistic studies of anti-cancer drugs, including components from different medical systems, such as traditional medicine, including traditional Chinese medicine, and the TCM. Since 2007, Dr. Jia’s office has established international collaborative research on Chinese medicine and cancer. There are established relationships with the Cancer Institute Hospital and China Academy of Chinese Medical Sciences, and also some universities of Chinese medicine and affiliated hospitals.

Through collaborative research and study of Chinese medicine, Chinese medicine drugs and their compounds have been studied at NCI Intramural labs. The research projects explore aspects of cancer prevention, botanical drug or mechanisms of anti-cancer action, component analysis like quality control of these components, and also anti-cancer activity screening.

These and other related projects have been presented at different conference and workshops. Interesting discoveries have been published. They have more than 12 papers and they have provided a workshop for promoting the new initiatives for future studies on Chinese medicine and cancer.

Dr. Jia discussed a paper was published in the Journal of the National Cancer Institute just in 201750. The paper summarizes comprehensively the U.S. NCI-supported research on Chinese medicine with the Chinese partners.

Dr. Jia’s talk provided a few examples of research conducted in his office. They studied compounds like Cryptotanshinone, CT, and also other compounds like Gambogic acid. Some are a mixture like a Fufang Kushen injection and the Shen Qi formula of Chinese medicine. Also, some are a single compound, like Berberine, Resveratrol, Toosendanin, and some Ping ointment.

The first example was as compound studied in the NCI Intramural lab and they found out that CT can inhibit a proliferation of Lewis lung carcinoma cell growths51. Also, cell mitosis was induced. In Panel C, a blot can be seen in the G2/M phase. Through the molecule analysis, the CT can up-regulate the P53 G expression and down-regulate Cdc2 and CyclinB1 and leads the cell mitosis on the G2 /M phase. Not only they can inhibit the growth of a Lewis lung carcinoma cell, but also it has another function, to induce, to promote the maturation of dendritic cells. Also, CT can inhibit the tumor growths. When the dosage is increased, you can see the tumor growths inhibited. Also, a mouse was cured with CT treatment52.

Another example provided was on a collaborative study with a mixture of powder for Fufang Kushen injection. This mixture is made in Chinese medicine with two herbs, Sophora flavescens and Rhizoma smilacis glabrae. It’s been used clinically in China for cancer patients. It can be used alone or combined with conventional therapy. Also, it has been found that it can inhibit tumor progression and improve the cancer-related symptoms, especially cancer-related pain. And of course, components analysis discovered that the main compounds are alkaloids, matrine, and oxymatrine.

An in vivo study showed that Fufang Kushen injection inhibits the S180 in vivo growth, dose dependent to manner53. Also, it is not harmful for the normal cell, because it is specific for the tumor cell.

Dr. Jia conducted an animal study using a pain test with the use of a hot plate. A mouse with a bearing tumor, would be sensitive to heat stimulation. The paw withdraw from the hot plate frequency is expected to be different if the mouse was tumor treated with Fufang Kushen injection. The results showed when you treat a mouse with Fufang Kushen injection the paw withdraw potency increased. There was a paw withdraw potency difference between the control and the tumor bearing mouse54. Last year, a drug manufacturer signed an agreement with MD Anderson Cancer Center in order to do clinical trials in Phase I and Phase II on various cancers.

Dr. Jia discussed the NCI Library of Traditional Chinese Medicinal Plant Extracts. The Library contains organic solvent in aqueous extracts for 332 samples of traditional medicines and herbs and these extracts are now available publicly in 96 and 384 well plates for high-scrutiny screening.

The methodology used to generate the library and the preliminary assessment of the anti-cancer activity of this crude extract library in NCI-60 human cancer cell lines screen. The chemical profiling and metabone comparison analysis of four commonly used TCM plants have been tested for the anti-cancer activity to lead into the bioassay testing on the NCI 60 cytotoxicity of potency. They analyzed the masses with organic extracts, aqueous extracts, and hot water extracts.

Traditionally, usually herbal extracts just use the hot water or aqueous. More components were found with the organic extracts. The crude extract library of an authentic collection of TCM herbs has been developed to facilitate systematic biological evaluation of the therapeutic potential of traditional medicines. It is a new natural product repository resource for those interested in understanding of the biological activity and chemical constituents of TCM.

Dr. Jia discussed an observational study at John Hopkins University by Harry Quon. The study observed use of Camwell skin cream, it is a six herbs mixture free of steroids, artificial color, fragrance, nut oils, alcohols and hypoallergenic. Patients who were treated with radiation therapy on their head and neck had skin dermatitis and peeling. When patients were administrated the skin cream, the skin improved or recovered55.

Dr. Jia closed by discussing by sharing that international collaborations lead to basic studies and clinical trials, provides a mechanism of understanding and public resources, and new initiatives and opportunities for conferences and fellowship training.

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6. AACR-AHNS Head and Neck Cancer Conference: Optimizing Survival and Quality of Life through Basic, Clinical, and Translational Research (Austin, TX, April 29-30, 2019**)**

**U.S. National Cancer Institute – India Collaboration**

**Dr. Jeffrey Buchsbaum**

**Radiation Research Program, DCTD, NCI/NIH**

Dr. Buchsbaum discussed the big picture — radiation therapy — treats half of cancer patients and it has side effects. It was important to develop a relationship with India for a host of reasons. The first, they had existing friendships that lasted decades. There are accrual issues, and then large numbers of patients, in India and the United States, who have very rare tumors.

The division could accrue if we work with India. They have proven this previously in the meantime, from the beginning of this project, international scientific opportunities that invited global applications, including members from India, to apply for highly rated biology research.

They initiated multiple discussions and meetings and have had probably 25 to 30 meetings over the last 4 years. It is key in the overall process to establish trust and a good working relationship. There are three factors to achieve this:

* “The how.” You have to define the process in the experiments. People do well together when they’re very different when they have a shared process and they agree upon how to do it
* “The who.” The collaboration of people. It’s important to get to know each other. It’s important that people understand each other’s strengths and weaknesses, and they work together to help each other
* “Find the what.” You have to know what you have. What data you do have. What data you don’t have. What machines you have. For example, they’re putting carbon therapy in Calcutta in the near future, we hope. They came up with this virtual biology, virtual scientific, almost an R1-type project. This has been adapted to allow virtualization across geographic, temporal, and expertise levels in an international setting. It was agreed upon that it was a good idea by the participants of the group, which included centers in Mumbai, Delhi, now Calcutta, and the United States

In order to reach this point, before the COVID-19 pandemic, they thought it would take a number of years in terms of developing structures, funding, processes, to get there. They decided to have multiple projects to help bring the team together while we were working on the less exciting, but just as important, pragmatic infrastructure of that bigger picture.

The three projects were an Ayurvedic Developmental Therapeutics Program (ADTP), which has been supported by leadership in the government of India, at the Primary Scientific Advisor’s Office of the Government of India and other agents from India, as well as a natural language processing project looking at AI and machine learning to study the Sanskrit language as it applies to Ayurveda to try to learn things. They have had about six total meetings. Number one, the Ayurveda Developmental Therapeutics Program.

He has met some of the speakers from the conference via multiple meetings in the ADTP. They have had multiple supporters and we are anticipating applications for NIH grants from the group. It is exciting to see people come together in that context and look at pragmatic studies. An interesting fact is that they had a Western scientist doing an Ayurvedic-style study, and they had an Ayurvedic physician doing almost a Western-style study in the context of some presented studies of the last several years.

He discussed the needs of the COLOSSUS project, and stated that you have to understand, in radiation oncology they believe that we have to change how we treat patients from a physical dose, meaning how much energy you give. The biological dose translates to what you’re doing to the patient, biologically. Meaning you need to know the context and not everyone responds the same way.

This is something that almost sounds like Ayurvedic thinking, if you think about it. In the beginning the process was one size fits all and everyone received the same dose. Now, they have moved to precision medicine, which means they customized dosage based upon your genetics or other measurable factors. They have adaptive therapy, which studies the tumor’s changing size and shape, and they adapt the size of the treatment to that and then we combine them.

The NCI has a funded study, TOPAS, this project looks at taking a very complex process—treatment planning—and simplifying it to one page to do an entire process56. The team existed across a number of institutions in the United States. Information on TOPAS is found at the following website: <http://www.topasmc.org/demos>. TOPAS is proton nozzle at Harvard that allows you to program how particles are processed. The researchers studied biological science and biological dose. They looked at a computationally intensive process to develop a collaboration between the U.S. scientists and the Indian scientists, and the Indian scientists were experts at the Field Programmable Gate Array (FPGA). They brought the teams together (e.g., TOPAS, CDAC, NCI).

They brought someone from the United States over for training. It was a popular event and they had to create extra session dates. The team set a goal to work together. They looked at the code, they wrote the code, and to some of the points of today’s lecture and some of the comments, to the more junior individuals, and included junior professionals in the process. It is a very well-run, efficient collaboration because they all had a common target and a common purpose.

The current standing of things with the COLOSSUS project is that they have 32 of these red FPGAs, and are looking to report the findings. This would have a global impact. This allowed treatment planning to be done in ways that it’s never been done before and help the peoples in both India and the United States.

The take-home messages of this talk are that collaboration and history bring people together and make people do things they could not do alone. Team building is a process. They were bringing high-performance computing that’s affordable, low energy, and hopefully it is translated to a global environment for good use.

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**International Center for Indigenous Phytotherapy Studies, Research Collaborations with Africa on Medicinal Plants—Dr. William R. Folk, University of Missouri, Columbia, Missouri, USA**

Dr. Folk described his experience with the International Center for Complementary and alternative Medicine in Africa. He was hesitant to be the only person scheduled to speak about Africa, because Africa is so diverse, as the United States in terms of traditional and complementary medicine, it is probably like the Wild West in contrast to traditional Chinese medicine or Ayurveda because there are many different cultures.

Nevertheless, about 12 years ago, 15 years ago, the National Center for Complementary and Alternative Medicine, which is now the National Center for Complementary and Integrative Health, took a giant leap, under the directorship of its first director, Dr. Steven Strauss, and agreed to fund several centers of international study for complementary and alternative medicine. The University of Missouri competed for those centers and was successful. They were one of two centers that were established at that time. Those centers no longer exist, but he described some of the lessons that they have learned and also provided some recommendations on how to go forward.

The reason that the international centers were developed was, in large part, because of the HIV/AIDS and tuberculosis pandemic, which had swept around the world. Africa was the nexus of many of those who were infected. Due to the partnership that had developed between the University of Missouri and the University of the Western Cape in South Africa, we competed for funds from the National Center for Complementary and Alternative Medicine.

Securing the funds helped develop very rich partnerships. It continued with the University of the Western Cape, but also with the University of KwaZulu-Natal and the KwaZulu-Natal Traditional Healers Council, the University of Cape Town, and Merritsburg Hospital. Dr. Folk continues to work, as do a number of other investigators, with investigators in those centers of research.

Meanwhile, they also have in the United States extended partnerships with the Missouri Botanical Garden, and importantly with the National Center for Natural Products Research, the University of Mississippi, whose leader, Dr. Ikhlas Khan (a conference speaker). This was a collaborative effort with the National Center within NIH through a U19 grant. Funders were the Fogarty International Center and the Office of Dietary Supplements. The goal was to study traditional complementary medicines that were being used by individuals who were infected with HIV/AIDS and susceptible to tuberculosis.

It was a major concern then that the effort that the South African Government was making to really push the use of traditional complementary medicines in lieu of the few anti-retrovirals that were available at that time because they were very expensive. Also, because some scientists viewed them as being ineffective, that the use of traditional and complementary medicines might be unsafe. A primary goal of the partnership—was to try to examine the safety of one or several traditional and complementary medicines. The program was the first, that they know of, which joined Western scientists and South African traditional healers.

Dr. Folk shared a letter from South Africa, from the American Embassy to the Government of South Africa describing the program once it got funded and read it aloud. “The International Center for Indigenous Phytotherapy Studies (TICIPS), is especially significant because it is one of the first opportunities for medical doctors, scientists in South Africa, and traditional healers to internationally cooperate as equal partners in exploring indigenous vital therapies for AIDS, secondary infection, and immune modulation. Furthermore, TICIPS creates a unique bridge between Western and African medicine systems with respect for both systems of practice and full protection of intellectual property rights”.

The collaboration had two main projects. One was to conduct several randomized control trials of Lessertia frutescens, also known as sutherlandia or unwelej57. There are a number of other names for it as well. It is widely used in South Africa and Southern Africa, and continues to be used for a number of health conditions. One of its other names is cancer bush; it was given that name by early colonialists in South Africa because it was being used to treat cancer.

The second project, which was really a lesser project, was studies of Artemisia annua, vital therapies, and the treatment of tuberculosis and cervical cancer. And the work that we did, part of the work that we did with sutherlandia, is described on a poster in the poster session, the virtual poster sessions posted number 25 that describes the outcomes of this work.

The research lasted six years and produced several outcomes. Here in the United States there was a much greater understanding of African traditional medicines and how to study them, and likewise for their African partners. There was improved understanding among health care providers, Western trained health care providers, and the traditional healers, all of whom have very different cultural norms. They trained a number of postgraduate medical and law students, and many undergraduates from U.S. and African universities. Leveraging NIH support with private support that helped build a number of state-of-the-art research and teaching facilities at the University of the Western Cape. They had more than 20 research publications.

Dr. Folk also discussed lessons learned. Which were trust and communication between partners are essential and require constant attention. Ethical norms, design of clinical trials of traditional healing practices are ill-defined and require much attention, much, much more attention by many stakeholders. The collaboration with their partnership with the NIH was very important because biostatisticians at NIH at the National Center for Complementary and Alternative Medicine really provided key input into the design of the randomized control trials of these traditional medical practices. Biodiversity, intellectual property protection, cash flow, IT, and other infrastructure needs can be huge barriers that really have to be addressed and overcome.

Dr. Folk provided his recommendations based upon his experience. In the future he believes that we have to strengthen understanding of indigenous practices and relationships among local biomedical scientists, the conventional health care providers, and the traditional healers. Research targets should be carefully chosen. There are so many different research targets and prioritized. There should be special attention to interactions between the traditional and conventional medicines.

We want to increase the research training of, and communication among social and biomedical scientists and health care providers. They are all critical elements of partnerships. We should promote communication and cooperation between the medicine regulatory agencies of high- and low- and middle-income countries. There has been a recent study in a national report, a National Research Council report, on the importance of this. We need to lessen barriers to implementation of research, ethical norms about diversity have gone on and on.

We need to pay particular attention in the United States and other high-income countries to those cancers that may not be well studied here in the United States because of either genetics or because of other ideologic agents of other causes. One being, for example, liver, certainly Kaposi’s sarcoma is another where the incidence of cancer in Africa is significantly greater than it is here in the United States. And as a result, here in the United States, these do not get anything like as much attention as they might, as they should, in Africa. These are particularly high, ought to be particularly high-priority targets.

Discussed the results of their studies which was the discovery of herb-drug interactions in the treatment of HIV that are very significant and probably compromise the treatment of tuberculosis, which continues to be a huge problem worldwide58. That was because of the presence of antioxidants and botanicals, which are very likely to interfere with the treatment of tuberculosis and may interfere also with the treatment of a number of cancers. There are also other botanicals that very likely will interfere with some of the newest treatments of cancers that are being developed here in the United States and in other wealthy countries using monoclonal antibodies and other treatments.

The reality is that the people in Africa, as occurs almost everywhere else in low- and middle-income countries, mix and use alternative and complementary medicines and Western treatments when they can reach them. Very little of this is understood when they are mixed. We do not understand these sorts of interactions and there’s great risk his opinion, for antagonistic interactions between the traditional and complementary medicines, which are well-established in the treatment of disease and cancers by themselves.

Nonetheless, when you introduce some of these modern treatments, and again, which are evidence-based, but the mixture we know very little about, and we have to be very concerned about those and recognize that those interactions really need to be studied because they can compromise the efficacy of both traditional medicine and Western medicine.

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2. Clairet, A., Boiteux-Jurain, M., Curtit, E. et al. Interaction between phytotherapy and oral anticancer agents: prospective study and literature review. Med Oncol 36, 45 (2019). https://doi.org/10.1007/s12032-019-1267-z

**Partnerships on Integrative Oncology, University of Texas, MD Anderson Cancer Center with Chile and Brazil**

**Dr. Gabriel Lopez**

**Houston, Texas, USA**

Dr. Lopez shared experiences that they have had with partnerships in particular programs in Chile and Brazil and he outlined how those partnerships were created. Additionally, Dr. Lopez shared some of the results that they had within collaborations and some of the challenges that they faced while working together. One of the connections that MD Anderson has created between a number of programs around the world is through a program called the Sister Institution Network.

The goal of this network is to be able to create connections between a number of cancer hospitals around the world to help to elevate the quality of care and research, and also to really create opportunities for not just elevating the quality of care, but also creating new opportunities for research and creating links between experts at MD Anderson and experts at these sister institution programs.

MD Anderson Cancer Center Sister institutions include Clinica Alemana in Santiago, Chile, Hospital de Amor in Barretos, Brazil, and the Instituto de Cancerologia Clinica Las Americas in Medellin, Columbia. A graph was presented and it showed how one institution can really connect with many other programs globally to help enhance the level of research in the area of cancer.

The graph is available on the MD Anderson website and provides a list of publications that have been done jointly between MD Anderson and institutions in that region. It provides an opportunity to learn about what kind of research is happening in collaboration between these programs, and also a way to connect with individuals who are interested in those specific areas around the world.

The more that we know about what research is going on, the better we can also work together more effectively and efficiently. With regard specifically to integrative oncology, there really is global growth in integrative oncology programs. The challenges and needs of the individuals who receive integrative oncology services are different around the world. It is important to be able to not just recreate the programs that are in existence already, but to understand what is going on in communities so that the needs of that community can be best served.

Dr. Lopez highlighted a collaboration with the Clinica Alemana in Santiago, Chile. This collaboration was with Dr. Marta Cioga, she’s the director of the palliative care program. The goal was to develop an integrative program and to learn more about their patient complementary and integrative medicine use and beliefs. There are many different factors that go into being able to create a new service. One is to actually identify what the unique needs are of the population that this institution is serving.

They decided to work together on distributing a survey to cancer patients, both inpatient and outpatients at their institution, to learn more about how they were already utilizing integrative approaches independently of there being a formal program at the Clinica Alemana. Regarding the survey methodology to identify the patterns of complementary and integrative medicine use at the Clinica Alemana, they used a survey that had already been developed at MD Anderson Cancer Center for learning more about complementary and integrative medicine use in Phase One clinical trials.

They adapted it to the Spanish language and really the challenge as part of doing this survey was not just translating the survey, but then finding out what resources were available locally to be able to distribute and collect the survey. The survey was one way to be able to directly get information from the patient population. A challenge was that more than half of those who were surveyed actually were discussing complementary and integrative medicine use with their oncology care team.

However, the decisions regarding their use of complementary and integrative approaches were not being guided or directed by their oncology physician. Patients were actually looking outside of the medical field for guidance. So, they were discussing it with their oncology teams, but their oncology teams were, in some way, unprepared or not ready to offer that information, to be able to provide the guidance necessary to implement these non-conventional approaches safely59.

It is important to understand what sources patients are using to learn about complementary and integrative medicine. Especially if they’re looking outside of their oncology care team, because that could potentially lead to harm either in the form of alternative drug-herb interactions, potential organ toxicity, depending on what natural products may be used or combined with their conventional therapeutics.

This all drives the idea of really helping to understand what information both the patient and the provider, in this case, the oncology care team, really needs to know to be able to provide evidence-based oncology care. Too often the oncology care teams may defer any discussion of integrative medicine to individuals outside of conventional medical care and that can lead to a lack of coordination and lack of safety regarding the use of potentially beneficial therapies. But if they’re not coordinated, they could potentially lead to harm.

An additional ongoing collaboration that MD Anderson has is with the Albert Einstein program in São Paulo, Brazil. This collaboration also is as part of the MD Anderson Sister Institution Network and its partners. The Albert Einstein program does have an integrative oncology program.

The goal with the program at Albert Einstein is to learn more about the local use of integrative oncology, and then also use this knowledge to compare across programs. This creates additional opportunities for collaboration, with eventual goal of completing the survey at Albert Einstein, comparing results both that we have at MD Anderson and at Clinica Alemana in Chile, and then learning about similar instances across these programs as we all work to develop evidence-informed integrative oncology practice.

Dr. Lopez shared limitations within the collaboration relationship. First, existing research infrastructure is not the same, MD Anderson is different from Clínica Alemana, and is different from Albert Einstein. Therefore, it is important to look at what can we benefit from that is already in existence at these programs or what do we need to look for to be able to create effective collaborations.

For example, fortunately, programs like REDCap are available across these different programs and really have been key to helping create unity in the survey distribution. Also, it is important to get buy-in from the institutions. Not all institutions have integrative oncology as a high priority. Some institutions may not have really an understanding of what integrative oncology is. Additionally, funding can be a challenge and competing priorities among faculty and staff.

Dr. Lopez’s solutions to overcoming these limitations were to view collaborations as an opportunity for programs to learn from each other. For example, sharing a developed survey with their sister institution helped to decrease any barriers of moving forward with the research. Hopefully, by providing some guidance and a foundation for what kind of research can be done across programs and within individual programs, will generate momentum for additional funding, staffing, and the creation of more knowledge within the programs.

1. Lopez G, Salas CA, Cadiz F, Barriga C, Gonzalez P, Acevedo S, Raimilla P, Pincheira P, Naing A, Quiroga M. Complementary and Integrative Medicine Use in Individuals Seeking Conventional Medical Oncology Care in Chile: Prevalence and Patient Characteristics. J Glob Oncol. 2019 May;5:1-6. doi: 10.1200/JGO.18.00190. PMID: 31095454; PMCID: PMC6550051.

**Brazilian Academic Consortium for Integrative Health (CABSIN)**

**Dr. Ricardo Ghelman**

**São Paulo, Brazil**

Dr. Ghelman shared some layers of partnerships and collaborative work of the Brazilian Academic Consortium that was inspired by the U.S. academic consortium first developed 12 or 18 years ago, and after the Dutch consortium that was established in 2017. They had the idea to organize the consortium in several committees to join researchers from different fields, with the mission to also contribute to the scientific validation of an integrative and complementary approach, as oncology is among one of the big 10 of integrative approaches. The consortium is comprised of several groups that all work collaboratively.

The consortium is a part of the Traditional Complementary Integrative Medicine (TCIM) Americas Network that engages 16 countries. This partnership allows for a library database with more than 1,500 TCM publications to be posted on the consortium’s website.

An international symposium of integrative pediatrics was held in 2019 and included leadership from 10 countries in the field of oncology. Around 400 people attended and they were from Brazil, Argentina, Israel, Germany, and the United States. A publication was developed from that conference and it provides a comprehensive definition for pediatric integrative oncology with international consensus. The paper should be released by 2021.

Dr. Ghelman shared an example of collaboration in the field of integrative pediatric at his institution. They have a long-standing partnership with the Charité group from Berlin, Germany. First, in the field of training nurses in strategy to implement an integrative approach in the hospital, they started within the first 3 years to train nurses in intensive care units, bringing external therapies and modalities to palliative care, particularly to nausea and vomiting control, and in pain control also. A paper was published from their collaboration and the results showed benefits of using mistletoe with patients diagnosed with osteosarcoma60.

The barrier of language, it’s a big thing to be overcome. Currently, they are helping their consortium to translate a course from Israel (on traditional herbal medicine for supportive cancer care that includes Ayurvedic and Chinese anthroposophical homeopathy approaches) into Italian, German, Spanish, and Portuguese.

Dr. Ghelman discussed a study using two medicinal plants, the results showed that there was better sleep quality after the use of guarana for group two, and no significant differences were found in the intergroup population of anxiety and depression symptoms. Additionally, there was better sleep quality after the use of guarana. The conclusion is that extract is an effective, cheap, and non-toxic alternative in the treatment of cognitive factors in women with breast cancer receiving chemotherapy, and further studies are needed to confirm the results and also the mechanism61.

Dr. Ghelman briefly mentioned another Amazon medicinal plant from the same region between Brazil and Peru, Uncaria tomentosa. It has been used to reduce fatigue related to cancer62.

In closing, the consortium is now starting collaborative work among three universities and also a company, one specific company; it’s very important for Brazil to continue to develop these partnerships.

1. Longhi A, Reif M, Mariani E, Ferrari S. A Randomized Study on Postrelapse Disease-Free Survival with Adjuvant Mistletoe versus Oral Etoposide in Osteosarcoma Patients. Evid Based Complement Alternat Med. 2014;2014:210198. doi: 10.1155/2014/210198. Epub 2014 Mar 31. PMID: 24803944; PMCID: PMC3988743.
2. Maira Paschoin de Oliveira Campos MD Department of Medical Oncology and Hematology ABC School of Medicine, Santo André São Paulo, Brazil Rachel Riechelmann MD PhD Associate oncologist Department of Medical Oncology and Hematology ABC School of Medicine, Santo André, São Paulo, Brazil Benjamin J Hassan MD PGY 3 Internal Medicine Jackson Memorial Hospital – University of Miami, Florida, USA Lourdes Conceição Martins Biostatistician ABC School of Medicine, Santo André, São Paulo, Brazil Fernanda Branco Assunção Casa Pharmaceutical Biochemistry Santo André, São Paulo, Brazil
3. MAGALHÃES, Lais Beltrão et al. Phase II Pilot Clinical Study of the Use of Uncaria tomentosa (Cat’s Claw) Combined with Paullinia cupana (Guarana) for the Treatment of Symptoms in Terminal Cancer Patienna (Guarana) for the Treatment of Symptoms in Terminal Cancer Patients. Journal of Natural Remedies, [S.l.], p. 55-62, sep. 2018. ISSN 2320-3358.

**Traditional, Complementary, and Integrative Medicine (TCIM) Americas Network**

**Dr. Natalia Aldana**

**Bogotá, Colombia**

On behalf of the Virtual Health Library on Traditional, Complementary, and Integrative Medicine and of the TCIM Americas Network, Dr. Aldana shared some the work of TCIM Americas Network collaborative work, and how that experience could contribute to research on integrative oncology.

The TCIM Americas Network is a collaborative initiative that was created with the objective of interconnecting several stakeholders that are involved. They are related to TCIM through the formulation of policies, regulations, training, promotion, practice, and use of research in the different countries of the Americas. And the TCIM Americas Network is then responsible for the content and development of the Virtual Health Library on Traditional, Complementary, and Integrative Medicine, with the technical support from the Biblioteca Regional de Medicina (Regional Library of Medicine), Pan American Health Organization/WHO.

The TCIM Americas Network was established in June 2017 at the regional meeting, Advancing Towards Universal Health Contributions on Traditional and Complementary Medicine, which was held in Managua, Nicaragua. Right now, the TCIM Americas Network has a huge mission that is all about partnership, because the TCIM Americas Network as a network of networks, and its mission is to gather together different institutions and organizations that are formulating policies for training health professionals, who are carrying out research, developing programs, and implementing programs.

Further, the mission is to be a global reference in network management to enhance the contribution of TCIM to the wellbeing of people and to the sustainability of health systems through informed decision making; access to information; or collaboration among health authorities, academy, indigenous and/or Afro-descendant organizations, professional associations, and service providers, among others.

In this moment, the TCIM Americas Network has institutions from 16 countries involved. They are conferring with national health authorities, professional associations, research groups, universities, providers of services, and indigenous organizations. They are encouraging people in each country to develop national networks, to be like a huge team in each country in order to advance the different goals that we have. They are also working with different networks outside of the region of the Americas to be a network of networks.

One big and really important example is the partnership that they have with the Academic Consortium of Brazil for Integrative Health for three years. To establish networks, they identify different actors and are working in a collaborative way to create interpersonal networks, interprofessional networks, and intersectional networks. This brings the opportunity to exchange experiences between countries and strengthens their research capacities in the different organizations and for the different stakeholders.

The biggest project that they have is the Virtual Health Library in Traditional, Complementary, and Integrative Medicine. The Virtual Health Library, right now, is available in English, Portuguese, and Spanish, and has the objective of promoting the visibility, access, use, and generation of scientific, technical, and educational content that could contribute to the promotion and development and integration of TCIM in the health services and systems in the Americas region. Its vision is that they can do it and they can get at a true collaboration of stakeholders.

The Virtual Health Library is accessible and is navigated through a main menu where you can find different sections. You can search database by using the search box. The interface is available in three languages. They also have news, information about different events, links of interest, and direct access to some research in the database.

One of the big themes that they are doing is developing this collection of information from different resources, from international, regional, and national database. They have specific strategy of research. They are collecting different articles and technical documents from all the database that are available. Right now, they have a collection of more than 1,000,500 documents. This is one way that the TCIM Americas Network is working to bridge the gap of research in integrative oncology.

They also have a Directory of Institutions and this means that you are able to find information, look for someone else you can join and start to work together. For example, there is a section about the regulations and policies, like a world landscape of the information of TCIM, of practitioners, products in each country, and also the practices. There is a specific section for traditional medicine in the Americas. Right now, there is general information about traditional medicine of indigenous peoples. They encourage people of different countries to join.

A e-learning course may be available in the future. They want to encourage people and have a tool to help with the enhancement of research in integrative oncology—pediatric, integrative, public health, traditional indigenous medicine, TCIM, and mental health are just some examples.

Currently, there are users from 142 countries. The network is growing, and the first area that they are focusing on ins developing the infrastructure to organize other projects. They are strengthening research in integrative oncology through collaborative work. Dr. Aldana shared that they would like to do a mapping, a kind of diagnosis of the region.

There are different issues with financial support for the research and issues with research capacity training. However, creating partner teams may be the solution, or at least contribute a lot for all the Latin American and Caribbean countries to improve their research capacities in integrative oncology and all the TCIM fields. This infrastructure was created with the help of Dr. Alejandro Salicrup. Dr. Salicrup was able to travel to Brazil, Argentina, Colombia, and Chile to meet with the network.

**Question & Answer Session**

**Question:** Dr. Buchsbaum, what was the role of the Ayurvedic Developmental Therapeutics Program (ADTP) in this project?

**Answer:** ADTP was one of the three projects developed along the route. The COLOSSUS project is currently focused on radiation biology; however, ADTP is going on in parallel. It represents a huge success in that it has brought a large number of people together to study Ayurvedic medicine prospectively in trials and to combine it and Western medicine in a way where open, unbiased questions can be asked. Because multiple projects are underway and are being developed, I did not want to focus on one for fear of not fairly sharing the spotlight with the group. The goal is to move and study things in a way so that real integration can take place. Some projects are looking at definitive (curing the cancer) hypotheses and others may be looking at the mitigation of side effects. Other projects are looking at integration of the electronic medical record.

**Question:** To William, what can clearly be done to bridge the gap of trust between traditional medicine/healing practitioners on one hand and clinician/research scientists on the other hand? Some of the problems are lack of trust, elitism, lack of understanding, etc., but it must be deeper than these issues.

**Answer:** Your question is extremely important. There is a need to identify and understand the cultural differences and motivations, then address them through communication, resolution!

**Question:** In creating partnerships among different countries and clinical/research institutions, how do investigators and clinicians approach requirement differences by research ethics review committees to be able to conduct integrative oncology studies?

**Answer:** We follow the lead of the NCTN, and I was a COG investigator before I was an NCI employee. Institutional Review Boards exist in both countries where the work is being done, and there has to be approval of the work getting done. So we very much don’t get involved at that level because ultimately people are going to open these trials at their institutions and they have to follow the rules at the local institution. Ideally, the work would be done in a way that could meet all the requirements across the board, and that’s obviously the intent.

In terms of intellectual property (IP), there are rules where the work is done. NCI has very formalized rules of IP and, Alejandro, I don’t think we have time for that. The bottom line is the IP resides where the work was done.

**Question:** How is your partnership, in this case, dealing with some of their research gaps pertaining to cancer prevention and treatment from the integrative oncology perspective?
 **Answer:** In the partnerships that we’ve been working with, it’s specifically looking at active treatment rather than in the area of cancer prevention. Our integrative oncology program at MD Anderson is very much focused on exploring lifestyle factors that are an important part of cancer prevention, and a lot of patients who go through treatment are looking at opportunities to decrease their risk of cancer recurrence. So that does become a part of integrative oncology, for sure, but not something that we’ve explored yet as part of the collaborations.

**Question:** What types of partnerships would you like to consider to advance integrative oncology in the region or sub-region, or country?

**Answer:** I think that there will be a different option. One option could be do partnerships with the universities, with the research groups of the universities, because we ... I remember what Paolo said in the last panel about what is happening with the research in integrative oncology, and he just found 17 articles. And that means that it’s not enough training and it’s not enough research skills and capacity.

I think that the partnerships could be done with different universities and groups to encourage people, to train people, to motivate people and different health professionals to do something related to integrative oncology research. I’ll mention that there’s such a diversity of what can be considered integrative oncology research that it is important to be open to learning about what the research efforts are, published or unpublished, in academic or private practice programs. So the more there’s communication about what expertise is out there, then the more we can learn about how to actually conduct quality research, because I think there’s just too much being done and maybe not enough collaboration, and when there’s not collaboration, a lot of what we learned might remain unpublished or the quality might be too low to have relevance and really affect and move practice.

**Question:** I was very impressed by the level of partnerships that MD Anderson Cancer Center has around the world. And I assume many of them are project-based and some other ones are more sustained, such as what you mentioned about the sister institution program. And I was wondering if you have an idea of what percentage of the global partnerships represent collaborations in integrative oncology on one hand? And if you could elaborate a little bit more about your plans toward expanding sustained collaborations, long-term partnerships, in integrative oncology?

**Answer:** The programs that MD Anderson has globally are a lot of research-based, more conventional medicine-based research studies. And so, really, when it comes to integrative oncology research, our collaborations are focused mostly on Latin and South America. And so, if you asked for a percentage, I would say it’s less than 1% of the broader research efforts. And my goal in working together with the sister institution programs in Latin and South America has really been to try to find what allows us to work together and what commonalities do we have as far as the research infrastructure, and then to see how we can really use the funding available through MD Anderson to allow for those partnerships to grow. For example, the Sister Institution Network has a special fund that we can apply to annually that allows for multi-institution collaborations. And we were going to apply for that grant this year to help us partner in creating a clinical research network across the institutions. However, that fund was suspended temporarily due to, I would say, the economic climate right now with the pandemic.

**Question:** Dr. Jia, you mentioned in your presentation about the creation that this partnership with colleagues in China has led to the creation of a new international consortium for Chinese medicine and cancer. And I was wondering if you could elaborate a little bit about this consortium and whether it has included other countries in addition to the United States and China.

**Answer:** Yes, we are open to welcoming all interested countries, organizations, to join this consortium. Currently, it has members from the United States, China, Singapore, Australia, South Korea, and some other interested countries. So, if you are interested in joining this consortium, contact me.

**Day 4: October 30, 2020**

**Location:**Zoom Webinar

**Time:**8:30 p.m. – 12:00 p.m., EST

**Date:**October 30, 2020

**Potential Mechanisms for Strengthening Integrative Oncology Research in LMICs**

**Moderators:**

**Dr. Satish Gopal**

**Director, Center for Global Health, NCI/NIH**

Dr. Gopal shared that at the NCI Center for Global Health, they support the NCI mission by seeking to advance global cancer research and coordinating NCI engagement and global cancer control. They hope to reduce worldwide cancer suffering through global scientific discovery dissemination. Additionally, its work is organized around four main goals: First, they support innovative, impactful research that addresses key scientific issues in global cancer control, and/or leverages unique scientific opportunities afforded by global collaboration, and there has been a lot of discussion about what those opportunities may be in integrative medicine throughout the conference.

They support global cancer research training. They promote the integration of current scientific knowledge in global cancer control, and then represent the NCI and promote its engagement with key partners in global cancer control. This is all in the context of the global cancer burden markedly increasing, with a 60% projected increase between 2018 and 2040 in the worldwide cancer burden.

Most of this proportional increase is actually occurring in LMICs, as compared with high-income countries. Currently, they are conducting fiscal year 2020 analyses now, but this is the fiscal year 2019 international portfolio for the NCI, largely focusing on extramural investments. NCI has made extramural awards to countries; many of the international investments are occurring in high-income countries.

**Dr. Alejandro Salicrup, Senior Advisor for Global Health Research, Center for Global Health and OCCAM-DCTD, NCI/NIH**

Related to the investments, for fiscal year 2019, the investment that NIH did in terms of millions of dollars in the area of complementary and alternative medicine research was quite high. NCI invested nearly $60 million, and there’s other institutes and centers, like the Institute of Aging, NIDDK, which is the one working in diabetes and kidney disease, and the one on neurological diseases (NINDS) that also invested a significant amount of money in this area.

In preparation for this conference, Dr. Salicrup and other members of the Planning Committee did a portfolio analysis, this time in the area of cancer, particularly, and complementary alternative medicine, to look at the international investments for fiscal years 2008 to 2018. What they found was a very low investment internationally, and most of it was into high-income countries. LMICs received very few grants over the ten-year span. All of them were in the modality of domestic with a foreign component. They were not direct grants. In fact, for this period of time, in this specific discipline, they did not find any direct award that was given to an LMIC.

**Speakers:**

**Dr. Avraham Rasooly**

**OCCAM-DCTD, NCI/NIH**

OCCAM is an office in the Division of Cancer Treatment and Diagnosis. OCCAM is responsible for the NCI research agenda in complementary medicine and alternative medicine as it’s related to cancer prevention, diagnosis, and treatment. There are several components of the OCCAM activities. First is the Extramural Research Program, which is essentially managing a grant, analyzing portfolios, advising on research, and promoting research on microbial-based cancer therapy.

A second important program is the Case Review and Intramural Science Program, which identified novel CAM interventions for evaluation as anti-cancer therapies. In the United Kingdom, summary data from patients promote support, collaboration between CAM, practitioners and researchers.

OCCAM has an international component. The main international program is collaboration with China, and we heard yesterday a lot about this program. In this program, there are collaborative research, conferences, programs from component analysis, and this is the most robust program, internal program of OCCAM. Recently, OCCAM developed a collaboration with India.

Only last week, OCCAM signed a letter of intent with the Indian government, AYUSH Ministry, and Central Council for Research in Ayurvedic Sciences for collaboration in the field of Ayurveda in cancer research. For the purpose of developing a new collaboration between NCI and India regarding CAM.

Historically, the utilization of natural products was limited to botanicals. However, the field can be expanded to include microorganisms, and OCCAM developed a funding opportunity for microbial-based cancer therapy vital drugs. The aim is to stimulate research and develop an overall microbial-based cancer therapy, utilizing naturally occurring microorganisms. In recent years, microbial cancer therapy has had several successes. The most notable is receiving U.S. Food and Drug Administration (FDA) approval.

There are several mechanisms for microbial-based cancer therapy. The microorganism can target directly, primarily in a metastatic tumor, or activate the immune system. In terms of targeting, bacteria can invade a tumor cell, it can be used as a vehicle for delivering a pharmaceutical, and it can activate the induced anti-tumor immunity. Dr. Rasooly’s view is that Western cancer therapy approaches cannot address all clinical need and is not sustainable in most LMICs.

Dr. Salicrup recently published a paper describing microbial-based cancer therapy for global health63. Microbial-based cancer therapy for LMICs is practical because the culturing of microorganisms is relatively simple and inexpensive, and the expertise and technical capability for culturing microorganisms already exist in all low-income countries. Microorganisms can be used as a self-regenerating cancer therapy.

This is the only therapy that can accurately reproduce itself. It can be utilized as a practical immunotherapy modality. I use the word “practical.” Yes, in the United States there is very well-developed immunotherapy, for example, CAR T-Cell therapy, but it costs something like $400,000 per patient. It is not practical, for example, if you take countries in South Africa with an expenditure of $50 a year for all medical expenses.

Obviously, $400,000 for one person is out of the question. Because this cancer therapy is a type of immunotherapy, however, despite the potential, there is very little research. More importantly, microbial-based cancer therapy is not well established yet, which actually limits the application of this field.

Dr. Rasooly discussed the main challenges in cancer-based therapy. First, the cost of current cancer therapy is probably expensive in the majority of the population. It does not mean that there is no potential for Western therapy. Because if you go, even in the LMICs, to urban centers, you can find it.

For example, several years ago, Dr. Rasooly moderated a session in India about the therapy of medicine. He was surprised to see how this was a conference of the Asian Cancer Society and the focus was on immunotherapy, which is counterintuitive. However, we have to remember that even in middle-income countries, there is a middle class, a substantial middle class.

For example, in India the middle class is something like 300 million or 200 million people, which is essentially the size of Europe. There is limited cancer-type infrastructure, especially in rural areas. There is relatively less expertise, equipment, and reagents, and international funding is limited. NIH funded, two grants for India, seven grants for China, and remember that NIH funds 60,000 grants every year, therefore, for CAM funding, two or three grants out of literally hundreds of thousands of grants is very little. Therefore, international funding is very limited and not as trainable and do not address borrowed research.

The main challenge is that integrative medicine in each LMIC has specific local needs, the issue of standardization of treatment. Basically, integrative medicine is less standardized across societies, and while conventional oncology practices are targeted, it is based on a single, active ingredient, for example, botanical, or however the modality is holistic.

It’s more complex, with numerous active ingredients and, therefore, it is very difficult to do a classical FDA trial on traditional medicine because it’s far more complex than holistic, while the FDA modality is based on a single active ingredient or single mechanism, very narrow. Therefore, that is essential in compatibility between the requirements of Western medicine and traditional literature medicine, which is very difficult to overcome.

Dr. Rasooly also discussed the mechanisms for strengthening integrative oncology in LMICs. He stated that collaboration is the main key because, especially in low-income countries, when there is very little infrastructure, there is very little expertise. Therefore, a collaboration, local collaboration with an investigator is key to sharing knowledge, expertise, equipment, funding, and everything else.

Another thing is regional integrated medicine, research centers, which can be used to utilize the resources of different countries. The best example for this is coming from CERN. CERN is a corporation, a European corporation, in nuclear physics. The CERN facility is located in Switzerland, but this is an example of what could be done with a corporation.

Europe is not the law in that country, but similar things can happen, even with the probably of a more limited budget, and there are scientific and clinical merit to do this because of geographic location, to have a regional collaboration, because of geographic location, shared philosophies, and addressing special needs.

1. Salicrup, Luis Alejandro et al. “Bugs as Drugs, potential self-regenerated innovative cancer therapeutics approach for global health.” Journal of global health vol. 10,1 (2020): 010311. doi:10.7189/jogh.10.010311

**Dr. Sudha Sivaram**

**Center for Global Health, NCI/NIH**

As we have heard from various presentations at the conference this week, there are really many exciting research opportunities in the field of integrative oncology, and we will agree that central to pursuing these opportunities is the development of a well-trained research workforce. Dr. Sivaram discussed some of the training opportunities for global cancer research.

There is wide recognition of a mismatch between interest and opportunity to pursue global cancer research training. This interest has been echoed by many experts at this conference, and it’s also widely expressed in the literature. In 2019, NCI and the American Society of Clinical Oncology conducted a survey of NCI-designated cancer centers that showed that there are few opportunities to match this interest64. Research training opportunities in the United States were low in terms of time, structure, and rigor, especially for trainees who intend to pursue global cancer research as a primary career focus, and even at cancer centers with formal global oncology programs.

That there are few opportunities for global research, it was also seen in a portfolio review of cancer training at the NCI, where only about 3% of the really larger training portfolio at NCI had a foreign component. Therefore, the Center sought to address this gap with a new program using the D43 mechanism at NIH that is designed specifically to allow for global workforce capacity building, and this program was developed in close partnership with NCI’s Center for Cancer Training, as well as the NCI Office of Cancer Centers.

The D43 program allows institutions to support training and research experiences that will develop or expand an ongoing collaboration with an LMIC institution. In addition to training support to conduct research, Dr. Sivaram anticipates that the awards will also facilitate research mentorship in the United States, as well as the LMIC institutions, and also provide long-term funding to allow for the development of multidisciplinary training programs.

This opportunity really allows for training in broad areas of cancer research, relevant to the scientific goals of the collaboration, and also provides a chance to train in critical areas that are key to successful global research, such as bioethics, and good clinical and laboratory practices, as well as allowing for discussions pertaining to the competencies needed for good cross-cultural collaborations.

Dr. Sivaram provided an example of how a D43 grant might be organized. The U.S. applicant institution and the U.S. principal investigator will collaborate with investigators and leaders in an LMIC institution to identify specific needs for developing research capacity, both in the United States and in the LMIC-based trainees that will enable the collaboration to advance its cancer research program goals.

The grant will then develop specific aims to meet these training needs, and can include a combination of long-, medium-, or short-term training to meet these research needs. Training can be proposed either at a U.S. or an LMIC institution, or both, which is a distinguishing feature of the NCI’s D43. U.S. trainees can be recruited at the postdoctoral level, whereas LMIC trainees can be recruited either at the pre- or postdoctoral levels. Hopefully, by the end of the award, at least 50% of the trainees will be from LMICs.

The grant will pay for trainee travel, tuition, stipend, and also support faculty efforts for mentorship in research. This program was published just this year, so it’s currently active. The Center has received the first round of applications and they are under review at the present time, and the receipt date is June 2021. You can reach out to Dr. Sivaram if one is interested in applying or has any questions about the program.

The D43 program really seeks to lay the foundation for research training initiatives at the NCI. The Center envisioned three main elements in our approach to research training: The first is improving global cancer research skills, the second is supporting global cancer investigators, and the third is building global cancer research environments, working primarily to increase access to cancer training opportunities by allowing for travel awards, by supporting conference attending for candidates from LMICs.

Dr. Sivaram mentioned some popular programs, such as the Implementation Science Training Institute at NCI, NCI’s summer curriculum for cancer prevention, as well as the National Human Genome Research Institute summer institute in genomics, and from time to time, they have also worked with different conferences and partners in supporting grant writing, as well as data analysis and science communication projects. The Center plans to continue to build on its work to support global cancer research investigators by supporting extramural grant programs, as well as facilitating training in our intermural research programs.

On the extramural side, they are seeking to increase the number of global cancer research applicants to suitable NCI career development awards, and will continue to strategically partner with the Fogarty International Center’s career development programs. The Center’s short-term scientist exchange program is an important program that allows scientists to come to NCI intramural labs and has been successful in building and supporting existing global research collaborations.

In closing, D43 is key to the continued work of building research environments. They also hope to continue to build partnerships with Fogarty, leverage other investments at the NIH, including those in HIV and other research areas that will allow us to continue supporting research environments in cancer.

1. Adapted from: Abudu et al, J Glob Oncol 2019

<https://www.cancer.gov/about-nci/organization/cgh/resources/globalonc-survey>

**Dr. Paige Green**

**DCCPS, NCI/NIH**

Dr. Green’s goals is to give a high-level overview of the Division of Cancer Control and Population Sciences and highlight a few funding opportunity announcements that might be considered as conduits of support for integrative oncology research in LMICs. The cancer control continuum is used to describe various stages in cancer control, research, and practice—from etiology, prevention, early detection, diagnosis, treatment survivorship, and end of life. While the continuum is oversimplified, it remains a useful framework for DCCPS, as it helps identify research gaps where we must collaborate with others to have an impact and where more resources are needed.

The division conducts and supports research in behavioral science, epidemiology, health services, implementation science, surveillance, and cancer survivorship. DCCPS funded research aims to understand the causes and distribution of cancer in populations, support the development and delivery of effective interventions, and monitor and explain cancer trends in all segments of the population, including populations outside of North America. In fiscal year 2019, the division supported research in Argentina, Australia, India, Nigeria, and Peru through collaborations with other NIH institutes.

This conference highlights integrative oncology as an evidence-informed field, including mind-body practices, natural products, and lifestyle modification approaches reflective of various traditions, cultures, and social norms that are used in combination with conventional cancer care. The behavioral targets are justifiable for integrative oncology research, and practice; there has been considerable progress on the development of testing and implementation of evidence-based approaches to scale population-level health promotion, behavior change, and quality of life improvement in high-, middle-, and low-income or low-resource environments as needed.

There are three funding opportunity announcements relevant to NCI’s intention to support and catalyze research on the discovery, development, testing, and implementation of effective strategies to promote healthy lifestyle behaviors for cancer prevention and control. Notice OD-20-106 emphasizes a particular interest in early-phase behavioral translation studies, including research that elucidates the causal factors related to cancer risk behaviors, identifying potential targets for intervention or research that involves the design and optimization of interventions to promote and sustain healthy behaviors related to cancer prevention and control.

PAR-19-309 seeks to support the development of innovative interventions that improve cancer-related health behaviors across diverse racial and ethnic populations; applications that test new theories and conceptual frameworks; develop and evaluate novel strategies to improve cancer-related health behaviors; investigate multi-level and multi-behavioral approaches; and utilize innovative research designs, methodologies, and technologies of interest. PAR-18-559 solicits investigator-initiated clinical trials that have the potential to reduce the burden of cancer through improvements in early detection, prevention, health care delivery, quality of life, and/or survivorship.

Proposed studies should have the potential to improve clinical practice and public health. Funding does not, however, support clinical trials for studies of cancer diagnosis or oncology therapy in patients. We know that care coordination challenges are growing as expanding treatment options, multimodality treatment regimens, and an aging population with co-morbidities intensify the demands for interprofessional team-based cancer care. Notice CA-19-059 calls for research that identifies effective strategies for improving the performance of interpersonal cancer care teams to address care coordination challenges within and between care settings and also for coordination during transition points across the continuum of care.

Studies that would be responsive should advance actionable knowledge about how to design and carry out effective, efficient interprofessional team-based cancer care that strives to improve quality and patient outcomes. Research that is focused on the needs of racial and ethnic minorities; medically underserved or low-income, low-resource populations; or those receiving care in community settings is strongly encouraged.

Adherence to oral anti-cancer agents, particularly molecularly targeted therapies, is critical to achieving an optimal clinical outcome, and suboptimal adherence may not only lead to poor survival, but to side effects and toxicities, unnecessary treatment changes, and increased use of health care resources and decreased patient satisfaction. So CA-20-026 invites research applications that strive to characterize the patient and provider factors influencing the use of oral anti-cancer agents to identify structural, systemic, and psychosocial barriers to adherence, or develop models and strategies to improve safe and effective delivery of oral anti-cancer agents. Research may be focused at the patient, caregiver, dyad, family, provider, health care team, or health care delivery system levels. Research that merges expertise from diverse areas of science and clinical disciplines, and addresses the needs of underserved populations is strongly encouraged.

Continued improvements in early detection, diagnosis, and anti-cancer treatment efficacy have increased the prevalence of cancer survivors globally. Yet as survivors live longer, challenges related to an increase in the incidence of cancer treatment-related cardiotoxicity that is consequent to morbidity and mortality have become apparent. Improving outcomes in cancer treatment-related cardiotoxicity encourages collaborative applications that will identify and characterize patients at risk of developing cancer treatment-related cardiotoxicity. Methods that evaluate cardiovascular risk prior to treatment and integrate evidence-based cancer regimens with cardiovascular screening, diagnostic, or management strategies are sought, and the primary intent of this particular call, which is offered in an R21 and an R01 mechanism format, is to mitigate the cardiovascular dysfunction while optimizing cancer outcomes.

Notice CA-20-025 reflects the interest of our institute in supporting implementation research related to cancer prevention and control in LMICs and in low-resource settings or environments. NCI encourages applications that pursue innovative approaches to identifying, understanding, and developing strategies for overcoming barriers to the adoption, adaptation, integration, scale-up, and sustainability of evidence-based interventions, tools, policies, and guidelines in those settings.

The research project should be focused on dissemination and implementation research for the primary and secondary prevention of cancer in LMICs or in populations facing conditions of particular vulnerability in high-income countries. The project should be built on evidence-based interventions for the respective population groups and those groups defined under contextual circumstances.

Similar research in all settings is called for through the PARs that are listed at the bottom of the slide, and these related announcements also highlight the benefit of understanding the circumstances that create a need to stop or reduce the use of interventions that are ineffective, unproven, of low value, or harmful.

In closing, the NCI Cohort Consortium is an extramural-intramural partnership created to address the need for large-scale collaborations to pull data and biospecimens to answer certain research questions. Through its collaborative network of investigators, the consortium provides a coordinated interdisciplinary approach to tackling important scientific questions. It offers economies of scale and opportunities to quicken the pace of research. The annual meeting for the Cohort Consortium occurred on November 16th and 17th.

**Dr. Della White**

**National Center for Complementary and Integrative Health (NCCIH), NIH**

Dr. White discussed the mission of NCCIH and that is to determine through rigorous scientific investigation, the fundamental mechanisms, usefulness, and safety of complementary and integrative health interventions and their roles in improving health and health care. The Center’s vision is that scientific evidence will inform decision making by the public, by health care professionals, and by health policy makers regarding the use and integration of complementary and integrative health approaches. Right now, NCCIH is right in the middle of strategic planning for the 5 years. Interested individuals can subscribe to follow the work at NCCIH and also follow the Center on different social media platforms to stay up to date on the new strategic planning process.

The Center has three scientific objectives. The first one is to advance fundamental science and methods development. The second is to improve care for hard-to-manage symptoms. The third is to foster health promotion and disease prevention. The cross-cutting objectives are to, of course, enhance the research workforce and to disseminate evidence-based information.

Dr. White discussed the types of projects funding by NCCIH. They study mind and body practices, as well as natural products. In terms of mind and body practices, they have an interest in acupuncture, massage, meditation, spinal manipulation, hypnosis, qi gong, tai chi, yoga, and different types of breathing exercises. In terms of natural products, they have an interest in botanicals, dietary supplements, probiotics, prebiotics, terpenes, cannabinoids, and special diets.

In the space of mind and body approaches, Dr. White share some of the Center’s interests as they relate to international integrative oncology. For mind and body approaches, they are interested in research to inform the use of these approaches to improve adherence to cancer treatment. The Center is interested also in research to inform the use of mind and body approaches for improving symptom management.

The priority symptoms would include pain, stress, depression, anxiety, sleep, and sleep disturbances. They do, however, have a low priority for the treatment and prevention of cancer. They are interested in secondary data analyses on animal studies, non-interventional studies, observational research, epidemiological clinical research, basic mechanistic research, and non-clinical translational research.

In the space of natural products, Dr. White shared that they have a keen interest in basic and mechanistic research to inform the use of natural products for improving symptom management. Specifically, in pain, stress, depression, anxiety, sleep, and sleep disturbances, again, with a low priority for projects focused on the treatment and prevention of cancer.

For international health research, in general, for NCCIH, foreign institutions are eligible for funding through direct mechanisms, but this is only when specified in the funding announcements. They mostly fund projects that have a foreign component. This is in order to foster and support collaborations offering thoughtful and impactful research around understanding mind and body approaches in natural products. This is specifically true for the types of symptoms that I mentioned before as it relates to pain, sleep disturbances, and anxiety, depression, and stress. Of note, NCCIH will not consider applications that involve interventional clinical trials outside of the United States and Canada, and there will be a slide in this link that takes you to a website that gives you some more details about our policies around international health research.

Dr. White shared some of the relevant funding opportunities for those who are interested in the topic. The first one, is a funding opportunity called Developing the Therapeutic Potential of the Endocannabinoid System for Pain Treatment. For this funding opportunity, there are no clinical trials allowed, and the interests are in understanding the role of naturally occurring phytocannabinoids and their derivatives, either alone or in conjunction with other complementary approaches, in modulating the biological and neural systems associated with pain perception and analgesia in relevant model organisms or human subjects.

They are also interested in understanding the mechanisms that are underlying cannabinoid analgesic and anti-inflammatory properties. The second one is a notice of special interest that they issued to let the investigative community know of their interest in the discovery of analgesic natural products through the National Institute of Neurological Disorders and Stroke IGNITE Program, which are innovation grants to nurture initial translational efforts, and this is going to be, therefore, related to assay development and neurotherapeutic agent identification.

Again, for this opportunity, clinical trials are not allowed. NCCIH’s interest in this IGNITE Program includes research geared toward the development of robust, validated analgesic assays suitable for medium to high throughput screening of natural product libraries, as well as analgesic targets relevant to different pain conditions.

Dr. White discussed a notice of special interest in nutrigenetics and nutrigenomics approaches for nutrition research. Again, these applications would come through the NIH parent-funding announcement, and NCCIH’s interests include research to understand the impact of selected nutrients, dietary supplements, the ketogenic diet, and prebiotic. There are supplements, and prebiotic and probiotic modulation of specific conditions, including pain.

They are also interested in understanding botanical products' underlying mechanisms, prebiotics, Omega-3 fatty acids, and other dietary supplements. Interest specifically lies in what their role is in delineating their relationship to pain and inflammation. There are two funding announcements that are related to probiotic and prebiotic and human microbiome research.

For this research, they are interested in nonclinical trials only. Specifically, they are looking for research on prevention and symptom management of inflammatory and pain conditions, mild-to-moderate anxiety, depression, sleep conditions, and behavioral research to promote healthier lifestyles.

Lastly, they are interested in applications focused on probiotics — with or without prebiotic studies — and their interactions with other natural products or the effects of mind-body modalities on microbes.

Those interested can send an email to Dr. White if there are any questions. Dr. White can connect individuals with the right program officer, who would help understand what our priorities are, especially as the new strategic plan becomes live. Also, she can direct them towards the right funding opportunity.

**Dr. Marya Levintova**

**Fogarty International Center, NIH**

Dr. Levintova’s presentation focused on the Fogarty International Center: One of the things that makes Fogarty truly different from the rest of the NIH institutes is focused specifically on supporting research and research training in LMICs. None of the Fogarty projects are specifically focusing on supporting a U.S.-based research or research training program. Fogarty supports every project that collaborates between a US investigator and an LMIC investigator or directly supports LMIC investigators.

About two-thirds of Fogarty’s portfolio is focused on research training. One example of such training is its K programs. They have a program that is a K01(<http://www.fic.nih.gov/programs/Pages/research-scientists.aspx>), specifically directed at US citizens or green card holders who are interested in working in a foreign country, in an LMIC.

The other K program they have is a K43 (<http://www.fic.nih.gov/Programs/Pages/emerging-global-leader.aspx>), which is for LMIC investigators. Both opportunities are for postdocs and have quite specific requirements. The links allow individuals to see the length of time for each of the programs and the time required. Physician-scientists have many questions because they have quite strict clinical requirements; individuals should review them carefully.

Fogarty has supported K awardees — throughout the world. There is more of a significant engagement on the African continent. It is also Central, and Latin America and Asia are also involved. To note, each one of these allows clinical trials. However, these clinical trials are not a requirement. There are two different announcements for each program; K01 has two announcements, and K43 has two announcements.

Fogarty has another program that allows applications focused on cancer, which allows for a broad spectrum of topics to be submitted. There have been research projects supported by Fogarty that focus on cancer-related topics in bioethics training. Dr. Levintoa shared two examples:

* The R25 is more of an educational didactic type of a program for master’s-level courses, and really developing the base for bioethics in the institutions, in the LMICs. The application period is summer
* The D43 program is more for a doctoral-level, a postdoctoral level of research training. Each one of these typically is a 5-year grant. They are really focused on developing the generation of researchers in bioethics in LMICs. The program director is Barbara Sina, who can provide all of the specific details

Another program is currently in process, for which Funding Opportunity Announcements are currently in the process of being developed. However, individuals can see that there are notices of intent to publish. A specific release date is not available. Health programs have supported cancer research in the past. More information is available online, and the contact person for the GEOHEALTH opportunities is Christine Jessup.

In closing, Fogarty has had long-running non-communicable diseases and disorders (NCD) D43 programs. This is a research capacity development program specifically focused on NCDs. Since NCI developed their own NCD D43 program, we are only supporting cancer-related applications submitted by an LMIC institution US investigator interested in this particular topic and would specifically inquire about NCI D43. However, LMIC investigators would inquire about Fogarty’s D43 NCD program.

**Questions and Answers About NCI and NIH Programs**

**Question:** Are there examples of D43 grant examples, particularly successful examples?

**Answer One:** The specific grants that are submitted for any program at NIH are actually private. We, at NIH, cannot share those materials with any researcher. But what I suggest you can do is go on Fogarty’s website, and you can find the specific projects you’re interested in. And there is a listing.

**Answer Two:** At the moment, we don’t have any sample grants to share. I’m aware that several institutes at NIH, including NCI, share other sample grants. I know Paige is nodding her head. There are sample grants at the Division of Cancer Control. Unfortunately, none of them are for the D43 mechanisms. But we hope to have these up in the coming years. In the meantime, as you’re developing the D43 application for the cancer program, do feel free to contact me. I have talked through several with several investigators who applied in the first round. And I’m happy to help in any way I can as you think about the second round of applications.

**Question:** What is the percentage of NIH investment in CAM, compared to the total amount of investment by NIH generally?

**Answer:** NIH funds, every year, approximately 50,000 grants. Ten of them go to CAM for an LMIC. That means 10 out of 50,000.

**Question:** Dr. Green, regarding some of the programs that you presented, people from LMICs can apply directly? Or do they have to be in a partnership with a US institution?

**Answer:** No, the program announcements that I highlighted are open to foreign institutions. We have many other funding opportunity announcements that are open to foreign components. But I specifically highlighted opportunities that were available to foreign institutions for direct application.

**Question:** What is an R21, which is the planning grant?

**Answer:** An R21 is a smaller scale grant mechanism. It normally is characterized as one that is highly exploratory and high risk. You officially do not need preliminary or pilot data, but I will say that this depends on the study section. It depends on your question. It depends on how you have built the case for exploring the particular aims that you are proposing. So it’s a smaller scale mechanism. At NCI, our funding for the R21 is considerably lower than the R1, but it is a 2-year grant mechanism. So, definitely, it can be used for exploratory work and high-risk, high-reward work.

**Question:** From a person who is a European Union citizen, but they are a resident of an African country where they are working with cancer prevention and treatment research with a local university in Africa, what grant might they be eligible for?

**Answer:** We’ve had situations where an individual interested in a K award was in the same kind of situation. It really depended on their legal status in the specific African country. If they’re just living there without a permanent residency status, then that makes it different versus living there as a permanent resident and having established a home there, even though you have dual citizenship with the European Union.

**Potential Mechanisms for Strengthening Integrative Oncology Research in LMICs (continued)**

**Moderators:**

**Dr. Satish Gopal**

**Director, Center for Global Health, NCI/NIH**

**Dr. Alejandro Salicrup**

**Senior Advisor for Global Health Research, Center for Global Health and OCCAM-DCTD, NCI/NIH**

**Speakers:**

**Dr. Partha Basu**

**Head, Screening Group, IARC, WHO, Lyon, France**

Dr. Basu identified a few challenges present in integrating traditional medicine into conventional oncologic care, especially from the perspective of research: I have identified a few solutions as well, but that is more to stimulate discussion because that may not be all. So, the number one challenge, I think, is that research is quite fragmented and lacks the vision to translate into practice, especially when it comes to low- and middle-income countries.

One of my colleagues has done a wonderful job in doing a systematic review, which is as yet unpublished, to see the role of Ayurveda on best breast cancer prevention, treatment, or survivorship. As you know, Ayurveda essentially deals with a lot of herbal projects and a traditional ancient medicinal practice in India.

This drawing essentially shows that there are definitely a few natural products that have shown their activities to promote or inhibit cancer growth or promote anticancer activities. These are all in the form of small research projects done by individual researchers, institutions that do not have crosstalk among them.

When we looked into the 63 articles identified, there are only three articles regarding a clinical intervention study, and all of these three articles were essentially validating the same herbal compounds. There is a disconnect somewhere, we know it, but then we have not translated it into some more advanced research.

The second challenge that I would highlight in integrative oncology research studies is the high risk of bias. Partly, it’s because of the nature of the interventions themselves. Again, this is a systematic review of different traditional practices from China on symptom management and improving the quality of life of cancer patients in practice — the meta-analysis. This meta-analysis identified 67 randomized controlled trials. Of these, 50 had a high risk of bias, and the rest had a moderate risk of bias.

And what are the major sources of bias? Number one was allocation concealment. This means that these were randomized studies. Ideally, in a randomized study, the person who is allocating patients or individuals to a particular study arm should not have any control over doing that allocation. This is avoidable in a proper design.

But the lack of blinding is a major problem. In fact — in some of the studies — it’s impossible to do blind. For example, if we’re comparing yoga in an intervention, how do I blind somebody? A practitioner of yoga? But again, the major factor was in any of the studies; they have not reported their complete outcome data, especially negative outcome data. It, too, is important. Then, of course, small sample size and high dropouts. So, these problems are there.

Possible solutions: Again, we should come to a pragmatic design. When we design studies, we need not always think of anonymized control studies. Well-designed cohort studies and case-controlled studies can address a lot of important questions. But if we do randomized studies — of course — we need to make sure that we follow all the processes and all the scientific rigors that are required to implement a randomized control study — specially to look at the co-funding factors.

Contamination is often a problem in the studies looking into traditional and conventional medicine. Because if I know that there is a study going on that shows the value of — for example — zinc, and then I am put into the control arm, I’ll go and buy zinc for the pocket and have it. So, contamination becomes a problem we need to be careful about.

Mainstream clinicians are not very attracted to this kind of research. This is from my own experience in doing a randomized control trial to evaluate curcumin in preventing cervical cancer. This was essentially initiated by the department of biotechnology in India for oncology centers that were supposed to participate.

Ultimately this became a negative trial, but that’s not the point. The point is that out of those four identified institutions, only our institution could successfully recruit patients in this study. The other three either didn’t initiate or started but didn’t take care of the blinding properly. So, none of the patients were evaluable. There was a huge protocol violation.

What do we need to do? First and foremost is fostering teamwork and multi-institution collaborations. That will give people a broader view of the entire ecosystem. Then, that trial design should be supported by robust preclinical data or data from observational studies to convince all who are associated with that study about the value, as well as the scientific rigor of the study. It is also important to follow the same rigorous standard of oversights as it is for the evaluation of conventional trials. So, that’s also important.

That brings us to the question of whether to do more implementation research studies. Essentially, we may have a lot of interventions proven through randomized control trials. As we look into their adoption, feasibility, and sustainability, evidence suggests these kinds of practices are never going to be adopted in mainstream practices.

My last is from IARC. We are investing in building capacity and research as the WHO cancer research organization. I am mentioning three different opportunities:

* Young scientists to spend 2 years at IARC through this IARC postdoctoral fellowship that is still open on our website. This is essential to continue with the existing research work or plan new research with the IARC teams. You’ll get all the details of the IARC teams on our website and the research projects
* A senior visiting scientist is utilized for 6 months or 1 year. Obviously, it is for senior researchers, but again, it gives us a great opportunity to build collaborations and expand our collaborators' network, which is our major strength. We are not a funding agency, so we have to depend on collaborations getting external, extramural funding
* Summer school: For the last 2 years, we have introduced a summer school on cancer control, which is becoming increasingly popular. And sometimes, for example, in the last summer school, the European Union, they wanted to participate, and they had a session

NIH may consider having a dialogue with IARC to have sessions in this kind of summer school or even postdoc fellowships. Senior research scientist positions are then done to support it through bilateral agreements between IARC and an individual institution. If NIH gives that consideration, that would be wonderful news for IARC, and that can certainly foster more research into integrative medicine because so many people interested in integrative oncology are listening to this.

**Dr. Geetha Gopalakrishna Pillai**

**WHO**

Dr. Krishnan described WHO’s cancer research: He explained collaborating or bringing in WHO in different arms or different ways of being useful for cancer as such and integrated oncology in low- and middle-income countries. Traditional, complementary, and alternative medicine can offer a few things to cancer therapy, especially integrative oncology.

Its inherent qualities are a holistic approach, cultural sensitivity, societal acceptance, experiential knowledge, empirical evidence, and individual categories: products, practice, and practitioners. In expected outcomes, it has better mass acceptance. It improves acceptance in patients, which you have seen in several of the studies that have been published.

Community engagement emphasizes quality of life, the extent of life, economic benefits, clinical benefits, prevention, and early detection — these are the broad areas where traditional medicine or traditional complementary. Alternative medicine can be useful at this particular moment in integrative oncology. WHO is not a funding agency. It is also not a research organization, as such. It helps in creating guidelines. It really helps in creating technical reports, and it publishes international norms and standards.

Dr. Krishnan stated that there are generally six expectations from integrative oncology:

* Primary prevention
* Early diagnosis and screening
* Management
* Supportive care
* Survivorship, and
* Palliative care

This is the entire spectrum of cancer management. Integrative oncology and the inclusion of traditional complementary and alternative medicine can be useful in all of these six areas. This can be immediate because there is evidence, and there are possibilities.

The outcomes of these expectations can be used immediately (short-term), medium-term, and long-term. For example, in the short term, we can use the huge resources of traditional medicine and human capital available around the world for primary prevention.

If they have good medical knowledge and clinical knowledge and understanding of diagnosis, you can use that. Alternatively, we can use that in a very appropriate manner to help give information to people based on already known factors for primary prevention. This can also be used in early diagnosis and improving screening. Traditional medicine can be used to manage conventional care for cancer by improving early access to care and human capital to help overcome barriers to care, etc. These are areas where conventional cancer care can use traditional medicine resources.

What is known could be immediately put into practice in LMICs for the use or benefit of the patients and the clinicians. For example, we can improve the quality of life and mental health in cancer survivors and palliative care. We can be very specifically using traditional medicine for improving pain management, disabilities of function, quality of life, and mental health.

However, in the medium-term, we are required to put in some resources, some kind of effort, which will improve the human resources for educating and informing the public of locally adapted healthy habits.

We also need to:

* Categorize them
* Create evidence of them
* Even create good communication processes for these healthy habits, which are locally adaptable or already existing in the community's culture

These are things that we need to identify, and it will take some time. Some concerted effort into this can bring a lot of benefit to the low- and middle-income countries.

Dr. Krishnan also shared that we can look at the alternative ways traditional medicine understands a disease — even cancer. It gives you a different perspective and a different approach to cancer cure. The field should move towards evidence-based medicines and practices, and complementary interventions are, of course, in the medium term.

Dr. Krishnan emphasized that it is no longer a question of whether traditional medicine needs to be integrated — whether it is useful. It is only how and what kind of traditional medicine do we include; that is the question. That is where we need to put our efforts and — of course — in complementary medicine.

Complementary and traditional medicine can improve supportive care and improve the effectiveness of medicines, reduce doses, and reduce side effects and nutrition deficiencies. This is something for which we can use traditional medicine. We can improve survivorship specifically in community-based rehabilitation programs and also in palliative care.

This is a bit far away from long-term — he believes that we require considerable resources and studies into this in primary prevention, interventions of traditional medicine, and innovation. Some traditional medicine knowledge could possibly help in primary prevention. Innovations — including new technology based on traditional medicine — and knowledge can help in early diagnosis and screening of cancer. This is due to using the alternative methods or alternative understanding and perspectives of traditional medicine of cancer as a disease.

We can improve life expectancy, and we can also work on improving the life expectancy of patients under palliative care. But in terms of low- and middle-income countries, immediately the areas we should focus on are the short term.

If one wants to achieve anything in this area, we should have decisive policies, strategic investments, and effective implementation. We have no doubt about it; all of us have been discussing that. We need to plan this and need to understand how we are going to do it. Probably, this is where WHO can be of help. We are probably good with creating these broad-based ideas and concepts on moving forward — and at roadmaps in general. We are good at bringing people together.

Dr. Pillai pondered and stated that these are not programs that are being run by WHO currently, but how can WHO be useful for this integrative oncology program globally? WHO could help create guidelines that could be research based, clinical guidelines, or integrative oncology approaches to pain management. They can implore all the countries. They can create research programs and documentation and develop a global guideline on utilizing pain management tools within integrative oncology.

WHO can create technical reports, which can talk about how product practices and their efficacies are being used appropriately in member states. Further, WHO can talk about norms and standards. For example, establish benchmarks for the safe use of traditional complementary and alternative products in cancer care. WHO can produce and provide tools for data and impact assessment, which could be the ICD terms for the common traditional medical classification of a cancer diagnosis. Lastly, WHO can create a training manual and approach training modules for integrative oncology.

**Prof. Vd. KS. Dhiman**

**Central Council for Research in Ayurvedic Sciences (CCRAS), New Delhi, India**

Professor Dhiman discussed research and the CCRAS Ministry of AYUSH's training opportunities on Ayurveda and integrative oncology. The first opportunity he foresees is developing a documentation format for reporting Ayurveda treatment as a stand-alone or add-on therapy. An attempt has been made in the form of a published short communication in one of the journals of this council65.

This database will lead to the identification of potential Ayurveda interventions and their possible role in cancer management. It can be the first area of collaboration. The research training component in integrative oncology from Ayurveda as a collaboration or research project(s) can be done on this.

The other area of opportunity is in research and training in designing integrated clinical research protocols to evaluate the safety and efficacy of Ayurveda interventions. This will be in the field as an add-on to the conventional treatment activity that is chemotherapy and radiation therapy, where synergism has been established by research studies. This is another way to enhance the quality of life and reduce the morbidity of the given chemotherapy and radiotherapy.

The other is a stand-alone for relapse and stable disease inoperable malignancy presentations and cases, unsuitable for chemotherapy and radiotherapy. This is an additional area where integrated clinical research protocols can be done. Research can be accomplished with suitable funding by any agency and rolled out in palliative care.

Preclinical research is also one of the areas where there is an activity from the NCI, and CCRAS has explored the potential of some botanicals as anticancer drugs. They have a list of 10 potential medicinal plants — botanicals where their anticancer activity has been screened on cell line studies. The in vitro and in vivo studies have already been completed. They can further be explored, taken for more vigorous in vitro and in vivo studies, and they can also be the potential botanical molecules for cancer studies.

The concept of a personalized approach to medicine is very much in a fundamental conception, which is practically utilized in medicine and the maintenance of health. That faculty or temperament has been standardized by this concept within the last 4 years. The Ayur Prakriti web portal is now available, a standardized faculty assessment tool, and there is great potential for training the researchers.

This exploration can bring out so many new research projects for a personalized approach and feasibly see this phenotype's relationship to the genotype in future studies. The other training programs can be short-term courses cum training programs on integrative oncology, in collaboration with a modern medicine counterpart.

This participation of Ayurveda and allopathic experts in that training program can help to understand each other. It can help bridge the gap and provide a common platform to share the sense and challenges of both the systems.

Areas of collaboration with this new initiative are the research programs in mutually identified research areas — including technical inputs — for the development of protocols for any collaborative research in the field of research and development in Ayurveda.

Another area of collaboration — CCRAS’ work related to preclinical and clinical studies already done —can be taken forward in collaboration, joint workshops, seminars, conferences, or training to identify key areas where such work can be intensified. This includes potential cooperation, research, and research training programs and activities related to the field of Ayurveda.

Exchanges of scientists in the field of complementary and alternative medicine — including Ayurveda and the identification of cancer, complementary approaches, research gaps, and any other potential complementary and alternative medicine — are with the research activities related to cancer, and an extension of technical support by OCCAM to CCRAS in the field of complementary Ayurveda medicine.

With these areas of collaboration, we foresee great collaboration and many opportunities from both sides. This collaboration letter of intent has been made possible by the very active and proactive involvement of Dr. Geetha Krishnan, a technical officer from WHO, from the India side. And he has taken very great pains in coordinating the Ministry of AYUSH and NCI/NIH.

1. Gundeti, M. S., et al. "Comprehensive, integrated format for systematic documentation of cancer management through Ayurveda interventions." *J Res Ayurvedic Sci* 1 (2017): 263-282.

**Dr. Jie Li**

**China Academy of Chinese Medical Sciences, Beijing, China**

Dr. Li discussed TCM oncology scientific funding in China. TCM has played an important role in cancer treatment in China. The Chinese government also showed great concern and great support for scientific research on TCM. There are many kinds of scientific funding projects in China. According to the different funding levels, the project can be developed at the national, ministry, administrative, provincial, and municipal levels; and research institutes or hospital levels.

Dr. Li shared a graph of the specific set of scientific funding in China.

* The first level—the national level—which also has funding support from our country, mainly consists of China's Natural Science Foundation. The second one is the National Key Research and Development Program. The National Natural Science Foundation of China is a general major project

The National Science Fund for Distinguished Young Scholars also set out some special funding for international cooperation, which we will discuss later. The National Key, Research, and Development Program can be developed into the 973 Program and the national 5-year plan

* The second level is about the ministry and administrative level from the Ministry of Health and National Administration of Traditional Chinese Medicine. This project focused on clinical research
* The third level is the provincial level from the local Natural Science Foundation. The fourth level is the research institute and hospital level. These are based on self-selection

According to the specific content of funding, scientific funding can be divided into three projects.

* The first one got the research project.
* The second, the talent project; and
* The third is the environmental condition project

The research project — both the clinical study and the basic research — is solid research of the foundation. The talent project pays more attention to the cultivation of talent and dreams of distinguished young scholars.

NSFC supported more than 2,000 projects over the past 10 years, with an amount of more than 1,000 yuan, equal to $115 US dollars. According to disease incidence, NSFC focused more on cardiovascular disease and cerebrovascular disease, and cancer. In TCM oncology, diseases included lung cancer, liver cancer, colon cancer, breast cancer, and gastric cancer in the most recent 5 years. Hot spots mainly involved tumor microenvironment and tumor immunity.

There were close to 13,000 papers published in the SCI journal, and about a quarter was funded by the NSFC.

The International of Chinese Medicine is very important to the development of the scientific fund. Until now, NSFC has already established international cooperation and exchange relationships with 94 science-funding organizations and research institutes in 49 countries and regions. They have funded an international academic conference held in China and international exchange programs.

Since 2007, we have set up cooperation with the NCI, and now 10 young scholars have started training in NCI as the paper has been published in the international journals. An ongoing research project, also supported by the National Natural Science Foundation, is focused on the effects of TCM on immune function and the molecule magnesium.

Dr. Li thanked the China Academy of Chinese Medical Sciences and the Natural Science Foundation of China. I also thank the Office of Cancer Complementary and Alternative Medicine, NCI. They showed great concern in cooperation over the last 12 years; we hope we’ll have a chance to cooperate with other countries.

**Dr. Roger Chammas**

**S****ão Paulo Research Foundation, São Paulo, Brazil**

Dr. Chammas presented what the São Paulo Research Foundation (FAPESP) has been doing in the past few years and opportunities for supporting research on integrative oncology. In the state of São Paulo, they have a very active environment of research. There are around 170 research and development organizations.

Most of them are higher educational institutions and universities. In the last 20 years, though, they changed this profile when more and more hospitals, research, and development strategies are coming in as clients. They are organizing their research centers, and they are now doing active research.

One percent of all the government of São Paulo's tax revenues goes into research, and here, most of the researchers have their salaries funded by either companies or universities. All the money allocated at FAPESP goes to fellowships, undergraduate and graduate students, postdoctoral fellows, and young investigators, and the great majority goes to cover the projects themselves.

The annual budget is around $0.6 billion, and it is divided into most of these activities. Around 35%, or even a little bit more, of the investment, is in the health area. They usually take a bottom-up strategy. Additionally, 40% of these initiatives go to our areas, health, and biological sciences.

There are some strategic projects, and one that may be of interest to most people — derivative oncology is the program by FAPESP that tackles the region's biodiversity. This is diverse botany here, and this is clearly an opportunity to interface with the huge biodiversity we have in the region with studies in health and biology. These initiatives do not exist right now, but there are clearly some things that we can learn, and this group can be actively doing.

They have been working over the last 20 years in increasing the integration of our research activities with groups of research agencies. Today, 38% of all papers in Brazil have international collaborations. FAPESP has a very large portfolio that can support activities of research.

A very successful NIH (R01) funding mechanism allows researchers from Brazil to team with researchers from the United States and have an NIH approved project. There are also collaboration opportunities with people from Iraq or China teaming up with FAPESP and organizing specific calls to fund cooperative research in the area. This is already in place with many universities abroad. These grants are usually the first grants to launch research project grants to establish the network necessary for supporting quality research in any field.

They also have something very similar to the D43 mechanism in the São Paulo School of Advanced Sciences, and these are strategies that bring students to the area from different countries. There are workshops and hands-on opportunities that would stimulate the development of specific areas. Again, this is a tremendous opportunity for bringing the concepts of integrative oncology to our researchers, and it’s an opportunity that is open to everyone.

Dr. Chammas shared that the most interesting mechanism they have at the FAPESP is called the Organization of Centers. These centers can be of two kinds: Research innovation or diffusion centers. Right now, there are 17 centers like this. They are essentially based on research, and they are fully funded by FAPESP and by the universities.

This concept gave rise to the second type of organization of centers: the engineer or applied research centers. Here they have a third party that could be either an international institute or a company that teams with FAPESP and the local universities and organizes a research center with a mission, a very specific mission, along 10 years.

It is a 10-year contract that would allow for the development of specific issues. Integrative oncology is very well adjusted. It would be a very interesting theme for developing an applied research center, considering the groups, the consortium that we have in Brazil, and groups from abroad that could team up to develop specific aspects.

Dr. Chammas provided some examples of applied research centers. The Human Well-Being Center is closely related to integrative oncology. This is something that is supported by Natura. Natura is a Brazilian company of cosmetics, and it is running in the Psychology Institute. So far, it has very little to add in terms of oncology, but they could obviously push in this direction if there are researchers interested in it.

FAPESP is the largest research finance institution in Brazil. For many years, 2% of income tax goes directly to science and technology and research. This is important for sustainability.

**Questions and Answers About Other Organizations**

**Question:** Dr. Basu, are IARC fellowships open only to candidates for LMICs. Might there be some consideration of the US and other investigators interested in doing this sort of work in international settings?

**Answer:** Yes, the IARC Fellowship is open to LMIC candidates only, but then an LMIC candidate working in the United States can also apply. However, beyond this fellowship, there is also an opportunity for bilateral fellowship grants. So just to give you an example, we had one postdoc fellow who came for a project through a bilateral grant agreement between IARC and the National Cancer Institute in Morocco. She worked for 2 years, then she managed to get her own grant, and then graduated to a research scientist position.

**Question:** Is there no need for a different paradigm or research methodology?

**Answer:** Yes, that’s right. A different research methodology approach is required for Ayurveda intervention. Many issues are there where blinding cannot be done. One of the issues is when you are doing some treatment procedure so far that the blinding is impossible. WHO has indicated certain different issues in the researcher setting for the traditional systems also. And they all have to be taken into account because all double-blind, placebo-control, all those parameters of a research treatment protocol approach are adopted for the patient's benefit.

**Panel Discussion: Potential Mechanisms for Strengthening Integrative Oncology Research in LMICs**

The panel discussion was on potential mechanisms for strengthening integrative oncology research in low- and middle-income countries. All of the panelists that you already saw doing their overviews participated in this panel.

**Question:** Moving forward, what do you envision that your institution, your agency, or program can contribute the most to advance integrative oncology research?

**Answer One:** For IARC, certainly, the main focus is cancer prevention and cancer detection research. And in that respect, we already have some of the groups that are working in various areas. Still, we have never tried to see how we can integrate this research into the ongoing research that is going on in traditional and complementary medicine. The outcome of this particular deliberation is to build some kind of consortium. IARC will be happy to be part of that consortium. And being a WHO organization, our major role is to generate evidence to inform policies, not only for the WHO but also for different countries and other international bodies. In a nutshell, apart is that IARC would be very open to joining any consortium focusing research on cancer prevention and cancer detection. (Dr. Rasooly)

**Answer Two:** Again, I just want to reiterate that, for us, I think our greatest contribution would definitely be supporting more basic and mechanistic research to understand the use of particularly natural products and improve symptomatology among those who are undergoing cancer treatment and then with cancer survivors. I think that’s going to be probably the place where we will have the greatest strength to contribute to these efforts. If I can add, we have in our programs in Brazil, we have the BIOTA program that looks at biodiversity. So, suppose we have a roadmap for exploiting this biodiversity to generate natural products and their use in integrative oncology. In that case, this will be, I think it could be, a very robust program for research in the country, in São Paulo, at least. (Dr. White, NCCIH)

**Question:** What type of partnerships do you look to or will consider to advance integrative oncology research and training?

**Answer One:** For the D43 program, we are not being very restrictive. You can have multiple principal investigators from the United States and the LMICs. Multiple LMICs can come in on the same application. So it’s really what type of training aligns best with your collaboration’s research goals. (Dr. Sudha Sivaram)

**Answer Two:** Can I just add a little bit? For Fogarty’s programs, some programs require a US lead with an LMIC partner, while other programs require an LMIC lead. And these are usually universities or research institutions in the countries. We have very few research grants where the collaboration is between nonprofit organizations, but not traditional research universities or research institutions. But those partnerships also exist with Fogarty funding, but most of it is a university or a research institution. (Dr. Levintova)

**Question:** What are some of the limitations of existing research methodologies, perhaps for moving science forward in this area? And if there are new, innovative, and evolving designs, we should be thinking about rigorously and impactfully studying integrated medicine. That’s probably a question that several people on the panel may want to address.

**Answer One:** The speaker discussed two examples: Let us look at the studies, randomized control studies and their systematic reviews that have shown that acupuncture is very useful in reducing cancer pain. Now there’s no point in going for more randomized controlled trials. The main point is, if we think realistically, who requires cancer pain management most? It’s the patient who is remaining at home and under some kind of care who requests pain medications, pain control.

For me, what is important to address whether it is possible to deliver acupuncture in a home setting, especially in an LMIC. It comes into the purview of implementation research. We need not think of controls, we need not think of blinding, we need not think of randomized control studies. We need to look at how best to implement this in a real intense setting. And looking at the health systems approach: What kind of training would be required, or what kind of leadership or governance would be required?—all those things. That is one example.

Another example that is often debated—and Dr. Dhiman touched upon it—is when we talk about Ayurveda research, is there anything different that we need to think about? Some basic tenants of research remain the same. Say, for example, you need to have a specific, measurable outcome. You need to have an appropriate design or the appropriate statistical power of the study. But then what may be different is when it comes to, for example, safety issues. With Ayurveda, it is very difficult to identify specific compounders. Maybe we need to learn from our pharmacologist friends, our regulators, other people who can really advise us how best to set up a clinical trial based on Ayurveda compounds. (Dr. Partha Basu)

**Answer Two:** I think it’s a growing area of need to identify innovative approaches to studying not only integrative oncology, but also the development and testing of behavioral interventions overall. So, I know that there are a number of new approaches that some behavioral investigators are beginning to adopt, things like optimization and things like stepped-care algorithms and other things that behavioral scientists, in particular, are about to adopt. (Dr. Paige)

**Answer Three:** I think we need to look at it from a new perspective. Because how integrative medicine or even cancer care happens in an LMIC is very different from what would happen in, of course, what we are discussing right now. I think we need to find methodologies for translating what is available in these settings and allow them to use it as early as possible if you are expecting something within the 15 years. Because it is not going to happen otherwise. It is not going to transfer itself into actual certified results on the ground. We will all be talking about LMICs, but LMICs will remain a faraway dream. They will not realize any of these things. Because of their set-up, their way of functioning, the way in which cancer is taken care of there, it is identified there very differently. We are talking from a different platform. We are talking about different things that are not even thinkable in all these countries.

I think we need to rethink what we are looking at. We should really look at what resources are available in these countries. We should find out where we can immediately use them. And how we can use them immediately, and how we can use them over a period of time. Because if you don’t examine them over a period of time, because if we don’t do it, it doesn’t work in this manner. This way of what we are talking about is integrating a new therapy into a high-end, highly sophisticated medical system that probably would be existing in the United States or in European countries. But LMICs, poor guys, do not have this. I think we need to really think about how we utilize this opportunity. We should create collaborations; we should start re-looking at the available resources in these countries. If we don’t re-look at them and generate an evidence base for them to utilize it, create mechanisms for them to translate their own resources into actionable, utilizable materials, we are not going to help them. We’re talking too far away from what the reality is. I’m sorry, but this is what came to my mind, because if you’re going to speak specifically on LMICs, this is what we should be approaching. (Dr. Pillai)

**Comment:** Regarding funding issues. I think, not surprisingly, at an integrative medicine meeting, the attendees and panelists feel that this is a vastly underfunded area of research.

**Answer:** The way that we operate is relatively simple. We have funding opportunities. And, essentially, we need to create a funding opportunity to address this issue. Because, normally, foreign grants are not very competitive compared to US grants. Therefore, we have to create funding opportunities that are very specific to LMICs, and which are very specific to integrative medicine because this is how NIH is operating. Therefore, the answer is relatively straight forward. But, obviously, the question is, okay, who is going to do this?

**Question:** Why has this not occurred already if it is relatively straightforward?

**Answer One:** I think that the question is this: If you look at the Center for Global Health, it’s the only really funded program that has to do with technology. Actually, I developed this program. And because when you deal with technology, you are dealing with very well-defined questions. Therefore, this is the low-hanging fruit. When you are dealing with integrative medicine, it is a far more complex issue; therefore, the bar is higher, because holistic medicine is different from Western medicine. And NIH thinking is more according to the traditional mechanistic studies, measurable things. There is a gap between Western medicine and traditional medicine. I think this gap is an issue because when NIH research is evidence-based, you have to provide an active ingredient, you have to provide a specific mechanism. And these things exist less in holistic, traditional medicine. This is a problem. Therefore, there has to be a specific funding opportunity to address these issues.

**Answer Two:** I’m Jeff White, director of NCI’s Office of Cancer Complementary and Alternative Medicine. And I think these are important issues. I’ll try to make my comments short, but this goes to what you asked Satish about. Well, why hasn’t this been done yet? There are various ways tried to attack pieces of this topic of integrative oncology, but not the whole thing, and not in the context of LMICs. And I think Jason made a great point about the uniqueness of that in those environments. It will take a lot of thinking and collaboration, I think, for NCI to target something that works, that is valuable, and that will make some steps forward for LMICs. I do think that this, what we’re doing with this meeting and what hopefully will come out afterwards, which is a continuing dialogue among groups like IR and WHO and the Central Council for Research in Ayurvedic Sciences and so on, can lead to that. Where we are probably the best at making some impact is on smaller pieces, like on the biological aspects of drug development. What was talked about in Brazil, the opportunities there, that’s something I think we could step into and perhaps make a more rapid impact on directly. But I think beyond that, it’s going to require collaborations.

**Question:** Based on what I heard over the last 3 days, there are so many differences across the geographical regions, and so many issues we can address. It would be more productive if NCI or other organizations, together with scientists, help organize some focus announcement, for example, a new mechanism, so researchers can work on a focus area and make a more cohesive impact rather than being really scattered for this new field.

**Answer One:** I was listening to what Dr. Geetha was saying earlier. I think for a moment, if you put aside the LMIC versus NIH/NCI piece aside, and think about it from a cancer patient’s perspective, I think there is a lot of opportunity to collect data on patient-centered outcomes. Some of the funding opportunities that Dr. Green mentioned earlier may lend to thinking of research studies where we can collect data on patients. Because patients, whether they are in India, China, or in the United States, are using a variety of traditional therapies concomitant with their cancer therapy at a cancer center, for instance. I think there is work to be done there, and there might be open opportunities at NCI or in governments elsewhere that have been represented here to pursue those specific questions. (Dr. Sivaram)

**Answer Two:** I think this gap in understanding can only be mitigated, and without doing this practice of bed to bench. In the case of the integration of traditional medicines in cancer care without a bed to bench approach, I think this will be very difficult. Otherwise, if we go by the conventional approach, what is acting and how it is acting, if we stick to this approach, I think we will never reach anywhere. So please think it over. If NCI and NIH agree to this approach, a new approach of bed to bench, first collect the data from the patients. Whether the traditional system, traditional treatment, is giving relief or a benefit to the patient. (Dr. Dhiman)

**Question:** What is one gap in integrative oncology that research could address? It’s innovative research at the interface of Western biomedicine and traditional medicine therapies, challenging the myths that could lead to new hypotheses and open new fields of research. They want your views on this.

**Answer One:** My suggestion is that we need a platform where this discussion can continuously happen. I am talking not as a WHO person, but as a clinician who had worked in a modern medical hospital with oncologists for about 10 years. This works only if the concepts of a traditional medical program can be understood by a modern medical doctor so that they can use it appropriately in the oncology protocol or otherwise.

The traditional medicine doctor has the freedom and the knowledge to go and ask the oncologist what they want in a particular condition, in a particular patient. This is how it functions. There are hundreds of different situations which we can really find out. I think in one of the presentations or several of the presentations, these were all given as examples during the last 2, 3 days. But what we lack is we don’t have this language translation mechanism. Modern medicine and traditional medicine speak two different languages, and there is no interpreter here. We require interpretations to evolve. And there is a new language that can be understood by both, or there should be an openness which should be enough, or put into practice where people can ask, “Okay, I don’t understand what that report means. Can you help me?” What is the intervention that you want from me that you are not able to achieve, that I might be able to give to you. For asking me, as a traditional medicine practitioner, an oncologist should know, which are the areas where I can give that information or that kind of support. As a traditional medicine practitioner, I should know, “Okay, what are the interventions in my hand, which I would be able to integrate safely into the particular protocol?”

This takes time; it is a slow, evolving process. It takes time. But if we don’t start that interface, we create a platform, we create ways of interacting with digital, and ways of documenting that and creating this process and make it perfect. As long as we don’t create it, we are not going to reach integrated medicine. This is my thought.

**Answer Two:** This is asking, if you want to ask, what can NCI do in this regard? It’s like, well, you say NCI has this office that deals with complementary and alternative medicine. Doesn’t that mean that it already has the capacity to look at these novel approaches or these different worldviews? And it already has developed a process to bring forward research in that. Well, to some degree, yes. But again, the way in which it actually happens is more the pieces of those worldviews that can be best understood by the Western biomedical worldview. And if you want to expand beyond that, to the things that these other traditional medical systems incorporate, that is a long-term interactive process, an educational process, a translation process. So it is all those things, and it’s a slow process that gets people a comfort level and some degree of belief that there is something of value there that needs to be followed upon. So, if I haven’t answered it, it’s just to say there’s one mechanism to do, but I just agree, it’s a complicated process that requires a lot of work. (Dr. Jeff White)

**Answer Three:** It’s, I think, a big concept that I more or less agree with and don’t necessarily have an easy answer for. I guess I should say that I don’t inhabit the integrative medicine field primarily. I’m a clinical translational person who worked on lymphoid malignancies, living primarily in Sub-Saharan Africa before I came to the NCI. A lot of our efforts were really focused on traditional biomedical science, improving allopathic programs, the bread and butter chemotherapy delivery, pathology infrastructure, etc., by which one could address cancer in low-income countries. We did become aware, of course, that integrated medicine or non-traditional medicines and herbal remedies and other things were being used frequently, and undertook some descriptive studies to try to understand that better, and what potential interactions might be. But we certainly didn’t go beyond that in my own clinical research program that I led before coming to the NCI. And I guess, to me, this meeting at least illustrates that there’s a lot of interest in this field from various parts of the NCI, as well as many international partners. And I think the NCI is often responsive when a field can articulate clear questions, opportunities, priorities. That’s something that we can try to help address again as an institute. Certainly, again, as someone who doesn’t inhabit this field primarily, I don’t quite know. I think if we had some help in articulating that clearly, hopefully as an outcome of this meeting, then that’s something that we could think about. How we might respond to the specific needs that are raised. (Dr. Gopal)

**Question:** There is a very low percentage of grants related to Ayurveda that are funded in the United States, besides supporting the grantees to increase the rigor of their submissions. How can we support the grant review process to find reviewers who can appreciate more integrative research projects with non-reductionist methods? As Dr. Dema noted, the Ayurvedic approach is a different paradigm for health. Do the other countries have a better mechanism in place to review integrative medicine grants?

**Answer One:** This is asking something specific to NCI in a way, and it’s a very specific question about how can we improve the review capacity and sensitivity to these issues. In order to really be helpful in answering this, we have to look at what the real situation is. I don’t know that we have, in fact, actually a lot of Ayurveda applications, because I’m not talking about an application that is about a component of ashwagandha or a lipid component, or whatever. These natural product applications, although they’re about natural products, compounds that come from Ayurvedic plants used in Ayurveda, I don’t know how much different their review is going to be if you incorporate somebody on the review panel who knows something about Ayurveda. Because, in fact, they probably aren’t really addressing Ayurveda issues. If there really is a problem about Ayurveda research not doing well in review, then there is the possibility of getting people on those committees that have Ayurvedic science backgrounds, more than likely in ad hoc capacities. Or, if there’s enough of them, as standing members of review committees. But these aren’t things that NCI actually does. Most of the review, as people know, maybe not the audience knows so much, but we only review a small fraction of the grants that come to us. Most of the applications that come to NCI come through the Center for Scientific Review. So, anyway, I think there are mechanisms to improve and review once you really understand what the issues are, but from an institute’s point of view, we generally can’t implement those things. We can only advise and support the development of better processes for review.

**Answer Two:** This is Della White from NCCIH and I would echo Jeff’s comments, too. You could send those names and we can pass those over to the scientific review office. When they have applications that require this expertise, then we can have some people who they can lean on. But I think the other point is really to be able to have some strong applications. So making sure that whatever work is being done in this space, whether it’s basic or mechanistic research to get those data published so that we can have a pool of investigators to have a demonstrated record of research in this area.

**Answer Three:** I think, in general, it’s a very good practice to contact us with a one-page description of the specific ideas, and we are happy to review them, put you in touch with other program directors at the NCI or at NIH, and help you develop your research ideas. (Dr. Sivaram)

**Question:** What about the possibility of research training merging either Ayurveda or traditional Chinese medicine with conventional Western medicine?

**Answer One:** As I noted in my presentation, our D43 does allow for training and integrative oncology. We have our application date this year in June, so do reach out. As you’re thinking about this topic, I really can’t say anything beyond this because we have tried to be very inclusive regarding important research areas for which training is needed in our program.

**Answer Two:** The best way to go about finding out if your project is appropriate for the Fogarty D43 NCD program, which has the last application deadline on November 13th, you have to send your specific ideas to the program director and then she would be able to tell you if it’s appropriate. The time is running short for that program, so make sure to sign up for Fogarty announcements and then you will be informed when the application is due. (Dr. Levintova)

**Answer Three:** I’m presently at the medical school here, and I’ve been analyzing the curriculum that we have in all medical schools in the country. And I fail to see any attempts or there’s very little discussion on integrative medicine at all. I understand that if we want to move forward into the integration, the incorporation of integrative medicine, I think we need to discuss this more with our colleagues and then try to change it, change the culture. And curriculum development is critical for that. (Dr. Chammas)

**Question:** In US national cooperative groups, some that are supported by the NCI are extremely successful in implementing clinical trials. Is there any possibility of developing similar mechanisms in LMICs, and perhaps having NCI co-sponsor and help to develop the infrastructure?

**Answer:** Certainly, some of the cooperative groups work internationally. That’s largely in high-income countries. The one NCI-supported cooperative clinical trials group that does have a substantial portfolio in LMICs is the AIDS Malignancy Consortium. And this was because of their specific scientific area. And I actually oversaw the African sites before coming to the NCI. So, this is something that I think we have a lot of interest in. Needless to say, there’s a whole variety of logistical issues, regulatory drug procurement, monitoring, that are necessary to do, cooperative cancer clinical trials that have to be addressed. There are probably ways of addressing them, and this is something that we certainly hope to think about as we go forward. A number of the other cooperative groups have actually approached me about their interests as well, and extending their portfolio into LMICs. Again, I think it’s the AIDS Malignancy Consortium primarily that has done this today. And this is something that we intend to think about with them and to see what kind of capacity we would need to build at the Center for Global Health in order to support these efforts. (Dr. Gopal)

Next Steps Discussion

**Moderators:**

**Dr. Alejandro Salicrup**

**Senior Advisor for Global Health Research, Center for Global Health and OCCAM-DCTD, NCI/NIH**

Dr. Salicrup discussed the next steps and some possible outcomes of this conference. First, a white paper will be produced for the journal, CA: A Cancer Journal for Clinicians. Dr. Jun Mao of Sloan Kettering and Dr. Salicrup will be the lead coordinators as well as several other people who had participated in the conference, will be invited to contribute. The white paper will summarize the conference outcomes, suggest future directions, and do an in-depth review of this field of integrative oncology, hopefully providing an excellent roadmap to advance this field internationally.

As many of you suggested throughout the conference, we believe that organizing a working group that can address some of the issues presented here related to integrative oncology research will be a crucial step, especially for LMICs. This is a good lesson learned — at least from his perspective, we have to work together — and this is not only NCI’s or NIH’s responsibility.

We have many hopes that people from all agencies, and many of the people who have participated in this conference — where we have more than 700 people registered from more than 24 countries — should chime in.

As we heard from the speakers in this last panel, some programs already in place that you can take advantage of immediately.

Dr. Salicrup mentioned that NCI has a program for short-term scientists. This is an exchange program where people can come to the intramural lab — and labs at NIH — to work on various specific and tangible projects for a short time. The program is perioded by The Center for Global Health also coordinates the program conference for research training. There are travel awards for LMICs, to attend conferences such as ASCO or the Society for Integrative Oncology, or any other. With these awards, interested individuals can also apply for funding to prove that they will be receiving a specific training or a very targeted session during the conference or workshop.

During the presentations, some of the NCI Designated Cancer Centers had a lot of interest in working internationally and with LMICs. In this conference, we heard from Dana-Farber, Sloan Kettering, and MD Anderson, but certainly, there are many others present. This is a potential opportunity to collaborate with some of their researchers from these cancer centers.

The other three scenarios are all examples, but Dr. Salicrup believes that people should take advantage.

* First, the Fogarty International Center, Dr. Levintova, described the K01 and the K43, and one of them could be a new U.S.-based investigator to work with an investigator for LMICs
* Also, there is another option where LMIC scientists could apply. Integrative oncology or related areas could be something that could be explored to be presented through these mechanisms
* There is also a trans-NIH funding opportunity announcement, R01, which is the most extensive mechanism available for collaboration, for researchers, between the United States and China, and the United States and Brazil
* This was alluded to in the last panel. Also, during the pharmacology of the traditional medicine panel, we have the intramural labs. 23 of the 27 institutes have laboratories where they do research and training in-house. They have always been very open to international colleagues, postdocs, or junior and senior scientists to come and work
* There are some areas related to integrative oncology—like the pharmacology of traditional medicine, population science, translational research—that apply to integrative oncology. There certainly will be opportunities for many people from LMICs to apply

Conference recordings and proceedings will be available on two websites, for the Center for Global Health and also on the website for the Office of Cancer Complementary and Alternative Medicine (OCCAM). This is just the beginning of a dialogue and an exchange of ideas that we intend to continue. We must hear from you, and we need to follow up regarding the committee proposed.

**Dr. Jeffrey White**

**OCCAM-DCTD, NCI/NIH**

Dr. White has noticed in emails that there has been an email exchange between some of the participants trying to express interest in collaborations. This was the exact purpose of the conference. I’m glad that’s happening already. If people have suggestions for other entities, some organizations they think should be engaged in this discussion and this ongoing discussion, we certainly would like to hear about it either. Just send us a note in one way or another, or ask someone from that organization to contact us. That would be very helpful because I think we are certainly planning on continuing the dialogue.

Dr. White believes that there is a lot of information from this meeting that we will be processing over time. There are a lot of motivations that people will have to join us. And I think some of them have been talked about that there’s the potential for real impact inpatient care. This comes about through the interaction between these medical systems and ways to create a better situation for patients that don't exist now.

Many patients use the combination of Western medicine and traditional medicines, in which Western medicine practitioners are not informed about the use of traditional medicine. That is a situation that could be quite a problematic one, and we need to improve that. We need to incorporate the voice of patients into this. As we move forward, he hopes that we will focus on how to do that.

He also believes another motivation is the expansion of this modern science that we have now. It will help us think more about underdeveloped areas within this in our medicine, some aspects of assessing risk for cancer, and some aspects of rehabilitation or getting patients in a better condition and more resilient for the therapy they are going to have.

Further, organizations and individuals who have an interest in these kinds of ideas, they can participate in our discussion. There is also some potential for traditional medicine here. Eventually, we will have more dialogue to hear from traditional medical systems about how they are noticing or see the potential for their own systems to develop through the incorporation of Western biomedical information. Hopefully, it will be a two-way street.

Lastly, I want to say that I think we’ve talked a lot about integration, in particular. If that is a goal, then the best thing that we are going to be able to do is to start with interaction, increase the interaction, and make it valuable to people from both, from all the worlds that are involved. Those are my comments.

**Dr. Alejandro Salicrup**

**Senior Advisor for Global Health Research, Center for Global Health and OCCAM-DCTD, NCI/NIH**

Two of the conference's objectives were to have a change between different groups that are working in this field and start a possible collaboration. Dr. Salicrup was happy to see this, and we are talking to researchers from Brazil, South Africa, the United States, and India. So, that is certainly showing good promise. Also, he noticed the networking through the chat. Even though we are virtual, we make many connections, get to know each other, and exchange ideas.

**Appendices**

**Appendix A**

**Recommendations**

Participants had the option of leaving open-ended feedback and recommendations. The majority of the comments thanked the organizers for hosting the conference and asked for ways to continue the conversation and collaborate with each other post-conference. Comments are included below.

|  |
| --- |
| Outstanding experience!! Thank you! I was able to get to know about new (for me) research areas. |
| This was a very informative conference. |
| The focus should be on science-based evidence that these alternative therapies actually work. I think Dr. Mustian stated that 50 clinical trials with 50 subjects each are not as useful or convincing as one collaborative trial of 2,500 subjects. Establishing large corroborative groups to accomplish this is a good goal of the conference.  |
| Many thanks to the Trans-NCI-NIH Conference on International Perspectives on Integrative Medicine for Cancer Prevention and Cancer Patient Management. And thanks to the participants, the panel members, especially the organizing committee, who have made this meeting on joint efforts a fulfilling, enriching forum to exchange minds and facilitate collaboration in the integrative oncology area. Looking forward to your next meeting! |
| We hope to have other meetings! Virtual conferences are OK, but we missed sharing with other people informally, which is a way to increase partnerships. Are we going to have access to presentations? Thank you, Alejandro and team, for this amazing opportunity. |
| Excellent conference. Since some of the questions were directed toward more allied health professionals, in the future, including speakers in behavioral health or nursing may be beneficial. |
| I would like to recommend interactive platforms. |
| Thanks for pivoting to an online format. Given the format, this conference was as good as I could expect. Obviously, the interaction between attendees is the main thing lost with an online format.I look forward to when it is safe for us to return to in-person conferences once again. One thing that was done well was paring down the conference to 3.5 hours—not an easy task—and prioritizing those sessions of most interest to the greatest number of attendees. A suggestion: Allow an opt-in to publish a list of attendees. This can help promote interaction and future collaboration.  |
| Have more of these! |
| I am hoping that all of the materials will be available. I live on the West Coast, so the time zones were EST. I am hoping to have the material to review more on my own time.  |
| This was great organization and content, and we were able to integrate multiple perspectives.We need to synthesize some concrete recommendations to move this field further. |
| Thank you! Overall, this was a terrific meeting! I want to sincerely thank all those who organized the meeting and all those who presented. I somehow managed to attend the entire meeting except for the 10:55 a.m. – 12 p.m. session on Wednesday, when I had to leave to teach a class. I enjoyed and learned from every bit of the meeting that I was able to attend. This meeting will help me with my research and my teaching in Mind-Body Medicine and TCM. I am fortunate to work (in the context of different courses) with undergraduate, graduate, and medical students and residents—almost all of whom show a great interest in this area.With all of the important ideas and recommendations presented over the last 4 days, I would like to highlight what Dr. Geetha Krishnan mentioned briefly in the final session regarding the critically important need for creating a common language and structure. This would facilitate communication between physicians and care providers trained in modern Western medicine and those trained in traditional medical systems. I strongly believe that everyone, and most importantly patients, would benefit tremendously from easy, constant, caring, trusting, and respectful communication between physicians and health care providers coming from different (modern Western and traditional) systems of medicine. It would take some work to make this happen everywhere, and in some cases, the process could be slow and challenging, but the time to start is NOW. Doing this successfully could be the glue that brings and keeps everything together for all of us!Thank you all. I wish everyone the very best and look forward to continuing interactions in this extremely important area, not only for integrative oncology but for medicine as a whole. Please contact me (dhabhar@gmail.com) if you feel that I can help at any point along the way.==================Firdaus S. Dhabhar, Ph.D.ProfessorDepartment of Psychiatry and Behavioral SciencesDepartment of Microbiology and ImmunologySylvester Comprehensive Cancer CenterMiller School of MedicineUniversity of Miami |
| In the next survey, provide an option for “did not attend” since it could have been the case that attendance was not 100%.I didn’t see an option to interact among attendees but rather interact with the speakers.Will the presentations be available for viewing in the future? |
| [I recommend] a regular meeting, maybe every 2 years. |
| Well done. |
| I could not attend much of the conference due to pressing issues in my academic job, hence my non-answers for much of question 5. I look forward to “attending” the recorded sessions. Despite what I thought was a very good effort on the organizers' part, it is clear that a virtual meeting really does not come close to an in-person one. I hope that changes in the year to come! |
| A professional platform like Whova may be considered for future conferences. |
| The Trans-NCI-NIH Conference on International Perspectives on Integrative Medicine for Cancer Prevention and Cancer Patient Management was very successful.Congratulations to the organizers and participants. |
| I would recommend more content focusing on true integration strategies, how difficulties and successes were achieved by integrating Chinese medicine and Ayurveda medicine into integrative oncology care to help patients where allopathic medicine has an overwhelming presence as, mainly, the only acceptable treatment option. There needs to be more input regarding how to incorporate TCM in a truly integrative approach. For example, in Canada, the USA, and Europe, TCM is one of the only truly licensed complementary health care professionals. Ayurveda medicine slowly has an increasing presence within schools that are teaching degrees in this area of expertise. I would recommend a separate conference incorporating expertise from countries in Asia, Europe, the Americas, and Africa that have successfully incorporated these licensed health care professionals into their integrative oncology model of care. What strategies and data are available about including interventions such as herbal treatments before, during, and after medical, radiation, and surgical oncology interventions? Herbal drug interactions from USA TCM expert providers such as John Chen, Pharm.D., L.Ac., Ph.D., OMD. Presentations are from Galina, Roofer Lac from the Cleveland Clinic on integrating TCM into patient’s care in this allopathic center of medicine. |
| Great organization. Thank you. |
| They should have more time to ask questions for each presentation. |
| Provide more information about integrative medicine and precise treatment of tumors. |
| The sequel effort would probably be better done in shorter and more focused meetings (virtual or in-person). |
| This conference was very well organized and conducted by Dr. Alejandro, Dr. Jeffrey, and their teams. It was a wonderful and fruitful experience.Recommendations: 1. Cancer Prevention: Success stories of cancer prevention measures in any region of the world, through lifestyle changes or intervention with integrative oncology, can serve as an inspiration and as guidelines for cancer prevention propaganda and research in LMICs.2. Cancer Patient Management: Guidelines for treatment in various integrative oncology branches to be addressed in groups. 3. Support innovative breakthrough research. Even from individuals in integrative oncology, it is likely to help advance science for future cancer research or treatment and facilitate collaborative research. |
| I loved this conference. As a second-year hematology/oncology fellow, I’m so glad this conference happened and that these resources exist. Some recommendations are to have opportunities for junior physicians, like me, to become more involved. If it is possible to pair us up with mentors. That would be even better. Also, I think it’d be valuable to have some presentations and insight from the Middle East, such as Egypt, Jordan, Iran, Palestine, and Syria. There is a lot of work done here with Unani to shed some more light and research opportunities for participants. Thanks again! |
| I would appreciate it if presentations from Africa are also presented.Also, it would be more engaging if it is in-person instead of virtual, so I pray that things around the world will change quickly. |
| Very well done. |
| This was an amazing space to be in, with so many people worldwide wanting the same outcomes. As a community-based researcher and practitioner, what is frustrating for me is the continued restrictive nature of research to meet the Western medicine RCT standards. Partha Basu brought up possibly needing novel research designs to study natural medicine. If that becomes an active study, please include me. During this conference, what came up for me was that it is somewhat of an insult, to begin with, the hypothesis that a natural practice is no better than a placebo. This takes a profession (something that someone has studied and practiced perhaps all their lives in the indigenous communities) and reduces it to an inert substance. What if we dismissed the whole notion of “does it work?” and began to replace it with “who does it work for?” What if we stopped looking for the control group and replaced it with a waitlist group (who also got the treatment eventually) or simply offered the treatment to everyone (in the case of oncological research) and focused instead on who got better, what got better, and, most importantly, dosages?I want to share this story. I am a professor and researcher of natural health practices. Two-and-a-half years ago, I discovered that I have an early stage carcinoid tumor at the distal end of my small intestine. The surgery seemed radical to me, and I believe in the power of natural health, so I decided to refuse the surgery. I began acupuncture, Chinese herbs, high-dose vitamin C, curcumin, mushrooms (what is the right dosage???), and my somatic movement practices. I also eliminated alcohol, caffeine, meat (for a year), worked on releasing anger, different diets, etc. My continued frustration was that no doctor could find in my insurance network was truly integrative. I went to some natural health practitioners who knew as much as I. I paid over $20K my first year out of my own health care pocket.I have not found a doctor to work with yet. I have had numerous CT and PET scans, blood work, and colonoscopies, but there is no one to compare them all. So, I decided to go see a neuroendocrine tumor oncologist at Mayo Clinic in Rochester, MN. I know, NOT integrative. They looked at everything and concluded that it is “about the same” as 2.5 years ago and recommended surgery. They refused to listen to what I had been doing or give me ANY help (because they don’t have the knowledge) with taking care of this naturally. They told me they could not give me a true size (to truly track its changes), as the technology does not offer that specificity. But the colonoscopy results told me it was 1.6 cm 2.5 years ago. That is pretty specific. I felt unheard again in the Western world.I do believe in the power of the case study. I also believe in the power of shifting paradigms.I was infused with hope after this conference. Maybe I can help in some way to begin to change the paradigm of natural medicine research. Barbara Wesson, Milwaukee, WI |
| Hopefully, we will be able to have a normal conference soon. |
| And enjoy a very well planned and organized meeting. It achieved all the goals it set out. The sessions were well planned, and the speakers were clear, with great presentations. The meeting was very timely and addressed an important issue of incorporating different medical systems toward providing personalized and appropriate treatment for patients.Great format3–4 hours each day was perfect and accommodated all the participants and speakers around the world. Congratulations to the organizers and the speakers!! |
| Very informative.  |
| I would love to have a list of participants, emails, areas of expertise and areas of interest in collaboration, and some sort of virtual meeting place (Facebook? WhatsApp?) to follow up and keep in touch with folks, but it was an excellent 4 days!! Thank you very much!! |

**Appendix B**

Virtual Poster Session

The poster presentations are listed under the following categories: Pharmacology of Traditional Medicine, Global Use of Natural Products in Cancer Patient Management, Global Approaches of Integrative Oncology, Global Integrative Oncology: Use in Cancer Prevention Global Integrative Oncology: Use in Cancer Treatment.

Select the title to view the poster presentation. Be sure to turn up your volume as some presentations have embedded audio. If you have any questions, contact the poster presenter directly.

Pharmacology of Traditional Medicine

1. **Title:** [*Viscum album* L. ethanolic extracts from different host trees show distinct metabolome and antitumor activity through the glycolytic pathway](https://events.cancer.gov/sites/default/files/assets/cgh-iio/posters/Michelle%20Nonato%20de%20Oliveira%20Melo.ppsx)

**Presenter:** Michelle Nonato de Oliveria Melo, Instituto de Química, Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil

[**Abstract**](https://events.cancer.gov/sites/default/files/assets/cgh-iio/abstracts/Poster%20%231.docx)

1. **Title:** [*Viscum album* topic and transdermal formulations: development, stability and *in vitro* cytotoxicity evaluation](https://events.cancer.gov/sites/default/files/assets/cgh-iio/posters/Joao%20Vitor%20da%20Costa%20Batista%20Pharmacology%20of%20Traditional%20Medicine%202020.pptx)

**Presenter:** João Vitor da Costa Batista, Federal University of Rio de Janeiro, Rio de Janeiro, Brazil, and Society for Cancer Research, Switzerland

[**Abstract**](https://events.cancer.gov/sites/default/files/assets/cgh-iio/abstracts/Poster%20%232.docx)

1. **Title:**[*Viscum album* use in pregnant rats – toxicity and safety evaluation](https://events.cancer.gov/sites/default/files/assets/cgh-iio/posters/Presentation%20Ghelman%2C%20Viscum%20album%20use%20in%20pregnant%20rats%20%E2%80%93%20%20toxicity%20and%20safety%20evaluation%20TRANS%20NCI%20NIH.pdf)

**Presenter:**Ricardo Ghelmann, MD, Ph.D., Chair, Brazilian Academic Consortium for Integrative Health, Coordinator, Integrative Pediatrics Unit, Faculty of Medicine, University of São Paulo, Brazil

[**Abstract**](https://events.cancer.gov/sites/default/files/assets/cgh-iio/abstracts/Poster%20%233.docx)

1. **Title:**[Safety evaluation of traditional medicines in Tanzania](https://events.cancer.gov/sites/default/files/assets/cgh-iio/posters/NDAHANI%20-%20%20PowerPoint%20slides%20%20for%20Safety%20evaluation%20of%20traditional%20medicines%20in%20Tanzania..ppt)

**Presenter:**Dr. Ndahani Msigwa, Traditional and Alternative Health Practice Council, Ministry of Health, Community Development, Gender, Elderly and Children, Dodoma, Tanzania

[**Abstract**](https://events.cancer.gov/sites/default/files/assets/cgh-iio/abstracts/Poster%20%234.docx)

1. **Title:**[Screening of Plants Used as Traditional Anticancer Remedies in Mkuranga and Same Districts, Tanzania, Using Brine Shrimp Toxicity Bioassay](https://events.cancer.gov/sites/default/files/assets/cgh-iio/posters/Trans%20NCI-NIH%20Conference%20October%202020.pptx)

**Presenter:**Pax Masimba, Senior Research Fellow, Department of Medical Botany, Plant Breeding and Agronomy, Institute of Traditional Medicine, Muhimbili University of Health and Allied Sciences, Dar es Salaam, Tanzania

[**Abstract**](https://events.cancer.gov/sites/default/files/assets/cgh-iio/abstracts/Poster%20%235.docx)

Global Use of Natural Products in Cancer Patient Management

1. **Title:**[Network pharmacology to unveil the biological basis of Yishengukang decoction in cancer-induced pain treatment](https://events.cancer.gov/sites/default/files/assets/cgh-iio/posters/Lixing%20Liu-Poster.ppt)

**Presenter:**Lixing Liu, Department of Chinese Medicine, Cancer Hospital Chinese Academy of Medical Sciences/National Cancer Center, Beijing, China

[**Abstract**](https://events.cancer.gov/sites/default/files/assets/cgh-iio/abstracts/Poster%20%236.docx)

1. **Title:**[The Prospects of *Croton membranaceus* Mull. Arg. (Euphorbiaceae) and *Momordica charantia* L. in cancer treatment and/or prevention](https://events.cancer.gov/sites/default/files/assets/cgh-iio/posters/NIH%20conference%20presentation.pptx)

**Presenter:**Mavis Boakye-Yiadom, Herbology Researcher, Clinical Research Department, Centre for Plant Medicine Research, Accra, Ghana

[**Abstract**](https://events.cancer.gov/sites/default/files/assets/cgh-iio/abstracts/Poster%20%237%20.docx)

1. **Title:**[Status of traditional medicines in the management of non-communicable diseases in Tanzania](https://events.cancer.gov/sites/default/files/assets/cgh-iio/posters/STATUS%20OF%20TRADITIONAL%20MEDICINES%20FOR%20MANAGEMENT%20OF%20NON%20COMMUNICABLE%20DISEASES%20IN%20TANZANIA%20-%20LUCY%20S.%20MZIRAY%20-%20NEW.ppt)

**Presenter:**Lucy Samwell, Traditional Medicine Section, Directorate of Curative Services, Ministry of Health, Community Development, Gender, Elderly and Children, Dar es Salaam, Tanzania

[**Abstract**](https://events.cancer.gov/sites/default/files/assets/cgh-iio/abstracts/Poster%20%238%20.docx)

1. **Title:**[Bitter Melon’s sweet promise: a novel chemopreventive agent by rejuvenating immune system and reprogramming of metabolism in oral](https://events.cancer.gov/sites/default/files/assets/cgh-iio/posters/Subhayan%20Sur_%20Poster_NIH2020.pptx) cancer

**Presenter:**Subhayan Sur, Department of Pathology, Saint Louis University, Saint Louis, Missouri, USA

[**Abstract**](https://events.cancer.gov/sites/default/files/assets/cgh-iio/abstracts/Poster%20%239%20.docx)

1. **Title:**[Preferential activity of *Petiveria alliacea* extract on primary myeloid leukemic blast](https://events.cancer.gov/sites/default/files/assets/cgh-iio/posters/Ballesteros-Ramirez%20et%20al%2C%2CNIC-NIH%20Conference%20Poster%20Presentation.pptx)

**Presenter:**Ricardo Ballesteros-Ramirez, Pontificia Universidad Javeriana, Colombia

[**Abstract**](https://events.cancer.gov/sites/default/files/assets/cgh-iio/abstracts/Poster%20%2310%20.docx)

1. **Title:**[Safety Evaluation in Healthy Colombian Volunteers of P2Et Extract Obtained from *Caesalpinia Spinosa*: Design 3+3 Phase I Clinical Trial](https://events.cancer.gov/sites/default/files/assets/cgh-iio/posters/Duran%20MI%20et%20al%2C%20NCI-NIH%20IO%2029092020.pptx)

**Presenter:**Maria Duran, Pontificia Universidad Javeriana, Colombia

[**Abstract**](https://events.cancer.gov/sites/default/files/assets/cgh-iio/abstracts/Poster%20%2311.docx)

1. **Title:**[Plant extract P2Et from *Caesalpinia Spinosa* inhibits *in vitro* generation of Cancer-Associated Fibroblasts](https://events.cancer.gov/sites/default/files/assets/cgh-iio/posters/Prieto%20K%20et%20al%2C%20NIC-NIH%20Conference%20Poster%20Presentation.pptx)

**Presenter:**Karol Mildred Prieto Sarmiento, Pontificia Universidad Javeriana, Colombia

[**Abstract**](https://events.cancer.gov/sites/default/files/assets/cgh-iio/abstracts/Poster%20%2312.docx)

Global Approaches to Integrative Oncology

1. **Title:**[Music therapy (MT) in Argentina for adult patients with Hematologic malignancies (APHM): challenges and opportunities](https://events.cancer.gov/sites/default/files/assets/cgh-iio/posters/Sofia%20Mountford%20-%20Poster%20Presentation.pptx)

**Presenter:**Sofia Mountford, Researcher at FUNDALEU, Buenos Aires, Argentina

[**Abstract**](https://events.cancer.gov/sites/default/files/assets/cgh-iio/abstracts/Poster%20%2313%20.docx)

1. **Title:**[Integrative Oncology in the Region of Tuscany: a Successful Integration in Public Health](https://events.cancer.gov/sites/default/files/assets/cgh-iio/posters/%2814%29%20Bethesda%202020%20%28I%29%20-%20Integrative%20Oncology%20Tuscany%20Region-2.pptx)

**Presenter:**Elio Rossi, MD, Clinic for Complementary Medicine and Diet in Oncology, North-Western Tuscan Local Health Authority, Lucca, Italy, Regional Center for Integrative Medicine, Region of Tuscany, Italy

[**Abstract**](https://events.cancer.gov/sites/default/files/assets/cgh-iio/abstracts/Poster%20%2314%20.docx)

1. **Title:**[Patients Refusing Anticancer Treatments and Complementary and Integrative Medicine](https://events.cancer.gov/sites/default/files/assets/cgh-iio/posters/%2815%29%20Bethesda%202020%20%28II%29%20-%20Patients%20Refusing%20Anticancer%20Treatments%20and%20CIM.pptx)

**Presenter:**Elio Rossi, MD, Clinic for Complementary Medicine and Diet in Oncology, North-Western Tuscan Local Health Authority, Lucca, Italy, Regional Center for Integrative Medicine, Region of Tuscany, Italy

[**Abstract**](https://events.cancer.gov/sites/default/files/assets/cgh-iio/abstracts/Poster%20%2315%20.docx)

1. **Title:**[PRINTER: Support and Revitalization Program in Integrative Oncology in Northern Brazil](https://events.cancer.gov/sites/default/files/assets/cgh-iio/posters/poster_Trans%20NCI-NIH%20%281%29.pdf)

**Presenter:**Paola Tôrres Costa, Brazilian Academic Consortium for Integrative Health Fortaleza, Ceará, Brazil

[**Abstract**](https://events.cancer.gov/sites/default/files/assets/cgh-iio/abstracts/Poster%20%2316%20.docx)

1. **Title:**[Acupuncture as a complementary therapy to minimize symptoms in cancer patients: a pilot study](https://events.cancer.gov/sites/default/files/assets/cgh-iio/posters/17%20Poster%20%20Acupuncture%20Sterline.ppt)

**Presenter:**Sterline Therrier, Nursing Graduate Program, Universidade Federal de Alfenas, Minas Gerais, Brazil

[**Abstract**](https://events.cancer.gov/sites/default/files/assets/cgh-iio/abstracts/Poster%20%2317%20.docx)

1. **Title:**[Perception of the patient undergoing cancer treatment on relaxation with guided visualization](https://events.cancer.gov/sites/default/files/assets/cgh-iio/posters/18%20Poster%20relaxation%20Sterline.ppt)

**Presenter:**Sterline Therrier, Nursing Graduate Program, Universidade Federal de Alfenas, Minas Gerais, Brazil

[**Abstract**](https://events.cancer.gov/sites/default/files/assets/cgh-iio/abstracts/Poster%20%2318%20.docx)

1. **Title:**[Breast Cancer and use of complementary therapies in the Chilean’s National Health Survey 2016–17](https://events.cancer.gov/sites/default/files/assets/cgh-iio/posters/NIH%20Breast%20Cancer%20and%20use%20of%20CT_PB_VL.pptx)

**Presenter:**Paula Bedregal, Ph.D., M.P.H., Associate Professor, Pontificia Universidad Catolica de Chile, Division of Public Health and Family Medicine, Santiago, Chile

[**Abstract**](https://events.cancer.gov/sites/default/files/assets/cgh-iio/abstracts/Poster%20%23%2019%20.docx)

1. **Title:**[Acupuncture in the treatment of cancer pain in a Chilean public Hospital](https://events.cancer.gov/sites/default/files/assets/cgh-iio/posters/Acupuncture%20in%20the%20treatment%20of%20cancer%20pain%20-%20CHILE.pptx)

**Presenter:**Sebastian Norambuena, Acupuncturist, Integrative Medicine Unit of the Sótero del Río Hospital, Santiago, Chile

[**Abstract**](https://events.cancer.gov/sites/default/files/assets/cgh-iio/abstracts/Poster%20%2320%20.docx)

1. **Title:**[Health Care Quality of Peruvian Breast Cancer Patients](https://events.cancer.gov/sites/default/files/assets/cgh-iio/posters/21%20Health%20Care%20Quality%20of%20Peruvian%20Breast%20Cancer%20Patients%20-%20Dr%20Juan%20Huaccho-Rojas.pptx)

**Presenter:**Juan Huaccho-Rojas, Faculty of Human Medicine, Universidad San Martin de Porres, Lima, Peru

[**Abstract**](https://events.cancer.gov/sites/default/files/assets/cgh-iio/abstracts/Poster%20%2321.docx)

1. **Title:**[Quality of Life of Peruvian Breast Cancer Patients](https://events.cancer.gov/sites/default/files/assets/cgh-iio/posters/22%20Quality%20of%20Life%20for%20Peruvian%20Breast%20Cancer%20Patients%20-%20Dr%20Juan%20Huaccho-Rojas.pptx)

**Presenter:**Juan Huaccho-Rojas, Faculty of Human Medicine, Universidad San Martin de Porres, Lima, Peru

[**Abstract**](https://events.cancer.gov/sites/default/files/assets/cgh-iio/abstracts/Poster%20%2322%20.docx)

1. **Title:**[Identifying Whole-Person Traditional Medical System Therapeutic Relationship Themes in Long-Term Breast Cancer Survivorship: Implications for Integrative Patient-Centered Care](https://events.cancer.gov/sites/default/files/assets/cgh-iio/posters/23%20TherapeuticRelationshipTheemes_PCC_NCI-CGH_assub.pptx)

**Presenter:**Vinita Agarwal, Ph.D., Salisbury University, Salisbury, Maryland, USA

[**Abstract**](https://events.cancer.gov/sites/default/files/assets/cgh-iio/abstracts/Poster%20%2323%20.docx)

1. **Title:**[Conceptualizing Pain in Ayurvedic Protocols for Chronic Pain Management: A Case Study of Ayurvedic Physicians from India](https://events.cancer.gov/sites/default/files/assets/cgh-iio/posters/24%20ConceptualizingPain_AyurvedaProtocolsPainManagement_NIH-CGA_assub.pptx)

**Presenter:**Vinita Agarwal, Ph.D., Salisbury University, Salisbury, Maryland, USA

[**Abstract**](https://events.cancer.gov/sites/default/files/assets/cgh-iio/abstracts/Poster%20%2324%20.docx)

1. **Title:**[International Center for Indigenous Phytotherapy Studies (TIPS) RCTs in South Africa](https://events.cancer.gov/sites/default/files/assets/cgh-iio/posters/Folk%20Trans%20NCI-NIH%20PP.pptx)

**Presenter:**William Folk, College of Agriculture, Food and Natural Resources, University of Missouri, Columbia, Missouri, USA

[**Abstract**](https://events.cancer.gov/sites/default/files/assets/cgh-iio/abstracts/Poster%20%2325.docx)

1. **Title:**[Traditional medicine in poor urban communities in India: a resource for prevention and early detection of oral cancer](https://events.cancer.gov/sites/default/files/assets/cgh-iio/posters/NCI%20NIH%20%28v4%29.pptx)

**Presenter:**Stephen L. Schensul, Ph.D., University of Connecticut, School of Medicine, Farmington, Connecticut, and Jean J. Schensul, Ph.D., Institute for Community Research, Hartford, Connecticut, USA

[**Abstract**](https://events.cancer.gov/sites/default/files/assets/cgh-iio/abstracts/Poster%20%2326%20.docx)

1. **Title:**[Palliative Care Link (mPCL): Examination of a digital solution to palliative care coordination among Tanzanian cancer patients](https://events.cancer.gov/sites/default/files/assets/cgh-iio/posters/NIH-NCI%20conference%20mPCL-comment%283%29.pptx)

**Presenter:**Mamsau Ngoma, Ocean Road Cancer Institute, Dar es Salaam, Tanzania

[**Abstract**](https://events.cancer.gov/sites/default/files/assets/cgh-iio/abstracts/Poster%20%2327%20.docx) **SEEMS TO BE A REPEAT OF 36**

1. **Title:**[FIPOL: An Initiative to Develop Networks, Collaborations, and Educational Opportunities in Psychosocial Oncology for Latin America](https://events.cancer.gov/sites/default/files/assets/cgh-iio/posters/FIPOL%20Pres%20NIH%202020%20IntOnc%20conference.pptx)

**Presenter:**Rosario Costas-Muñiz, Memorial Sloan Kettering Cancer Center, New York, New York, USA

[**Abstract**](https://events.cancer.gov/sites/default/files/assets/cgh-iio/abstracts/Poster%20%2328%20.docx)

Global Integrative Oncology: Use in Cancer Prevention

1. **Title:**[Prostate cancer screening perception, beliefs, and practices among men in Bamenda, Cameroon](https://events.cancer.gov/sites/default/files/assets/cgh-iio/posters/Ernie%20Kaninjing_Prostate%20Cancer%20Screening%20Perceptions%2C%20Beliefs%20and%20Practices.pptx)

**Presenter:**Ernie Kaninjing, Dr.P.H., M.P.H., CHES, Assistant Professor, Public Health, School of Health and Human Performance, Georgia College, Milledgeville, Georgia, USA

[**Abstract**](https://events.cancer.gov/sites/default/files/assets/cgh-iio/abstracts/Poster%20%23%2029.docx)

1. **Title:**[Prevalence, incidence, and distribution of human papillomavirus types in female sex workers in Kenya](https://events.cancer.gov/sites/default/files/assets/cgh-iio/posters/PrevalenceIncidenceHPVtypes%20in%20FSW_BosireC.pptx)

**Presenter:**Claire Bosire, Sc.D., MSPH, RD, Postdoctoral Fellow, Cancer Health Disparities Program, Department of Health Behavior, Gillings School of Global Public Health, University of North Carolina at Chapel Hill, North Carolina, USA

[**Abstract**](https://events.cancer.gov/sites/default/files/assets/cgh-iio/abstracts/Poster%20%2330%20.docx)

1. **Title:**[Potential mHealth application for cancer prevention in Cambodians living with HIV](https://events.cancer.gov/sites/default/files/assets/cgh-iio/posters/IMCP%20Poster_200924.pptx)

**Presenter:**Thanh Cong Bui, M.D., Dr.P.H., Assistant Professor of Research, University of Oklahoma Health Sciences Center, Stephenson Cancer Center, Oklahoma Tobacco Research Center, Oklahoma City, Oklahoma, USA

[**Abstract**](https://events.cancer.gov/sites/default/files/assets/cgh-iio/abstracts/Poster%20%2331.docx)

1. **Title:**[Clinician Perspectives of Complementary and Integrative Medicine (CIM) at an Academic Cancer Center](https://events.cancer.gov/sites/default/files/assets/cgh-iio/posters/Poster_32_Updated_10.19.2020.pptx)

**Presenter:**Marium Husain, MD, MPH, Ohio State University, James Comprehensive Cancer Center, Hematology/Oncology Fellow, Riverside Methodist Hospital, Internal Medicine, Ohio State University, College of Medicine, Columbus, Ohio, USA

[**Abstract**](https://events.cancer.gov/sites/default/files/assets/cgh-iio/abstracts/Poster%20%2332%20and%20%2343%20repeat.docx)**SEEMS TO BE A REPEAT OF 43**

1. **Title:**[Step up to health, Nigeria! Utilizing information from Abuja’s 2020 World Cancer Day Walk for equity-based cancer prevention interventions](https://events.cancer.gov/sites/default/files/assets/cgh-iio/posters/Step%20up%20to%20Health%2C%20Nigeria%20power%20point%20with%20audio.pptx)

**Presenter:**Leigh Leibel, M.Sc., Integrative Oncology, Division of Hematology/ Oncology, Columbia University Irving Medical Center, New York, New York, USA

[**Abstract**](https://events.cancer.gov/sites/default/files/assets/cgh-iio/abstracts/Poster%20%2333.docx)

1. **Title:**[Molecular pathways of IL-16 in relation to cancer therapy and prevention: An integrative approach examining its mechanisms of immune regulation in neurological diseases and experimental autoimmune encephalomyelitis (EAE)](https://events.cancer.gov/sites/default/files/assets/cgh-iio/posters/NCI%2C%20NIH%2C%202020.ppt)

**Presenter:**Dusanka Skundric, MD, Ph.D., Department of Biochemistry, Microbiology, and Immunology, School of Medicine, Wayne State University, Detroit, Michigan, USA

[**Abstract**](https://events.cancer.gov/sites/default/files/assets/cgh-iio/abstracts/Poster%20%2334%20.docx)

1. **Title:**[Biological and Demographic Factors Influencing Stage at Diagnosis of Cervical Cancer in Botswana](https://events.cancer.gov/sites/default/files/assets/cgh-iio/posters/Friebel_Klingner_Factors%20associated%20with%20late%20stage%20CC%20in%20Botswana.pptx)

**Presenter:**Tara Friebel, M.P.H., Doctoral Candidate in Epidemiology, University of Pennsylvania, Philadelphia, Pennsylvania, USA

[**Abstract**](https://events.cancer.gov/sites/default/files/assets/cgh-iio/abstracts/Poster%20%2335%20.docx)

1. **Title:**[Palliative Care Link (mPCL): Examination of a digital solution to palliative care coordination among Tanzanian cancer patients](https://events.cancer.gov/sites/default/files/assets/cgh-iio/posters/36NIH-NCI%20conference%20mPCL-comment%283%29.pptx)

**Presenter:**Mamsau Ngoma, Ocean Road Cancer Institute, Dar es Salaam, Tanzania

[**Abstract**](https://events.cancer.gov/sites/default/files/assets/cgh-iio/abstracts/Poster%20%2336.docx)**SEEMS TO BE A REPEAT OF 27**

1. **Title:**[Characterization of Normal Cell and Cancer Cell Attachment Using Electric Impedance Sensing](https://events.cancer.gov/sites/default/files/assets/cgh-iio/posters/Maddy%20Behravan-NCI%20NIH-09%2027%202020.ppt)

**Presenter:**Maddy Behravan, Assistant Professor, Biology, Chemistry, and Physics Department, Converse College, Spartanburg, South Carolina, USA

[**Abstract**](https://events.cancer.gov/sites/default/files/assets/cgh-iio/abstracts/Poster%20%2337%20.docx)

1. **Title:**[A preventive vaccine targeting both Human papillomavirus α genotypes causing anogenital cancers and β genotypes causing non-melanoma skin cancers](https://events.cancer.gov/sites/default/files/assets/cgh-iio/posters/20200929%20Olczak%20NIH%20conference_0.pptx)

**Presenter:**Pola Olczak, Department of Pathology, Johns Hopkins University, Baltimore, Maryland, USA

[**Abstract**](https://events.cancer.gov/sites/default/files/assets/cgh-iio/abstracts/Poster%20%2338%20.docx)

Global Integrative Oncology: Use in Cancer Treatment

1. **Title:**[Supportive Oncology Metabolic Syndrome Clinic Within Integrative Oncology](https://events.cancer.gov/sites/default/files/assets/cgh-iio/posters/NIH%20Poster%20Metabolic%20Clinic_9.30.20_SUBMITTED.pptx)

**Presenter:**Danielle Gentile, Ph.D., Health Services Researcher, Assistant Professor of Medicine, Department of Supportive Oncology, Levine Cancer Institute, Atrium Health, Charlotte, North Carolina, USA

[**Abstract**](https://events.cancer.gov/sites/default/files/assets/cgh-iio/abstracts/Poster%20%2339%20.docx)

1. **Title:**[The immunotherapeutic potential of soy extract in the treatment of urothelial carcinoma of the bladder](https://events.cancer.gov/sites/default/files/assets/cgh-iio/posters/Lifschutz_Brian%20The%20immunotherapeutic%20potential%20of%20soy%20extract%20in%20the%20treatment%20of%20bladder%20cancer.pptx)

**Presenter:**Brian Lifschutz, Des Moines University College of Osteopathic Medicine, Des Moines, Iowa, USA

[**Abstract**](https://events.cancer.gov/sites/default/files/assets/cgh-iio/abstracts/Poster%20%2340%20.docx)

1. **Title:**[The popular vegetable asparagus’s surprising pro-tumor effect on pancreatic cancer](https://events.cancer.gov/sites/default/files/assets/cgh-iio/posters/Jacob%20Hough%20NCI_NIH%20Presentation%20%281%29%20%281%29.pptx)

**Presenter:**Jacob Hough, Department of Microbiology, Immunology, Des Moines University College of Osteopathic Medicine, Des Moines, Iowa, USA; Department of Surgery, University of Missouri School of Medicine, Columbia, Missouri, USA

[**Abstract**](https://events.cancer.gov/sites/default/files/assets/cgh-iio/abstracts/Poster%20%2341.docx)

1. **Title:**[Everyday Spice, Cilantro, Exhibits Promising Health Benefits Against Lung Cancer](https://events.cancer.gov/sites/default/files/assets/cgh-iio/posters/Vlad%20Husyev%20NCI_NIH%20presentation.pptx)

**Presenter:**Vlad Husyev, Department of Microbiology, Immunology, and Pathology, Des Moines University College of Osteopathic Medicine, Des Moines, Iowa, USA; Department of Surgery, University of Missouri School of Medicine, Columbia, Missouri, USA

[**Abstract**](https://events.cancer.gov/sites/default/files/assets/cgh-iio/abstracts/Poster%20%2342.docx)

1. **Title:**[Clinician Perspectives of Complementary and Integrative Medicine (CIM) at an Academic Cancer Center](https://events.cancer.gov/sites/default/files/assets/cgh-iio/posters/Poster_43_Updated_10.19.2020.pptx)

**Presenter:**Marium Husain, MD, MPH, Ohio State University, James Comprehensive Cancer Center, Hematology/Oncology Fellow Riverside Methodist Hospital, Internal Medicine, Ohio State University College of Medicine, Columbus, Ohio, USA

1. **Title:**[A randomized controlled pilot study of a yoga skills training compared to an attention control implemented in the clinic during chemotherapy](https://events.cancer.gov/sites/default/files/assets/cgh-iio/posters/Sohl_Trans-NCI-NIH%20091720.pptx)

**Presenter:**Stephanie Sohl, Wake Forest School of Medicine, Winston-Salem, North Carolina, USA

[**Abstract**](https://events.cancer.gov/sites/default/files/assets/cgh-iio/abstracts/Poster%20%2344.docx)

1. **Title:**[An immunomodulatory gallotanin-rich fraction from *Caesalpinia Spinosa* enhances the therapeutic effect of anti-PD-L1 in melanoma](https://events.cancer.gov/sites/default/files/assets/cgh-iio/posters/Lasso%20et%20al%20290920%20V1.pptx)

**Presenter:**Paola Lasso, Pontificia Universidad Javeriana, Colombia

[**Abstract**](https://events.cancer.gov/sites/default/files/assets/cgh-iio/abstracts/Poster%20%2345.docx)

1. **Title:**[Effect of P2Et extract alone or in combination with chemotherapy in ex-vivo derived tumor organoids from breast cancer patients](https://events.cancer.gov/sites/default/files/assets/cgh-iio/posters/Urue%C3%B1a%20et%20al%2C%20NIC-NIH%20Conference%20Poster%20Presentation.pptx).

**Presenter:**Claudia Urena, Pontificia Universidad Javeriana, Colombia

[**Abstract**](https://events.cancer.gov/sites/default/files/assets/cgh-iio/abstracts/Poster%20%2346%20.docx)

1. **Title:**[Cranberry: a powerful anti-cancer superfruit for patients with lung adenocarcinoma](https://events.cancer.gov/sites/default/files/assets/cgh-iio/posters/Cranberry%27s%20are%20a%20powerful%20anti-cancer%20superfruit%20for%20patients%20with%20lung%20adenocarcinoma%20speech%20%281%29.pptx)

**Presenter:**Marco Lequio, Des Moines University, Des Moines, Iowa, USA; University of Missouri, Columbia, Missouri, USA

[**Abstract**](https://events.cancer.gov/sites/default/files/assets/cgh-iio/abstracts/Poster%20%2347%20.docx)

1. **Title:**[Intermittent Fasting for ovarian cancer reduction](https://events.cancer.gov/sites/default/files/assets/cgh-iio/posters/RattanR_Poster.pdf)

**Presenter:**Ramandeep Rattan, Ph.D., Associate Scientist, Gynecology Oncology, Women’s Health Services, Henry Ford Hospital, Detroit, Michigan, USA

[**Abstract**](https://events.cancer.gov/sites/default/files/assets/cgh-iio/abstracts/Poster_%2348.docx)

**General Information**

**For logistics questions**, contact Jessica Freer at jfreer@seiservices.com.

**For program questions**, contact Dr. Alejandro Salicrup, Senior Advisor for Global Health Research, Center for Global Health and OCCAM-DCTD, National Cancer Institute, National Institutes of Health luis.salicrup@nih.gov.