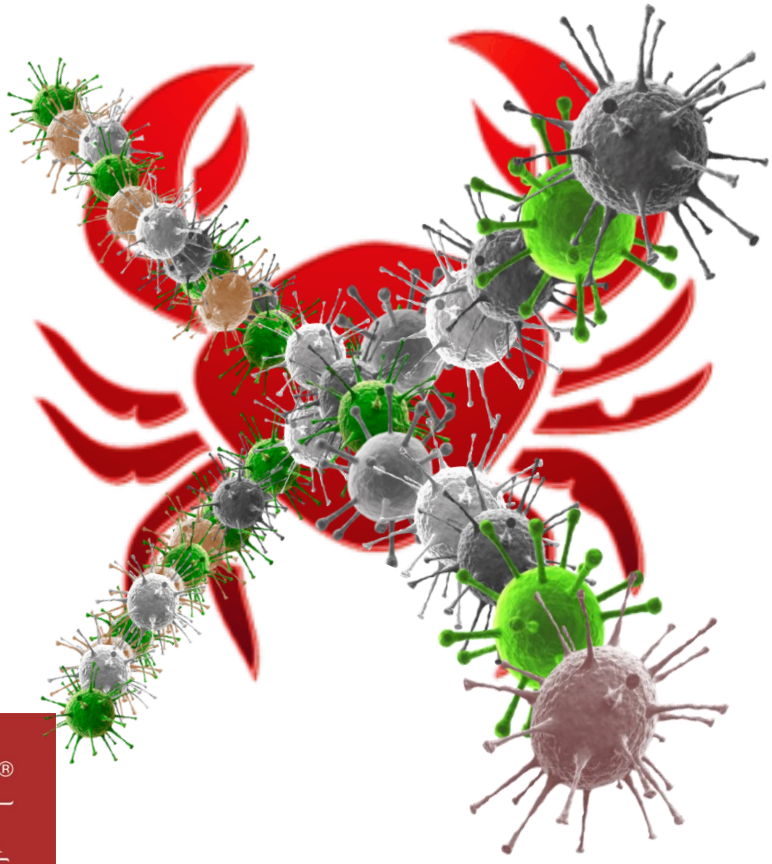
NCI Microbial Based Cancer Therapy Conference



Technologies to Overcome Cancer Challenges

Conference sponsored by the National Cancer Institute

July 11-12, 2017

Natcher Center, NIH campus- Building 45, Bethesda, Maryland

Wednesday, June 28, 2017

On behalf of the National Cancer Institute and the conference organizing committee, I welcome the attendees and the speakers to the "Microbial based cancer therapy" conference, which was initiated by the NCI Office of Cancer Complementary and Alternative Medicine.

While microbial based therapy is one of the oldest cancer therapy modalities, dating from the bacterial therapies of the late 19th and early 20th centuries, the subject is not well studied and research has yielded few effective and safe cancer treatments. Recent scientific advances in tumor biology, microbial pathogenesis, cancer immunity and new molecular tools make it possible to revisit the old concept from new perspectives, utilizing current scientific technologies.

At this conference, which is the first NIH-sponsored comprehensive meeting on this topic, speakers will describe the complex nature of the microbe-tumor interaction and discuss recent advances in the field. The goal is to present current research and to stimulate new research to harness the unique potential of viruses and bacteria to invade, damage or destroy human cells and induce immune responses to create new safe and effective therapeutic approaches to selectively eliminate cancer cells.

The conference's agenda includes sessions on the biology of microbe-tumor interactions, virus- and bacteria-based therapies, and translational aspects of microbial-based therapies. One of the main themes is highlighting opportunities for microbial based therapy where conventional therapy is inadequate such as tumor cell dormancy, tumor cells that are not well accessed by drugs, hypoxia or poorly vascularized tumors.

More than 550 scientists, from academia, industry and government, have registered for this multidisciplinary conference. A working group from across the NCI has brought together staff from the Divisions of Cancer Biology, Cancer Treatment and Diagnosis, Cancer Prevention and the NCI Small Business Innovation Research program to plan and support this important meeting.

I hope that the conference will stimulate more research interest in the field and unleash new tools based on bacteria and viruses against cancer, augmenting NCI's efforts to find novel approaches to combat cancer.

Best regards,

Jeffrey D. White, M.D.
Director, Office of Cancer Complementary and Alternative Medicine
Division of Cancer Treatment and Diagnosis
National Cancer Institute, NIH

NCI Microbial Based Cancer Therapy Conference

Natcher Conference Center, July 11-12, 2017

Day 1, July 11

8:30-8:45 AM Welcome
Jeffrey D. White, Director, NCI Office of Cancer Complementary and Alternative Medicine

8:45-9:20 Keynote Speaker: Microbial based cancer therapy
Robert M. Hoffman, Univ. of California San Diego and AntiCancer, Inc.

9:20 -11:35 Modes of action of microbial mediated cancer therapy

Chairs: Robert Mufson, DCB/NCI; Phil Daschner, DCB/NCI; Steve Nothwehr, DCTD/NCI; Steve Thorne, Univ. of Pittsburgh

9:20-9:45 Engineered Salmonella for Drug Delivery to Solid Tumor
Neil S. Forbes, Univ. of Massachusetts Amherst

9:45-10:10 *In situ* vaccination for cancer immunotherapy: treat locally, respond systemically
Steve Fiering, Geisel School of Medicine at Dartmouth

10:10-10:25 Break

10:25-10:50 Oncolytic viruses as novel, multi-mechanistic immunotherapies
Steve Thorne, Univ. of Pittsburgh

10:50-11:15 Viral Vectors as Vaccines Targeting Cancer Antigens
Kim Lyerly, Duke Univ.

11:15-11:35 Panel Discussion

11:35-1:30 *LUNCH and POSTER SESSION*

1:30-4:45 Bacterial based cancer therapy

Chairs: Elad Sharon, DCTD/NCI; Jacob Kagan, DCP/NCI; Daniel A. Saltzman, Univ. of Minnesota

1:30-1:55 Site-Specific Immunomodulators: Harnessing the Intrinsic Immune Capacity to Prevent and Fight Malignancy
Hal Gunn, Qu Biologics

1:55-2:20 Tumor-Targeting *Salmonella typhimurium* A1-R
Robert M. Hoffman, niv. of California San Diego and AntiCancer, nc.

2:20-2:45 Therapy with Oncolytic Bacterium *Clostridium novyi-NT*: From Mice to Men
Shibin Zhou, Johns Hopkins Univ.

2:45-3:00 Break

3:00-3:25 *Salmonella* derived immunotherapy for solid malignancies
Daniel A. Saltzman, University of Minnesota/SALSPERA LLC.

3:35-4:00 Vectors to Guide Anti-Tumor Immune Responses
James L. Gulley, NIH

4:00-4:25 TBD
Tom Dubinsky, Aduro Biotech, Inc.

4:25-4:45 Panel Discussion

Day 2, July 12

8:30-8:35 AM Welcome

8:35 -10:45 Cancer virotherapy

Chairs: Jason Yovandich, DCTD/NCI

8:35-9:00 T-VEC, an oncolytic *Herpes virus* for melanoma treatment.
Robert H. I. Andtbacka, Univ. of Utah

9:00-9:25 Targeted Adenoviruses at the Level of Infection: Development and Application, Masato Yamamoto, University of Minnesota

9:25-9:50 Developing immunomodulatory anti-cancer vectors from tiny viruses
Peter Tattersall, Yale Univ. School of Medicine

9:50-10:05 Break

10:05-10:30 MAP3K7 and CHD1 are novel mediators of resistance to VSV oncolysis in prostate cancer, David A. Ornelles, Wake Forest School of Medicine

10:30-10:45 Panel Discussion

10:45-11:45 Poster oral presentations. *Chair Claudia Gravekamp, Albert Einstein College of Medicine*

1. Tumor localized inhibition of the PD1/PDL1 checkpoint enhances the efficacy of oncolytic *myxoma* virus against both local and metastatic melanoma; Eric Bartee, Medical Univ. of South Carolina
2. Attenuated LListeria monocytoenes as a delivery platform in cancer immnotherapy. Cladia GGravekamp, Albert EEinstein College of Medicine
3. Engineered *Reoviruses* Have Enhanced Oncolytic Properties Against Triple-Negative Breast Cancer; Bernardo A. Mainou, Emory Univ.
4. Reenergized Adoptive Cell Transfer (ReACT)- A Multi-Pronged Strategy to Treat Solid Tumors; Weiguo Cui, Blood Center of Wisconsin
5. Cancer therapy in a microbial bottle: Uncorking the remarkable anti-cancer biology of *Toxoplasma gondii*; David J. Bzik, Geisel School of Medicine at Dartmouth
6. Cloud-based Microbe Identification and Characterization Pipeline; Hsinyi Tsang, National Cancer Institute

11:45-12:40 *LUNCH*

12:40-15:20 Bringing microbial based cancer therapy to the patient: Industrial research efforts

Chairs: Min He, DCTD/NCI; Jonathan Franca-Koh, SBIR/NCI; Grant McFadden, Biodesign Institute

12:40-1:05 Translational and clinical development of Clostridium novyi-NT
Halle H. Zhang, BioMed Valley Discoveries, Inc.,

1:05-1:30 Cancer bacterial vaccines - live, attenuated strains of *Listeria* and *Salmonella* as vaccine vectors in cancer treatment
Michael F Princiotta, Advaxis, Inc.

1:30 1:45 Break

1:45-2:10 Clinical Considerations on Microbes-based Cancer Therapy - a Regulatory Perspective
Ke Liu, CBER/FDA

2:10-2:35 Bacterial minicell-based oncolytic therapy for non-muscle invasive bladder cancer and beyond
Matthew Giacalone, Vaxiion Therapeutics

2:35-3:00 *Ex vivo* virotherapy with oncolytic *Myxoma Virus* improves cancer-free outcomes after either allo- or auto- hematopoietic stem cell transplantation
Grant McFadden, Biodesign Institute, Arizona State Univ.,

3:00-3:20 Panel Discussion

POSTER SESSION

No	Name	Title
		Cancer virotherapy
1	Eric Bartee	Tumor localized inhibition of the PD1/PDL1 enhances the efficacy of oncolytic myxoma
2	David A. Ornelles	MAP3K7 and CHD1 are novel mediators of resistance to VSV oncolysis in prostate cancer
3	Lauren Oldfield	Rapid, genome-wide modification of herpesvirus genomes using synthetic genomics methods
4	Bernardo A. Mainou	Reoviruses Have Enhanced Oncolytic Properties Against Triple-Negative Breast Cancer
5	Liang Deng	Intratumoral delivery of inactivated modified vaccinia virus Ankara (iMVA)
6	Liang Deng	Intratumoral Delivery of Modified Vaccinia Virus Ankara Expressing Human Flt3L
7	Kate Chiappinelli	Epigenetic control of endogenous retroviruses in cancer: implications for immune therapy
8	Biswajit Biswas	Therapeutic and Prophylactic Applications of Bacteriophages in Cancer Therapy
9	Ann B. Hill	Cytomegalovirus-based vaccines in breast and melanoma mouse tumor models
9b	Jorge G. Gomez Gutierrez	Enhancement of Triple Negative Breast Cancer Virotherapy via Alkylating Agent-Induced Autophagy
		Bacteria and eukaryotes based cancer therapy
10	Abel Baerga-Ortiz	Direct detection of genotoxic or pro-inflammatory bacterial genes in stool samples
11	Adam Fisher	Modulation of the Tumor Microenvironment using Synthetic Biotics™
12	Hassan Brim	Gut microbiome analysis reveals dysbiosis in sickle cell diseases patients with veillonella
13	Weiguo Cui	Reenergized Adoptive Cell Transfer -A Multi-Pronged Strategy to Treat Solid Tumors
14	David J. Bzik	Uncorking the remarkable anti-cancer biology of Toxoplasma
15	Jill Zeilstra-Ryalls	Developing a photosynthetic bacterial vector for intratumorial photodynamic therapy
16	Greg Phillips	Use of a gnotobiotic mouse model to characterize bacteria/colorectal tumor interactions
17	Wei Kong	TRAIL-armed Self-destructing *Salmonella* serve as “Time-Bombs” to Combat Cancer
18	Bin Xue	Multiple Responding Mechanisms in Intestinal Cancer Tissues Mediated by Microbiome
19	Shiladitya DasSarma	An Archaeal Therapeutic Drug and Antigen Delivery Employing Proteinaceous Nanoparticles
20	Qiuhong He	Loss of Cancer Immune Privilege in Bacterial-based Therapy
21	Roger A Laine	Bacterial Secreted Polysaccharide Toxins Bind to Sialin on Tumor Capillary Endothelium
22	Gilad Bachrach	Tumor targeting by *Fusobacterium nucleatum*
23	Mark Gomelsky	Optogenetic and chemogenetic platforms for listeria-mediated intratumoral drug delivery
24	Alejandro Alice	Vγ9Vδ2 T cells dominate the response to Listeria monocytogenes-based vaccines
25	Shifeng Wang	Regulated invasion, chemotaxis, attenuation and endotoxicity of Salmonella

Technologies to Support Research on Microbial based cancer therapy

NCI Conference on Microbial-Based Cancer Therapy

July 11th - 12th, 2017

Natcher Conference Center, NIH campus - Building 45
Bethesda, Maryland 20894

Microbial-based cancer therapy is an old concept that dates from the 19th century using live and heat-killed bacteria with reported effectiveness. As a treatment, microbial-based therapies for cancer were discontinued in the 1930's because of side effects, toxicity, varied effectiveness, limited reproducibility and the advancement of radiotherapy and later chemotherapy.

However, the scientific advances in the last decades make it timely to revisit microbial-based cancer therapy from new perspectives. There are new research molecular tools and tremendous amounts of new scientific knowledge about cancer and microorganisms that can provide insights into ways of tapping the potential of microbial-based cancer therapy.

One important motivating factor for revisiting the concept of microbial cancer therapy is that there are areas that existing cancer therapies cannot address. While most existing cancer therapies have a single mode of action, oncolytic viruses are a new class of therapeutic agents with a dual mechanism of action; selective tumor cell killing and induction of systemic anti-tumor immunity. Moreover, current cancer treatments, such as chemotherapy and radiation therapy, continue to have limited efficacy due to their relative lack of specificity in targeting tumor cells, tumor cell dormancy, accessibility of the drug to tumor cells or hypoxia as these therapies predominantly target the well-vascularized active component of tumors limiting the effectiveness of conventional therapies on poorly vascularized tumors or dormant cancer cells. In contrast, bacteria can infect many tissues and microorganisms have the unique ability to grow in anaerobic conditions, damage host cells and activate the immune system which may provide long lasting effects and potential broader tumor targeting. For example, it was demonstrated in vitro that tumor targeting bacteria can prompt quiescent, drug resistant cells, which are the majority in many tumors, to enter the cell cycle and become drug sensitive. Therefore, microbes are a potentially valuable multimodal tool to specifically target and invade cancer cells including cells that are resistant to current therapies, while activating the immune system.

The purpose of this conference is to stimulate research on microbial-based cancer therapy through presentation of current advances in the field from the perspectives of cancer biology and cancer therapy. The sessions will include talks on microbes-tumor interactions, virus and bacteria based therapies and translational aspects of microbial-based therapies. The speakers and attendees will discuss the mechanisms of microbial-based therapy, ways to avoid the failures of the past and potential strategies for successful microbial cancer treatment. The overall goal of the conference is to generate interest and facilitate new scientific collaborations and interactions that will lead to novel research studies that take advantage of the potential capabilities of microorganisms for cancer therapy.

Organizing committee

Elad Sharon	DCTD/CTEP
Robert Mufson	DCB
Jason Yovandich	DCTD/DTP
Jonathan Franca-Koh	SBIR
Min He	DCTD/DTP
Phil Daschner	DCB
Jacob Kagan	DCP
Steven F. Nothwehr	DCTD/SPORE
Peter Ujhazy	DCTD/SPORE
Giorgio Trinchieri	CCR
Andrew Kurtz	SBIR
Helen Chen	DCTD/CTEP
Magdalena Thurin	DCTD/CDP
Avi Rasooly	DCTD/OCCAM