Introduction

On May 5, 2005, Lorenzo Cohen, PhD, presented *Traditional Chinese Medicine for Cancer: The Road to China*, the fourth program in OCCAM’s Invited Speakers Series, held at Lipsett Auditorium in Building 10 at NIH. Dr. Cohen reported on the initial findings of the International Center of Traditional Chinese Medicine for Cancer, which is supported by an NCI planning grant and represents a collaboration between The University of Texas M. D. Anderson Cancer Center and the Fudan University Cancer Center in China. The basic aims of the International Center fall into the main areas of focus within traditional Chinese medicine (TCM): Evaluating herbal/natural products that target disease outcomes and treatment and disease-related symptoms; determining the effects of acupuncture on specific clinical symptoms in cancer patients; and quantifying the biobehavioral effects of *qigong*, a traditional practice of movement and meditation that focuses on energy and the mind/body connection.

The collaboration has included training and exchange programs and studies focused on traditional Chinese therapies used to treat cancer and its symptoms. These studies have looked at acupuncture and its effects on cancer-related symptoms; *qigong* as an adjuvant to radiotherapy for breast cancer patients; Tibetan meditation and yoga for reducing sleep disturbances in lymphoma patients; and Huachansu, a traditional Chinese extract often used to treat pancreatic cancer. Researchers will also develop a methodology for examining traditional Chinese diagnostic techniques. Each of these studies moves the group toward an important goal: To create an ongoing research partnership between these institutions in order to share knowledge and develop the most effective treatments for cancer patients in the United States and abroad.
Traditional Chinese Medicine for Cancer: The Road to China

Lorenzo Cohen, Ph.D.
Director, Integrative Medicine Program

THE UNIVERSITY OF TEXAS
MD ANDERSON CANCER CENTER
Making Cancer History™

FUDAN UNIVERSITY CANCER HOSPITAL
Medicines and treatment methods were found inscribed on oracle bones from the Shang Dynasty (1766 to 1122 BC) and on silk banners and bamboo slip records between the Chin and Han Dynasties (221 BC to 220 AD), which represent the oldest surviving Chinese medical literature.
The New Face of Traditional Chinese Medicine

TOKYO—Epidemiologists had long suspected that the low cancer rates in southeast China might be related to coix, a grasslike relative of maize that is a dietary staple in the region and a key ingredient of many traditional Chinese herbal medicines. But no one had as much faith in coix as pharmacologist Li Dapeng, who in 1975 began trying to coax the anticancer compounds out of the plant’s seed. Twenty years later, Li won government approval to market the fruits of his research, a drug he calls Kanglaitie, to help cancer patients fight their disease and reduce the side effects from other treatments.

Although scientists still don’t know how it works, the injected drug has been taken by more than 200,000 patients and is China’s best-selling cancer treatment. This year, the U.S. Food and Drug Administration approved a phase II trial to test its efficacy in treating non-small-cell lung cancer. It’s the first drug derived from a traditional Chinese herbal remedy to go into clinical trials in the United States, and officials and scientists in mainland China, Hong Kong, and Taiwan are betting it won’t be the last. All three regions are ramping up efforts to screen the 10,000 or so plants described in the Chinese herbal medicine literature. In addition to searching for new drug leads, they are investigating the herbal remedies themselves.

Traditional Chinese medicine (TCM) has also made it onto the region’s political agenda. Hong Kong Chief Executive Tung Chee Hwa has laid out a 10-year plan for making the city an “international center for Chinese medicine,” and his government is currently funding 18 TCM research projects that include clinical trials, developing quality standards, and basic pharmacological studies. The Hong Kong Jockey Club Charities Trust is equipping research labs and donating $64 million to get research started at a new Institute of Chinese Medicine. Last year, Taiwanese President Chen Shui-bian proposed spending as much as $1.5 billion over 5 years to develop Taiwan’s Chinese medicinal herb industry, although a detailed spending plan is still pending and will need legislative approval. China’s Ministry of Science and Technology has made the modernization of TCM one of 12 focal points in its current Five-Year Plan, with $3.6 million budgeted for screening both conventional chemical compounds and medicinal herbs for drug leads.

Officials see these efforts as a way to use rising research budgets to boost domestic biotechnology research efforts and capitalize on a cultural treasure. “Screening herbal remedies is a way for China to try to catch up with Western research at Hong Kong University of Science and Technology (HKUST). A new generation of Western-trained scientists is eager to take on the challenge of “demonstrating the efficacy of traditional remedies.”” he says. Chinese researchers and officials also want to stay ahead of the growing Western interest in herbal medicine. “This is our culture!” says Yang Ning Sun, director of the Institute of Agro-biotechnology at Academia Sinica in Taipei. “We should be interested in making good use of it.”

Ironically, as interest in herbal remedies and acupuncture has boomed in the West, the Asian public is turning increasingly to modern medicine. According to a 1999 survey by the Hong Kong government, only 22% of outpatient medical consultations in the city were provided by Chinese medicine practitioners. Officials think the percentage in mainland China is even lower, and they believe the safety concerns are driving people away from TCM. To address that problem, Hong Kong is drawing up regulations to ensure the quality of herbal medicines and the qualifications of practitioners. “Once the regulatory system is in place and we upgrade professional standards, I’m sure the usage rate [for TCM] will increase,”
Learning From China

Researchers are finding that traditional Chinese medicine may have a lot to offer
International Center of Traditional Chinese Medicine for Cancer

Lorenzo Cohen, Ph.D., Principal Investigator/Co-Director

Luming Liu, M.D., Co-Principal Investigator/Co-Director

Zhiqiang Meng, M.D., Ph.D., Deputy Director

NCI: R21 CA10808
Aims

- Evaluate herbal/natural product treatments that target disease outcomes and treatment- and disease-related symptoms.
- Determine the effects of acupuncture on specific clinical symptoms in patients with cancer.
- Quantify the biobehavioral effects of qigong and other mind/body-based interventions.
Department of Traditional Chinese Medicine

Professors: 3
Associate professors: 6
Attending: 5
Residents and Clinical Fellows: 5
Graduate students: 6

Ward: 1
Cooperative Cancer Center: 1
Beds: 100
国际整合医学肿瘤中心

INTERNATIONAL CENTER OF INTEGRATIVE ONCOLOGY (ICIO)

FUDAN UNIVERSITY
CANCER HOSPITAL

The University of Texas
MD Anderson Cancer Center

2004年7月
July 2004
Education

- Research training
- Long-term exchange
- TCM training
- Unique opportunities
Preclinical Research and Phase I Clinical Trial

- Examining Huachansu in preclinical studies at MDACC and conducting a Phase I clinical study at Cancer Hospital.
Huachansu or Ch’an su

- Bufo toads excrete from their parotid glands substances known as bufotoxins.
- Bufalin is one such toxin known to be a cardiac glycoside.
- Huachansu is an important component in the treatment of cancer in China.
Quality Control Determination of Huachansu Preparations

- Color and appearance
- UV absorbance
- Cytotoxicity against human malignant cell lines
- Bufalin content
- Nonpolar compound profile
Relative growth inhibition of human BRO melanoma cells when treated with Huachansu preparations (72 hr continuous exposure)
The relative growth inhibition of human malignant cell lines by huachansu

<table>
<thead>
<tr>
<th>Cell lines</th>
<th>Lot 30202</th>
<th>Lot 31001</th>
<th>Lot 30902</th>
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<tbody>
<tr>
<td>Hep 3 B</td>
<td>25.0*</td>
<td>20.07</td>
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<td>BRO</td>
<td>12.7</td>
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<td>4.1</td>
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<tr>
<td>HT29</td>
<td>7.3</td>
<td>9.5</td>
<td>2.9</td>
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<tr>
<td>Panc-1</td>
<td>4.7</td>
<td>4.0</td>
<td>0.5</td>
</tr>
</tbody>
</table>

*Data are presented as the IC$_{50}$ value (units/ml, assuming the concentration of extract is 100 unit/ml).
The Effect of Polar and Non-polar Components of Huachansu on the Growth of Panc-1 Cells
Chemical Composition

Huachansu: A. Bufalin

B: Resibufoegenin

Nerium oleander: Oleandrin

Endogenous cardiac glycoside: Ouabain
Selective Ion Chromatograms Analyzed by High Performance Chromatography/Tandem Mass Spectrometry

Cinobufotalin
M/z = 459.1 > 363.0

Cinobufagin
M/z = 443.1 > 150.8

Bufalin
M/z = 387.1 > 161.0

Resibufagenin
M/z = 385.1 > 144.9
Concentration of cardiac glycosides in three different lots of huachansu

<table>
<thead>
<tr>
<th>Sample</th>
<th>Bufalin (ng/ml)</th>
<th>Resibufagenin (ng/ml)</th>
<th>Cinobufagin (ng/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lot 31001</td>
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<td>17.8 ± 0.7</td>
<td>1.2 ± 0.1</td>
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<td>19.5 ± 1.8</td>
<td>19.0 ± 1.3</td>
<td>2.9 ± 0.2</td>
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<tr>
<td>Lot 30202</td>
<td>18.4 ± 2.6</td>
<td>17.7 ± 0.7</td>
<td>1.2 ± 0.1</td>
</tr>
</tbody>
</table>
The Effect of Cardiac Glycosides on Proliferation of Human Melanoma BRO Cells.
Mechanisms

- Regulation of Na, K-ATPase pump.
- Cardiac glycosides bind to the alpha subunit.
- There are four alpha subunits (1-4).
- Cardiac glycosides bind strongly to alpha 3.
Human Tumor Cell Lines Differ in Their Relative Content of α3 Subunit Relative to α1 Subunit
It is little wonder that cardiac glycosides failed in early *in vitro* cytotoxicity screens that used murine tumor cells.
All human malignant cell lines tested to date are more sensitive than murine tumor cell lines.
# The Cytotoxic Effect of Bufalin and Huachansu in Human and Murine Melanoma Cells

<table>
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<tr>
<th>Compounds</th>
<th>IC50, BRO</th>
<th>IC50, B16</th>
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<tr>
<td>Oleandrin</td>
<td>0.007 μM</td>
<td>&gt; 10.0 μM</td>
</tr>
<tr>
<td>Bufalin</td>
<td>0.01 μM</td>
<td>&gt; 10.0 μM</td>
</tr>
<tr>
<td>Huachansu</td>
<td>1.7 units/ml</td>
<td>&gt; 12.5 units/ml</td>
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</table>

1 unit was defined as 0.01 ml of huachansu solution.
Control

Oleandrin 3.3 ng/ml

Oleandrin 10 ng/ml

NAC 10 mg/ml

NAC + Oleandrin (3.3 ng/ml)

NAC + Oleandrin (10 ng/ml)
Phase I Clinical Trial

- Determine the MTD and DLT of Huachansu in advanced hepatocellular carcinoma, non-small cell lung cancer, and pancreatic cancer.
- Determine the side effects.
- Assess anti-tumor responses in a descriptive fashion.
- Examine bufalin content from plasma samples.
Phase II Trial

- Randomized, double-blind, placebo-controlled, trial for patients with pancreatic cancer.
- Assess the efficacy based on tumor response and 6-month survival.
- Huachansu will be given along with gemcitabine and radiotherapy. Patients will be randomized to either receive gemcitabine, radiotherapy, and huachansu or gemcitabine, radiotherapy, and placebo.
Acupuncture

- Examining the effects of acupuncture to prevent prolonged post-operative ileus in patients undergoing ileostomy or colostomy at Cancer Hospital.

- Compare postsurgical quality of life status between treatment and control groups in terms of pain, use of opioid analgesics, nausea, vomiting, insomnia, abdominal distension/fullness, activity, and sense of well-being.
Acupuncture

- 28 patients have been recruited and randomized.
- The trial should be completed this fall.
Acupuncture for Xerostomia

- Some research has been conducted in the United States and Europe suggesting that acupuncture may be a useful treatment for radiation-induced xerostomia.

- However, there have been few randomized trials, the treatment schedules have varied greatly, and the research has never been conducted in China.
A phase I study will evaluate two different treatment schedules. Patients will be randomized to one of two groups that will receive acupuncture treatment using a fixed set of points over a 5-week period. The various treatment schedules are designed to help establish maximum results with the least patient burden.
Qigong
A pilot study of qigong is being conducted to determine the feasibility of conducting biobehavioral research at the Cancer Hospital.
Tibetan Yoga
(Trul khor or Magical Wheel)
7-Week Program of Tibetan Meditation and Yoga

- Breathing and visualization
- Mindfulness techniques
- *Tsa lung*
  - Incorporating body movements
- *Trul khor*
  - Integrating body, energy, and mind
Study Population

- Thirty-nine patients with lymphoma who were undergoing active treatment or had received active treatment within the past 12 months.
Assessments

Seven Yoga Sessions

Assessment Session I
Assessment Session II
Assessment Session III
Assessment Session IV

0.5” Represents approximately 1 week

Controls were assessed at corresponding time points relative to the initial assessment.
Sleep Disturbances During Follow-up

- T-Yoga
- Control

p < .004

Cohen et al., 2004
Sleep Disturbances - Subscales

Cohen et al., 2004
Qigong for Women with Breast Cancer

- Examine the feasibility and initial efficacy of implementing a Qigong program for patients with breast cancer as an adjuvant to their radiotherapy.

- Patients with breast cancer who are undergoing radiotherapy are randomly assigned to either a Qigong group or a wait-list control group.

- Participants in the Qigong group attend daily Qigong sessions 5 days/week throughout their 6-week radiotherapy schedule.
Guo Lin

- Modified Guo Lin qigong for health
  - I. Preparation Exercise (yubei gong)
    - Qi Breathing (qi huxi)
    - Opening and Closing of Dantian (kai he dantian)
  
  - II. Main Exercise (zhuyao lianxi)
    - Slow Exercise (manbu xing gong)
    - Wind-like breathing (huxi ru feng)
  
  - III. Ending exercise (shou gong)
    - Qi Breathing (qi huxi)
    - Opening and Closing of Dantian (kai he dantian)
    - Rubbing Chest & Andomen (Cha Xiong Mo Fu) (not part of guolin qigong)
Timeline

@3 months

0.5" Represents approximately 1 week

1 " Represents approximately 1 month
Cognitive Processing

Stressors
Cancer/
Radiotherapy

Finding Meaning
Qi (TCM diagnosis)

Cognitive Processing

Primary Outcomes
Fatigue
Sleep Quality

Secondary Outcomes
QOL
Mental Health
Physiological Parameters

Qigong
Epidemiology

- Establish a methodology to examine reliability and validity of TCM diagnostic techniques.
- Identify markers for genetic susceptibility and prognosis that may be associated with TCM diagnosis and TCM treatment of cancer.
Epidemiology

- Collect epidemiological information from all the patients who are part of the three main projects.
- Examine changes in TCM diagnosis over time and to correlate this with possible changes in Western-based diagnostic techniques, changes in symptoms, and possibly with molecular markers.
Epidemiology

- Collect data prospectively from all newly diagnosed pancreatic, head and neck, and breast cancer patients.

- Patients will be recruited around the time of diagnosis before the start of any treatment.
Epidemiology

- Questionnaire
- TCM pattern differentiation
  - Asking – history and symptoms
  - Looking – tongue, skin, etc.
  - Touching/feeling – pulse diagnosis and palpation
  - Smelling
- ZM-III pulse analyses
- Tongue photographs
- Blood sample
- Clinical data
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<td>5</td>
<td>170.9</td>
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增益 1

原始脉图
最佳脉图及参数

最佳取脉压力： 123.4g  增益： 1.0

最佳脉图

最佳脉图速率图

<p>| | | | | | | | | | |</p>
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<td>h1</td>
<td>19.3g</td>
<td>As</td>
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<td>w1</td>
<td>0.12s</td>
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<td>h2</td>
<td>14.0g</td>
<td>Ad</td>
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脉率：平（63.9次/分）
节律：不齐
脉形：abc
脉名：平弦脉(II)(不齐)

确定 显示参数
card or credit card number in an instant message conversation.

Start viewing webcam. Please wait for a response or Cancel (Alt+Q) the pending

invitation to start viewing webcam.

viewing webcam. Do you want to Accept (Alt+C) or Decline (Alt+D) the

invitation to start viewing webcam.
M. D. Anderson Cancer Center

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