

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™

美國德州大學
M.D. 安德森
癌癥中心



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 Kanglaite, 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

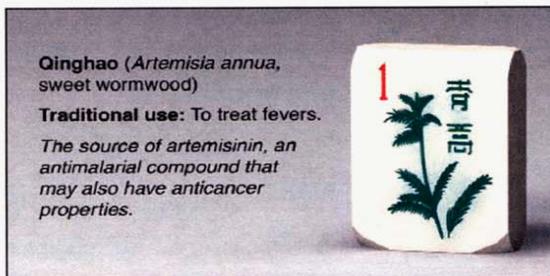
include clinical trials, developing quality standards, and basic pharmacological studies. The Hong Kong Jockey Club Charities Trust is equipping research labs and donating \$64 million to get research started at a new Institute of Chinese Medicine. Last year, Taiwanese President Chen Shui-bian proposed 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

Rooting around for drugs. Shanghai's Li Dapeng found the active compound for his cancer-fighting Kanglaite drug in a traditional medicinal herb.

countries in developing new drugs," says chemist Yang Xiuwei, director of the National Research Lab of Natural and Biomimetic Drugs at Beijing University of Medical Sciences.

The timing is right, says biochemist S. D. Kung, who is coordinating herbal medicine



Qinghao (*Artemisia annua*, sweet wormwood)

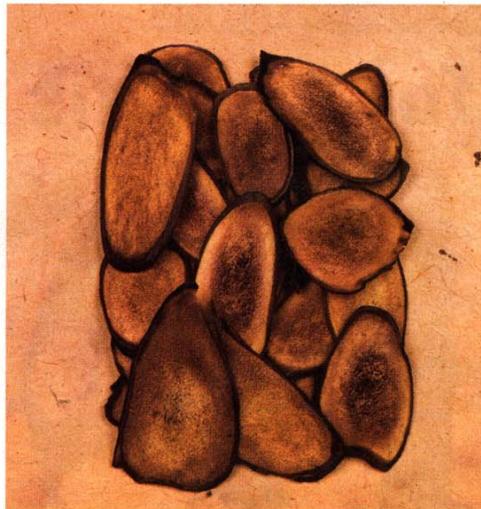
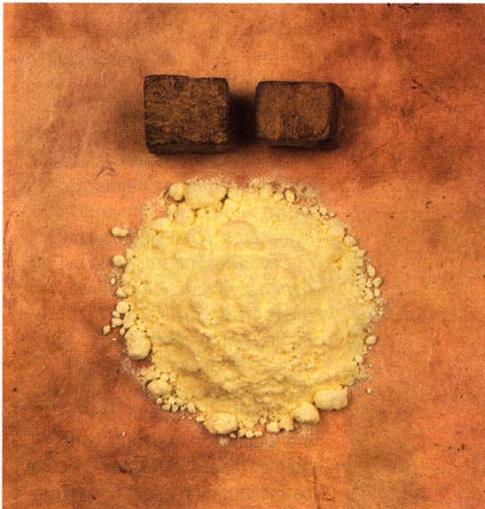
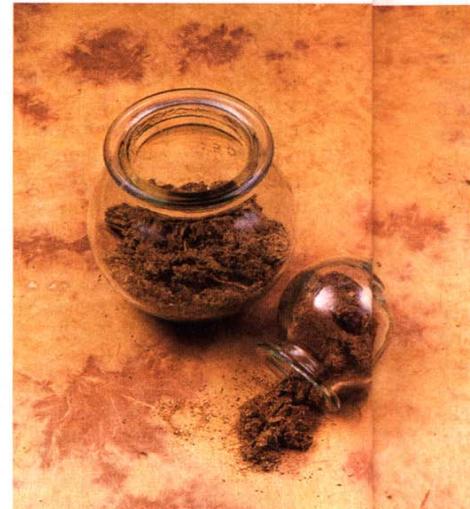
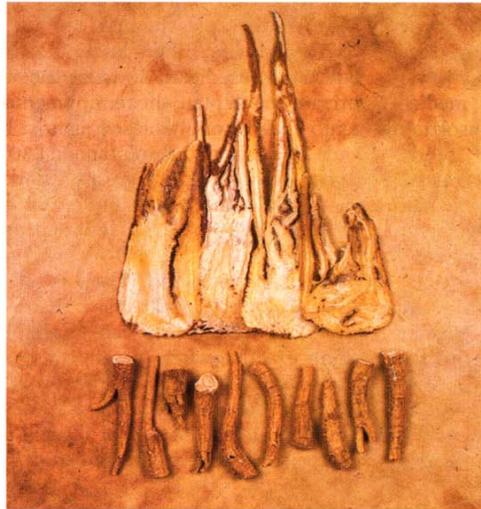
Traditional use: To treat fevers.

The source of artemisinin, an antimalarial compound that may also have anticancer properties.

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] to [meet] the standards of the U.S. Food and Drug Administration," 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 Agrobiotechnology 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 that 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."

CREDITS: (LEFT TO RIGHT) ZHE JING; KANGLAITE PHARMACEUTICAL CO. ILLUSTRATION: C. SANDEN



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











建设一流
肿瘤中西
医结合学
科



Y7-1-3-2 白茯苓 20g

厚栝子 15g 香薷子 15g 桂枝 15g

Y7栝子 15g

Y21180 12g







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中国复旦大学
附属肿瘤医院

美国德克萨斯州大学
安德生肿瘤医院

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



Bluebonnets



Magnolia

Sister Institutions

M. D. Anderson Cancer Center

Fudan University Cancer Hospital

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.



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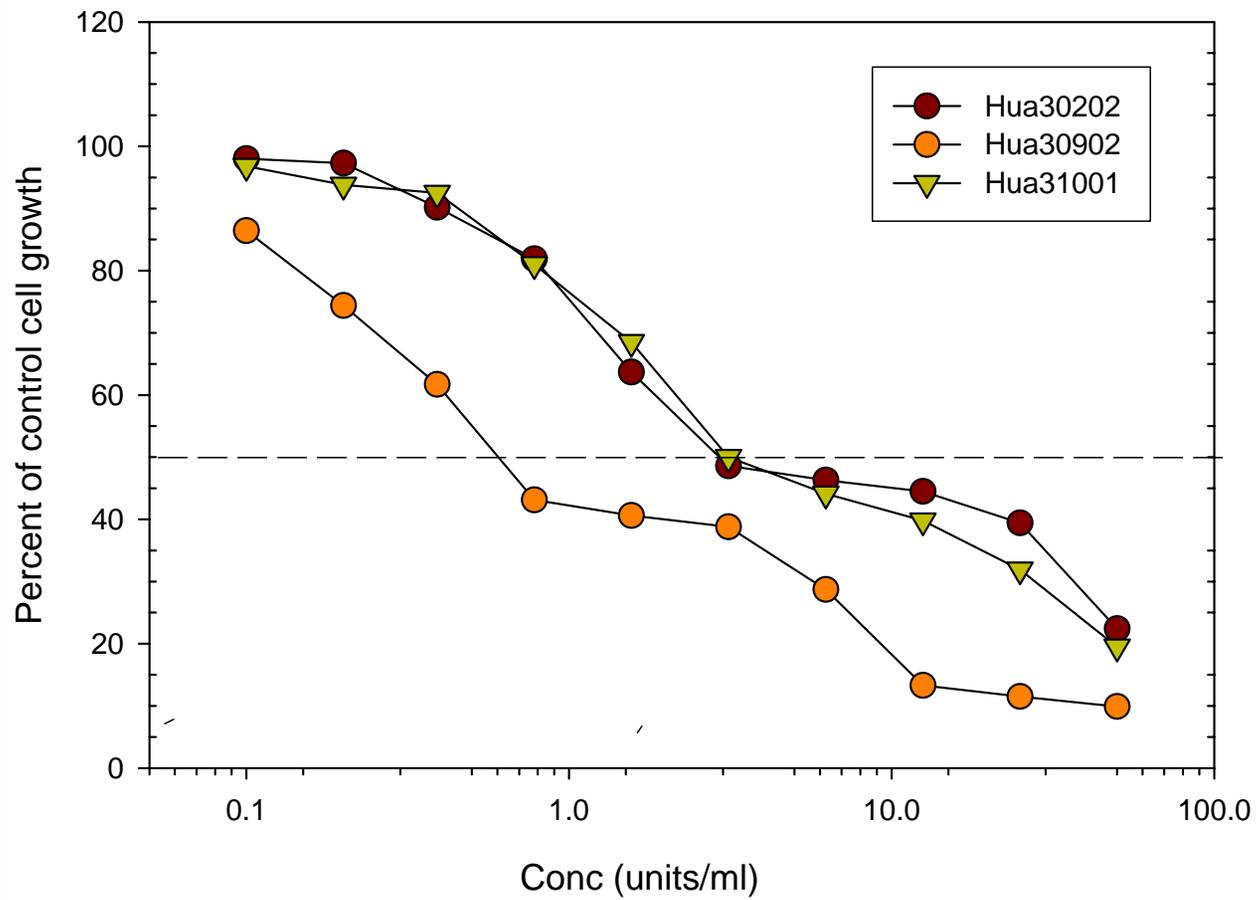
电话号码：0561-3152828（传真）3152828
地址：安徽省淮北市人民路168号 邮编：235000

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)

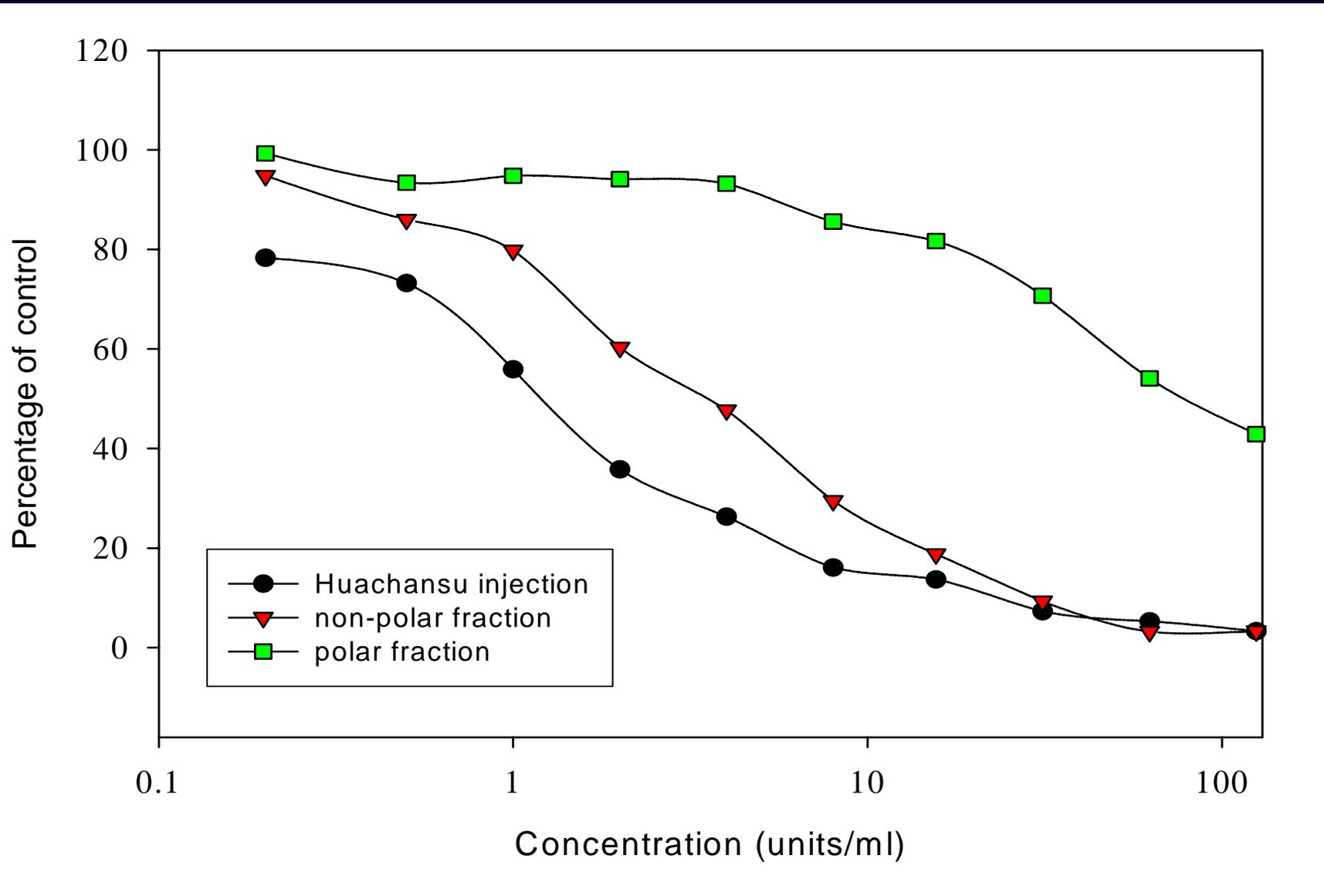


The relative growth inhibition of human malignant cell lines by huachansu

Cell lines	Lot 30202	Lot 31001	Lot 30902
Hep 3 B	25.0*	20.07	13.9
BRO	12.7	10.8	4.1
HT29	7.3	9.5	2.9
Panc-1	4.7	4.0	0.5

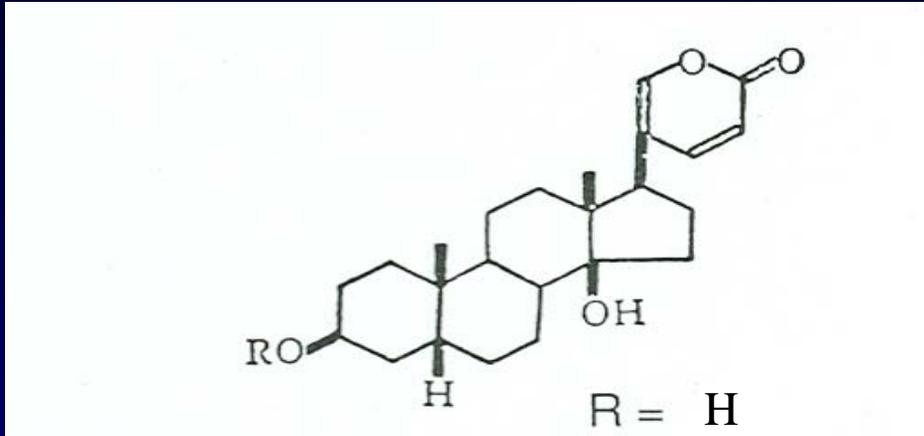
*Data are presented as the IC₅₀ value (units/ml, assuming the concentration of extract is 100 unit/ml).

The Effect of Polar and Non-polar Components of Huachansu on the Growth of Panc-1 Cells

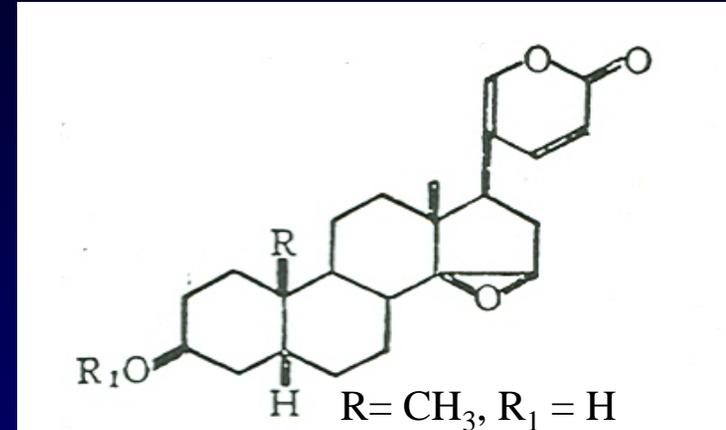


Chemical Composition

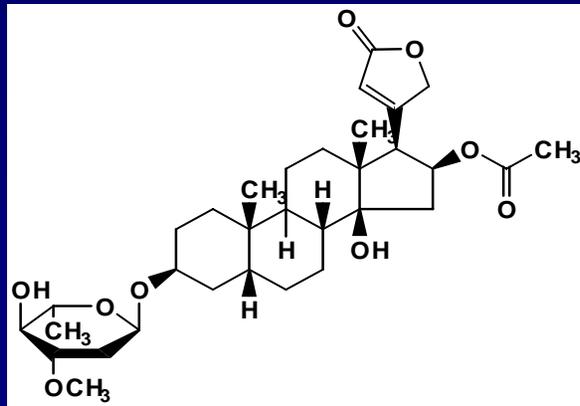
Huachansu: A. Bufalin



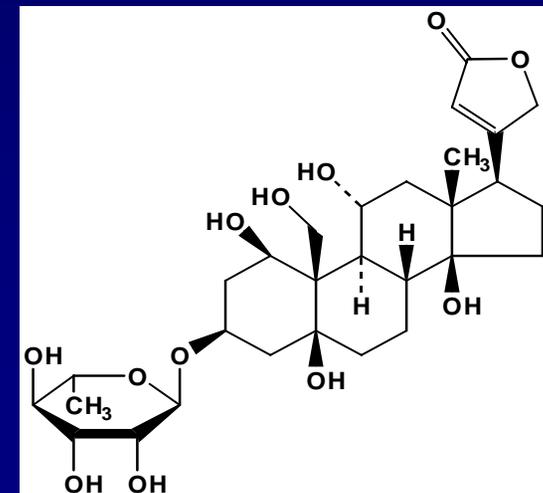
B: Resibufogenin



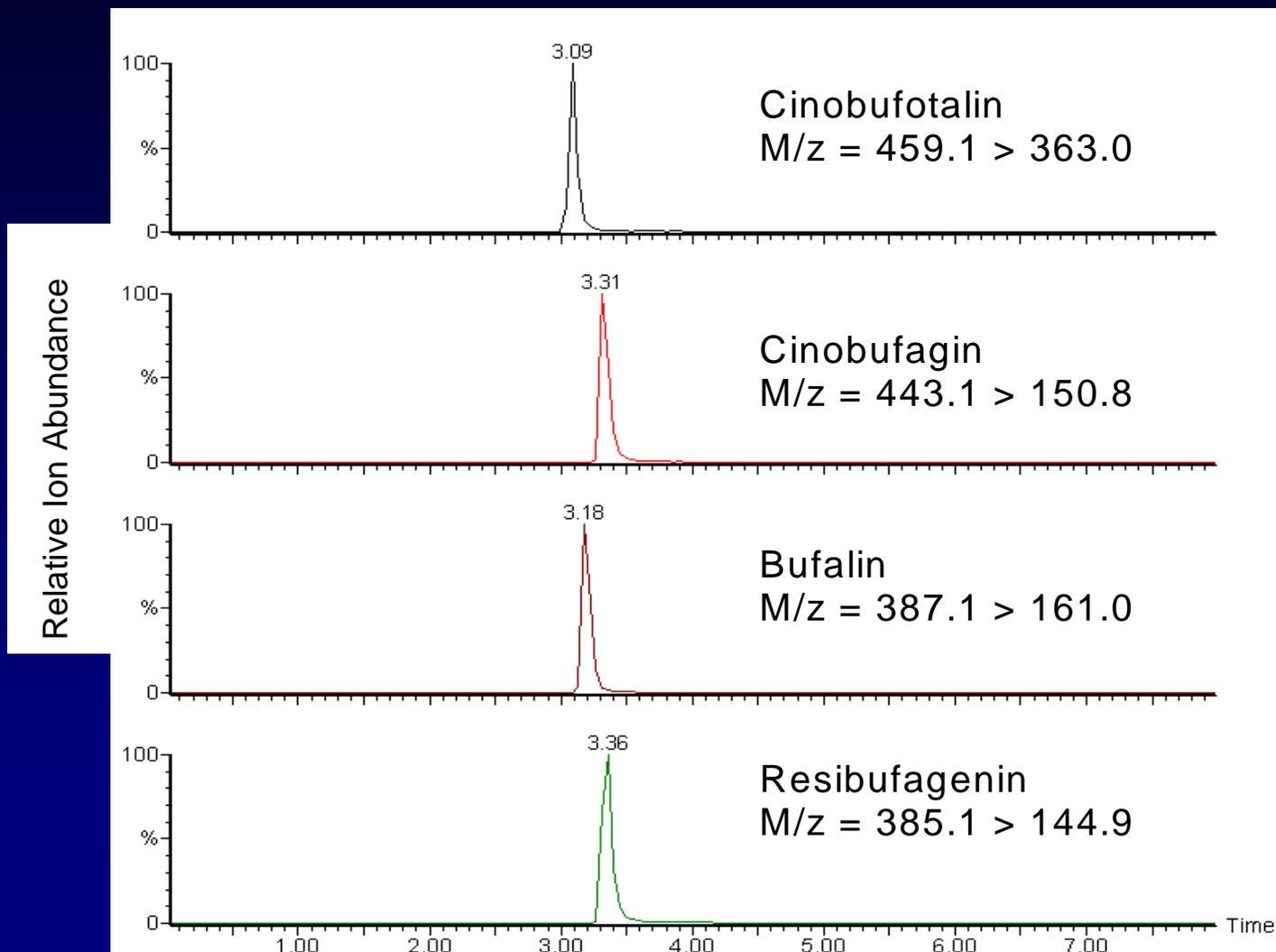
Nerium oleander: Oleandrin



Endogenous cardiac glycoside: Ouabain



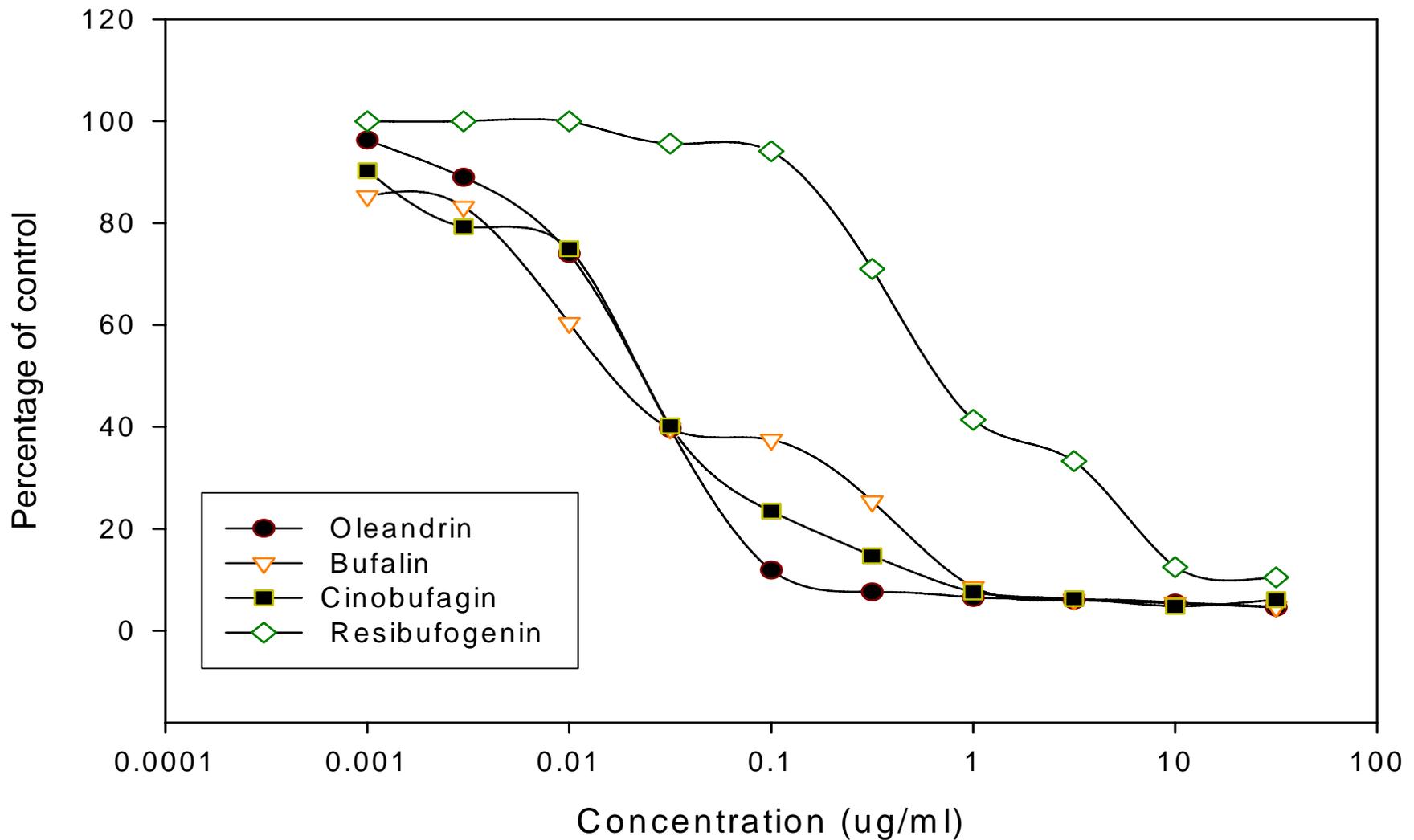
Selective Ion Chromatograms Analyzed by High Performance Chromatography/Tandem Mass Spectrometry



Concentration of cardiac glycosides in three different lots of huachansu

Sample	Bufalin (ng/ml)	Resibufagenin (ng/ml)	Cinobufagin (ng/ml)
Lot 31001	18.0 ± 0.6	17.8 ± 0.7	1.2 ± 0.1
Lot 30902	19.5 ± 1.8	19.0 ± 1.3	2.9 ± 0.2
Lot 30202	18.4 ± 2.6	17.7 ± 0.7	1.2 ± 0.1

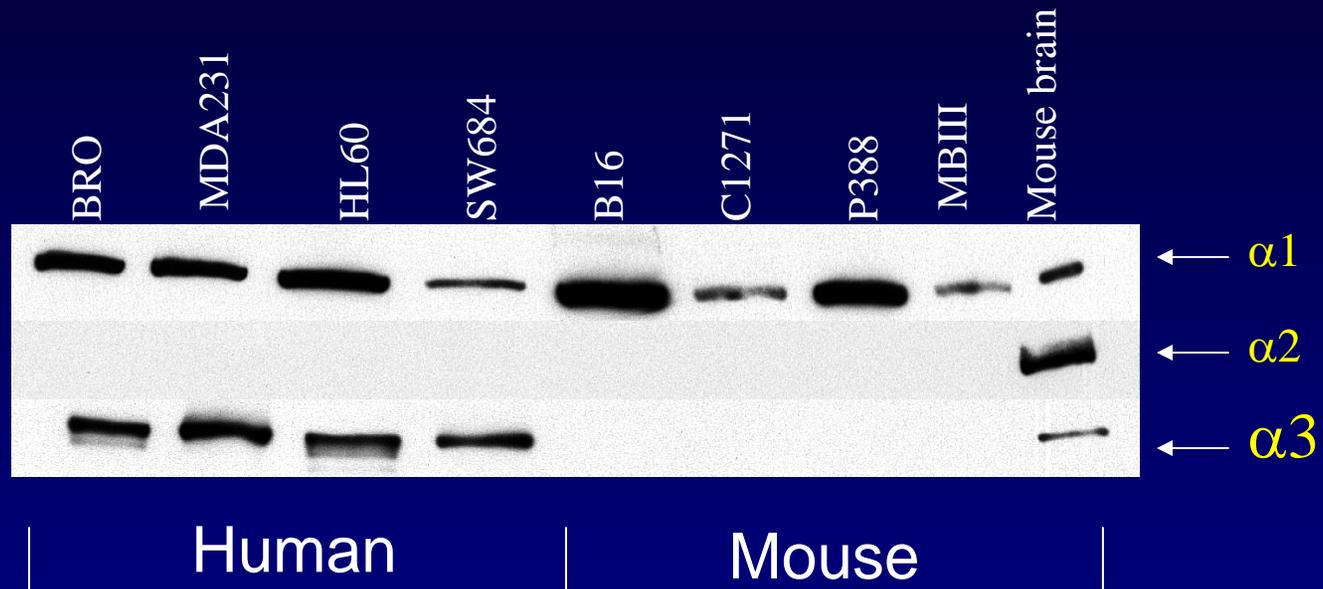
The Effect of Cardiac Glycosides on Proliferation of Human Melanoma BRO Cells.



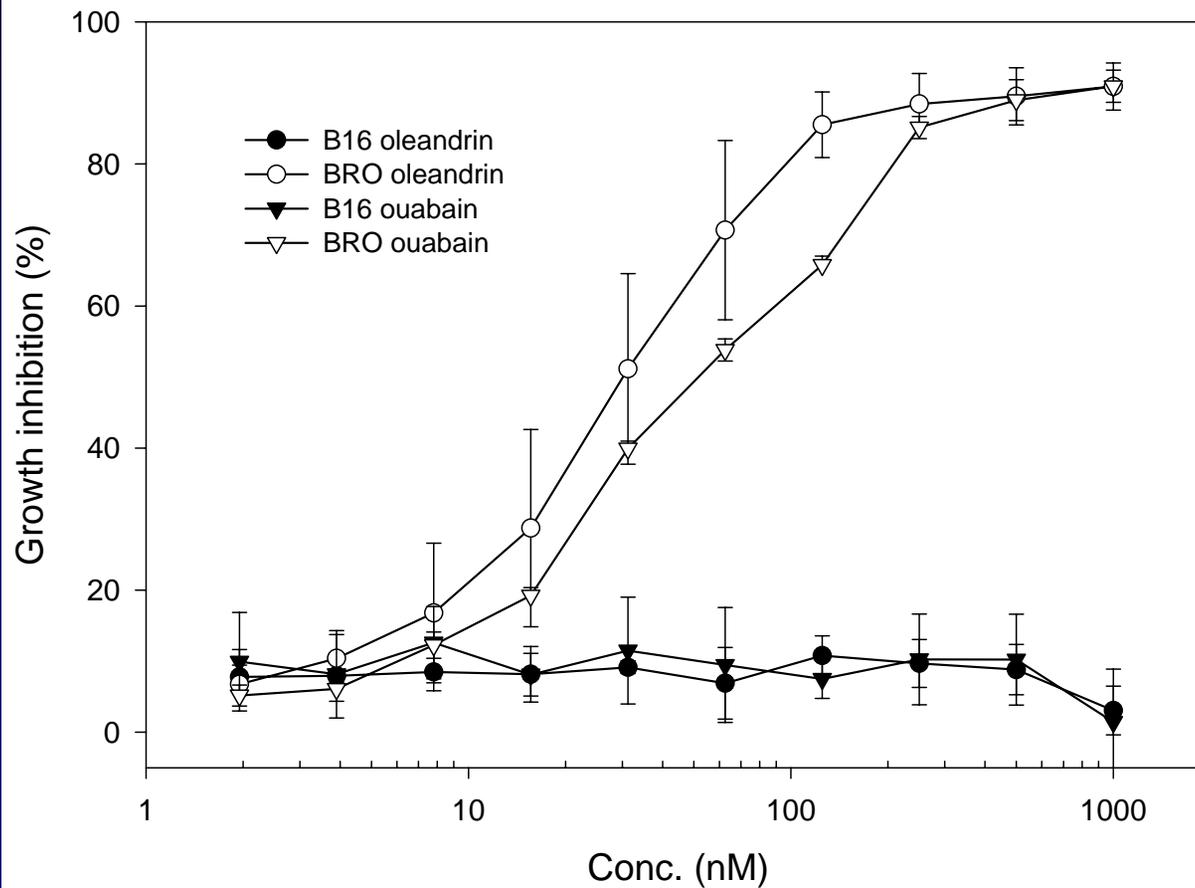
Mechanisms

- 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.

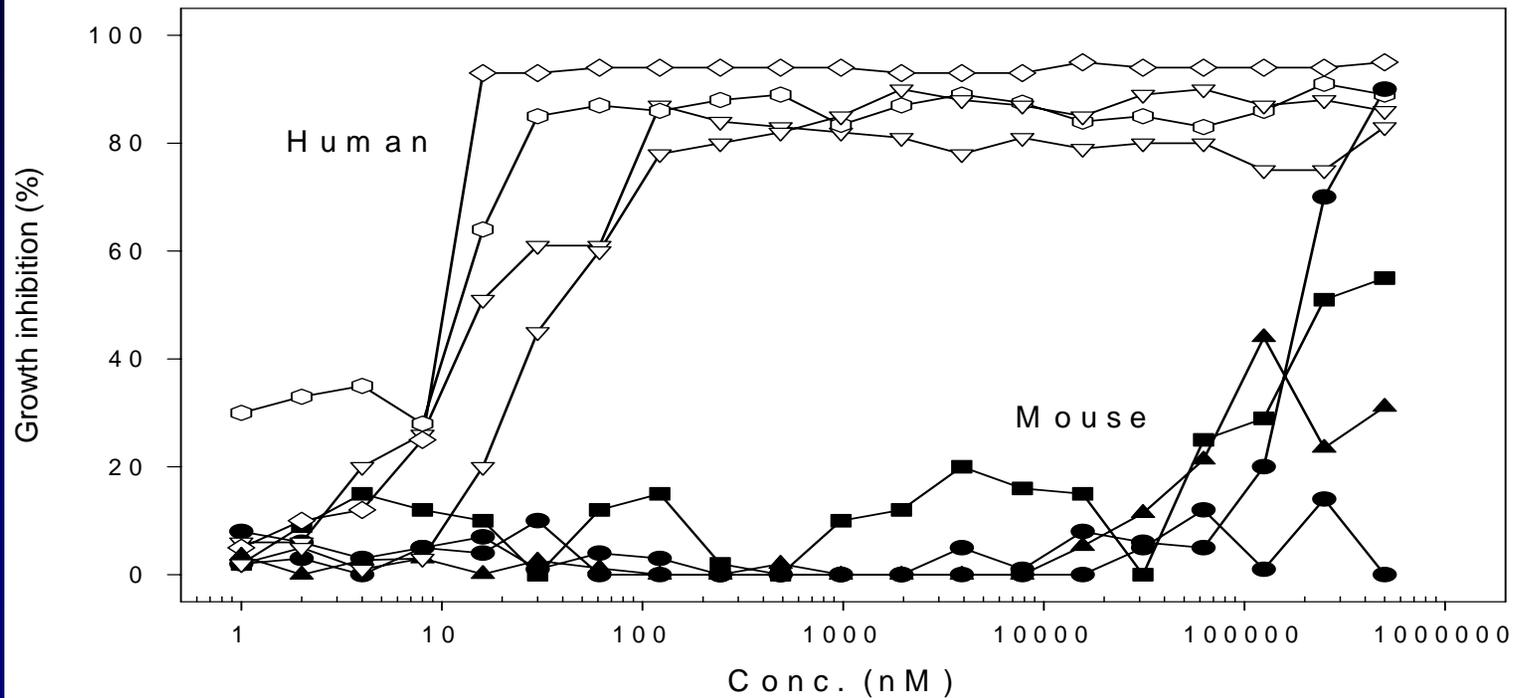
Human Tumor Cell Lines Differ in Their Relative Content of $\alpha 3$ Subunit Relative to $\alpha 1$ Subunit



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.

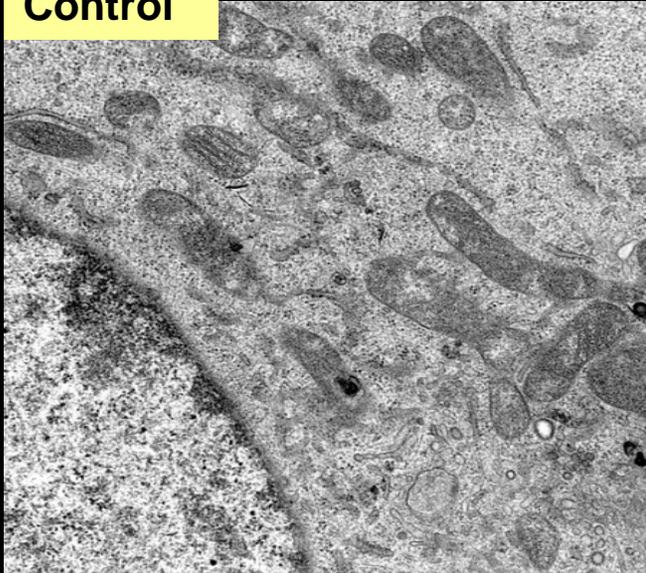


The Cytotoxic Effect of Bufalin and Huachansu in Human and Murine Melanoma Cells

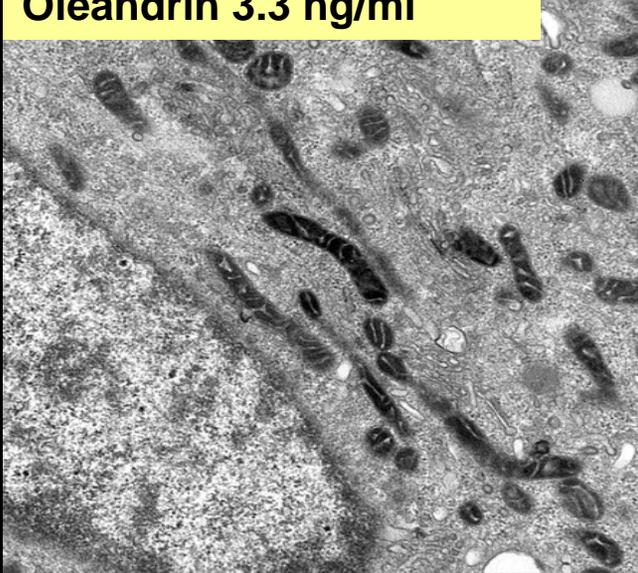
Compounds	IC50, BRO	IC50, B16
Oleandrin	0.007 μM	> 10.0 μM
Bufalin	0.01 μM	> 10.0 μM
Huachansu	1.7 units/ml	> 12.5 units/ml

1 unit was defined as 0.01 ml of huachansu solution.

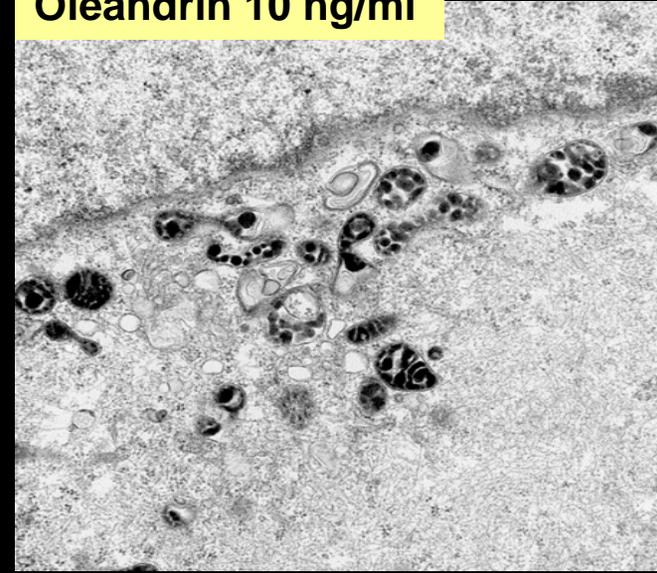
Control



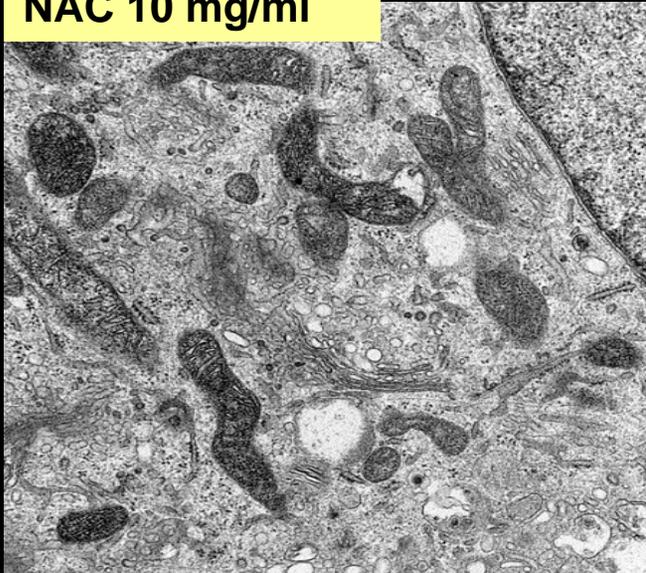
Oleandrin 3.3 ng/ml



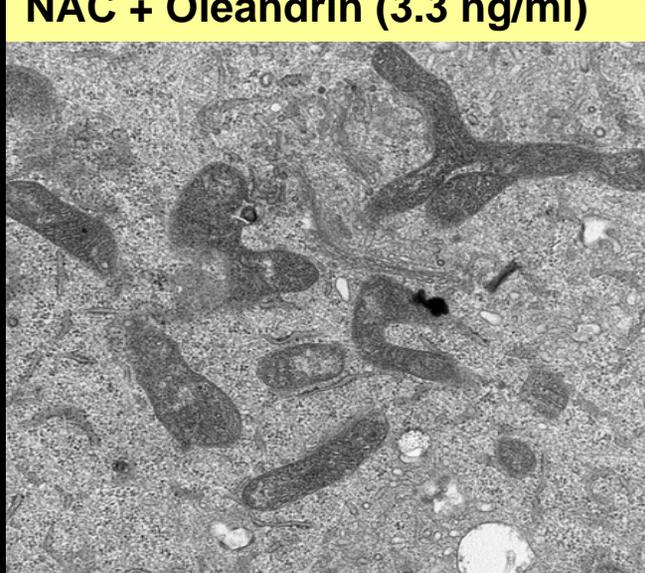
Oleandrin 10 ng/ml



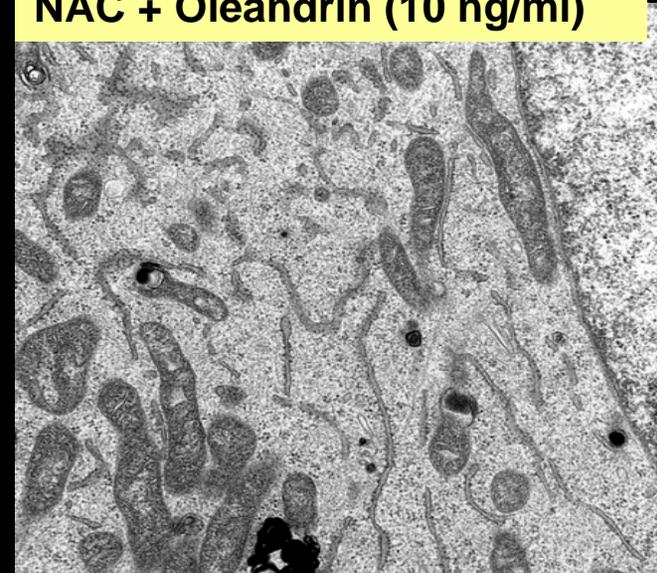
NAC 10 mg/ml



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.

THE SAUDIS: A NEW LINK TO THE 9/11 HIJACKERS

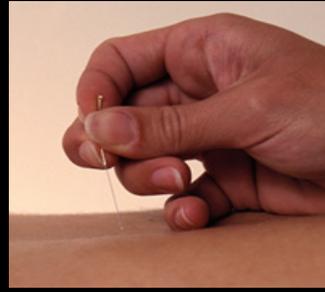
Newsweek

December 2, 2002

The Science of Alternative Medicine

Depression Treatments
Acupuncture & Herbs
Natural HRT

PLUS Insights
From Harvard
Med School



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.

Acupuncture for Xerostomia

- 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.

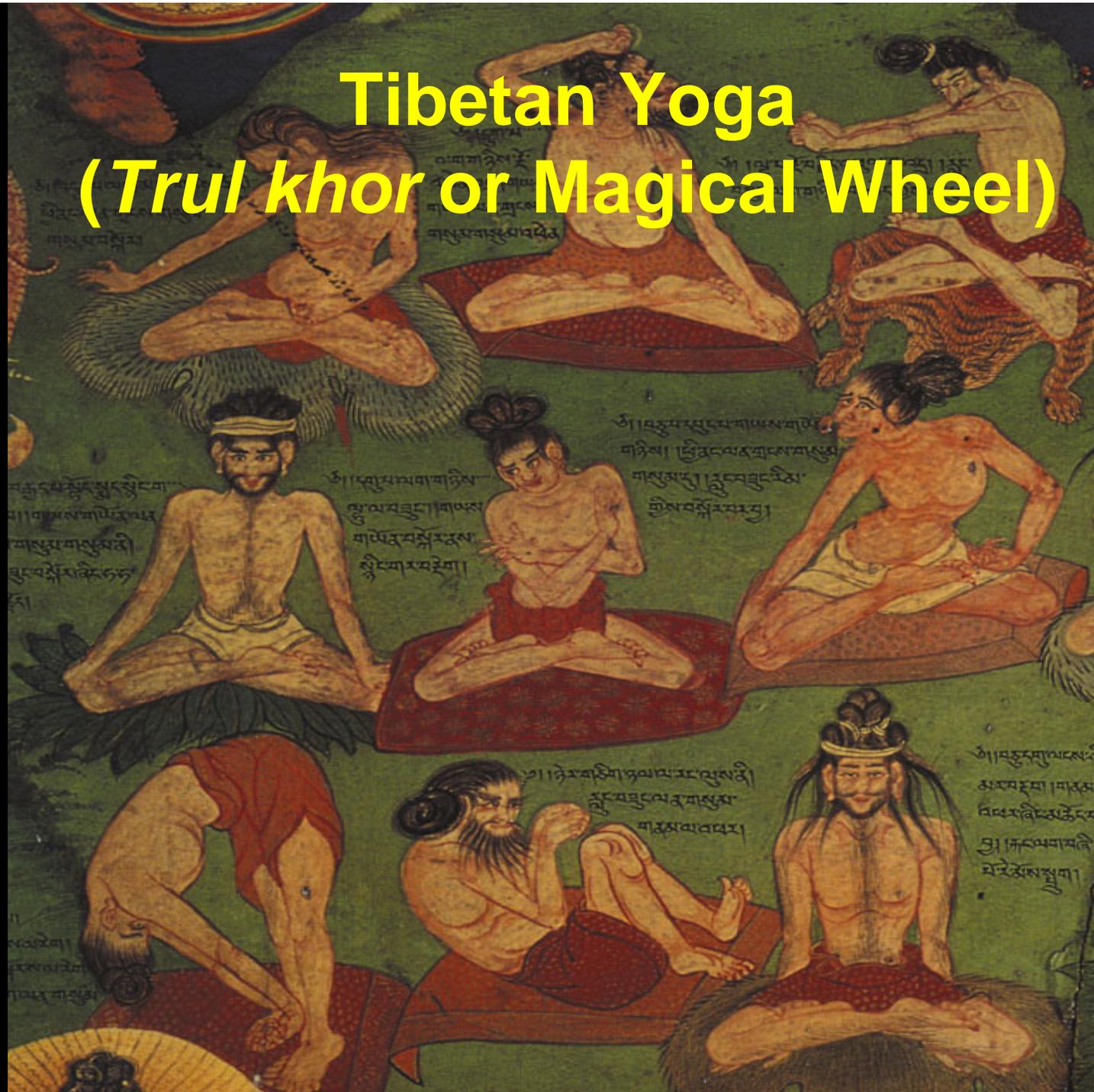
Qigong



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)



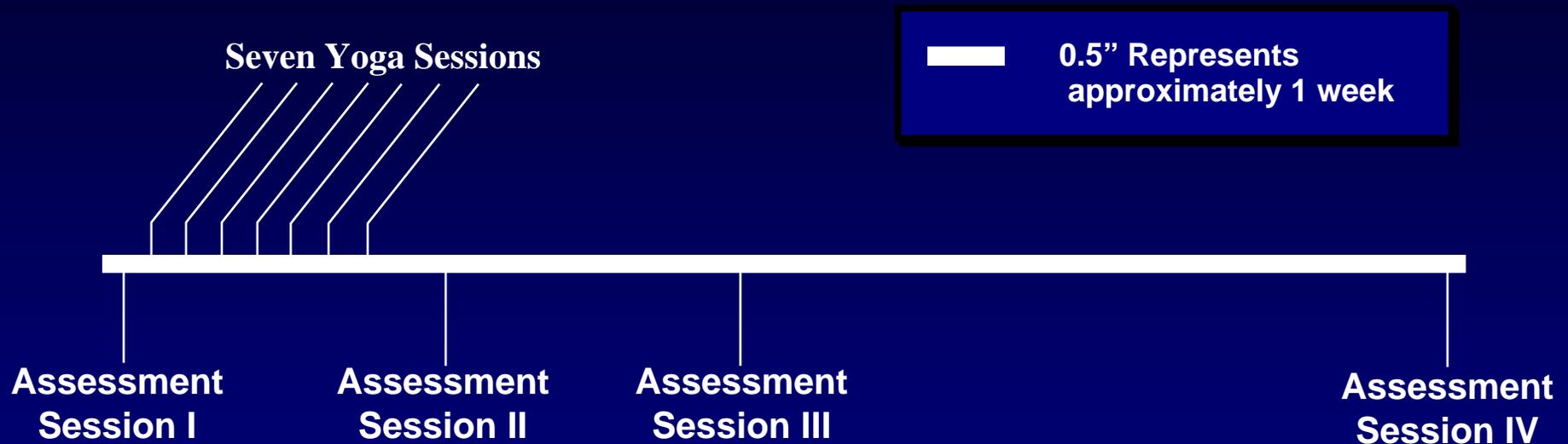
7-Week Program of Tibetan Meditation and Yoga

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

Study Population

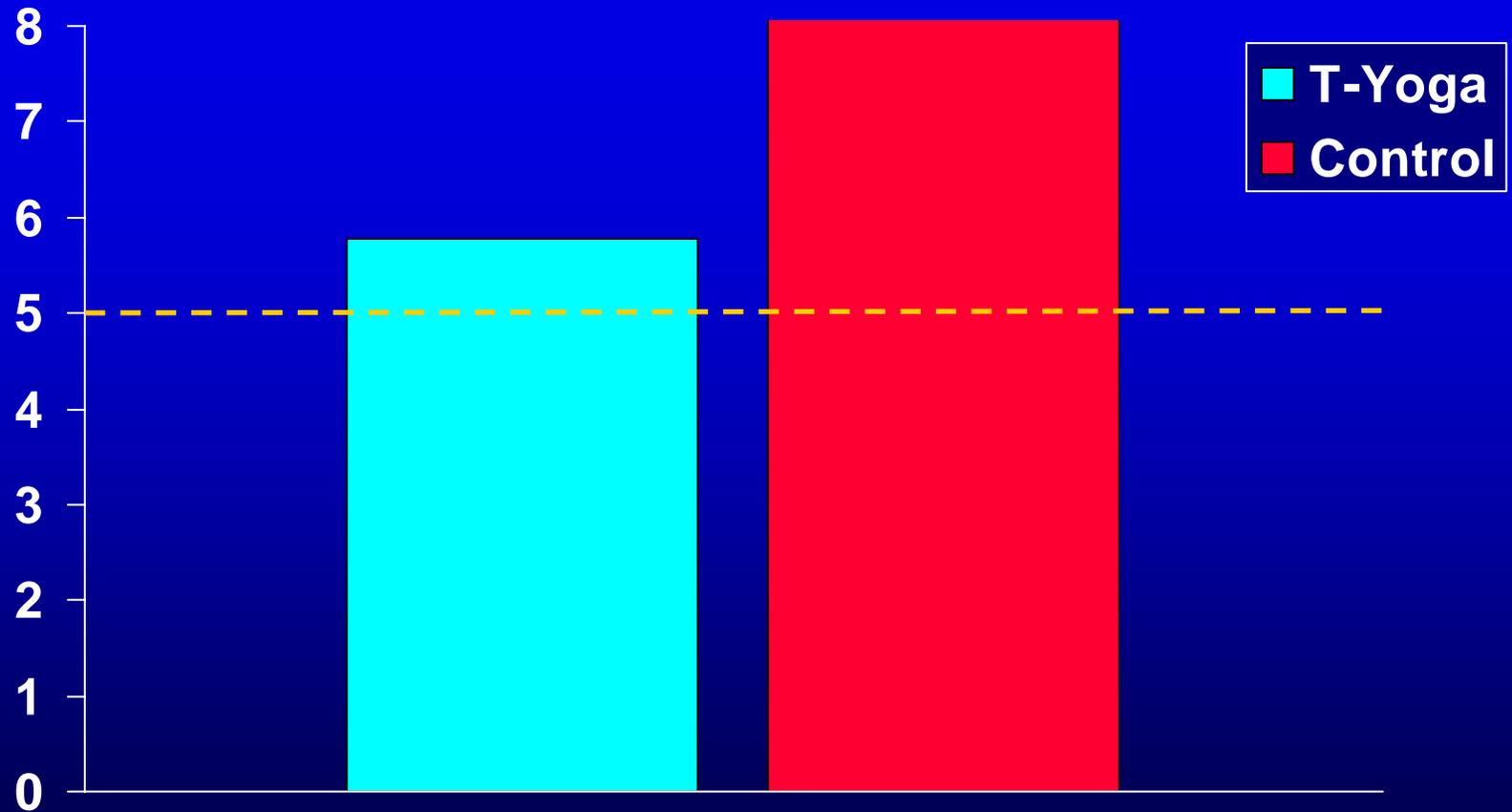
- **Thirty-nine patients with lymphoma who were undergoing active treatment or had received active treatment within the past 12 months.**

Assessments



Controls were assessed at corresponding time points relative to the initial assessment.

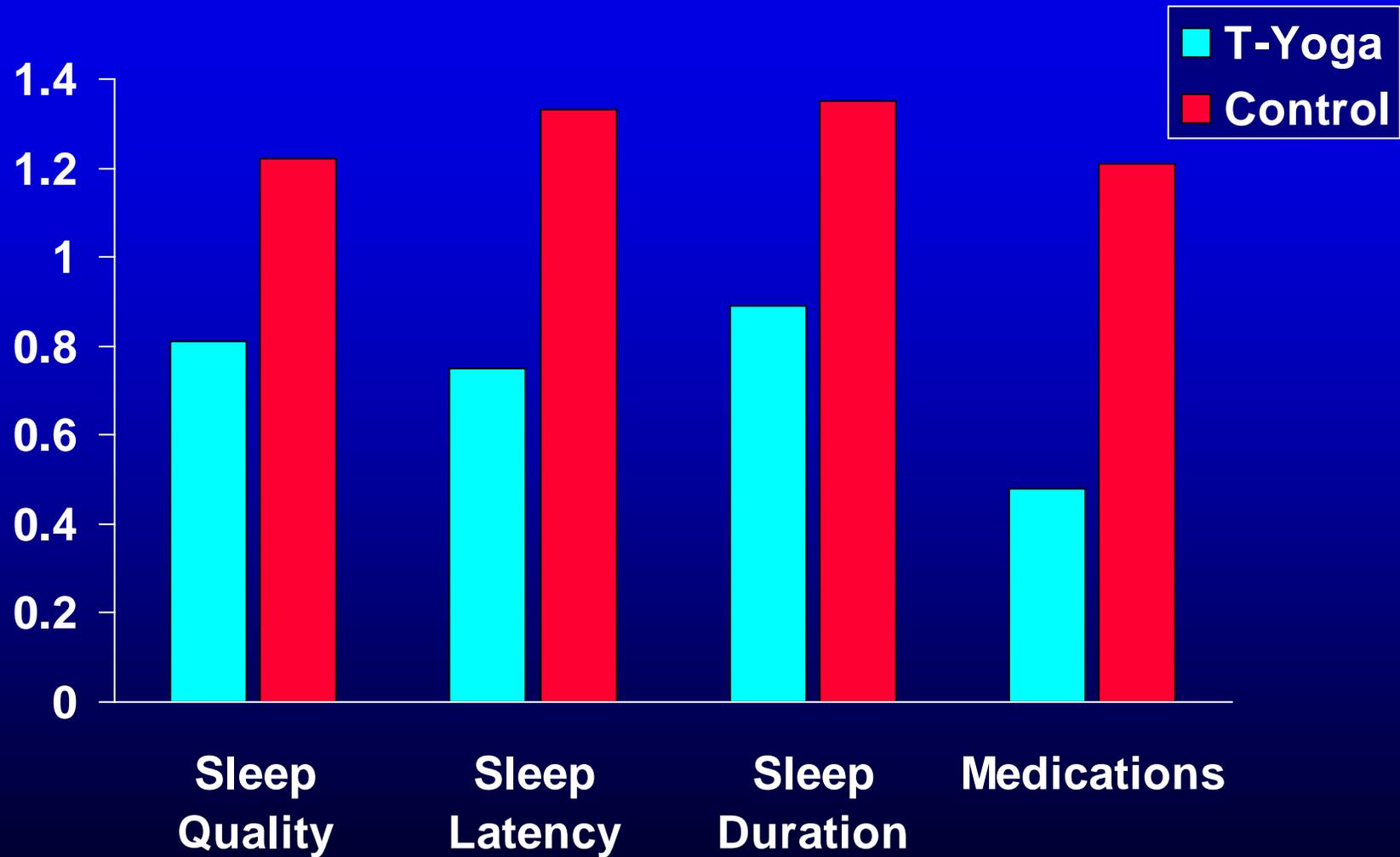
Sleep Disturbances During Follow-up



Total Score (adjusted for baseline)

$p < .004$

Sleep Disturbances - Subscales



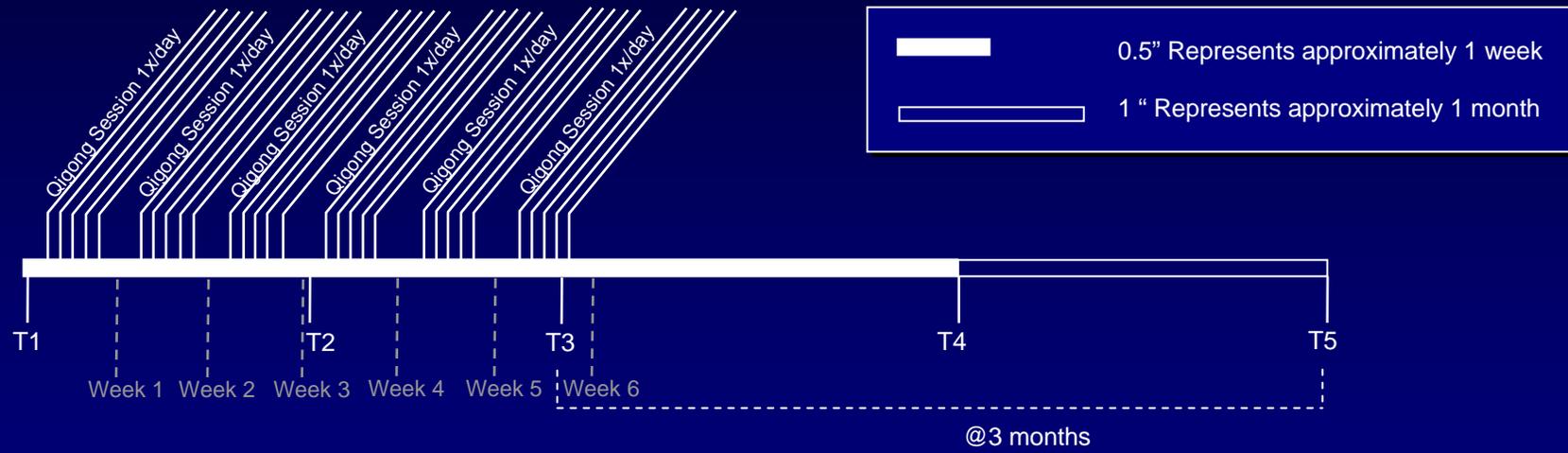
Qigong for Women with Breast Cancer

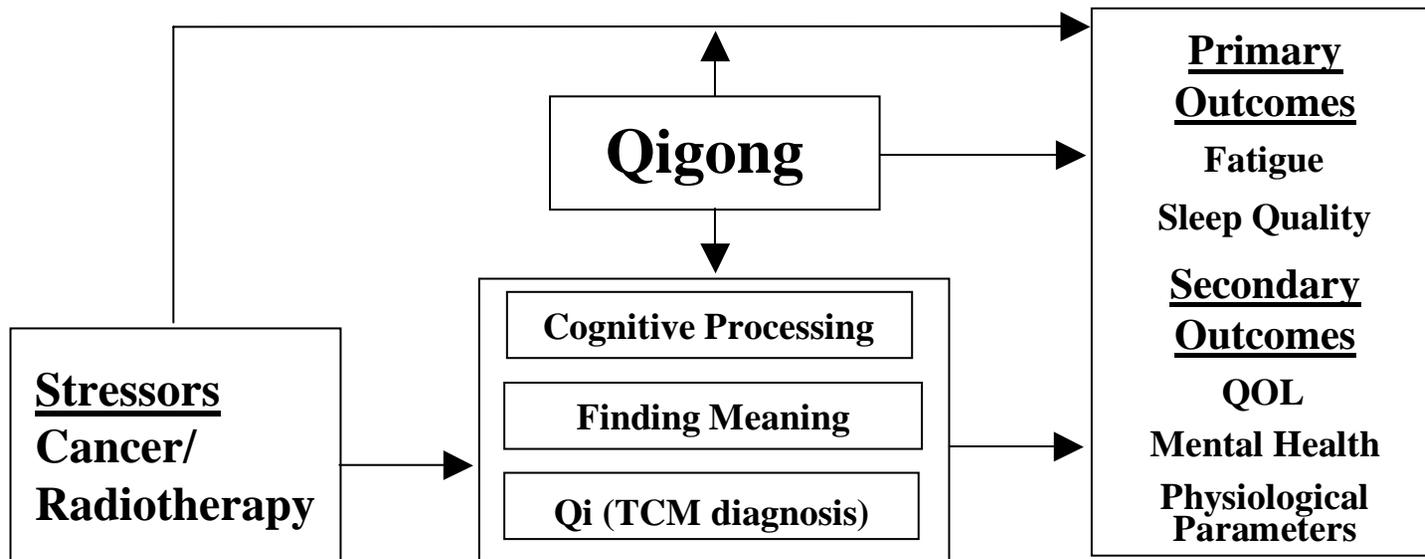
- **Examine the feasibility and initial efficacy of implementing a Qigong program for patients with breast cancer as an adjuvant to their radiotherapy.**
- **Patients with breast cancer who are undergoing radiotherapy are randomly assigned to either a Qigong group or a wait-list control group.**
- **Participants 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





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

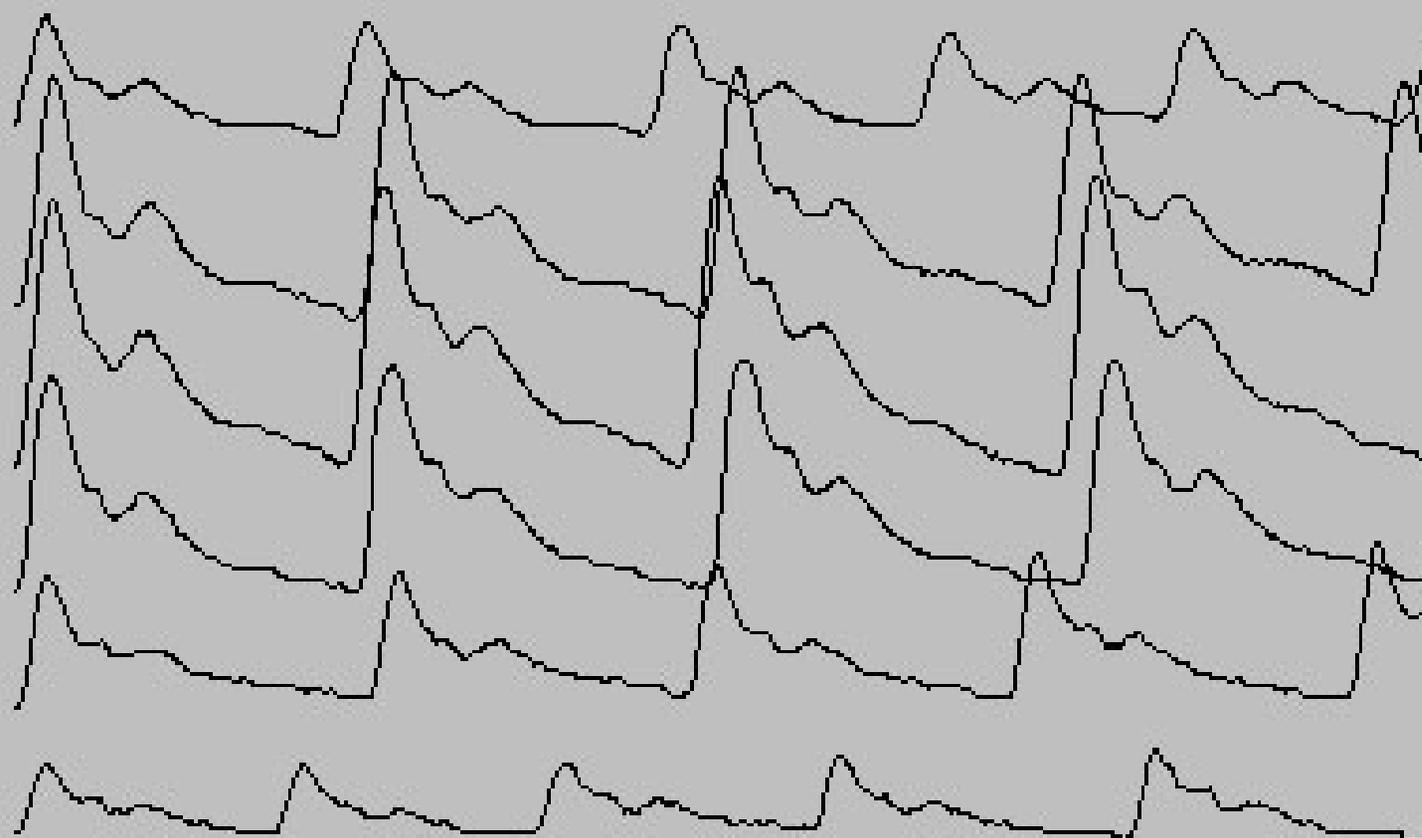




系列脉图

增益 1

NO.	P (g)
1	52.8
2	88.8
* 3	123.4
4	137.8
5	170.9
6	219.9



原始脉图

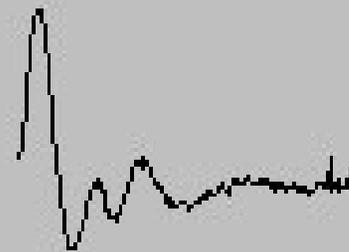
确 定

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

t1=	0.12s	h1=	19.3g	As=	3.7g.s	h3/h1=	0.61	w1=	0.12s
t2=	0.17s	h2=	14.0g	Ad=	2.8g.s	h4/h1=	0.43	w2=	0.08s
t3=	0.24s	h3=	11.7g	A =	6.5g.s	h5/h1=	0.08	w1/t=	0.12
t4=	0.31s	h4=	8.3g	t =	0.96s	t5/t4=	2.05	w2/t=	0.08
t5=	0.64s	h5=	1.5g						

确 定

测脉结论

脉 位： 中 脉 力： 中

脉 势： 正常 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





MM-3 脉象模型

D组模型：输出沉、细、涩、弱脉（依次排列）。

沉脉
脉象特征：脉位深沉，重按始得，举之不足，按之有余，其脉体沉而位较深。
临床意义：主气病内伤，各种虚证；又主邪盛，脉沉而实者为主。

细脉
脉象特征：脉细如线，应指明显，触脉感觉为脉管细小，硬而脆，按之不绝。
临床意义：主气血两虚，各种虚证；又主邪盛，脉沉而实者为主。

涩脉
脉象特征：形如刮竹，往来艰涩不畅，脉律与脉力不匀，应指如轻刀刮竹。
临床意义：主气滞、血少、痰食内停、气虚血瘀等证。

弱脉
脉象特征：脉微而沉，轻按则沉取方得，沉而无力。
临床意义：主阳虚或气虚血衰，多见于久病体弱之体。

MM-3 脉象模型

C组模型：输出弦、洪、代、促脉（依次排列）。

弦脉
脉象特征：脉体端直，如按琴弦，脉管紧张度增高，脉力较强，脉位较浅。
临床意义：主肝胆病、疼痛、痰饮、诸实、诸紧、诸弦等证。

洪脉
脉象特征：脉体宽大，来盛去衰，脉管扩张度增大，脉力较强，脉位较浅。
临床意义：主热证。

代脉
脉象特征：脉来数而时有一止，止有定数，脉律不匀。
临床意义：主脏气衰微，诸虚百损，亡阳等证。

促脉
脉象特征：脉来急数，时有一止，止无定数，脉律不匀。
临床意义：主阳盛实热，痰饮，气滞等证。

MM-3 脉象模型

B组模型：输出滑、数、弦、紧脉（依次排列）。

滑脉
脉象特征：脉体流利，应指圆滑，脉管扩张度增大，脉力较强，脉位较浅。
临床意义：主痰饮、食积、实热、诸实、诸滑等证。

数脉
脉象特征：脉来急促，脉率增快，脉律不匀，脉力较强，脉位较浅。
临床意义：主热证。

弦脉
脉象特征：脉体端直，如按琴弦，脉管紧张度增高，脉力较强，脉位较浅。
临床意义：主肝胆病、疼痛、痰饮、诸实、诸紧、诸弦等证。

紧脉
脉象特征：脉体紧张，如按绳索，脉管紧张度增高，脉力较强，脉位较浅。
临床意义：主寒证、痛证、痰饮、诸实、诸紧、诸弦等证。

MM-3 脉象模型

A组模型：输出浮、沉、迟、数脉（依次排列）。

浮脉
脉象特征：脉位浅显，轻按即得，重按反减，脉力较弱，脉位较浅。
临床意义：主表证、虚证、诸浮、诸数等证。

沉脉
脉象特征：脉位深沉，重按始得，举之不足，按之有余，脉力较弱，脉位较浅。
临床意义：主气病内伤，各种虚证；又主邪盛，脉沉而实者为主。

迟脉
脉象特征：脉来迟缓，脉率减慢，脉律不匀，脉力较弱，脉位较浅。
临床意义：主寒证、阳虚、痰饮、诸迟、诸数等证。

数脉
脉象特征：脉来急促，脉率增快，脉律不匀，脉力较弱，脉位较浅。
临床意义：主热证。







Fun & Games



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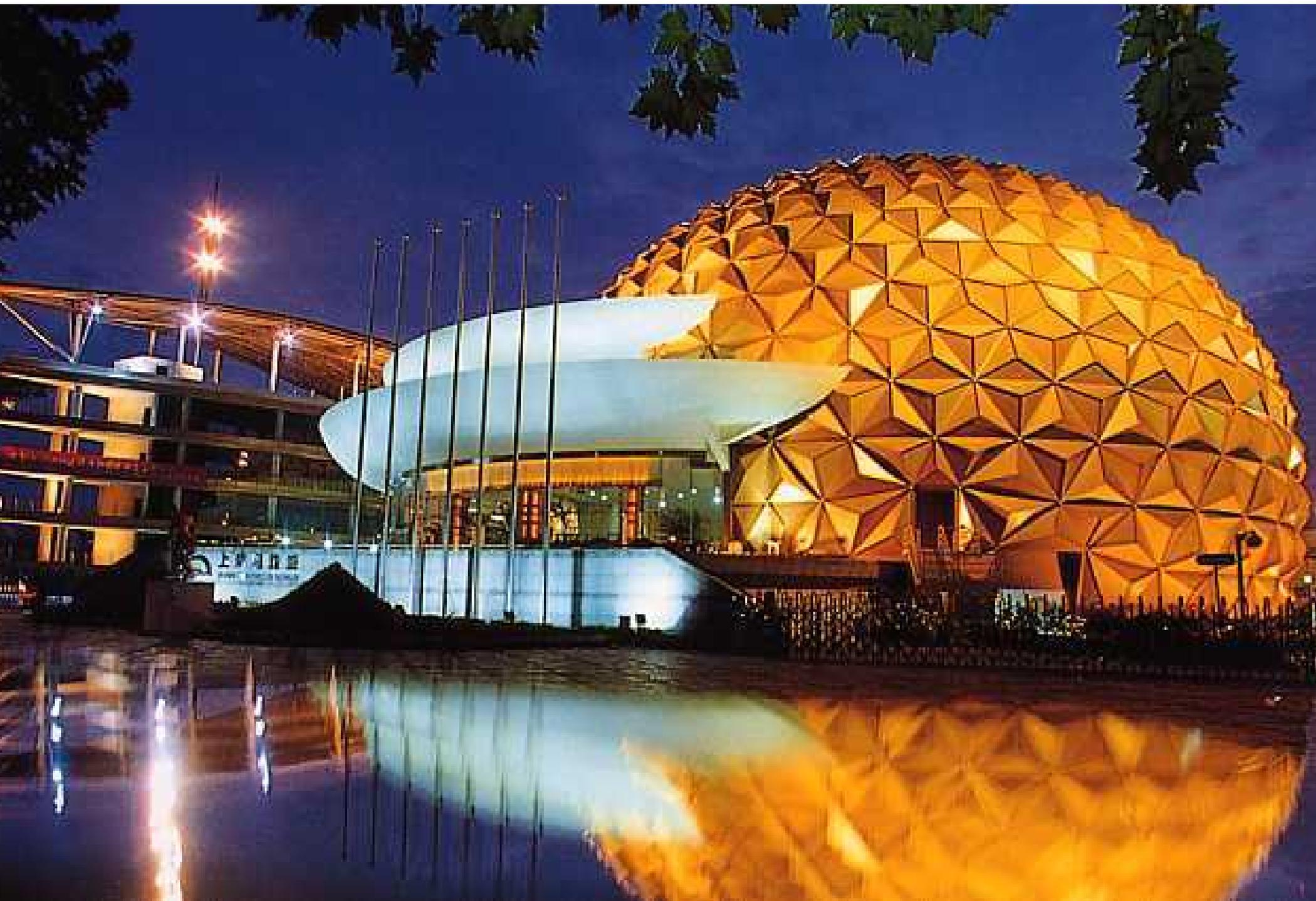
The text "Shanghai Today" is written in a bold, italicized, sans-serif font. The letters are filled with a vertical gradient from light blue at the top to yellow at the bottom. Below the text is a dark, semi-transparent shadow of the same text, which is slightly offset to the right and bottom, creating a 3D effect. The background is a solid, deep blue.

















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