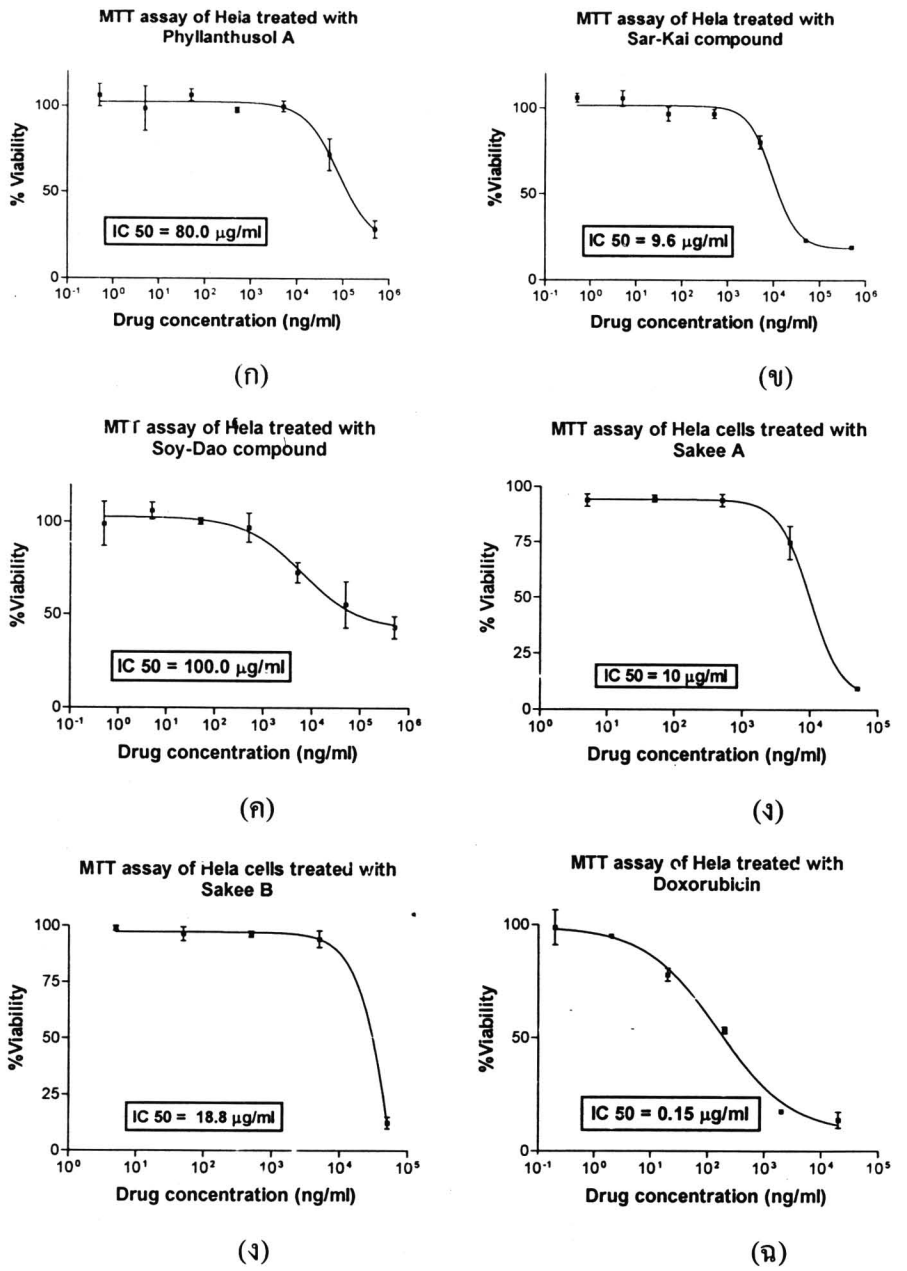
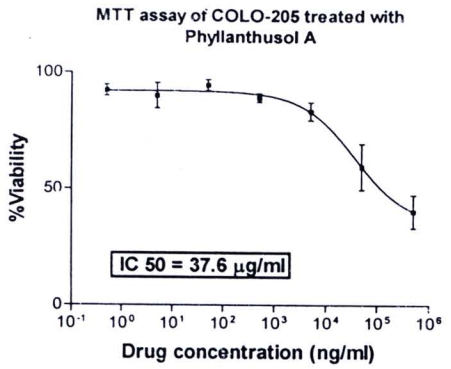
ภาคผนวก: รูปผลของการวิจัย



รูปที่ 1 ผลการทดสอบความเป็นพิษต่อเซลล์มะเร็งปากมดลูก (Hela) ด้วยสาร Phyllanthusol A (ก) สารสกัดจากสมุนไพรซาไก (ข) สารสกัดจากต้นสอยดาว (ค) สารสกัดจากต้นสักขี A (ง) สารสกัดจากต้นสักขี B (จ) และ ยา Doxorubicin (ฉ) โดยใช้วิธี MTT ในการทดสอบ (n=3)



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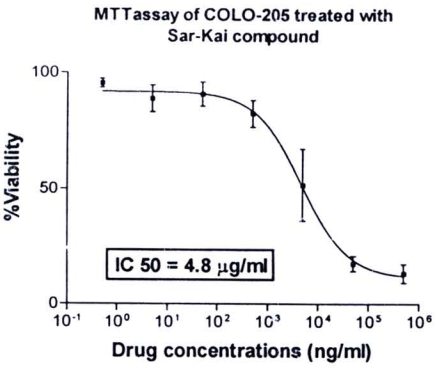

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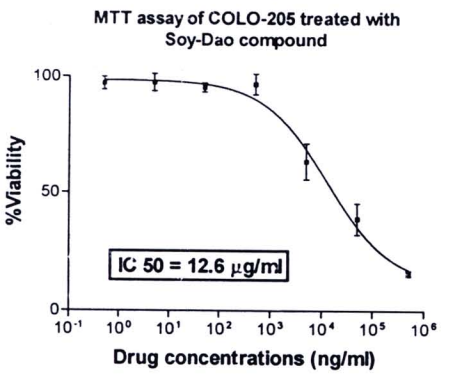

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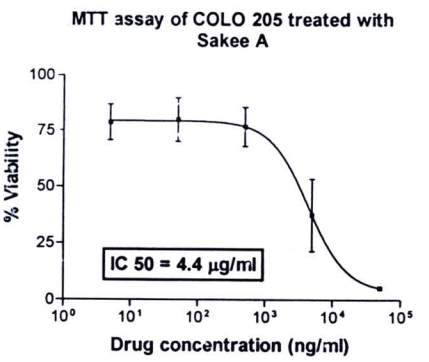

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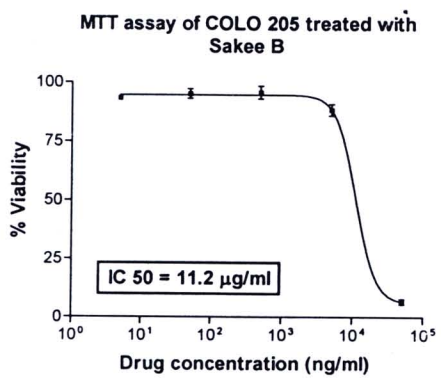

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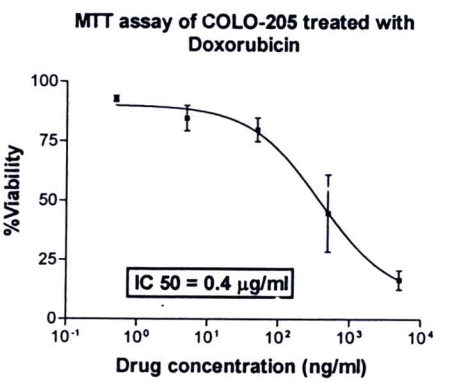
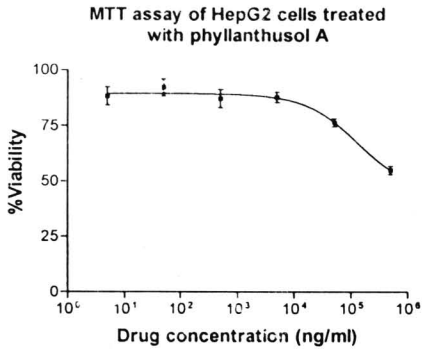


(ฉ)

รูปที่ 2 ผลการทดสอบความเป็นพิษต่อเซลล์มะเร็งลำไส้ (COLO 205) ด้วยสาร Phyllanthusol A (ก) สารสกัดจากสมุนไพรซาไก (ข) สารสกัดจากต้นสอยดาว (ค) สารสกัดจาต้นสักขีA (ง) สารสกัดจากต้นสักขี B (จ) และ ยา Doxorubicin (ฉ) โดยใช้วิธี MTT ในการทดสอบ (n=3)



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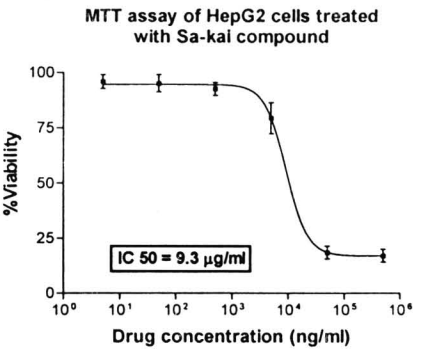

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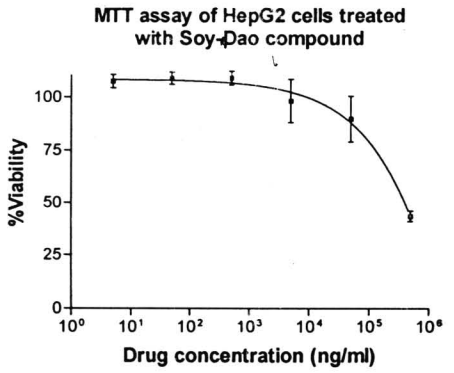

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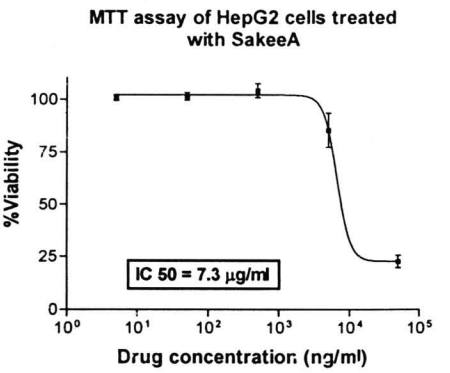

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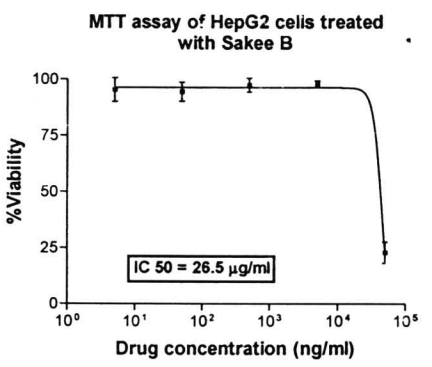

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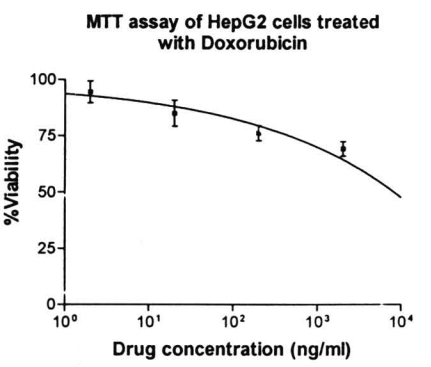
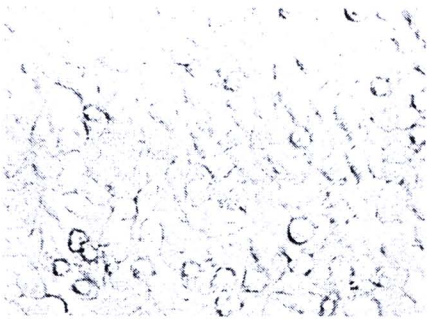


(ฉ)

รูปที่ 3 ผลการทดสอบความเป็นพิษต่อเซลล์มะเร็งตับ (HepG2) ด้วยสาร Phyllanthusol A (ก) สารสกัดจากสมุนไพรซาไก (ข) สารสกัดจากต้นสอยดาว (ค) สารสกัดจากต้นสักขี A (ง) สารสกัดจากต้นสักขี B (จ) และ ยา Doxorubicin (ฉ) โดยใช้วิธี MTT ในการทดสอบ (n=3)

ตารางที่ 1 ผลการทดสอบความเป็นพิษของสารสกัดบริสุทธิ์โดยวิธี MTT assay

สารที่ใช้ทดสอบ	IC 50 (μg/ml)		
	มะเร็งปากมดลูก (Hela)	มะเร็งลำไส้ (COLO 205)	มะเร็งตับ (HepG2)
สาร Phyllanthusol A	80.0	37.6	>100.0
สารสกัดจากสมุนไพรซาไก	9.6	4.8	9.3
สารสกัดจากต้นสอยดาว	100.0	12.6	>100.0
สารสกัดจากต้นสักขี A	10.0	4.4	7.3
สารสกัดจากต้นสักขี B	18.8	11.2	26.5
ยา Doxorubicin	0.15	0.4	>10.0



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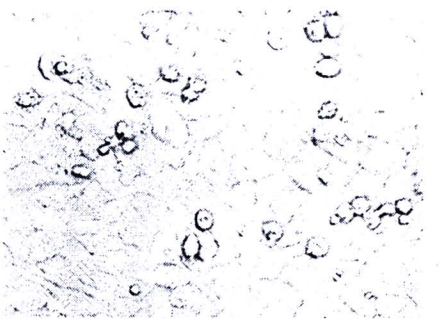

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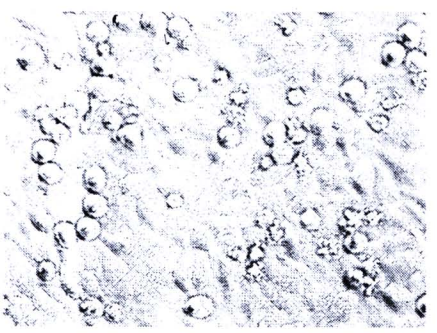

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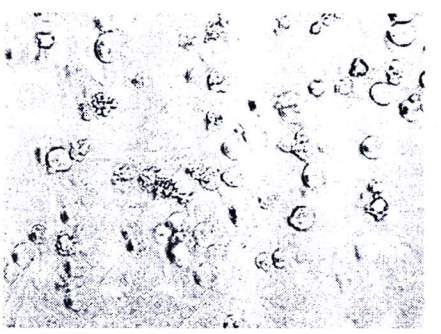
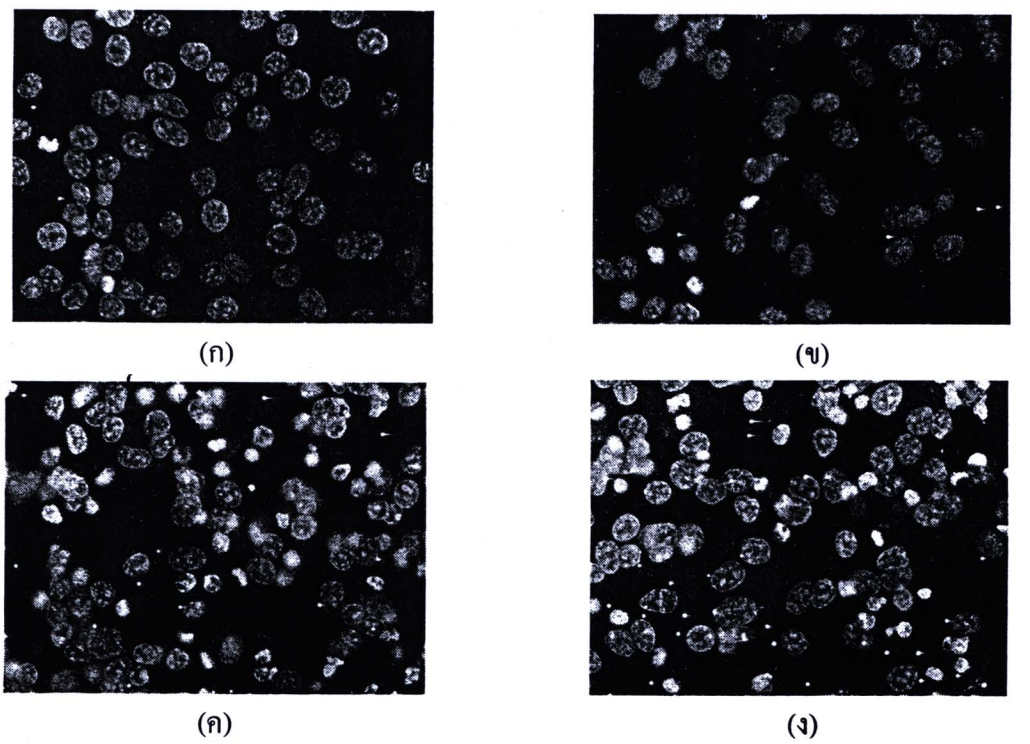
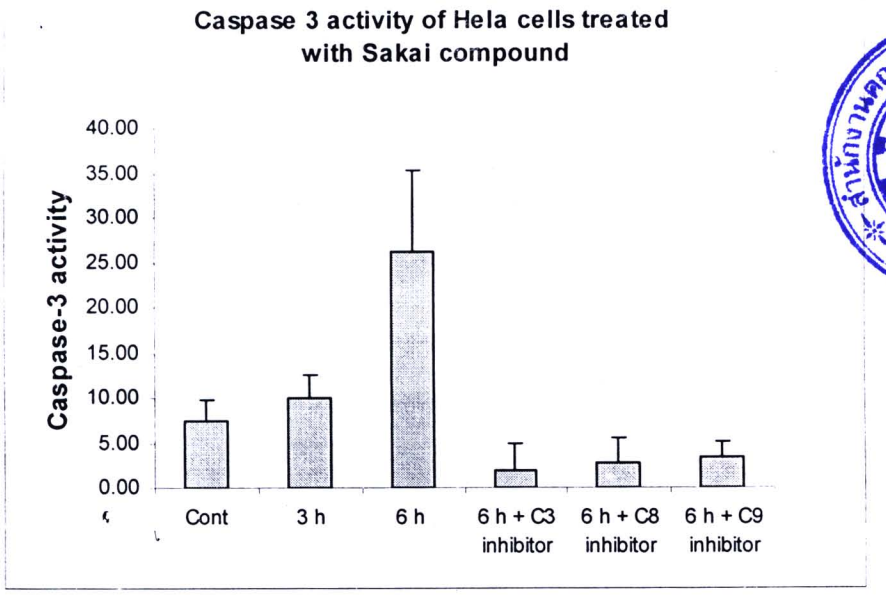


(ง)

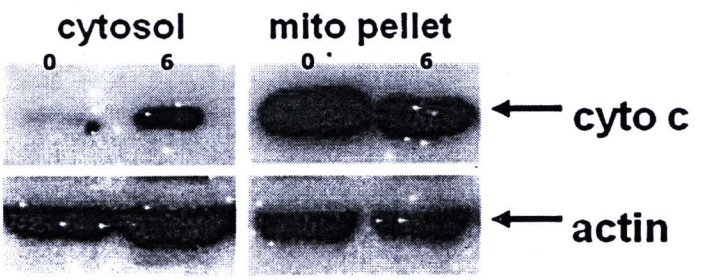
รูปที่ 4 ลักษณะภายนอกของเซลล์มะเร็งปากมดลูก (Hela cells) เมื่อถูกกระตุ้นด้วยสารสกัดจากสมุนไพรชาไกที่ความเข้มข้น 20 ไมโครกรัมต่อมิลลิลิตร เวลา 0 3 5 และ 7 ชั่วโมง (ก-ง) ที่อุณหภูมิ 37 องศาเซลเซียส ปริมาณ CO_2 เท่ากับ 5 % (กำลังขยาย 100 เท่า)



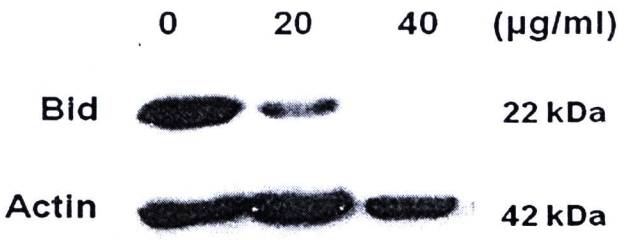
รูปที่ 5 ลักษณะของนิวเคลียสที่ย้อมด้วยสี DAPI ของเซลล์มะเร็งปากมดลูก (Hela cells) เมื่อถูกกระตุ้นด้วยสารสกัดจากสมุนไพรซาไกที่ความเข้มข้น 20 ไมโครกรัมต่อมิลลิลิตร เวลา 0 3 5 และ 7 ชั่วโมง (ก-ง) (กำลังขยาย 100 เท่า)



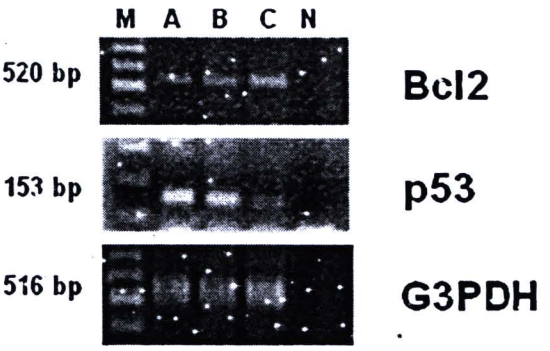
รูปที่ 6 ผลการทำงานของ caspase-3 เมื่อถูกกระตุ้นด้วยสารสมุนไพรซาไกเป็นเวลา 3 และ 6 ชั่วโมงและเป็นเวลา 6 ชั่วโมงเมื่อกระตุ้นร่วมกับการทำงานของ caspase-3 caspase8 และ caspase-9 inhibitor (n=5)



รูปที่ 7 การกระตุ้นการหลั่งของ cytochrome c จากไมโตคอนเดรีย โดยนำเซลล์มะเร็งปากมดลูกมาทดสอบด้วยสารสกัดสมุนไพรซาไกที่ความเข้มข้น 40 µg/ml เป็นเวลา 0 และ 6 ชม แล้ววิเคราะห์ผลด้วย 12% SDS-PAGE ตรวจสอบผลด้วย supersignal chemiluminescent kit



รูปที่ 8 การกระตุ้นการทำงานของ Bid โดยนำเซลล์มะเร็งปากมดลูกมาทดสอบด้วยสารสกัดสมุนไพรซาไกที่ความเข้มข้น 0, 20 และ 40 µg/ml เป็นเวลา 6 ชม แล้ววิเคราะห์ผลด้วย 12% SDS-PAGE ตรวจสอบผลด้วย supersignal chemiluminescent kit



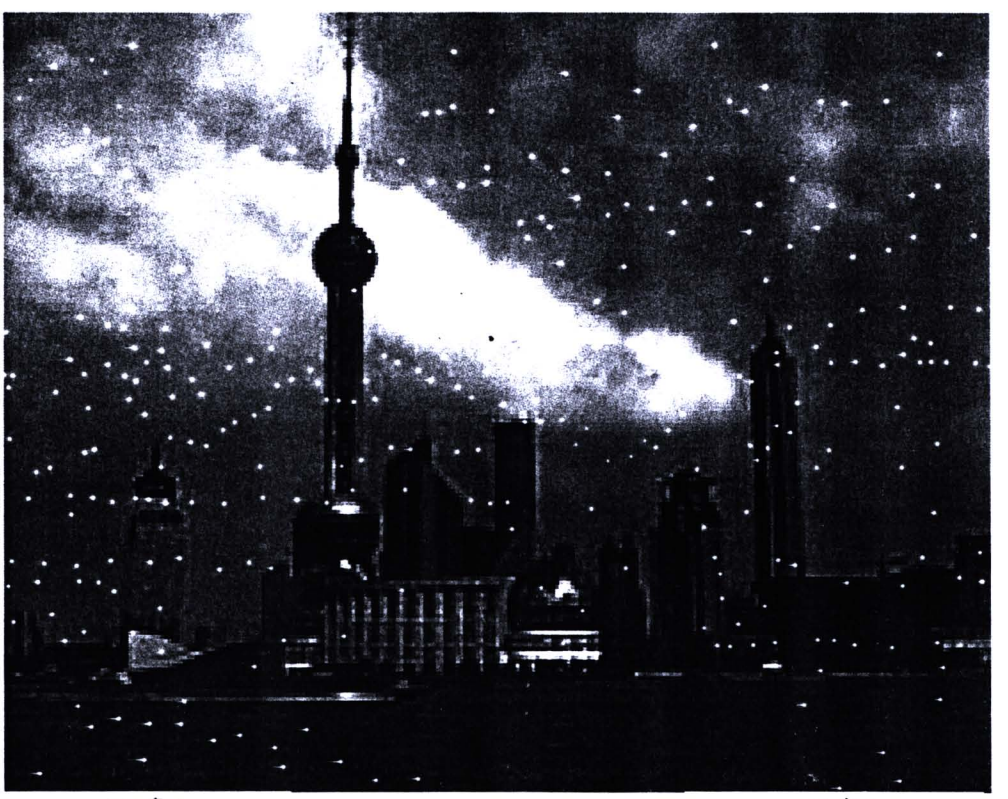
M = 100 bp DNA standard marker
A = Hela cells treat with altholactone 40 µM
B = Hela cells treat with altholactone 20 µM
C = Untreated Hela cells
N = Negative control

รูปที่ 9 การแสดงออกของโปรตีน p53 และ Bcl-2 โดยตรวจสอบด้วยวิธี RT-PCR นำเซลล์มะเร็งปากมดลูกมาทดสอบด้วยสารสกัดสมุนไพรซาไกที่ความเข้มข้น 0, 20 และ 40 µg/ml เป็นเวลา 6 ชม แล้ววิเคราะห์ผลด้วย 12% SDS-PAGE ตรวจสอบผลด้วย supersignal chemiluminescent kit

PROGRAM AND ABSTRACT BOOK

INTERNATIONAL CELL DEATH SOCIETY PRESENTS

"Targeting cell death pathways for human diseases"



Shanghai, China
June 6-9, 2008

Organized by:
Zahra Zakeri, Richard Lockshin, Junying Yuan, Jiarui Wu,
Dengxi Zheng, Yun Bo Shi

Grateful Acknowledgement Is Given For The Support From The Following Sponsors:

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Local Organizers:
-Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences
-Chinese Society of Biochemistry and Molecular Biology

Sponsors:
National Natural Science Foundation of China
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Shanghai Institutes for Biological Sciences, CAS

Local host: Shanghai National Accounting Institute

上海国家会计学院交通地理指南

学院坐落在上海市西南面的青浦区蟠龙路200号。距离上海市中心人民广场22公里，距离虹桥机场8公里。318国道和沪青平高速公路从学院旁穿过，出入非常方便，交通极为快捷。

到达学院的快捷线路:

虹桥机场出发：行程约10公里，出租车费约为30元。

浦东机场出发：行程约60公里，出租车费约为200元。（最快捷的方式可选择乘坐磁悬浮列车到龙阳路换乘地铁2号线到终点站淞虹路，再换乘出租车到达学院；也可以选择在浦东机场乘坐机场巴士到虹桥机场，再换乘出租车到达学院）

上海火车站出发：行程约25公里，出租车费约为80元。

上海火车南站出发：行程约22公里，出租车费约为70元。

到达学院的经济线路:

上海火车站出发：由北出站口出站，乘地铁3号线，再中山公园下车，换乘776路公交车，到徐泾中路蟠龙路站下车即到。

上海火车南站出发：乘坐上朱线公交车，到谢家宅站下车向回走到蟠龙路即到。

经过学院的其他公交线路

上朱线：(首/末班时间：上海南站05:00-18:30 朱家角05:10-18:40)

谢家宅站下车

运行路线：上海南站 - 桂林路桂林西街 - 桂林路冠生园路(上海师大) - 桂林路田林路 - 桂林路吴中路 - 虹桥路伊犁路 - 虹桥路程家桥(上海动物园) - 沪青平公路吴家巷 - 杨家泾 - 卫家角 - 谢家宅 - 徐泾 - 蟠城中东路 - 朱家角

票价：按路段收费

沪青盈专线：(首/末班时间：普安路07:00-09:30大盈乡15:00-16:00)

谢家宅站下车

运行路线：普安路 - 谢家宅 - 青安路 - 城中北路 - 胜利路 - 青浦汽车站 - 大盈乡

票价：全程8元

沪朱专线：(首/末班时间：老成都北路07:00-17:45朱家角05:50-17:15)

谢家宅站下车

运行路线： 老成都北路 - 谢家宅 - 徐泾 - 赵巷 - 青浦 - 朱家角

票价：全程8元

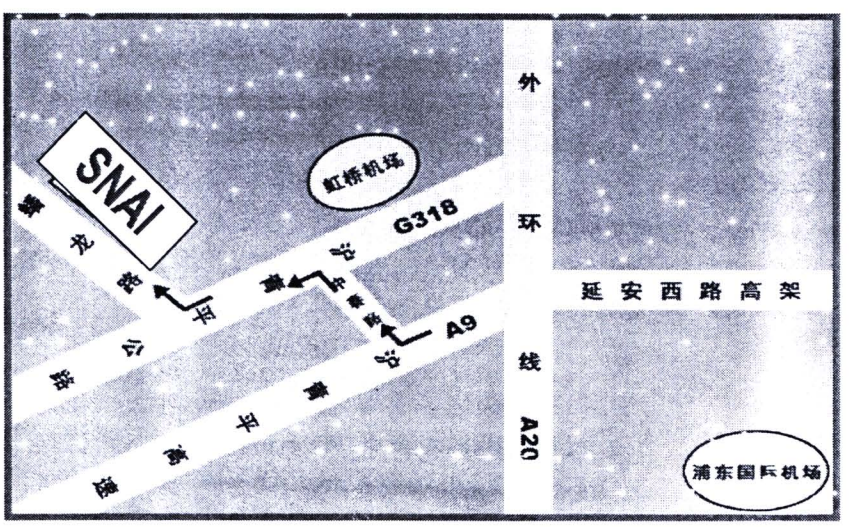
776（原中卫线）：(首/末班时间：凯旋路近长宁路：6:20-20:30 联民路（青浦）6:20-19:30)

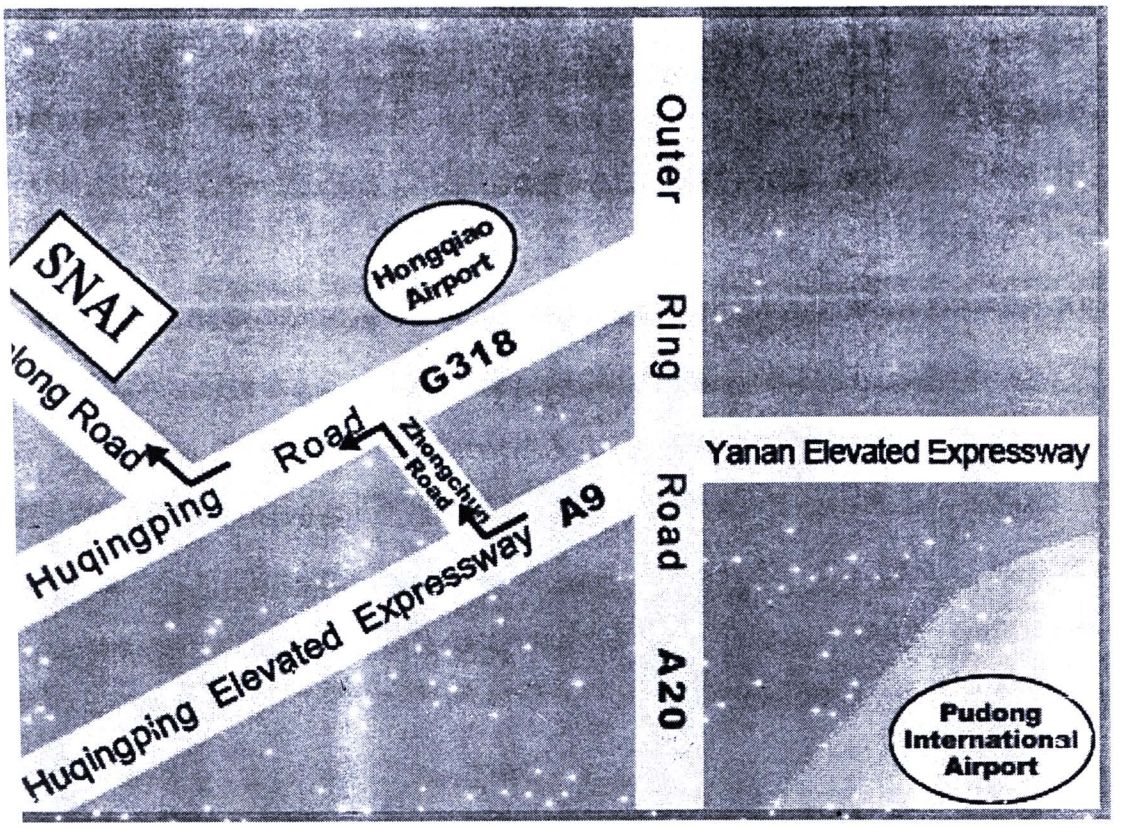
徐泾中路蟠龙路站下车

运行路线：中山公园地铁站 - 中山公园 - 定西路武夷路 - 延安西路中山西路 - 中山西路安顺路 - 中山西路虹桥路 - 西区汽车站 - 吴中路张虹路 - 古北新城 - 虹桥镇 - 吴中路虹桥路 - 吴中路合川路 - 吴中路虹井路 - 吴中路航中路 - 航北路航中路 - 航华一村 - 航东路沪清平公路 - 沪清平公路航新路 - 吴家老 - 杨家泾 - 卫家角 - 诸光路 - 久事花园 - 徐泾中路诸光路 - 徐泾中路蟠龙路 - 广虹馨苑 - 徐泾中路明珠路 - 联民路沪清平公路 - 联民路(青浦)

票价：按路段收费

具体可参考网站：www.snai.edu "交通地理"内容。





d Map to Shanghai National Accounting Institute (SHAI)

(No. 200 Pan-Long Road , Shanghai)

(The meeting-place for "The Seventh International Cell Death Society Symposium")

ving on Shanghai Pu-Dong Airport

: One:

a taxi directly from Shanghai Pu-Dong airport to No.200 Pan-Long Road, Shanghai National inting Institute (about 60 Km; Taxi fee: about 200RMB).

e Two:

ake an airport shuttle bus from Shanghai Pu-Dong airport to the stop "Shanghai Hong-Qiao Airport" n Shuttle Bus No.1 (bus fee: 30RMB); then take a taxi from Shanghai Hong-Qiao Airport to No.200 ong Road, Shanghai National Accounting Institute (Taxi fee: about 30RMB).

riving on Shanghai Hong-Qiao Airport

a taxi directly from Shanghai Hong-Qiao airport to No.200 Pan-Long Road, Shanghai National nting Institute (about 10 Km; Taxi fee: about 30RMB).

上海国家会计学院（蟠龙路200号）的路线图

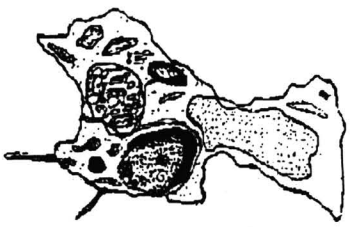
Road Map to Shanghai National Accounting Institute (No. 200 Pan-Long Road)

Table of Contents

Welcome

On behalf of the International Cell Death Society, the organizing committee, and our hosts, we welcome you all and offer our wishes for a successful meeting and very pleasant stay in China.

Welcome to China!



The International Cell Death Society
"The Death Poet's Society"

YOUR SOCIETY: THE INTERNATIONAL CELL DEATH SOCIETY

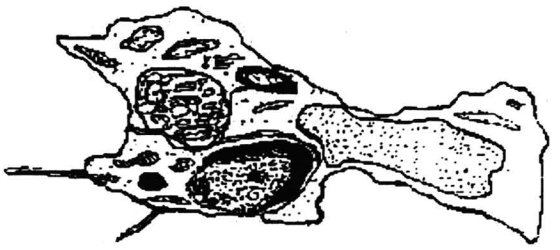
- The society promulgates a better understanding of the mechanisms of cell death, establishing communication among the various branches of the research and communicating and coordinating the application of research findings. We sponsor monthly meetings in New York City and other cities, a biannual meeting, and a web page. We have approximately 600 members. Members receive discounts to Apoptosis, and discounted registration for the annual meetings.

- We sponsor local meetings approximately monthly in New York City, and we encourage other groups to establish similar local forums. We can provide logistic support and advices, as well as announcements on our webpage. We encourage you to put your group together and let us know so we can let others know about you.

- This is your society. We solicit your ideas and suggestions. Our aim is to promote integration of the ideas in the field and to support communication of knowledge in the broadest interpretation of the field. We are instituting short courses on the aspect of Cell Death & aging in this years meeting. Please give us your comments either on the questionnaire to be distributed at the end of the meeting or by direct communication to us (see website for addresses).

YOUR WEB PAGE (http://www.celldeath-apoptosis.org): The society's web page is for benefit of the research and clinical communities. Please us to build it. It has been quite popular since its inception (over 100 hits/day since September 1997), but it needs and update. We solicit both suggestions and contributions. We would like to rewrite various sections concerning general areas of apoptosis. Contributions should be one to two typewritten pages in length. We welcome clear illustrative material. Original artwork or digital images (tiff, jpeg, gif files preferred, pdf and other files possible) can be accepted. Editorial assistance is available, and full credit will be given on the website. Contact Richard Lockshin, lockshin@stjohns.edu or send a message to webmaster@celldeath-apoptosis.org.

JOIN THE INTERNATIONAL CELL DEATH SOCIETY



The International Cell Death Society

MEMBERSHIP 2008

The Society has been formed for the purposes of promulgating a better understanding of the mechanisms of cell death and apoptosis, establishing communication among the various branches of research, and communicating and coordinating the application of research findings in biology and medicine.

ITS ACTIVITIES INCLUDE:

- Monthly meetings in New York City and other cities as demand warrants;
- Annual international meeting in years alternating with the Keystone, and Cold Spring Harbor meetings;
- A web page with discussion sections, job mart, education pages

BENEFITS FOR MEMBERS INCLUDE:

- Discounted admission to the annual meeting;
- Access to other club services.

MEMBERSHIP FEES:

Industry: US $125.00; Academia: US $75.00; Students and Post-docs: US $35.00

I hereby authorize the amount of $_____ to be charged to my ____Visa ___MC by the Queens College Foundation for the Cell Death Society.
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A non-profit organization. For further information contact: Dr. Zahra Zakeri, Queens College of CUNY, Flushing, NY 11367. Tel: 718: 997-3417, Fax: 718: 997-3429, email: Zahra_Zakeri@hotmail.com or Victoria Matassov Cell Death Secretary, email: victoriamatassov@hotmail.com. ICDS Web Page: http://www.celldeath-apoptosis.org

Conference Program
The Seventh International Cell Death Society Symposium on
Targeting cell death pathways for human diseases

Shanghai Mega City, China
June 6-9, 2008

Registration Opens **9:00am—6pm**

Friday 6th June 2007

11:00-12:00pm **Meeting on establishing ICDS China chapter**

Welcome and Introduction

Session 1: Introduction and Keynote Speaker
Chair: Zahra Zakeri: Queens College, U.S.A

2:00-2:15pm **Introduction and Welcome**
Zahra Zakeri: Queens College, U.S.A

2:15-2:30pm **Welcome**
Jiarui Wu: Shanghai Institutes for Biological Sciences, China

2:30-3:00pm **Presentation of Award to Dr. H. Robert Horvitz**
Richard Lockshin: St. Johns University, U.S.A

3:00-4:00pm **Genetic Control of Programmed Cell Death in *C. elegans***
H. Robert Horvitz: MIT, U.S.A

4:00-4:30pm **COFFEE**

Session 2: Research and Development in China
Chair: Jiarui Wu: Shanghai Institutes for Biological Sciences, China

4:30-5:00pm **R & D in China - New adventure for Astrazeneca**
Xiaolin Zhang: AstraZeneca Globla R&D, China

5:00-5:30pm **TRPC channels and neuronal survival**
En Li: Novartis, Shanghai, China

5:30-6:00pm **A New Model in Discovery of Innovative Medicine: a Look at Roche R&D Center China**
Li Chen: Roche R&D center, China

7:00pm **DINNER, Awards**

Registration Opens **8:00am**

Saturday 7th June 2008
Session 3: Pathways: Apoptosis, Necrosis, Autophagy and more
Chairs: Roya Khosravi-Far: Harvard Medical School, U.S.A

9:00-9:30am **Molecular connections between different cell death pathways**
Xiaodong Wang: Southwestern Medical Center, U.S.A

9:30-10:00am **System level analysis of programmed cell death: switching between different death modalities**
Adi Kimchi: Weizmann Insitute of Science, Israel

10:00-10:15am **Pretaporter, A *Drosophila* Endoplasmic Reticulum Protein Serving As A Ligand For Draper In Phagocytosis Of Apoptotic Cells**
Takayuki Kuraishi: Kanazawa University, Japan

10:15-10:30am **Imaging Of Caspase Activation During Drosophila Development**
Erina Kuranaga: University of Tokyo, Japan

10:30-11:00am **COFFEE**

Chair: Dengxi Zheng: Chinese Academy of Medical Science, Beijing

11:00-11:30am **Regulation of autophagy**
Patrice Codogno: INSERM U756, France

11:30-12:00pm **Regulation of autophagy in mammals by Ambra-1 and its partners**
Mauro Piacentini: University of Rome, "Tor Vergata", Italy

12:00-12:30pm **NF-kB as a regulator of apoptosis of human leukemia**
Marc Diederich: Hopital Kirchberg, Luxembourg

12:30pm-2:00pm **Lunch**

Session 4: Signaling in Cell Death
Chair: Simone Fulda: Ulm University, Germany

2:00-2:30pm **Molecular mechanisms of cytotoxic lymphocyte mediated cell death**
Nigel Waterhouse: Peter MacCallum Cancer Centre, Australia

2:30-3:00pm **Death pathways mediated by the granules of NK/CTLs**
Zusen Fan: Institute of Biophysics, CAS, China

3:00-3:15pm **Cloning and expression Of Bir3 Domain Of mouse Naip1 protein**
Jamshid Davoodi: University of Tehran, Iran

3:15-3:30pm **Erucylphosphohomocholine-Induced Apoptosis In Human Glioma Cells: Role Of The Oligomycin-Sensitive F0 Part Of Mitochondrial H^+-Atp-Synthase**
Wilfried Kugler: Universitats-Kinderklinik, Germany

3:30-4:00pm **COFFEE**

Chair: Marianne Cronje: University of Johannesburg, South Africa

4:00-4:30pm **Death in the Oocyte**
Sally A. Kornbluth: Duke University Medical Center, U.S.A

4:30-5:00pm **Diversity of the roles of caspase activation during development**
Masayuki Miura, University of Tokyo, Japan

5:00pm-7:00pm **Poster Session**

7:00pm **DINNER**

Registration Opens **8:00am**

Sunday 8th June 2008
Session 5: Regulation of Cell Death I
Chair: Marie-Lise Gougeon: Institut Pasteur, France

9:00-9:30am **Regulation of DNA-damage-induced apoptosis by protein arginine methylation in *C. elegans***
Chong-Lin Yang: Institute of Genetics and development, CAS, China

9:30-10:00am **Molecular regulation of mitochondrial dynamics**
Quan Chen: Inst. Of Zoology, Chinese Academy of Sciences, China

10:00-10:15am **Cellular Pro-Apoptotic Bax and Bak Play Opposing Roles During Influenza A-Induced Cell Death**
Jeff Mclean: Queens College, U.S.A

10:15-10:30am **Oxidative Stress And Chaperone-Mediated Cancer Cell Death**
Pedro Calderon: Université Catholique de Louvain, Belgium

10:30-11:00am **COFFEE**

Session 6: Regulation of Cell Death II

Chair: Nader Maghsoudi: Shaheed Behesti Medical University, Iran

11:00-11:30am **Negative Regulation of caspases**
Herman Steller: Rockefeller University, U.S.A

11:30-12:00pm **New apoptotic complexes including mitochondrial AK2 and caspase-10 in Cell Death and Tumor**
Yong-Keun Jung: Seoul National University, Korea

12:00-12:15pm **Calpain Inhibitors Delay Injury-Induced Apoptosis In Adult Mouse Spinal Cord Motor Neurons**
Hamid Reza Momeni: University of Arak, Iran

12:15-12:30pm **Perturbations In Bioenergetics Of Mitochondria Mediate The Induction Of Apoptosis By Perfluoroalkyl Acids**
Konrad Kleszczynski: Medical University of Gdansk, Poland

12:30-2:30pm **LUNCH**

Chair: Shazib Pervaiz: Singapore

2:30-3:00pm **FoxO Transcription Factors in the Regulation of Blood**
Saghi Ghaffari: Mount Sinai School of Medicine, U.S.A

3:00-3:30pm **TRPC channels and neuronal survival**
Yi-Zheng Wang: Institute of Neuroscience, SIBS, CAS, China

3:30-4:00pm **Function And Mechanism Of Stromelysin-3 In Thyroid Hormone Induced Apoptosis During Amphibian Metamorphosis**
Yon-Bo Shi: NIH, U.S.A

4:00-4:30pm **COFFEE**

Session 7: Phagocytosis
Chair: Ray Birge: New Jersey Medical School, U.S.A

4:30-5:00pm **Engulfment of apoptotic cells**
Shigekazu Nagata: Kyoto University, Japan

5:00-5:30pm **Role of TAM (Tyro-3, Axl, Mertk) receptors in immune moduation and phagocytosis of apoptotic cells**
Ray Birge: New Jersey Medical School, U.S.A

5:30- 7:30pm **Poster Session**

7:30pm **DINNER**

Registration Opens **8:00am**

Monday 9th June 2008
Session 8: Targeting Cell Death for Therapeutics
Chair: Boris Zhivotovsky: Karolinska Insitut, Sweden

9:00-9:30am **p53 orthologue regulates metabolic enzyme in repairing DNA damage**
Mian Wu: Chinese University of Science and Technology, China

9:30-10:00am **Modulation of apoptosis-associated gene products by Resveratrol: role in chemo-sensitzation of myeloma and lymphoma tumor cells**
Ali Jazirehi: Howard Hughes Medical Insitute, U.S.A

10:00-10:15am **Prion Protein and Breast Tumor Resistance to Cell Death**

Maryam Mehrpour: CAS, Beijing, China

10:15-10:30am **Selective Death Of Tumor Cells By Interference Of The Antisense Non-Coding Mitochondrial Rna (Ncmtrna) With Oligonucleotides**
Soledad Viduarre: Chile

10:30-11:00am **COFFEE**

Chair: Jean-Ehrland Ricci: INSERM, France

11:00-11:30am **Mechanisms of cell death/survival in ischemic cardiac diseases**
Sergio Lavandero: University of Chile, Chile

11:30-12:00pm **Effects of hypoxia on chemotherapeutic drug-induced apoptosis in different cancer cell lines**
Carine Michiels: Facultés Universitaires Notre Dame de la Paix, Belgium

12:00-12:30pm **Targeting cell death pathways for human diseases**
Silvia Soddu: Regina Elena Cancer Insitute, Italy

Session 9: **Wrap-up**
12:30-1:00pm **Perspective of the field and how this meeting fits in it**
Guido Kroemer: INSERM, U848, Institut Gustave Roussy, France

1:00-2:00pm **LUNCH**

Poster Abstracts

Session Number: A

N-BAK IS REGULATED POST-TRANSCRIPTIONALLY AND CAUSES APOPTOTIC CHANGES IN THE SYMPATHETIC NEURONS

Jakobson M (1), Yabal M (2), Jokitalo E (1),* ***Arumäe U@ (1)***
(1) Institute of Biotechnology, University of Helsinki, Biocenter 1, Viikinkaari 9, P.O. 56, FIN-00014, Helsinki, Finland; (2) Walter and Eliza Hall Institute of Biomedical Research, 1G Royal Parade, Parkville Victoria 3050, Australia

mRNA for N-Bak, a BH3-only splice variant of Bak is expressed only in neurons, whereas Bak mRNA is expressed in all tissues but not in the neurons. Despite the normal levels of N-Bak mRNA, endogeneous N-Bak protein is difficult to demonstrate, suggesting a post-transcriptional regulation. Although N-Bak mRNA meets the formal criteria for nonsense-mediated decay, our preliminary results show that it is not the case in the primary neurons. When overexpressed in the cultured sympathetic neurons deprived of nerve growth factor (NGF), N-Bak retards their apoptotic death. In the NGF-maintained neurons, overexpressed N-Bak localized to Golgi in a C-tail-dependent manner. It caused Golgi dispersal, apoptotic morphology of the mitochondria and release of cytochrome c from the mitochondria to the cytosol. The death of the neurons was still retarded, probably by blockage of caspase activation.

Presenter: Urmas Arumae

DJ-1 MEDIATED NEUROPROTECTION IS CONTROLLED BY CASPASES PROTEOLYSIS

Giaime, E (1), Sunyach, C (1), Grosso, S (2), Auberger, P (2), Goldberg, M (3), Shen, J (3), Heutink, P (4), Pagès, G (5), Checier, F (1) ***and Alves da Costa, C* (1),***
(1) Institut de Pharmacologie Moléculaire et Cellulaire, UMR6097 CNRS/UNSA; (2) Faculté de Médicine, INSERM U526, Avenue de Valombrose, 06107 Nice, France; (3) Center of Neurologic Diseases, Harvard Medical School, Boston, Massachusetts, USA; (4) Department of Clinical Genetics, Erasmus MC Rotterdam, P.O. Box 1738, 3000, DR Rotterdam, The Netherlands; (5) Institute of Signaling, Developmental Biology and Cancer Research, CNRS UMR 6543, Centre A. Lacassagne, 33 Avenue de Valombrose, 06189 Nice, France

Autosomal recessive genetic cases of Parkinson's disease are usually characterized by early onset and aggressive evolution. Several gene candidates have been identified which account for these familial cases, among which DJ-1, a cytosolic oxidative stress regulator. The mechanisms by which mutations on DJ-1 could alter its function and account for PD-related pathology is poorly understood. We have analyzed the ability of DJ-1 to modulate cell death as well as its influence on p53 pathway at both transcriptional and post transcriptional levels. The effect of either wild-type or mutated DJ-1 in the control of cell death was performed in various cell systems including neuronal dopaminergic cells such as SH-SY5Y neuroblastoma cells and mouse embryonic fibroblasts depleted or not in DJ-1 and p53. Here we show that overexpression of DJ-1 elicits an antiapoptotic phenotype by regulating the p53-dependent cell death pathway at both transcriptional and post-transcriptional levels. The inverse phenotype was observed when DJ-1 was depleted both *in vitro* and *in vivo*. We show that DJ-1 is proteolytically processed to generate a catabolite that is responsible for the DJ-1-associated protective phenotype. Of most importance, a pathogenic DJ-1 mutation abolished both DJ-1 cleavage and associated protective phenotype. Overall, our data show that DJ-1 triggers a p53-dependent antiapoptotic phenotype and that this function is proteolytically regulated and impaired by pathogenic mutations.

Presenter: Cristina Alves da Costa

JNK MEDIATES UVB-INDUCED APOPTOSIS BY TRIGGERING LYSOSOMAL MEMBRANE PERMEABILIZATION AND BIM PHOSPHORYLATION

Bivik C *(1)*, Rosdahl I (1), Öllinger K @(2). Divisions of (1) Dermatology and (2) Experimental Pathology, Faculty of Health Sciences, Linköping University, SE-581 85, Linköping, Sweden.*

UVB irradiation induces phosphorylation of JNK and subsequent apoptosis in human melanocytes. Depletion of JNK expression using siRNA transfection, protected against apoptosis, as detected by decreased nuclear fragmentation and caspase-3 activity, as well as reduced translocation of Bax to

hydroxitamoxifen. E2F1 activation produced apoptosis in naive and post-mitotic cells; serum and NGF respectively protected them from E2F1 apoptotic stimuli. The presence of SB216763, a GSK3 inhibitor, completely protected cells from the apoptosis induced by E2F1 activation. The effect of SB216763 occurred upstream from the activation of caspase 3 and cytochrome C release. Significative change on the expression of members of BCL2 family was not detected after E2F1 activation. However, over-expression of E2F1 produced the oligomerization of Bax in the mitochondria; inhibition of GSK3 activity reverse this effect; this effect is concomitant with the loss of mitochondrial membrane.potential. Studies are in progress to elucidate the involvement of GSK3 on the oligomerization of Bax.

Presenter: Albert Tauler

SEARCHING FOR TUMOR SUPPRESSOR-LIKE GENES IN YEAST

Xinchen Teng*, *Wen-chih Cheng, Kelly M. Leach, Kalyani Ramachandran and J. Marie Hardwick , Departments of Pharmacology and Molecular Microbiology, Schools of Medicine and Public Health, Johns Hopkins University, Baltimore, Maryland, 21205*

Fis1 is a highly conserved mitochondrial fission protein and has been implicated in mammalian cell death. We found that *FIS1* knockout yeast strains develop a specific secondary mutation in a stress-response gene that also causes increased programmed cell death susceptibility. Interestingly, this secondary mutation also causes overgrowth on low leucine media and sensitivity to rapamycin, suggesting that this secondary mutation leads to constitutive activation of the TOR (target of rapamycin) pathway, which is commonly activated in human cancers. Taken together, these phenotypes of our *FIS1* knockout yeast are reminiscent of human tumor cells, as they are sensitive to cell death stimuli, fail to respond to nutrient limitation, are sensitive to rapamycin (TOR-dependent), and exhibit lower O_2 consumption (possible reduced mitochondrial oxidative phosphorylation). The human *fis1* gene is located in a region on chromosome 7 that is commonly deleted in AML, but no tumor suppressor has yet been identified in this region. Preliminary experiments in mammalian cells suggest that knockdown of human Fis1 can cause some of the same phenotypes observed in yeast. While the yeast community generally regards these secondary mutations as trivial consequences to improve cell growth/survival, we suggest that this selection process is reflective of early tumorigenesis. Therefore, we analyzed the ~5000 strains in the yeast genome knockout collection in a three-way screen for cell death, low leucine growth and rapamycin sensitivity. Preliminary results have identified several Fis1-like candidates, consistent with the possibility that yeast will be a powerful tool to study the initial steps in tumorigenesis.

Presenter: Xinchen Teng

ALTHOLACTONE INDUCES APOPTOSIS VIA CASPASE-8 AND -9 DEPENDENT PATHWAYS INCERVICAL CARCINOMA CELL.

Uthaisang-Tanechpongtamb W*(1), and Wilairat P@(2), (1) Department of Biochemistry, Faculty of Medicine, Srinakharinwirot University, Bangkok, Thailand 10110, (2) Department of Biochemistry, Faculty of Science, Mahidol University, Bangkok, Thailand 10400*

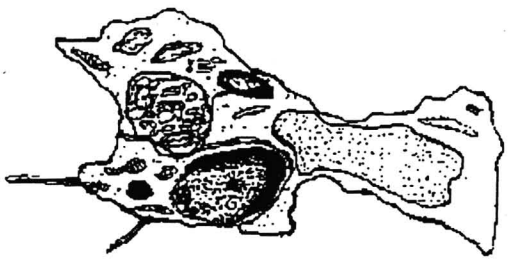
As part of a program to develop anticancer drugs from natural agents, altholactone extracted from Goniothalamus macrophyllus (FamilyAnnonaceae) was investigated for cytotoxicity and induction ofapoptosis in cervical carcinoma HeLa cell line. MTT assay showed thataltholactone had IC50 value of 9.6 ug/ml. Blebbing formation at theplasma membrane, chromatin condensation and caspase-3 activation, characteristics of apoptosis, increased in a time-dependent manner.Interestingly, caspase-3 activation was inhibited by both inhibitorsof caspase-8 and caspase-9 suggesting the possibility of a type IIapoptotic signaling pathway which has mitochondria as amplifier.This notion was supported by the release into cytosol of cytochrome cfrom mitochondria.

Presenter: Wanlaya Uthaisang-Tanedchpongtamb

GENETIC ANALYSIS OF NEURONAL CELL DEATH MECHANISM IN DROSOPHILA OPTIC LOBE CELLS THAT FAILED TO GET RETINAL INNERVATION.

Yu Togane*, *Rie Ayukawa, Keiichiro Hirai, Kengo Beppu, Yusuke Hara, Tatsuro Enomoto, Hiromi Akagawa, and Hidenobu Tsujimura@. Tokyo University of Agriculture and Technology, Developmental Biology.*

During neuronal development, synaptic connection plays an essential role in the development and survival of pre- and post-synaptic neuronal cells. When pre-synaptic cells or axons get damaged and their correct projection is interrupted, post-synaptic cells can die or fail to differentiate properly. This suggests that neuronal connection transmits survival/differentiation signals to post-synaptic cells during



International Cell Death Society Symposium On

"Targeting cell death pathways for human diseases"

April 3, 2008

To Whom It May Concern:

This is to confirm that ____ **Dr.Wanlaya Uthaisang-Tanechpongtamb** _ has been accepted to attend the International Cell Death Society Meeting to be held at the Shanghai National Accounting Institute in China June 6-9, 2008. I am the President of the Cell Death Society and a organizer for this meeting and can be contacted in relation to this at Tel: (US) 718-997-3417, E-mail: Zahra_zakeri@hotmail.com. You may also contact Victoria Matassov Cell Death Assistant Coordinator at Tel: (US) 718-997-3450, Fax: (US) 718-997-3429, E-mail: victoriamatassov@hotmail.com.

Sincerely,

Zahra Zakeri
Professor of Biology
Deputy Chair of Graduate Program at Queens College
President of the International Cell Death Society
Queens College of City University of New York
Flushing New York
NY, 11367
Tel # 718-997-3417Fax # 718-997-3429
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Last (family) Name of Senior Author	Wilairat
First (given) Name(s) of Senior Author	Prapon
Last (family) Name of Presenter	Uthaisang-Tanechpongtamb
First (given) Name(s) of Presenter	Wanlaya
Check if you wish to be considered for an oral presentation	☐

Abstract: Please use the format below:

ACTIVATION OF CASPASE-3 BY CATHEPSIN B DURING CELL STRESS.
Authorlastname AB(1), Authorlastname CD(1), PresentingAuthor EF*(2), and Seniorauthor GH@(2), (1) Address1, (2) Address2

Abstract will begin here with 5 spaces indent. If you need to use non-English letters or symbols please cut-and-paste them from below or paste from a word processing program (base font: Times New Roman or equivalent, 10 point). For Greek letters, type your abstract, then cut and paste the l in the box below and insert them into your text. Otherwise the fonts will be confused.)

MAXIMUM 2000 CHARACTERS (APPROXIMATELY 280 WORDS)

Altholactone induces apoptosis via caspase-8 and -9 dependent pathways in cervical carcinoma cell.
Uthaisang-Tanechpongtamb W*(1), and Wilairat P@(2), (1) Department of Biochemistry, Faculty of Medicine, Srinakharinwirot University, Bangkok, Thailand 10110, (2) Department of Biochemistry, Faculty of Science, Mahidol University, Bangkok, Thailand 10400

As part of a program to develop anticancer drugs from natural agents, altholactone extracted from *Goniothalamus macrophyllus* (Family Annonaceae) was investigated for cytotoxicity and induction of apoptosis in cervical carcinoma HeLa cell line. MTT assay showed that altholactone had IC_{50} value of 9.6 μg/ml. Blebbing formation at the plasma membrane, chromatin condensation and caspase-3 activation, characteristics of apoptosis, increased in a time-dependent manner. Interestingly, caspase-3 activation was inhibited by both inhibitors of caspase-8 and caspase-9 suggesting the possibility of a type II apoptotic signaling pathway which has mitochondria as amplifier. This notion was supported by the release into cytosol of cytochrome c from mitochondria.

Greek letters:

ΑΒΧΔΕΦΓΗΙϑΚΛΜΝΟΠΘΡΣΤΥςΩΞΨΖ αβχδεφγηιφκλμνοπθρστυϖωξψζ

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