目 錄 Contents

理事長的話

各位會員朋友們：

歡迎參加第二十八屆生物醫學聯合學術年會。與往年一樣，本屆年會中，各學會安排非常精彩學術演講、研討會及壁報。估計這兩天的議程會有將近 2000 位會員來參與，在國內而言，這是一個相當重要的生物醫學相關的會議。更難得的，這個年會由 7 個不同學會組成，具不同專長領域的各學會會員一起互動交流，激發新的想法，對於臺灣生物醫學研究的推動一直是扮演重要角色。本屆籌備會亦首次嘗試將大會會場的安排、參展廠商的聯繫等交予專業的私人公司規劃。希望這個安排能為本屆年會增添豐富性及創意性，也希望能為下一屆的主辦單位省下不少精力與時間。

最後還是要感謝在籌備過程中各學會理事長及秘書長的參與及幫忙。
並預祝今年年會活動圓滿成功。

毒理學會理事長

郭明良 敬上

參加年會注意事項

1. 會議會場禁止攜帶食物及飲料入內，會議進行中禁止飲食，敬請共同維護會場清潔
2. 年會將提供餐點，用餐相關事宜：
   a. 年會將於一樓，第 1 教室及第 2 教室前方，提供精緻茶點供大家食用
      (請參照生物醫學會 1F 平面圖，P6)
   b. 中餐請持餐券至三軍總醫院地下一樓商店街使用
   c. 請詳閱餐券上之注意事項
   d. 餐券僅供年會兩日用，敬請依標示日期使用
3. 停車相關事宜 :
   a. 國防醫學院之停車場為免費停放
   b. 三軍總醫院之停車場，採計時方式計費，每小時 40 元
   c. 請勿占用專用停車位

※ 因車位有限，參加會議敬請盡量搭乘大眾運輸系統，會議期間於捷運昆陽站一號出口提供免費接駁車

前往國防醫學院交通示意圖

地址：

台北市內湖區民權東路六段 161 號

1. 大會接駁專車： (20 人巴士)

至捷運台北車站搭乘**藍線** (板南線) -- **昆陽站 1 號出口**搭乘往國防醫學院接駁車。

3 月 23-24 日 07:30-18:00 (每 15 分鐘一班)

07:30-13:00　昆陽站前往國防醫學院 單向發車

13:00-18:00　國防醫學院前往昆陽站 雙向發車

2. 轉乘公車前往國防醫學院：

(1) 捷運板南線 -- 昆陽站 (出口 4 對面)：轉乘 藍 20 於國防醫學中心站下車

(2) 捷運淡水線 -- 民權西路站 (出口 1)：轉乘 617 於國防醫學中心站下車

(3) 捷運木柵線 -- 中山國中站：轉乘 617 於國防醫學中心站下車

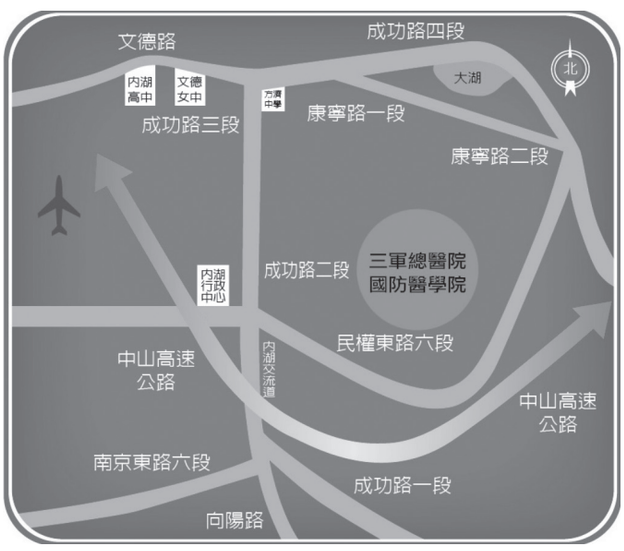
(4) 松山火車站：轉乘 棕 1 於國防醫學中心站下車

國防醫學院附**近的公車資訊：** (只標出明顯路標)

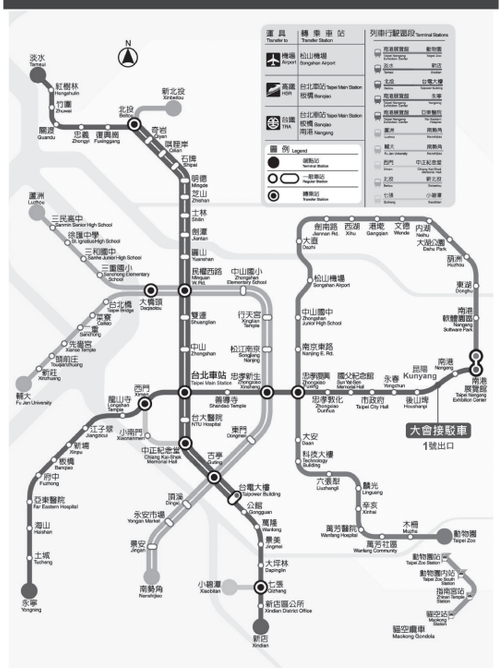
藍20：金龍路口－西湖圖書館－國防醫學中心－捷運昆陽站（05：50-22：30，尖峰 7-10 分，離峰 15-20 分）

617：新莊－三重－民權西路站－復興北路（中山國中站）－松山機場－時報廣場－國防醫學中心－湖光市場－大湖公園－民權隧道（05：30-22：00，尖峰 6-10 分，離峰 10-12 分）

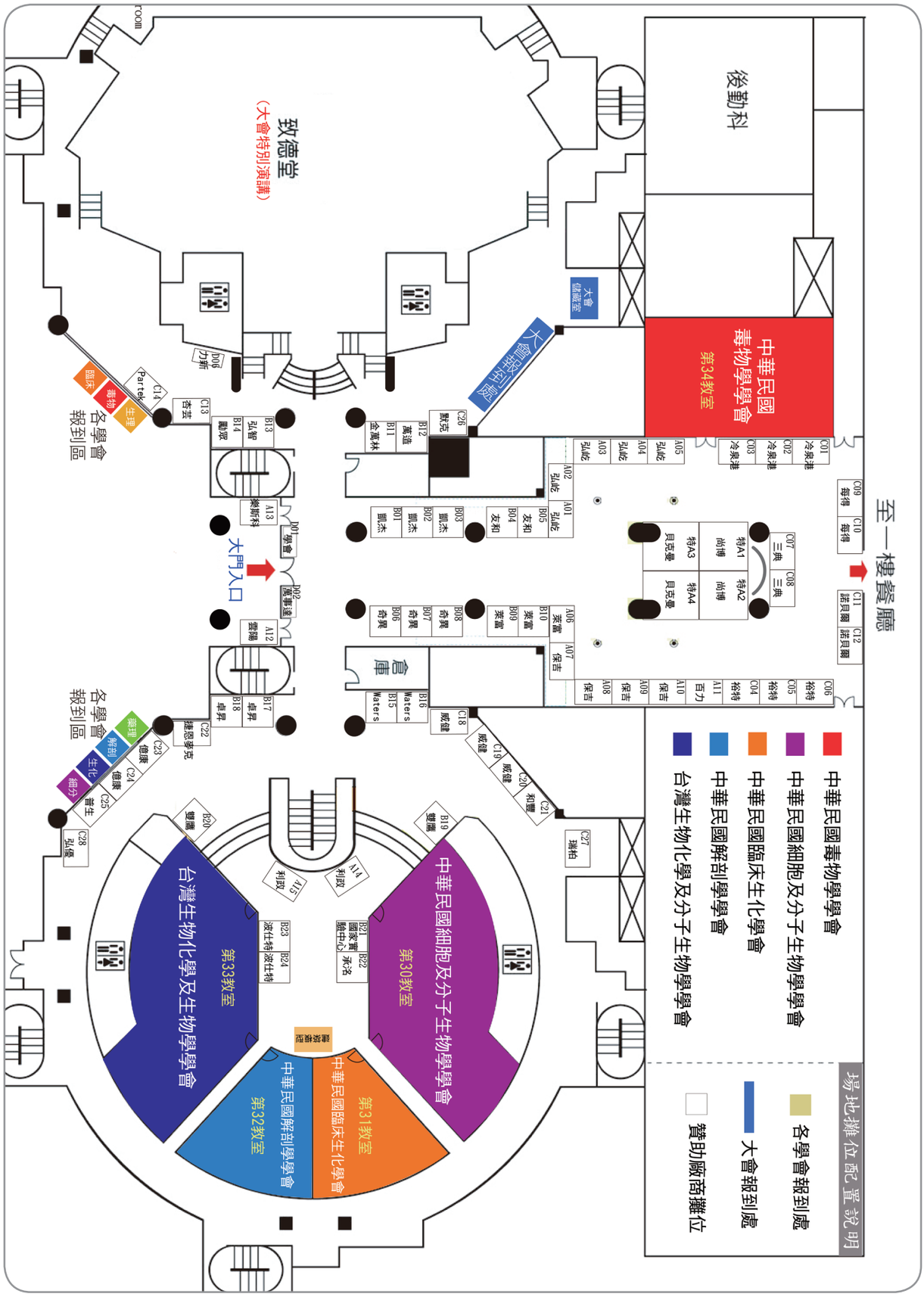
棕 1：麥帥新城－時報廣場－國防醫學中心－松山車站－饒河街口－復興北路－中山國中站－松山機場（06:00-23:20，尖峰 10 分，離峰 15 分，22:00 以後固定班次 22:15；22:25； 22:45）



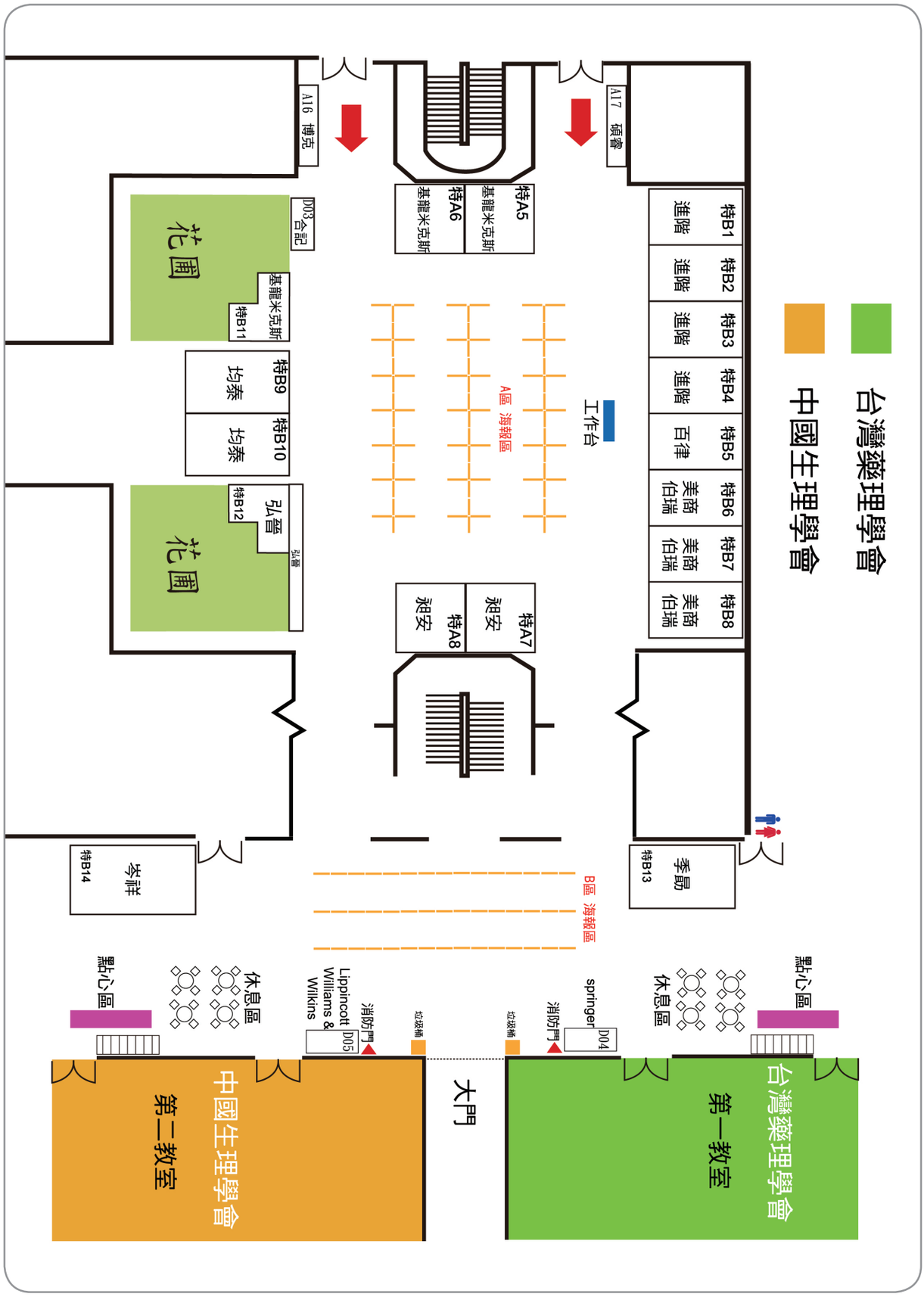
台北捷運路線圖



生物醫學會 3F 平面圖



生物醫學會 1F 平面圖



第 28 屆 (102 年度) 生物醫學聯合學術年會
參與學會暨理事長及秘書長名單

中華民國毒物學學會 (本屆主辦單位)	理事長：郭明良 秘書長：張正琪
中國生理學會	理事長：謝博軒 秘書長：何應瑞
中華民國解剖學學會	理事長：錢宗良 秘書長：龔秀妮
中華民國細胞及分子生物學學會	理事長：王陸海 秘書長：羅秀容
中華民國臨床生化學會	理事長：方偉宏 秘書長：張雅雯
臺灣生物化學及分子生物學學會	理事長：陳鴻震 秘書長：洪慧芝
臺灣藥理學會	理事長：符文美 秘書長：陳文彬

第 28 屆 (102 年度) 生物醫學聯合學術年會
籌備委員名單

總　召　集　人：郭明良
總　連　絡　人：張正琪
學　　術　　組：何應瑞、洪慧芝、陳文彬、張正琪、張雅雯、
　　羅秀容、龔秀妮
文 書 出 版 組：張正琪、張雅雯
廠 商 展 示 組：何應瑞、張正琪
會　　場　　組：陳文彬、張正琪
報　　到　　組：張正琪、龔秀妮
會　　計　　組：洪慧芝、張正琪
公　　關　　組：張正琪、羅秀容
（依姓名筆劃排列）

主要工作人員名單
學　　術　　組：陳心怡
會　　計　　組：范家睿
資　　訊　　組：田孟于
美　　工　　組：吳旻芳
展　　場　　組：李月如、楊振寧、楊珊珊、吳品嫻、黃紫虹、黃靖雅、顧佳芳
（依姓名筆劃排列）

第 28 屆生物醫學聯合學術年會 會議資訊

	時 間	地 點
大會特別演講	102 年 3 月 24 日 10:15-11:15	三樓 致德堂

生物處業務說明會

	時 間	地 點
生物處業務說明會	102 年 3 月 23 日 11:15-12:00	三樓 第 30 教室

學會特別演講及會員大會時間表

學 會	學會特別演講	學會會員大會	地 點
台灣藥理學會	102 年 3 月 23 日 13:45-15:45	102 年 3 月 23 日 13:45-15:45	一樓 第 1 教室
中國生理學會	102 年 3 月 23 日 13:45-14:45	102 年 3 月 23 日 14:45-15:45	一樓 第 2 教室
中華民國細胞及 分子生物學學會	102 年 3 月 23 日 10:15-11:15		三樓 第 30 教室
中華民國臨床生化學會	102 年 3 月 23 日 10:15-11:15	102 年 3 月 23 日 10:15-11:15	三樓 第 31 教室
中華民國解剖學學會	102 年 3 月 23 日 09:30-10:30	102 年 3 月 23 日 10:40-11:10	三樓 第 32 教室
台灣生物化學及 分子生物學學會	102 年 3 月 23 日 09:00-10:00	102 年 3 月 23 日 10:00-10:40	三樓 第 33 教室
中華民國毒物學學會	102 年 3 月 23 日 10:15-11:15	102 年 3 月 24 日 09:00-10:00	三樓 第 34 教室
	102 年 3 月 24 日 09:00-10:00		

第 28 屆生物醫學聯合學術年會議程

March 23 (六), 2013

	一樓		三樓				
	藥理學會	生理學會	細分生學會	臨床生化	解剖學會	生化學會	毒物學會
	1 教室	2 教室	30 教室	31 教室	32 教室	33 教室	34 教室
09:00 | 10:00	研究生 論文獎 決選演講 主持人： 張文昌院士	研討會 轉譯醫學 專論： 從生理到 臨床 演講者： 楊松昇教授 鄭劍廷教授 蔡少正教授 主持人： 樓迎統教授	學生、博士後 與助理 口頭論文報告 O17-O20 主持人： 王廷方 副研究員		9:30-10:30 特別演講 演講者： Dr. Feng C. Zhou 主持人： 錢宗良教授	特別演講 演講者： 蕭介夫教授 主持人： 陳鴻震教授	研討會 The Interplay of Environmental Factors and Estrogen in Cancer 演講者： 李立安 副研究員 林伯雄教授 主持人： 林嬪嬪研究員
10:00 | 10:15	10:10-11:10 口頭論文 競賽 O1-O5 主持人： 林琬琬教授 陳炯東教授		休息 (大會提供茶點於 1 樓休息區)			10:00-10:40 會員大會	
10:15 | 11:15			特別演講 演講者： 程淮榮教授 主持人： 王陸海理事長	特別演講 演講者： Dr. David G. Grenache 主持人： 方偉宏副教授 & 會員大會	10:40-11:10 會員大會		特別演講 演講者： 羅浩院士 主持人： 郭明良教授
11:15 | 12:00	看板論文競賽		生物處說明會 演講者： 裘正健處長 主持人： 郭明良教授	看板論文競賽			
12:00 | 13:00 午餐	科技新知演講						
	美商沃特斯國際股份有限公司台灣分公司	基龍米克斯生物科技股份有限公司	金萬林企業股份有限公司	萊富生命科技股份有限公司	諾貝爾生物有限公司	世翔國際有限公司	均泰生物科技有限公司
13:00 | 13:45	看板論文競賽						
13:45 | 14:45	特別演講 會員大會 演講者： Dr. Tamotsu Yoshimori 主持人： 符文美教授	特別演講 演講者： Dr. William Chilian 主持人： 謝博軒教授	研討會 Neuroscience 演講者： 陳俊安 助研究員 莊志立研究員 蔡坤哲副教授 鄭函若副教授 主持人： 高閬仙教授	研討會 Current Trend in Clinical Biochemistry 演講者： 劉燦榮教授 林植培主任 楊雅倩副教授 蘇剛毅 助理教授 主持人： 方偉宏副教授	研討會 Neural Science 演講者： 曾拓榮 助理教授 王詔絹 助理教授 王先逸 助理教授 郭余民教授 主持人： 郭余民教授	研討會 Drug discovery 演講者： 張明熙教授 黃奇英教授 Dr. Geraldine Wee 謝興邦教授 主持人： 洪慧芝教授	14:00-15:45 口頭論文競賽 O52-O59 主持人： 張正琪副教授
14:45 | 15:45		會員大會 主持人： 謝博軒理事長					
15:45 | 16:00	休息 (大會提供茶點於 1 樓休息區)						
16:00 | 17:00	口頭論文 競賽 O6-O10 顧記華教授 石宜銘教授	博士生暨新科 博士口頭論文 競賽 O11-O16 主持人： 童吉士教授 陳景宗教授	學生、博士 後與助理 口頭論文報告 O21-O24 主持人： 楊昀良教授		口頭報告 O37-O39 主持人： 龔秀妮 助理教授		

第 28 屆生物醫學聯合學術年會議程

March 24（日）, 2013

	一樓		三樓				
	藥理學會	生理學會	細分生學會	臨床生化	解剖學會	生化學會	毒物學會
	1 教室	2 教室	30 教室	31 教室	32 教室	33 教室	34 教室
09:00 | 10:00		研討會 生理學在醫學教育改革中所扮演的角色 演講者： 蔡美玲教授 許　勤 教授 湯志永教授 卓貴美教授 謝博軒教授 主持人： 蔡美玲教授	學生、博士後與助理 口頭論文報告 O25-O28 主持人： 楊瑞彬研究員		口頭報告 O40-O42 主持人： 龔秀妮 助理教授		特別演講 演講者： Dr. Myung-Haing Cho 主持人： 郭明良教授 & 會員大會
10:00 | 10:15	休息 (大會提供茶點於 1 樓休息區)						
10:15 | 11:15	生醫年會大會特別演講（致德堂） 演講者：李林衡教授 主持人：郭明良教授						
11:15 | 12:00	看板論文競賽						
12:00 | 13:00 午餐	科技新知演講						
	財團法人國家實驗研究院國家實驗動物中心	弘晉 有限公司	承洛科技 有限公司	卓昇 有限公司	百律 有限公司	Promega Corporation	凱杰生物科技 有限公司
13:00 | 13:45	看板論文競賽						
13:45 | 15:45	研討會 Translational Research in Cancers 演講者： 李新城教授 林家齊醫師 康宏佑教授 陳宜民教授 主持人： 林滿玉教授 康宏佑教授	研討會 生理學專題 演講者： 盧主欽 助理教授 余青翰 助理教授 李季湜副教授 林詠凱副教授 主持人： 李小媛教授	學生、博士後與助理 口頭論文報告 O29-O32 主持人： 陳紀如副教授 O33-O36 主持人： 李心予教授		研討會 Vascular disorder 演講者： 王家儀教授 賴逸儒副教授 王淑慧 助理教授 李學德 助理教授 主持人： 葉添順教授	口頭論文競賽 13:45-14:45 O43-O45 主持人： 高銘欽教授 14:55-15:55 O46-O48 主持人： 李明學教授 16:05-17:05 O49-O51 主持人： 陳佩燁教授	
15:45 | 16:00	休息						
16:00 | 17:00		生理學會 口頭及壁報論文競賽 頒獎典禮 主持人： 李怡萱教授					

大會特別演講 (Keynote Lecture)

102 年 3 月 24 日 (週日) 10:15-11:15

論文編號：K1

地　　點：三樓，致德堂

主 持 人：郭明良 教授 / 國立臺灣大學 生命科學院

講　　題：Niche, Signaling, and Epigenetic Regulation of Stem Cells

演 講 者：李林衡 教授

單　　位：Stowers Institute for Medical Research, Kansas City, Missouri 64110, USA

K1

3 月 24 日 (週日) 10:15-11:15
三樓，致德堂

Niche, Signaling, and Epigenetic Regulation of Stem Cells

Dr. Lin-Heng Li
Stowers Institute for Medical Research, Kansas City, Missouri 64110, USA

Hematopoietic stem cells (HSCs) are maintained in balance between quiescent state and proliferating state. While proliferating HSCs are critical for supporting routine blood production, quiescent HSCs are essential for long-term maintenance and also can be roused to replenish lost active HSCs. How the different states of HSCs are regulated is a fundamental question.

First, we investigated underlying signaling that regulates the quiescence and activation in different niches, which remains largely unknown. To address this question, we have analyzed the expression profile of Wnt receptors, Frizzleds, in HSCs. We found that noncanonical Wnt signaling -- via receptors Frizzled8 (Fz8) and Frizzled5 (Fz5) -- are expressed in dormant (or reserve) and active (or primed) HSCs respectively. We further detected Fz8 and Fz5 localized at N-cadherin+ preosteoblasts in the endosteal niche and in Nestin-GFP+ mesenchymal stem cells (MSCs) in the perivascular niche respectively. Functionally, we found that Fz8 and Fz5 mediate noncanonical Wnt signaling to maintain HSCs in the endosteal niche and to regulate active HSCs in the perivascular niche.

Second, our earlier studies have revealed expression of a cluster of imprinting genes, such as H19 and Gtl2, predominantly in the dormant or reserve HSC population, suggesting a role for these genes in regulation of HSC state and function. Since imprinting genes are regulated by differential methylated domains (DMD) and are mono-allelic in expression, we carried out experiments in animals with a conditional deletion of the DMD of the H19 imprinting gene in an allele specific manner and analyzed the corresponding phenotypic changes in hematopoiesis. Unlike inheritance of the deletion from the paternal allele (H19ΔDMD), inheritance of the deletion from the maternal allele resulted in sequential reduction in HSCs and compromised function as assessed by long-term engraftment assays. Mechanistically, downregulation of H19 led to reciprocal upregulation of IGF2 and loss of suppression on Igf1r translation imposed by H16-encoded mi675. In conclusion, our data from a combination of genetic and functional approaches clearly demonstrate that imprinting as a specific epigenetic regulation plays a critical role in control of HSC state and function.

Dr. Lin-Heng Li
Co-leader, Cancer Biology, University of Kansas Cancer Center (NCI-CC) Fairway, Kansas USA
Affiliate Professor, Department of Pathology University of Kansas Medical Center (KUMC), Kansas City, Kansas USA
Investigator, Stowers Institute for Medical Research, 1000 East 50th Street Kansas City, Missouri 64110 USA

APPOINTMENT HISTORY

2010-present	Co-leader, Cancer Biology, University of Kansas Cancer Center (NCI-CC) Fairway, Kansas USA
2009-present	Affiliate Professor, Department of Pathology University of Kansas Medical Center (KUMC), Kansas City, Kansas USA
2008-present	Investigator, Stowers Institute for Medical Research, 1000 East 50th Street Kansas City, Missouri 64110 USA
2006-2008	Associate Investigator, Stowers
2006-2009	Affiliate Associate Professor, KUMC
2001-2006	Affiliate Assistant Professor, KUMC
2000-2005	Assistant Investigator, Stowers
1999-2000	Affiliate Assistant Professor, Department of Molecular Biotechnology & affiliate position in Pediatrics Department /Division of Genetics and Development University of Washington Medical Center, Seattle, Washington USA
1995-1998	Senior Associate, Laboratory of Dr. Leroy Hood, Department of Molecular Biotechnology, University of Washington, Seattle, Washington USA

EDUCATION

1995	Post-Doc., Molecular and Cellular Biology, New York University, Medical Center, New York USA
1993	M.S., Molecular and Cellular Biology, New York University, Medical Center, New York USA
1988	M.S., Genetics, Fudan University, Shanghai, P.R. China
1985	B.S., Biology, Fudan University, Shanghai, P.R. China

HONORS AND AWARDS

2011	Fellow of the American Association for the Advancement of Science (AAAS)
2003	Missouri Biotechnology Association Excellence in Life Sciences Award in Basic Research
2004	Hudson Prize for excellence in basic biomedical research, presented by the M.R. and Evelyn Hudson Foundation

REVIEWER

Academy of Sciences
Blood
Cancer Cell
Cell
Cell Stem Cell
Development Cell
Developmental Biology
Gastroenterology
Gene Therapy
Genes & Development
Immunity
J. Am Soc Nephrology
J. Cell Biology
J. Cellular Physiology
J. Clinical Investigation
J. Clinical Investigation
J. Experimental Medicine
J. Molecular Cell Biology
Leukemia
Nature
Nature Genetics
Nature Insight
Nature Medicine
Nature Review Cancer
Nature Review Genetics
Nature Review MCB
Oncogene
Plos Biology
Procedures of the National Science
Trends

PUBLICATION

- M Wang, S Keilbaugh, T Cash-Mason, X He, L Li, G Wu (2008). Immune-mediated signaling in intestinal goblet cells via PI3-Kinase and AKT-dependent pathways. American Journal of Physiology-Gastrointestinal and Liver Physiology 2008; 295:G1122-G1130.

- Yucai Xie, Tong Yin, Winfried Wiegraebe, Xi He, Diana Miller, Danny Stark, Katherine Perko, Richard Alexander, Joel Schwartz, Justin Grindley, Jungeun Park, Jeff Haug, Joshua Wunderlich, Hua Li, Simon Zhang, Teri Johnson, Ricardo Feldman & Linheng Li (2009). Detection of functional haematopoietic stem cell niche using real-time imaging. Nature. 2009 Jan; 457:97-102. doi:10.1038; published online 3 Dec. 2008.

- Jeffrey B Brown, Goo Lee, et al, Linheng Li, Terrence A Barrett (2009). 5-ASA inhibits epithelial β-catenin activation in chronic ulcerative colitis. Gastroenterology, 2009 Oct 28.

- J Brown, G Lee, E Managlia, G Grimm, R Dirisina, T Goretsky, P Cheresh, N Blatner, K Khazaie, G Yang, L Li, T Barrett (2010). Mesalamine Inhibits Epithelial Beta-Catenin Activation in Chronic Ulcerative Colitis. Gastroenterology 2010, 138:595-605.

- Kentaro Hosokawa, Fumio Arai, et al, Linheng Li and Toshio Suda (2010). Cadherin-based adhesion is a potential target for niche manipulation to protect HSCs in adult bone marrow. Cell Stem Cell, 5 March 2010.

- Nava, P, Koch, S, Laukoetter, MG, Lee, WY, Kolegraff, K, Capaldo, CT, Beeman, N, Addis, C, Gerner-Smidt, K, Neumaier, I, Skerra, A, Li, Linheng, Parkos, C.A., Nusrat, A. (2010). Interferon-γ Regulates Intestinal Epithelial Homeostasis through Converging β-Catenin Signaling Pathways. Immunity. 2010 March;32(3):392-402.

- Da Zhang, Maura F O' Neill, Mark T Cunningham, Fang Fan, Moitaba Olvasee, Linheng Li. (2010). Abnormal Wnt signaling and stem cell activation in reactive lymphoid tissue and low-grade marginal zone lymphoma. Leukemia & Lymphoma, May 2010; 51(5):906-910.

- G Lee, T Goretsky, E Managlia, R Dirisina, A Singh, J Brown, R May, G Yang, J Rogheb, B Evers, C Weber, J Turner, X He, R Katzman, L Li, T Barrett (2010). Phosphoinositide 3-Kinase Signaling Mediates Beta-Catenin Activation in Intestinal Epithelial Stem and Progenitor Cells in Colitis. Gastroenterology 2010, 139:869-881.

- N He, Z Xiao, T Yin, J Stubbs, L Li, D Quarles (2011). Inducible expression of Runx2 results in multi-organ abnormalities in mice. Journal of Cellular Biochemistry 2011, 112:653-665.

- Helen He Zhu, Kaihong Ji, Nazilla Alderson, Zhao He, Shuangwei Li, Wen Liu, Dong-Er Zhang, Linheng Li and Gen-Sheng Feng (2011). Kit-Shp2-Kit signaling acts to maintain a functional hematopoietic stem and progenitor cell pool. Blood 2011; 117 (20), 5350-5361.

- P Nava, C Capaldo, S Koch, K Kolegraff, C Rankin, A Farkas, M Feasel, L Li, C Addis, C Parkos, A Nusrat (2011). JAM-A regulates epithelial proliferation through Akt/Beta-catenin signaling. EMBO Reports 2011; 12:314-320.

- S Koch, P Nava, C Addis, A Kim, T Denning, L Li, C Parkos, A Nusrat (2011). The Wnt antagonist Dkk1 regulates intestinal epithelial homeostasis and wound repair. Gastroenterology 2011; 141:259-268.

- C Arnold, R Tan, B Zhou, S Yue, S Schaffert, J Biggs, R Doyonnas, M Lo, J Perry, V Renault, A Sacco, T Somervaille, P Viatour, A Brunet, M Cleary, L Li, J Sage, D Zhang, H Blau, C Chen, CZ Chen (2011). MicroRNA programs in normal and aberrant stem and progenitor cells. Genome Research 2011; 21:798-810.

- JM Perry, XC He, R Sugimura, JC Grindley, JS Haug, S Ding, and L Li (2011). Cooperation between both Wnt/β-catenin and PTEN/Akt signaling promotes primitive hematopoietic stem cell self-renewal and expansion. Genes and Development 2011; 25:1928-1942.

- Sugimura, R., He, X.C., Venkatraman, A., Arai, F., Box, A., Semerad, C., Haug, J.S., Peng, L., Zhong, X., Suda, T., and Li, L. Non-canonical Wnt Signaling Maintains Hematopoietic Stem Cell through Flamingo and Frizzled8 in the Niche. Cell 2012; 150:351-365.

- M Zhao, JT Ross, T Itkin, JM Perry, A Venkatraman, JS Haug, M Hembree, C Deng, T Lapidot, XC He, and L Li. FGF Signaling Facilitates Post-injury Recovery of Mouse Hematopoietic System. Blood 2012; 120 (9), 1831-1842.

生物處業務說明會

102 年 3 月 23 日 (週六) 11:15-12:00

地　　點：三樓，第 30 教室
主 持 人：郭明良 教授 / 國立臺灣大學 生命科學院
講　　題：生物處業務說明會
演 講 者：裘正健 院士
單　　位：行政院國家科學委員會 生物科學發展處

裘正健 Jeng-Jiann Chiu (Cheng-Chien Chiu)

EDUCATION

1992	Ph.D., Blood Flow Dynamics, Institute of Aeronautics and Astronautics, National Cheng Kung University, Taiwan
1986	Mechanical Engineering, Department of Mechanical Engineering, Chung-Yuan University, Taiwan

PRESENT AND PREVIOUS POSITION

2013-present	Joint-Appointment Professor, Institute of Biomedical Engineering, National Cheng Kung University, Taiwan
2012-present	Director General, Department of Life Sciences, National Science Council, Taiwan
2012-present	Investigator, Institute of Cellular and System Medicine, National Health Research Institutes, Taiwan
2012-present	Joint-Appointment Professor, Institute of Biomedical Engineering, National Tsing Hua University, Taiwan
2012-present	Director of The Board, Development Center for Biotechnology, Taiwan
2012-present	Director of The Board, Animal Technology Institute, Taiwan
2012	Director, Institute of Cellular and System Medicine, National Health Research Institutes, Taiwan
2012	Director, Department of Administration, National Health Research Institutes, Taiwan
2009-present	Joint-Appointment Professor, Institute of Aging Medicine, China Medical University, Taiwan
2009	President, TienTe Lee Award Laureate Club
2008-present	Joint-Appointment Professor, Biotechnology Center, National Chung Hsin University, Taiwan
2008-2012	Investigator, Division of Medical Engineering Research, National Health Research Institutes, Taiwan
2007-2011	Secretary-general, The Chinese Society of Cell and Molecular Biology, Taiwan
2004-2008	Associate Investigator, Division of Medical Engineering Research, National Health Research Institutes, Taiwan
2003-2008	Joint-Appointment Associate Professor, Institute of Biomedical Engineering, National Yang-Ming University, Taipei, Taiwan
2000-2004	Assistant Investigator, Division of Medical Engineering Research, National Health Research Institutes, Taiwan
1999-2008	Adjunct Associate Professor, Graduate Institute of Life Sciences, National Defense Medical Center, Taipei, Taiwan
1993-2000	Postdoctoral Research Fellow, Division of Cardiovascular Research, Institute of Biomedical Sciences, Academia Sinica, Taiwan

AWARDS AND HONORS

2012	Outstanding Research Achievement Award. National Health Research Institutes
2011	Cover story of the 2011 January Issue of Physiol Rev (Impact Factor: 28.417).
2010	Frontier Science Research Grant by National Science Council
2009	Outstanding Research Award. National Science Council
2008	Best Engineering Paper Award. Chinese Institutes of Engineers
2007	Tiente Lee Award (Young Scientist). Tiente Lee Biomedical Foundation
2007	Academia Sinica Junior Research Investigators Award. Academia Sinica, Taiwan
2006	Outstanding Research Award. National Science Council
2006	Young Investigator Distinguished Research Achievement Award. National Health Research Institutes
1994, 1997-1999	Research Award. National Science Council
1992	The Best Ph.D. Thesis Award, Li-Ching Culture and Education Foundation
1986-1991	National Defense Industrial Scholarship Award. Aerospace Industry Development Center, Chung-Shun Institute of Science and Technology (CSIST), Branch of Defense Ministry
1983	Education Scholarship Award. Ministry of Education

PUBLICATIONS (2009 to present)

- Zhou J, Lee PL, Lee CI, Wei SY, Lim SH, Lin TE, Chien S, Chiu JJ*. BMP receptor-integrin interaction mediates responses of vascular endothelial Smad1/5 and proliferation to disturbed flow. J Thromb Haemost. Feb 7. [Epub ahead of print], 2013.
- Lien SC, Wei SY, Chang SF, Chang MD, Chang JY, Chiu JJ*. Activation of PPAR-α induces cell cycle arrest and inhibits transforming growth factor-β1 induction of smooth muscle cell phenotype in 10T1/2 mesenchymal cells. Cell Signal. Feb 4. [Epub ahead of print], 2013.
- Chen LJ, Chiu JJ*. Mechanical regulation of epigenetics in vascular biology and pathobiology. J Cell Mol Med. (In press)
- Zhou J, Li YS, Nguyen P, Wang KC, Weiss A, Kuo YC, Chiu JJ, Shyy JY, Chien S. Regulation of vascular smooth muscle cell turnover by endothelial cell-secreted microRNA-126: Role of shear stress. Circ Res. (In revision).
- Zhou J, Lee PL, Tsai CS, Lee CI, Yang TL, Chuang HS, Lin WW, Lin TE, Lim SH, Wei SY, Chen YL, Chien S*, Chiu JJ*. Force-specific activation of Smad1/5 regulates vascular endothelial cell cycle progression in response to disturbed flow. Proc Natl Acad Sci U S A. 109:7770-5, 2012. (Highlight by the A-IMBN Research Network)
- Lee DY, Lee CI, Lin TE, Lim SH, Zhou J, Tseng YC, Chien S*, Chiu JJ*. Role of histone deacetylases in transcription factor regulation and cell cycle modulation in endothelial cells in response to disturbed flow. Proc Natl Acad Sci U S A. 109:1967-72, 2012.
- Yeh YT, Lee CI, Lim SH, Chen LJ, Wang WL, Chuang YJ, Chiu JJ*. Fibrillar Collagen-Regulated P66Shc Converges Physical and Chemical Signaling in Modulating Vascular Smooth Muscle Cell Cycle and Proliferation. Biomaterials. 33:6728-38, 2012.
- Shih YT, Wang MC, Peng HH, Chen TF, Chen L, Chang JY, Chiu JJ*. Modulation of Chemotactic and Pro-inflammatory Activities of Endothelial Progenitor Cells by Hepatocellular Carcinoma. Cell Signal. 24;779-793, 2012.
- Shih YT, Wang MC, Yang TL, Zhou J, Lee DY, Lee PL, Yet SF, Chiu JJ*. β2-Integrin and Notch-1 differentially regulate CD34+CD31+ cell plasticity in vascular niches. Cardiovasc Res. 96:296-307, 2012.
- Chen LJ, Lim SH, Chiu JJ*. Roles of microRNAs in atherosclerosis and restenosis. J Biomed Sci. 29;79-89, 2012.
- Yeh YT, Hur SS, Chang J, Wang KC, Chiu JJ, Li YS, Chien S. Matrix Stiffness Regulates Endothelial Cell Proliferation through Septin 9. PLoS One 7;e46889, 2012.
- Chiu JJ, Chien S. Effects of disturbed flow on vascular endothelium: pathophysiological basis and clinical perspectives. Physiol Rev. 91:327-387, 2011. (Cover Story of the Issue)
- Zhou J, Lim SH, Chiu JJ*. Epigenetic regulation of vascular endothelial biology/pathobiology and response to fluid shear stress. Cell Mol Bioeng 4:560-578, 2011.
- Zhou J, Wang KC, Wu W, Subramaniam S, Shyy JY, Chiu JJ, Li JY, Chien S. MicroRNA-21 targets peroxisome proliferators-activated receptor-alpha in an autoregulatory loop to modulate flow-induced endothelial inflammation. Proc Natl Acad Sci U S A. 108:10355-60, 2011
- Yang TL, Lin FY, Chen YH, Chiu JJ, Shiao MS, Tsai CS, Lin SJ, Chen YL. Salvianolic acid B inhibits low-density lipoprotein oxidation and neointimal hyperplasia in endothelium-denuded hypercholesterolaemic rabbits. J Sci Food Agric. 91:134-41, 2011.
- Lee DY, Li YS, Chang SF, Zhou J, Ho HM, Chiu JJ*, Chien S*. Oscillatory flow-induced proliferation of osteoblast-like cells is mediated by αvβ3 and β1 integrins through synergistic interactions of FAK and Shc with PI3K and the Akt/mTOR/p70S6K pathway. J Biol Chem. 285, 30-42, 2010.
- Wang YL, Kuo JH, Lee SC, Liu JS, Hsieh YC, Shih YT, Chen CJ, Chiu JJ*, Wu WG*. Cobra CRISP functions as an inflammatory modulator via a novel Zn2+- and heparan sulfate- dependent transcriptional regulation of endothelial cell adhesion molecules. J Biol Chem. 285:37872-83, 2010.
- Yeh CR, Chiu JJ, Lee CI, Lee PL, Shih YT, Sun JS, Chien S, Cheng CK. Estrogen augments shear stress-induced signaling and gene expression in osteoblast-like cells via estrogen receptor-mediated expression of beta1-integrin. J Bone Miner Res. 25, 627-39, 2010
- Tsai MC, Chen L, Zhou J, Tang Z, Hsu TF, Wang Y, Shih YT, Peng HH, Wang N, Guan Y, Chien S, Chiu JJ*. Shear stress induces synthetic-to-contractile phenotypic modulation in smooth muscle cells via peroxisome proliferator-activated receptor alpha/delta activations by prostacyclin released by sheared endothelial cells. Circ Res 105, 471-80, 2009.

學會特別演講 (Special Lecture)

102 年 3 月 23 日 (週六)

論文編號：L1　　時間：09:00-10:00
地　　點：三樓，第 33 教室
主 持 人：台灣生物化學及分子生物學學會 陳鴻震 教授
講　　題：Biocatalysis in Green Biotechnology
演 講 者：蕭介夫 教授
單　　位：中央研究院農業生物科技研究中心特聘研究員兼義守大學校長

論文編號：L2　　時間： 09:30-10:30
地　　點：三樓，第 32 教室
主 持 人：中華民國解剖學學會 錢宗良 教授
講　　題：從 Epigenetic Medicine 到 21 世紀解剖細胞學之再出發
演 講 者：Dr. Feng C. Zhou
單　　位：Indiana University Purdue University at Indianapolis

論文編號：L3　　時間：10:15-11:15
地　　點：三樓，第 30 教室
主 持 人：中華民國細胞及分子生物學學會 王陸海 理事長 / 國家衛生研究院
講　　題：Neuropsychiatric disorders and axon pruning
演 講 者：程淮榮 教授
單　　位：國立臺灣大學 腦與心智科學研究所

論文編號：L4　　時間：10:15-11:15
地　　點：三樓，第 31 教室
主 持 人：中華民國臨床生化學會 方偉宏 副教授 /
　　國立臺灣大學醫學院 醫學檢驗暨生物技術學系
講　　題：Macroprolactin: what laboratorians need to know
演 講 者：Dr. David G. Grenache
單　　位：Department of Pathology, University of Utah

論文編號：L5　　時間：10:15-11:15
地　　點：三樓，第 34 教室
主 持 人：中華民國毒物學學會 郭明良 教授 / 國立臺灣大學 生命科學院
講　　題：Receptor Engineering in the Development of Ideal Analgesics
演 講 者：羅浩 院士
單　　位：Department of Pharmacology, University of Minnesota Medical School

論文編號：L6　　時間：13:45-15:45
地　　點：一樓，第 1 教室
主 持 人：台灣藥理學會　符文美 教授 / 國立臺灣大學 醫學院藥理學科
講　　題：50 Years of Autophagy: towards Understanding The Intracellular Self-Degradation System Sustaining Life
演 講 者：Dr. Tamotsu Yoshimori
單　　位：Department of Genetics, Graduate School of Medicine, Osaka University

論文編號：L7　　時間：13:45-15:45
地　　點：一樓，第 2 教室
主 持 人：中國生理學會　謝博軒教授 國防醫學院 生理學研究所
講　　題：Regulation of Blood Flow to the Heart: A feed-forward process that is regulated by H2O2-dependent redox signaling
演 講 者：Dr. William Chilian
單　　位：Department of Integrative Medical Sciences, Northeast Ohio Medical University

學會特別演講 (Special Lecture)

102 年 3 月 24 日 (週日)

論文編號：L8　　時間：09:00-10:00
地　　點：三樓，第 34 教室
主 持 人：中華民國毒物學學會　郭明良 教授 國立臺灣大學 生命科學院
講　　題：GOLGA2/GM130, cis-Golgi Matrix Protein, is a Novel Target of Anticancer Gene Therapy
演 講 者：Dr. Myung-Haing Cho
單　　位：Laboratory of Toxicology College of Veterinary Medicine, Seoul National University

L1

3 月 23 日 (週六) 09:00-10:00
三樓，第 33 教室

Biocatalysis in Green Biotechnology

Dr. Jei-Fu Shaw
Chair Professor and President, I-Shou University
Distinguished Research Fellow, Agricultural Biotechnology Research Center, Academia Sinica

Biocatalysts including enzymes and microorganisms can be used to replace chemical catalysts for the production of useful industrial products, which have the advantage of environmental friendliness and consumer acceptance as a green process. For example, lipases have different substrate specificities, enantioselectivities and regioselectivities, which are not only important for various biological functions but also widely used for industrial applications. Lipases can catalyze fat splitting, esterification, interesterification, aminolysis, oximolysis and thiotransesterification, therefore they are very useful in organic synthesis, biodiesel production, medicial-,agrochemical- ,flavor- and food-industries. Commercial preparations of Candida rugosa lipase (CRL) are mixtures of five lipase isoforms used for the hydrolysis and synthesis of various esters. The presence of variable isoforms and the amount of lipolytic protein in the crude lipase preparations lead to a lack of reproducibility of biocatalytic reactions. We have used recombinant enzyme technologies to produce five individual isoforms which have different biochemicial properties and applications. Since C. rugosa does not utilize the universal codon CTG for leucine; therefore, the CTG codons were converted to universal serine triplets by multiple site-directed mutagenesis to gain expression of functional lipase in heterologous hosts. Protein engineering of recombinant CRL isoforms allows the tailoring of enzyme function to improve the enantioselectivity, thermostability, and substrate specificity of CRL isoforms and increase their biotechnological applications.

Chitinolytic enzymes can be applied in pharmaceutical production, single-cell protein preparation, protoplasts isolation, chitinous waste treatment, and pathogenic fungi control. From the study on the senescence associated genes, papaya chitinase was cloned and overexpressed in *E. coli.* It appears to be a novel type of chitinase which can reduce the fungal activity of *Rhizoctonia solani, Sclerotium rolfsii, Phytophthora capsici, and Alternaria brassicicola.* We introduced the CpCHI into melon and successfully improved its antifugal ability against *R. solani*. Recombinant CpCHI is not only a chitinolitic enzyme for industrial applications but also potentially useful as a bio-control agent that can protect plants against agricultural pathogens.

Biocatalysts can also be used for the production of useful industrial products and functional foods from cheap agricultural produce. For example, rice can be converted into useful functional foods, high fructose and high maltose syrups, wine, glucose, and trehalose. The conversion process involves fermentation by microorganisms and use of biocatalysts such as hydrolases of the amylase superfamily. Amylases catalyze the process of liquefaction and saccharification of starch. It is possible to perform complete hydrolysis of starch by using the fusion product of both linear and debranching thermostable enzymes. This will result in saving energy otherwise needed for cooling before the next enzyme can act on the substrate, if a sequential process is utilized. Recombinant enzyme technology, protein engineering, and enzyme immobilization are powerful tools available to enhance the activity of enzymes, lower the cost of enzyme through large scale production in a heterologous host, increase their thermostability, improve pH stability, enhance their productivity, and hence making it competitive with the chemical processes involved in starch hydrolysis and conversions.

Transgenic plants which harbor enzyme genes can also be used to produce biobased products directly without adding exogenous enzymes. For example, a transgenic “Sweet rice” containing an amylopullulanase (Apu) gene under the control of rice glutelin gene promoter can be used to produce sugar syrup and protein enriched flour upon heating at 80°C for a few hours. The new transgenic plant technology is expected to be a more simple and efficient process for the application of enzymes in producing high-value-added products from cheap agricultural produce. Other applications of enzyme genes in transgenic plants for disease control and postharvest biotechnology will also be demonstrated.

Dr. Jei-Fu Shaw
Distinguished Research Fellow, Agricultural Biotechnology Research Center, Academia Sinica
President and Chair Professor, I-Shou University

EDUCATION

1997	Ph.D., Biochemistry , University of Arkansas
1970	B.S., Agricultural Chemistry, National Taiwan University

EXPERIENCE

2012	President of International Symposium on Biocatalysis and Agricultural Biotechnology (Taiwan)
2011	Distinguished Research Fellow, Agricultural Biotechnology Research Center, Academia Sinica
2010-2012	President of Association of National University of Taiwan
2010-2012	Standing Committee Member, International Union of Biological Science (IUBS)-Taiwan
2008	President of Academia-Industry Consortium of Central Taiwan - Science Park
2008	Adviser of National Museum of Natural Science
2007	President-elect of International Society for Biocatalysis and Biotechnology
2004-2011	President and Chair professor, National Chung Hsing University

AWARDS AND HONORS

2011	Fellow, International Society for Biocatalysis and Biotechnology
2010	Award of Merit, International Society of Biocatalysis and Biotechnology
2008	TWAS (Academy of Sciences for Developing World) Prize in Agricultural Science
2008	Storer Lectureship of UC Davis, USA
2008	Honorary Doctor degree (Biotechnology) of Maejo University, Thailand
2008-present	New Biotechnology Special Issues Editor-in-Chief.
2007	Distinguished Research Fellow Award of National Science Council
2005	Fellow of American Association for the Advancement of Science(AAAS)

EXPERTISE

1. Functional genes and biotechnology
2. Production of industrial products and functional food from agriculture produce by biocatalysis
3. Protein engineering and biotechnology of enzymes

ACADEMIC AND SCHOLASTIC CONTRIBUTIONS

I. Biochemistry and biotechnology of lipase/esterases

Lipases and esterases are very efficient biocatalysts that not only regulate the metabolism of lipids and esters but also are widely used in industry for biotransformation. Professor Shaw has made many important contributions to our knowledge of the structure, function and applications of these important serine-hydrolase family enzymes. His achievement earns international recognitions and he was invited to write two review papers in top-notched Journals (Progress in Lipid Research (43: 528-544, 2004); Lipids (39:513-526,2004))

(1) Dr. Shaw discovered a novel multi-function arylesterase which has arylesterase, thioesterase and protease-like activities. This led to the discovery of a new GDSLS protein family. Further studies on the structure of another GDSLS member E. coli thioesterase revealed that flexibility in the active site is crucial for the multi-functions of these GDSLS enzymes. These discoveries pioneered the protein engineering of the enzymes in this novel family.

(2) Dr. Shaw demonstrated that the different properties of Candida rugosa lipase from various suppliers were a result of the different percent composition of five isozymes which are differentially regulated by culture conditions. He developed a multiple mutagenesis method to overcome the codon usage problem hampering CRL gene expression in industrial expression systems. This solved a long-standing dispute and has had a great impact on bioindustry.

(3) He invented numerous new methods for the lipase-catalyzed synthesis of many important compounds such as carbohydrate esters, fatty acid esters, propylene glycol esters and diethanolamide. These novel enzymatic methods replace previous chemical methods and show potential for saving energy and reducing pollution, since they have high catalytic efficiency and specificity at ambient temperature. In contrast, conventional chemical methods require high temperature and produce undesirable byproducts.

II. Plant functional genes and agricultural biotechnology

1. Dr. Shaw characterized the active site of ACC oxidase, a key enzyme in ethylene biosynthesis, and discovered a novel ACC oxidase associated with late-stage plant senescence which may regulate irreversible plant cell death. His laboratory also cloned and characterized the first broccoli ethylene receptor and transferred the mutated ers gene to heterologus plants such as flowers to delay senescence and hence reduce postharvest loss of perishable agricultural produce.
2. He discovered the novel plant tubby-like protein gene family which plays important functions in plant hormone and stress signaling through ubiquitin-mediated proteolysis pathway.
3. He discovered an enzymatic method for simultaneous production of syrup and high-protein food from crops. In collaboration with Dr. Su-May Yu, he transferred the amylopullulanase gene into rice and produced transgenic "sweet rice", which expressed high amounts of the enzyme amylopullulanase. Without exogenous addition of amylases, the rice grain starch was completely degraded into syrup while the protein remained. This method has great promise for improving the nutrition of low protein crops and at the same time producing syrups for industrial uses, which greatly increases the added-value of agricultural products.

PATENTS

- Shaw, J. F. Production of fatty acid esters by enzyme catalyzed alcoholysis. (TW39390)
- Shaw, J. F. Production of high maltose syrup and high protein byproduct from materials containing starch and protein.(TW60191) (US5312739)
- Yu. S.M., Shaw, J.F. Transgenic seeds expressing amylopullulanase and uses therefor. (US6737563) (TW1322664)
- Shaw, J. F., G. C. Lee and S. J. Tang. Recombinant Candida rugosa lipases. (Taiwan1233450) (US7052879) (JP4074078) (US7468429) (EP1288294 B1)
- Shaw, J. F., R. C. Chang and S. J. Chou. Mutant-type lipases and applications thereof.(US7049122)
- Shaw, J. F., and G. P. Lai. Plant TULP gene family. (US US7314756)(TW 1338695)
- Shaw, J.F., G. C. Lee and C. T. Chen. Method of preparing starch-derived products. (TWI284151)
- Shaw, J.F., Y.T. Chen, L.H. Hsu. A novel anti-fungal chitinase. (US7,670,820B2)
- Shaw, J.F., G. C. Lee and Chen YS. Gene cloning, expression and applications of a novel acid and heat resistant trehalose synthesise.(TW1328611)

TECHNOLOGY TRANSFER

- Recombinant Candida rugosa lipases. TW1233450, US7052879, JP4074078, EP1288294B1, Licensed to Polyamine Co.
- Transgenic seeds expressing amylopullulanase and uses there for , US6737563, Licensed to Nugenplasm LLC Co.
- Starch derived products, US7981639B, Licensed to Shang-Ping Co.

L2

3 月 23 日 (週六) 09:30-10:30
三樓，第 32 教室

從 **Epigenetic Medicine** 到 **21** 世紀解剖細胞學之再出發

Dr. Feng C. Zhou
Department of Anatomy & Cell Biology/Stark Neuroscience Research Institute, Indiana University School Medicine, Indianapolis, USA

Epigenetic medicine is still in its infancy. Its impact, however, has expanded the perception and scope of life science. Life science studies how a specific organ, tissue, or cell is structured, how it functions, and how it maintains its normalcy or becomes diseased. These elements are integral function of protein and gene expression. However, there is little knowledge as to how these complex proteins and genes are coordinately instructed upstream at the genomic level to arrive to the sophisticated lives and shapes. Epigenetics has been recently reintroduced to life science. In general, this means that every cell in the body is equipped with the same genomic code (like computer chips), though how each individual cell specifically functions (normal) or dysfunctions (ill) is in a large part dictated by the epigenetics instructed transcription (like software). Epigenetics is a chemical coding (e.g. methylation) on top of the DNA or at the histone tail (e.g. acetylation) that conforms the 3D packing of DNA which dictates the transcription factor accessibility for transcription. Recently, it is also gaining evidence that the part of the complexity of genes and proteins may also be a result from the editing of another component of epigenetics, non-coding RNA. Therefore, this talk will discuss epigenetics, epigenomics and their dynamic nature as intrinsic programs and as functions of environmental impacts. Their application crosses fields of stem cell, cell biology, development, neuroscience, and genetics. Since epigenetics is acquirable and inheritable through generations, its impact on diseases traces back to ancestors. Epigenetic medicine is one of the most exciting milestones in the 21st century.

Dr. Feng C. Zhou
Professor of Psychology, Indiana University Purdue University at Indianapolis
Professor of Anatomy/ Cell Biology and Medical Neurobiology, Indiana Univ. Sch. Med.

EDUCAITON

1983-1985	Post-Doc., Neurobiology, New York University
1983	Ph.D., Neuroanatomy, Mt. Sinai School of Medicine, City Univ. of New York
1981	M.Phil., Anatomy, Mt. Sinai School of Medicine, City Univ. of New York
1975	B.S., Biology, National Taiwan Normal University/ Taiwan

POSITION AND EMPLOYMENT

2009-present	Professor of Psychology, Indiana University Purdue University at Indianapolis
1997-present	Professor of Anatomy/ Cell Biology and Medical Neurobiology, Indiana Univ. Sch. Med.
1991-1997	Associate Prof. Anatomy and Med. Neurobiology, Tenured, Indiana Univ. Sch. Med.
1987-1991	Assistant Professor of Anatomy and Med. Neurobiology, Indiana Univ. Sch. Med.
1985-1987	Assistant Research-Anatomist, UCLA, School of Medicine
1984-1987	Adjunct Assistant Professor of Biology, New York University
1983-1985	Assistant Professor of Anatomy, New York College, Podiatric Medicine

EXPERIIENCE AND HONORS

1990-Present	NIH Section and Ad hoc grant reviewer
2007-2008	Vise President, Fetal Alcohol Spectrum Disorder Study Group, USA
2008-2009	President, Fetal Alcohol Spectrum Disorder Study Group, USA
2005-present	Project principle investigator in Consortium in Fetal Alcohol Spectrum Disorder
2000-2002	Editorial board: Experimental Neurology
2003-Present	Editorial board: Current Neurovascular Research
2005-present	Editorial board: Recent Patent Review on CNS Drug Discovery
2009-present	Editorial board: Anatomy Research International
2011-present	Editorial board: Frontiers in Genetics: (Section) Frontiers in Epigenomics

PUBLICATIONS (2009 to present)

- Resendiz M, Chen Y, Öztürk NC, Zhou FC. Epigenetic Medicine and Fetal Alcohol Spectrum Disorders. Epigenomics. 2013 (5) 73-86 (doi: 10.2217/epi.12.80).
- Zhou, FC. DNA Methylation Program During Development. Frontiers in Biology, 2012 (7) 485-494. ISSN: 1674-7984 (Print) 1674-7992 (Online). DOI: 10.1007/s11515-012-9246-1.
- Zhou, F. C. and R. L. Bell (2012). "Editorial: Pharmacotherapies for the treatment of alcohol abuse and dependence." Recent Pat CNS Drug Discov 7(2) 91-92.
- Mason S, Anthony B, Lai X, Ringham H, Wang M, Witzmann FA, You JS, Zhou FC. Ethanol Exposure Alters Protein Expression in a Mouse Model of Fetal Alcohol Syndrome. International J Proteomics. Int J Proteomics 2012: 867141.
- Beversdorf DQ, Nordgren RE Bonab A A , Fischman A J , Weise S B, Dougherty DD, Felopulos G J, Zhou FC , Bauman ML. 5-HT2 receptor distribution shown by [18F] setoperone PET in high-functioning autistic adults. Neuropsychiatry Clin Neurosci 2012 (24)191-197.
- Zhou FC, Balaraman Y, Teng M, Liu Y, Singh RP, Nephew KP (2011a) Alcohol Alters DNA Methylation Patterns and Inhibits Neural Stem Cell Differentiation. Alcohol Clin Exp Res, in press. NIHMSID: NIHMS252373
- Zhou FC, Zhao. Q., Liu Y, Goodlett CR, Liang T, McClintick J, Edenberg HJ, Li L (2011b) Alteration of Gene Expression by Alcohol Exposure At Early Neurulation. BMC genomics, 12:124. PMCID:PMC3056799
- Zhou FC, Chen, Y., Love, A. (2011c) Cellular DNA Methylation Program during Neurulation and its Alteration by Alcohol Exposure. Birth Defects Res A Clin Mol Teratol. 2011 91(8)703-15. doi: 10.1002/bdra.20820; PMID:21630420.
- Singh RP. Cheng YH, Nelson P, and Zhou FC, Tenacious Multipotency of Adult Dorsal Root Ganglial Stem Cells. Cell Transplant. 2009;18(1):55-68
- Singh RP, Shiue K, Schomberg D, Zhou FC. Cellular Epigenetic Modifications of Neural Stem Cell Differentiation. Cell Transplant. 2009; 18(10): 1197–1211. PMCID: PMC2812652
- Liu Y, Balaraman Y, Wang G, Nephew K, and Zhou FC. Alcohol Exposure Alters DNA Methylation Profiles in Mouse Embryos at Early Neurulation. Epigenetics, 2009(4)1-12. PMCID: PMC2805036

Ongoing Research Support

12/1/2012- 11/31/2017
PHS P60 AA007611-200012 (PI: Zhou/Muir)
NIH/NIAAA
"Genomics of alcohol preferring P and HAD rats"
Investigate the genomic and signature and epigenomic potential of the alcohol preferring rats. Identify the fixed genomic mutation of the alcohol preferring traits over generation of screening using next generation sequencing on DNA and coding & non-coding RNA.
Role: Principal investigator

3/1/2012-2/28/2015
W. M. Keck Foundation
(Co-PI: Irudayaraj, Zhou)
"Live Single Cell Epigenetic Profiling and Regulation at Single Molecule Resolution"
Role: Subcontract PI
The goal of this project is to understand the epigenetic mechanism on gene expression at single cell level. This project will create a new nano-tool to identify and manipulate epigenetic marks at single locus level and meanwhile detecting gene expression at single live cell.

3/1/2012-2/29/2013
IUCRG (PI: Zhou)
"Ionizing Radiation Induced DNA Demethylation and Brain Development"
Study the effect of radiation on brain development through alteration of epigenetics. The therapeutic and diagnostic levels of radiation will be studied on their alteration of epigenetics during Brain development. The studies will inform how ionizing radiation in the clinic setting will alter the epigenetics in brain development.

12/1/2014-11/30/2016
PHS P60 AA007611: (Pilot Project: Lossie; Co-PI: Zhou)
NIH NIAAA
Alcohol-drinking induced DNA methylation-binding Protein changes in P rats
This study investigate how alcohol exposure would alter the DNA methylation binding protein in the alcohol preferring rats, and through its epigenetic changes to influence the gene expression in the key brain regions.

Recently Completed Research Projects

10/1/06-9/30/2011
R01AA016698 (Zhou)
NIH/NIAAA
"Epigenetics of Fetal Alcohol Syndrome"
The goal of this project is to study the epigenetic mechanism of the developmental deficit including neural and periperhal dysmorphogenesis caused by alcohol exposure during pregnancy. The effect of modification of DNA methylation and histone code on development are being studied using high throughput analysis.

9/30/2007-9/29/2012
UO1 AA14819 (Zhou)
NIH/NIAAA
"Mouse Model Neuro-Facial Dysmorphology: Translational and Treatment Studies"
The goal of this study is to develop diagnostic criteria for developmental disorder caused by pregnancy drinking in animal model that can be adopted for translational application. Further, neurotrophic and neuroprotective peptides against brain growth deficit will be tested in the animal model for potential translational application.

12/1/2007- 11/31/2012
PHS P60 AA007611 Component 7, P60 AA007611-200012 (Zhou)
NIH/NIAAA
"Genetics of Fetal Alcohol Syndrome" in "Alcohol Research Center- Center on Genetic Determinants of Alcohol Ingestion"
Examine the genes and biology of the alcohol related neurodevelopmental deficit in an embryonic culture and in vivo model. Identify the genes that mediate the individual differential sensitivity.

9/30/2007-9/29/2012
UO1AA017120-01 (Cudd)
Translational Studies of FASD Using a Sheep Model
Use long-gestational sheep model to investigate the prolong alcohol exposure including late gestations on developmental brain and neuronal circuitry and functional deficits.
Role: Co-Investigator

8/1/2010-7/31/2011
CTSI (Zhou)
Development of a High Throughput Metabolomic Screening of Biomarkers in Zebrafish and Mouse for the Translational Evaluation of Fetal Alcohol Syndrome.

L3

3 月 23 日 (週六)10:15-11:15
三樓，第 30 教室

Neuropsychiatric disorders and axon pruning

程淮榮 教授
國立臺灣大學 腦與心智科學研究所

Many common neuropsychiatric disorders ranging from autism to schizophrenia are complex in their disease nature such that the causes and effective methods for cure are largely unknown. Evidence from multiple lines of research, which include molecular genetics, neuroimaging and clinical neuroscience, indicates that neural connectivity is apparently altered in these disorders. My research focuses on the regulatory mechanisms of the formation of neuronal network in the brain. We use various genetic systems to study axon pruning, a process that is important for fine-tuning our neural connectivity. Mistakes in pruning have been implicated in neuropsychiatric disorders. In my presentation, I will first discuss the implications of abnormal axon pruning in neuropsychiatric disorders and then use my research data as an example to illustrate how the axon pruning process is regulated.

Dr. Hwai-Jong Cheng
Research Scholar, Graduate Institute of Brain and Mind Sciences
(腦與心智科學研究所), College of Medicine, National Taiwan University, Taiwan
Professor, Center for Neuroscience, Department of Neurobiology, Physiology and Behavior, College of Biological Sciences, and Department of Pathology and Laboratory Medicine, School of Medicine, University of California, Davis
Director, Diagnostic and Research Electron Microscopy Laboratory, Department of Pathology and Laboratory Medicine, School of Medicine, University of California, Davis

EDUCATION

1989	M.D. Medicine, National Taiwan University, Taiwan
1995	Ph.D., Cell & Developmental Biology, Harvard University
1997-2002	Postdoctoral Training, Neurobiology, UC San Francisco / Stanford University

POSITIONS AND PROFESSIONAL EXPERIENCE

1982-1989	Medical Student, College of Medicine, National Taiwan University, Taipei, Taiwan
1987	Summer Student, Drs. Kung-Ming Jan and Shu Chien, Institute of Biomedical Sciences, Academia Sinica, Taipei, Taiwan
1989-1991	Clinical Resident, Pathology, National Taiwan University Hospital, Taipei, Taiwan
1991-1995	Graduate Student, Dr. John G. Flanagan, Department of Cell Biology, Harvard Medical School, Harvard University
1996-1997	Clinical Resident, Pathology, National Taiwan University Hospital, Taipei, Taiwan
1997-2002	Postdoctoral Fellow, Dr. Marc Tessier-Lavigne, Howard Hughes Medical Institute, Department of Anatomy, University of California at San Francisco, and Department of Biological Sciences, Stanford University
2002-2008	Assistant Professor, Center for Neuroscience, and Department of Neurobiology, Physiology and Behavior, College of Biological Sciences, University of California, Davis
2003-2008	Assistant Professor, Department of Pathology and Laboratory Medicine, School of Medicine, University of California, Davis
2008-2011	Associate Professor, Center for Neuroscience, Department of Neurobiology, Physiology and Behavior, College of Biological Sciences, and Department of Pathology and Laboratory Medicine, School of Medicine, University of California, Davis
2002-now	Faculty Member, Neuroscience Graduate Group, and Biochemistry, Molecular, Cellular and Developmental Biology (BMCDB) Graduate Group, University of California, Davis
2004-now	Advisory Research Committee (ARC), Department of Pathology and Laboratory Medicine, School of Medicine, University of California, Davis
2008-now	Executive Committee, NIH Training Grant Program in Molecular and Cellular Biology (MCB), College of Biological Sciences, University of California, Davis
2008-now	Master Adviser, Neuroscience Graduate Group, University of California, Davis
2010-now	Director, Diagnostic and Research Electron Microscopy Laboratory, Department of Pathology and Laboratory Medicine, School of Medicine, University of California, Davis
2011-now	Professor, Center for Neuroscience, Department of Neurobiology, Physiology and Behavior, College of Biological Sciences, and Department of Pathology and Laboratory Medicine, School of Medicine, University of California, Davis
2012-now	Research Scholar, Graduate Institute of Brain and Mind Sciences, College of Medicine, National Taiwan University, Taiwan

HONORS AND PROFESSIONAL ACTIVITIES

1996	Pharmacia Biotech & Science Prize for Young Scientists in Molecular Biology, Regional winner from North America
1997-2002	Howard Hughes Medical Institute Physician Postdoctoral Fellowship
2003	Whitehall Foundation Grant Award
2004	Alfred P. Sloan Research Fellow
2004	Klingenstein Fellowship Award
2004	The M.I.N.D. Institute Research Grant Award
1997-now	Pathologist Board Certification, Taiwan
2002-now	Member, Society for Neuroscience

PUBLICATIONS (2009 to present)

- Maro, G. S., Shen, K., and Cheng, H.-J.. Deal breaker: semaphorin and specificity in the spinal stretch reflex circuit. Neuron 63:8-11 (2009) (Invited Preview)

- Chen, S.-Y. and Cheng, H.-J.. Functions of axon guidance molecules in synapse formation. Curr. Opin. Neurobiol. 19:471-478 (2009) (Invited Review). PMCID: PMC2812565

- Vanderhaeghen, P.* and Cheng, H.-J.*. Guidance molecules in axon pruning and cell death. Cold Spring Harb. Perspect. Biol. 2:a001859 (2010) (Invited Review). (*Co-corresponding authors) PMCID: PMC2869516

- Cheng, T.-W., Liu, X.-B., Faulkner, R. L., Stephan, A. H., Barres, B. A., Huberman, A. D., and Cheng H.-J.. Emergence of lamina-specific retinal ganglion cell connectivity by axon arbor retraction and synapse elimination. J. Neurosci. 30:16376-16382 (2010). PMCID: PMC3073606

- Chen, S.-Y., Huang, P.-H.* and Cheng, H.-J.*. Disrupted-in-Schizophrenia 1-mediated axon guidance involves TRIO-RAC-PAK small GTPase pathway signaling. Proc. Natl. Acad. Sci. USA 108: 5861-5866 (2011). (*Co-corresponding authors) PMCID: PMC3078365.

- Tseng, C.-H., Murray, K. D., Jou, M.-F., Hsu, S.-M., Cheng, H.-J.* and Huang, P.-H.*. Sema3E/Plexin-D1 mediated epithelial-to-mesenchymal transition in ovarian endometrioid cancer. PLoS One 6(4):e19396. (2011). (*Co-senior authors)

L4

3 月 23 日 (週六)10:15-11:15
三樓，第 31 教室

Macroprolactin: What Laboratorians Need To Know

Dr. David G. Grenache
Associate Professor of Pathology, University of Utah School of Medicine
Medical Director, ARUP Laboratories

Summary:

Hyperprolactinemia is caused by excessive production of prolactin by the anterior pituitary gland. Common physiologic causes include pregnancy and lactation while a pituitary adenoma is a frequent pathologic cause. However, the presence of a high molecular mass prolactin-IgG complex can also cause increased concentrations of prolactin. This can lead to a misdiagnosis of hyperprolactinemia that results in inappropriate and unnecessary follow-up procedures such as radiologic imaging, drug therapy, or surgery. This presentation will describe the biochemistry and clinical significance of macroprolactin, its reactivity in prolactin immunoassays, and methods for detecting macroprolactin and reporting test results.

Learning Objectives:

1.Describe the nature of macroprolactin and explain why it is an important issue for laboratorians and clinicians to understand.
2.Discuss the reactivity of macroprolactin by prolactin immunoassays.
3.Explain analytical methods for determining if macroprolactin is present in a serum specimen.

Dr. David G. Grenache
Medical Director, Special Chemistry and EME Laboratories, ARUP Laboratories

EDUCATION

1983-1988	B.S., Massachusetts College of Liberal Arts (Medical Technology) North Adams, MA
1983-1987	B.A., Massachusetts College of Liberal Arts (Biology) North Adams, MA
1989-1994	Ph.D., Worcester Polytechnic Institute (Biomedical Sciences) Worcester, MA
2000-2003	Fellow, Washington University (Clinical Chemistry and Laboratory Medicine) Saint Louis, MO

EMPLOYMENT

1988-1991	Medical Technologist, Clinical Chemistry and Immunology Laboratories, University of Massachusetts Medical Center, Worcester, MA
1991-2000	Medical Technologist, Tranfusion Medicine, University of Massachusetts Medical Center, Worcester, MA
1994-2000	Assistant Professor, Department of Clinical Laboratory Sciences, Fitchburg State College, Fitchburg, MA
1996-2000	Lecturer, Department of Laboratory Medicine, Northeastern University, Boston, MA
2003-2007	Director, Special Chemistry and Blood Gas Laboratories, UNC Hospitals, Chapel Hill, NC
2003-2007	Associate Director, Core Laboratory, UNC Hospitals, Chapel Hill, NC
2003-2007	Assistant Professor, Department of Pathology & Laboratory Medicine, University of North Carolina School of Medicine, Chapel Hill, NC
2007-2010	Assistant Professor (Clinical), Department of Pathology, University of Utah, Salt Lake City, UT
2007-Present	Medical Director, Special Chemistry and EME Laboratories, ARUP Laboratories, Salt Lake City, UT
2009-Present	Co-Director, Clinical Chemistry Fellowship, University of Utah, Salt Lake City, UT
2010-Present	Associate Professor (Clinical), Department of Pathology, University of Utah, Salt Lake City, UT

REVIEWER EXPERIENCE

American Journal of Obstetrics & Gynecology; Annals of Clinical & Laboratory Science; Clinica Chimica Acta; Clinical Biochemistry; Clinical Chemistry; Clinical Chemistry and Laboratory Medicine; Clinical Journal of the American Society of Nephrology; European Heart Journal; Placenta; Reproduction; Tumor Biology

PUBLICATIONS (2009 to present)

- Furtado LV, Lehman CM, Thompson C, Grenache DG. (2012). Can the qualitative serum pregnancy test be considered obsolete? Am J Clin Pathol, 137(2), 194-202.
- Greene DA, Schmidt RL, Wilson AR, Freedman MS, Grenache DG. (2012). Cerebrospinal fluid myelin basic protein is frequently ordered but provides little value: a test utilization study. Am J Clin Pathol, 138(2), 262-72.

- Greene DN, Procter M, Krautscheid P, Mao R, Lyon E, Grenache DG. (2012). Alpha-1-antitrypsin deficiency in fraternal twins born with familial spontaneous pneumothorax. Chest, 141(1), 239-41.

- Lu J, Grenache DG. (2012). Development of a rapid, microplate-based kinetic assay for measuring adenosine deaminase activity in body fluids. Clin Chim Acta, 413, 1637-40.

- Erickson JA, Grenache DG. (2011). Comparison of three assays for quantifying S-100B in serum. Clin Chim Acta, 412, 2122-27.

- Greene DN, Procter M, Grenache DG, Lyon E, Bornhorst JA, Mao R. (2011). Misclassification of an apparent alpha-1-antitrypsin "Z" deficiency variant by melting analysis. Clin Chim Acta, 412(15-16), 1454-6.

- Haddow JE, Neveux LM, Palomaki GE, Lambert-Messerlian G, Canick JA, Grenache DG, Lu J. (2011). The relationship between PTH and 25-hydroxy vitamin D early in pregnancy. Clin Endocrinol (Oxf), 75, 309-14.

- Parnas ML, Procter M, Schwarz M, Rong M, Grenache DG. (2011). Concordance of butyrylcholinesterase phenotype with genotype: implications for biochemical reporting. Am J Clin Pathol, 135, 271-76.

- Woodworth A, Grenache DG, Gronowski A. (2011). Cervicovaginal interleukin-6 as a predictor of preterm birth in African American women. Clin Chim Acta, 412(11-12), 988-92.

- Erickson JA, Lu J, Smith JJ, Bornhorst JA, Grenache DG, Ashwood ER. (2010). Development of a reliable immunoassay for quantifying squamous cell carcinoma antigen in serum. Clin Chem, 56(9), 1496-499.

- Grenache DG, Greene DN, Dighe AS, Fantz CR, Hoefner D, McCudden C, Sokoll L, Wiley CL, Gronowski AM. (2010). Falsely decreased human chorionic donadotropin (hCG) results due to elevated concentrations of the free beta subunit and the beta core fragment in quantitative hCG assays. Clin Chem, 56(12), 1839-44.

- Grenache DG, Wilson AR, Gross GA, Gronowski AM. (2010). Clinical and laboratory trends in fetal lung maturity testing. Clin Chim Acta, 411(21-22), 1746-49.

- Lockwood CM, Crompton JC, Riley JK, Landeros K, Dietzen DJ, Grenache DG, Gronowski AM. (2010). Validation of lamellar body counts (LBC) using three hematology analyzers. Am J Clin Pathol, 134, 420-28.

- Lu J, Grenache DG. (2010). High-throughput tissue homogenization method and tissue-based quality control materials for a clinical assay of the intestinal disaccharidases. Clin Chim Acta, 411(9-10), 754-757.

- Lu J, Snider JV, Grenache DG. (2010). Establishment of reference intervals for soluble ST2 from a United States population. Clin Chim Acta, 411(21-22), 1825-26.

- McCudden CR, Sharpless JL, Grenache DG. (2010). Comparison of multiple methods for identification of hyperprolactinemia in the presence of macroprolactin. Clin Chim Acta, 411(3-4), 155-60.

- Patel JL, Erickson JA, Roberts WL, Grenache DG. (2010). Performance characteristics of an automated assay for the quantitation of CYFRA 21-1 in human serum. Clin Biochem, 43, 1449-52.

- Whittington J, Fantz CR, Gronowski AM, McCudden C, Mullins R, Sokoll L, Wiley C, Wilson A, Grenache DG. (2010). The analytical specificity of human chorionic gonadotropin assays determined using WHO international reference reagents. Clin Chim Acta, 411(1-2), 81-5.

- Wu AHB, Lewandrowski K, Gronowski AM, Grenache DG, Sokoll L, Magnani B. (2010). Antiquated tests within the clinical pathology laboratory. Am J Manag Care, 19(9), e220-27.

- Cervinski MA, Lockwood CM, Ferguson AM, Odem RR, Stenman UH, Alfthan H, Grenache DG, Gronowski AM. (2009). Qualitative point-of-care and over-the-counter urine hCG devices differentially detect the hCG variants of early pregnancy. Clin Chim Acta, 406(1-2), 81-5.

- Fritchie K, Zedek D, Grenache DG. (2009). The clinical utility of parathyroid hormone-related peptide in the assessment of hypercalcemia. Clin Chim Acta, 402(1-2), 146-9.

- Lockwood CM, Grenache DG, Gronowski AM. (2009). Serum human chorionic gonadotropin concentrations greater than 400,000 IU/L are invariably associated with suppressed serum thyrotropin concentrations. Thyroid, 19(8), 863-8.

L5

3 月 23 日 (週六)10:15-11:15
三樓，第 34 教室

Receptor Engineering in the Development of Ideal Analgesics

H. H. Loh[1], S. H. Yeh[2], S. H. Ueng[2], J. H. Xi[1], P.L. Tao[2], P. Y. Law[1], and Y.S. Chao[2]
[1]University of Minnesota, Department of Pharmacology, Minnesota, USA
[2]National Health Research Institutes, ROC

Opioids are the most efficacious compounds in the treatment of moderate to severe pain. However, with chronic use, many adverse effects including tolerance and dependence development will result. Differential tolerance development between the analgesic and respiration depression responses decreases the therapeutic index of opioids during chronic administration, which is also a concern. In order to overcome this obstacle, the holy grail of opioid research has been the development of an “ideal analgesic,” i.e., one that has minimal or no side effects. In the past decades, thousands of specific orthosteric ligands have been developed that will active morphine receptor (MOR) with limited success. In these studies, we have pursued a novel approach to develop an opioid receptor mutant that can be activated by the opioid antagonist. This approach was based on our several experimental findings:

1) In our original studies to determine the functional domain of MOR we have found that a mutation of a conserved serine in the transmembrane region (TM)-4 of all opioid receptors confers agonistic properties to classical antagonists (PNAS.93:5715-5719, 1996). In other words, the observed agonist properties by an antagonist were due to the mutations of the conserved serine to leucine (or ala) in the fourth TM domain (S196L).

2) To determine the pharmacological significance of this mutation in vivo we have used homologous recombination gene-targeting strategies and have introduced the MOR- S196A mutants into the mouse MOR gene by a knock-in strategy. In homozygous mice the opioid antagonists such as naloxone or naltrexone elicited antinociceptive effects the same as the agonists. More importantly, chronic treatment of these mice with antagonists did not produce the expected tolerance and physical dependence associated with morphine treatment (PNAS.100:2117-2121, 2003).

3) In order to test the feasibility of utilizing such receptor mutations in the treatment of chronic pain, our recent works have shown preliminary success by using gene therapy approaches. Using a well-defined delivery vehicle, we are able to see the expression of this mutant receptor in the nociceptive neurons of the proper segment of the spinal cord. By systemic administration of opioid antagonists, which are devoid of opioid side effects, activation of this mutant MOR occurred while the endogenous wild type MOR were not activated. These results have provided a “proof of principal” that this should be a feasible approach to make an “ideal pain killing paradigm” for the treatment of chronic pain (PNAS.104:20096-20101, 2007).

Currently our group has developed a new target to screen for a new non-addictive narcotic analgesic, which I will present in my talk.

Supported by grants from NIDA-NIH of USA, and NHRI and NSC of ROC.

Dr. Horace H. Loh
Regents Professor, Department of Pharmacology, University of Minnesota Medical School, Minneapolis, Minnesota
Frederick and Alice Stark Professor, Department of Pharmacology, University of Minnesota Medical School, Minneapolis, Minnesota
Professor, Department of Pharmacology, University of Minnesota Medical School, Minneapolis, Minnesota

EDUCATION

1965-67	Postdoctoral Training, Department of Pharmacology, University of California Medical Center, San Francisco, California
1965	Ph.D., Biochemistry, School of Medicine, University of Iowa
1958	B.S., Department of Agricultural Chemistry (Biochemistry), National Taiwan University

PROFESSIONAL EXPERIENCE

2010-present	Regents Professor, Department of Pharmacology, University of Minnesota Medical School, Minneapolis, Minnesota
1990-present	Frederick and Alice Stark Professor, Department of Pharmacology, University of Minnesota Medical School, Minneapolis, Minnesota
1989-present	Professor, Department of Pharmacology, University of Minnesota Medical School, Minneapolis, Minnesota
1989-2012	Department Head, Department of Pharmacology, University of Minnesota Medical School, Minneapolis, Minnesota
1975-88	Professor, Departments of Psychiatry and Pharmacology and Langley Porter Neuropsychiatric Institute, University of California School of Medicine, San Francisco, California
1972-75	Associate Professor, Departments of Psychiatry and Pharmacology and Langley Porter Neuropsychiatric Institute,University of California School of Medicine, San Francisco, California
1970-72	Lecturer and Research Associate, Departments of Psychiatry and Pharmacology and Langley Porter Neuropsychiatric Institute, University of California School of Medicine, San Francisco, California
1970-72	Director, Drug Dependence Research Center, Mendocino State Hospital, Department of Mental Hygiene, Talmage, California
1968-70	Associate Professor of Biochemical Pharmacology, Wayne State University, Detroit, Michigan
1967	Lecturer, Department of Pharmacology, University of California School of Medicine, San Francisco, California

AWARDS AND HONORS

2010-present	Appointed Regents Professor, University of Minnesota
1990-present	Holder of the Dr. Frederick and Alice Stark Chair in Neuroscience, Medical School, University of Minnesota
2010	Recipient of the First University of Minnesota's Medical School Senior Investigator Award
2007	Recipient of the Founders' Award from the International Narcotics Research Conference
2007	Recipient of the University of Iowa Carver College of Medicine's Distinguished Alumnus Award for Achievement,
2006	Co-Recipient of The Japanese Society of Toxicology "Tanabe Award,"
2002	"Recognition of Excellence" for Outstanding Contributions and Achievements in Teaching, Research, or Service, from the Academic Health Center, University of Minnesota, 2002. Dr. Loh was in the first group (one of 4) to receive this honor when this program was initiated.
2002	Recipient of the Nathan B. Eddy Memorial Award for Lifetime Excellence in Addiction Research, from the College on Problems of Drug Dependence (CPDD)

2002	Recipient of the 1999 Otto Krayer Award in Pharmacology, from the American Society for Pharmacology and Experimental Therapeutics (ASPET)
1999	Recipient of the First "Award in Excellence for Basic Pharmacology" from the Pharmaceutical Research and Manufacturers of America (PhRMA) Foundation
1999	Recipient of the First "Presidential Award" from the Society of Chinese Bioscientists in America (SCBA)
1988-1998	National Institutes of Health (NIH) Method to Extend Research in Time (MERIT) Award (National Institute on Drug Abuse) (Dr. Loh was one of three of the very first scientists to receive this award.)
1976	Humboldt Research Award (West Germany)

National Institutes of Health (NIH) Research Scientist Award (1983-88, 1989-94, 1994-99, 1999-04, 2004-09, five five-year terms)

National Institutes of Health (NIH) Career Development Award (1973-78, 1978-83, two five-year terms)

PROFESSIONALLY RELATED SERVICE

National Institutes of Health (NIH)

2006-2010	Standing Committee Member, National Institute on Drug Abuse (NIDA) K Scientific Review Group
2006	Member, NIDA Special Emphasis Panel (ZDA1-MXG-S-19) on Prescription Opioid Use and Abuse in the Treatment of Pain, NIH
1998	Chair, Molecular, Cellular and Developmental Neuroscience-4 (Study Section), NIH
1997	Ad Hoc Committee Member, NIDA Study Section, NIH
1995	Member, Search Committee for Scientific Director, Division of Intramural Research, National Institute on Drug Abuse, NIH
1994-1995	Member, Search Committee for Addiction Research Center (ARC) Director, National Institute on Drug Abuse, NIH
1992-1996	Council Member, NIDA National Advisory Council, NIH
1989-1993	Chair, NIDA Drug Abuse AIDS Research Review Committee (Study Section), NIH
1989	Chair, NIDA Special Review Committee for Drug Development (Study Section), NIH
1986-1988	Chair, Biochemistry Subcommittee, NIDA Biomedical Research Review Committee (Study Section), NIH
1984-1988	Member, NIDA Biomedical Research Review Committee (Study Section), NIH
1983-1984	Ad Hoc Committee Member, NIDA Study Section, NIH
1980-1981	Member, National Institute of Mental Health (NIMH) Basic Psychopharmacology and Neuropsychopharmacology Research Review Committee (Study Section), NIH
1977-1979	Member, NIMH Preclinical Psychopharmacology Study Section, NIH
1976-1977	Ad Hoc Committee Member, NIDA Study Section, NIH

U. S. Government

1980-1984	Scientific Consultant, U.S. Army Research and Development Command, Department of Defense
1974-1975	Chinese Biologists' Association President

Academic Service

Academia Sinica, Taiwan ROC

2005-2011	Chair, Academic Advisory Council, Institute of Biological Chemistry
1993-present	Member, Academic Advisory Committee, Institute of Biomedical Sciences
1994-2004	Member, Institute of Biological Chemistry
1995	Member, Search Committee for Institute of Biomedical Sciences Director
1994-1998	Member, Biotechnology Development Action Committee

Hong Kong University of Science and Technology, Hong Kong

2005-2008	Member, Advisory Committee, School of Science

2003-2006 Member, International Advisory Committee, Department of Biochemistry Chinese Academy of Sciences, China
2005-2008 Member, International Scientific Advisory Board, Guangzhou Institute of Biomedicine and Health

Hong Kong University
2000-present Member, International Advisory Committee, Institute of Chemical Biology

National Tsing Hua University, Institute of Life Sciences, Taiwan ROC
1985-1989 Member, Advisory Committee

Governmental Service

Department of Higher Education, Ministry of Education, Taiwan ROC
2000-present Member, Scientific Advisory Committee

National Health Research Institutes (NHRI), Taiwan ROC
1991[present Chair, Scientific Review Committee
1991-present Member, Scientific Advisory Council
1989-present Chair, Scientific Advisory Committee, Institute of Biotechnology and Pharmaceutical Research

Ministry of Economics, Taiwan ROC
1998-2000 Member, Advisory Board of Development Center for Biotechnology

Scientific/Professional Society Service

International Narcotic Research Conference (INRC)
1997 Scientific Program Chair for Annual Meeting in Hong Kong
1984-1987 Member, Executive Committee, Scientific Program Chair for 1986 Annual Meeting in San Francisco

L6

3 月 23 日 (週六)13:45-15:45
一樓，第 1 教室

50 Years of Autophagy: towards Understanding The Intracellular Self-Degradation System Sustaining Life

Dr. Tamotsu Yoshimori
Department of Genetics, Graduate School of Medicine, Osaka University

Autophagy is an evolutionarily conserved membrane trafficking from the cytoplasm to lysosomes. As the term “autophagy”(self-eating in Greek), was officially used for the first time in 1963, we are cerebrating the 50th anniversary of the autophagy studies in this year. In autophagy, the unique double membrane-bound autophagosomes transiently emerge in the cytoplasm, sequester portion of the cytosol and organelles, and eventually fuse with lysosomes to degrade the contents. In addition to the basic role in nutrient supply under starvation conditions, the process unexpectedly functions in development, longevity, immunity, and suppression of various diseases including tumorigenesis, neurodegeneration, and inflammatory diseases.

My group has been working on unraveling the molecular machinery and roles of mammalian autophagy for the last 16 years. LC3, a first protein we identified, has been mostly used golden marker in autophagy studies. This single paper (EMBO J, 2000) has been cited in over 1,800 papers (second best in the field). Recently, we have provided new insights into biogenesis of autophagosome, which have been topic of longstanding debate. We showed that autophagosome forms at the ER-mitochondria contact site. Furthermore, we found that autophagy eliminates invading pathogenic bacteria. Now we are focusing on how cells recognize the intracellular bacteria and envelop them specifically by autophagosome. I also would like to introduce our recent finding about a new role of autophagy in selective elimination of damaged lysosomes to defense against dieases.

Related papers:

1.Hamasaki et al. Autophagosomes form at ER−mitochondria contact sites. *Nature.* in press (2013)
2.Matsunaga et al. Two Beclin-1 binding proteins, Atg14L and Rubicon, reciprocally regulate autophagy at different stages. *Nat Cell Biol.,* 11, 385-396 (2009)
3.Nakagawa et al. Autophagy defenses cells against invading group A Streptococcus. *Science.* 306, 1037-1040 (2004)
4.Kabeya et al. LC3, a mammalian homolog of yeast Apg8p, is localized in autophagosome membranes after processing. *EMBO J.* 19, 5720-5728 (2000)

Dr. Tamotsu Yoshimori
Professor, Laboratory of Intracellular Membrane Dynamics, Graduate School of Frontier Biosciences, and in Department of Genetics, Graduate School of Medicine (concurrently), Osaka University, Osaka, Japan

EDUCATION AND EMPLOYMENT

1977-1981	Undergraduate Student in Department of Biology, Faculty of Scinence, Osaka University, Japan
1981-1986	Graduate Student in Institute for Molecular and Cellular Biology, Osaka University, Japan, with Prof. Yoshio Okada
1986-1996	Assistant Professor in Department of Physiology, Kansai Medical University, Japan, with Prof. Yutaka Tashiro
1989	Ph.D. in Medical Science from Osaka University, Japan
1993-1995	Postdoctoral Fellow in the Cell Biology Program, European Molecular Biology Laboratory, Heidelberg, Germany, with Prof. Kai Simons
1996-2002	Associate Professor in Department of Cell Biology, National Institute for Basic Biology, Okazaki, Japan, with Prof. Yoshinori Ohsumi
1999-2002	Associate Professor (concurrently) in Department of Molecular Biomechanics, School of Life Science, The Graduate University for Advanced Studies, Japan
2002-2006	Full Professor in Department of Cell Genetics, National Institute of Genetics, Mishima, Japan
2002-2006	Full Professor (concurrently) in Department of Genetics, School of Life Science, The Graduate University for Advanced Studies, Japan
2002-2008	Group Leader in CREST (Core Research for Evolutional Science and Technology) Program, Japan Science and Technology Agency, Japan
2006-2010	Full Professor in Department of Cellular Regulation, Research Institute for Microbial Diseases, Osaka University, Osaka, Japan
2008-2012	Area Leader in Grant-in-Aid for Scientific Research on Innovative Areas (Team-based research) “Intracellular Logistics: Interdisciplinary approaches to pathophysiology of membrane traffic”
2010-present	Full Professor in Laboratory of Intracellular Membrane Dynamics, Graduate School of Frontier Biosciences, and in Department of Genetics, Graduate School of Medicine (concurrently), Osaka University, Osaka, Japan
2012-2017	Group Leader in CREST (Core Research for Evolutional Science and Technology) Program, Japan Science and Technology Agency, Japan

AWARD

Human Frontier Science Program Long Term Fellowship 1993-1995
Osaka University Presidential Award for Achievement 2012
Roche Distinguished Lecturer 2012

MANUSCRIPT REVIEWS

Invited referee for scientific journals including: Nature, Science, Cell, Nat. Cell Biol., Mol. Cell, Immunity, J. Cell Biol., Proc. Natl. Acad. Sci. USA, Nat. Struct. Mol. Biol., Nat. Nanotec., J. Exp. Med., J. Clin. Invest., EMBO J., PLoS Pathogens, Hum. Mol. Genet., Cell Death Differ., Cell Host Microbe, EMBO rep., Mol. Biol. Cell., J. Cell Sci., J. Biol. Chem., Cell Microbiol., Traffic, Autophagy, J. Immunol., PLoS One, and so on.

PUBLICATION (2012 to present)

- Hamasaki M, Furuta N, Matsuda A, Nezu A, Yamamoto A, Fujita N, Oomori H, Noda T, Haraguchi T, Hiraoka Y, Amano A*, Yoshimori T*. Autophagosomes form at ER mitochondria contact sites. Nature. in press (2013)

- Raju D, Hussey S, Ang M, Terebiznik MR, Sibony M, Galindo-Mata E, Gupta V, Blanke SR, Delgado A, Romero-Gallo J, Ramjeet MS, Mascarenhas H, Peek RM, Correa P, Streutker C, Hold G, Kunstmann E, Yoshimori T, Silverberg MS, Girardin SE, Philpott DJ, El Omar E, Jones NL. Vacuolating Cytotoxin and Variants in Atg16L1 That Disrupt Autophagy Promote Helicobacter pylori Infection in Humans. Gastroenterology 142, 1160-71. (2012)

- Shimizu S, Takehara T*, Hikita H, Kodama T, Tsunematsu H, Miyagi T, Hosui A, Ishida H, Tatsumi T, Kanto T, Hiramatsu N, Fujita N, Yoshimori T, Hayashi N. Inhibition of autophagy potentiates the antitumor effect of the multikinase inhibitor sorafenib in hepatocellular carcinoma. Int J Cancer. 131, 548-57. (2012)

- Takahashi A, Kimura T, Takabatake Y, Namba T, Kaimori J, Kitamura H*, Matsui I, Niimura F, Matsusaka T, Fujita N, Yoshimori T, Isaka Y*, Rakugi H. Autophagy guards against Cisplatin-induced acute kidney injury. Am J Pathol. 180, 517-25. (2012)

L7

3 月 23 日 (週六)13:45-15:45
一樓，第 2 教室

Regulation of Blood Flow to the Heart: A feed-forward process that is regulated by H_2O_2-dependent redox signaling

Dr. William M. Chilian
Department of Integrative Medical Sciences, Northeast Ohio Medical University, Rootstown, Ohio USA

Under normal conditions, myocardial blood flow is dynamically adjusted to the oxygen requirements of the myocardium. If oxygen demands increase, as during exercise, blood flow increases to match the heighted metabolic demands. Because coronary flow and myocardial metabolism can increase several-fold without any signs of insufficiency or reductions in venous PO_2 (which would suggest inadequate perfusion), coronary flow is likely controlled, at least in part, in a feed forward manner. A feed-forward metabolic factor would be produced by myocardial oxygen metabolism and not when oxygen delivery is limited. One possible feed-forward metabolic dilator is H_2O_2, which is largely produced by mitochondria in cardiac myocytes. H_2O_2 is derived from the dismutation of $O_2^{\cdot -}$, which is produced when electrons leak from mitochondrial complexes and reduce O_2. The higher the electron flux—as during increased oxygen metabolism—the greater the production of H_2O_2. H_2O_2 produces dilation in a redox-dependent manner via oxidation of thiol groups of proteins that activate potassium channels in vascular myocytes. Opening of potassium channels results in hyperpolarization, reduced levels of calcium, relaxation of the vascular myocytes and vasodilation. Coronary resistance vessels express certain Kv channels that are known to be redox sensitive, especially those in the Kv1 family, which mediate dilation to H_2O_2. Kv1 family channels are critical to the coupling of flow to metabolism in the heart and if these channels are dysfunctional (or not expressed), improper coupling of flow to metabolism occurs. This impaired coupling can lead to age-related decrements in function, as well as heart failure. Taken together, the regulation of coronary blood flow is a process that is critically dependent on the feed-forward, mitochondrial production of H_2O_2 in cardiac myocytes, with subsequent activation of Kv1 family channels in vascular smooth muscle. These events are critical for the proper coupling of flow to metabolism. Impairment in this coupling leads to inadequate myocardial perfusion and impaired cardiac pump function.

Dr. William M. Chilian
Department of Integrative Medical Sciences, Northeast Ohio Medical University

EDUCATION

1974	B.A., Honors in Biology, St. Olaf College, Northfield, Minnesota
1976	M.S., Texas Tech University, Lubbock, Texas
1980	Ph.D., University of Missouri, Columbia, Missouri

EMPLOYMENT

2002-2007	Department of Physiology, LSU Health Sciences Center in New Orleans, Kenneth A. Ardoin/Pfizer Superchair of Basic Cardiovascular Research
2007-present	Department of Integrative Medical Sciences, Northeast Ohio Medical University, Professor and Chair
2009-present	Member, Center for Biomaterials and Medicine and the Wound Healing Consortium, Austen BioInnovation Institute of Akron
2010-present	Adjunct Professor, Department of Chemical and Biomolecular Engineering, University of Akron

RESEARCH AND OTHER SCHOLARLY ACTIVITIES:

Areas of Research:
Regulatory Mechanisms in the Coronary Microcirculation
Coronary Angiogenesis and Arteriogenesis
Non-linear behavior of biological systems
Mechanosensitive Gene Expression and Signal Transduction
Redox-dependent signaling processes

PUBLICATIONS (2009 to present)

- Adapala RK, Thoppil RJ, Luther DJ, Paruchuri S, Meszaros JG, Chilian WM, Thodeti CK. Trpv4 channels mediate cardiac fibroblast differentiation by integrating mechanical and soluble signals. J Mol Cell Cardiol. 2013;54:45- 52
- Guarini G, Capozza PG, Huqi A, Morrone D, Chilian WM, Marzilli M. Microvascular function/dysfunction downstream a coronary stenosis. Curr Pharm Des. 2012
- Pung YF, Rocic P, Murphy MP, Smith RA, Hafemeister J, Ohanyan V, Guarini G, Yin L, Chilian WM. Resolution of mitochondrial oxidative stress rescues coronary collateral growth in zucker obese fatty rats. Arterioscler Thromb Vasc Biol. 2012;32:325-334
- Luther DJ, Thodeti CK, Shamhart PE, Adapala RK, Hodnichak C, Weihrauch D, Bonaldo P, Chilian WM, Meszaros JG. Absence of type vi collagen paradoxically improves cardiac function, structure, and remodeling after myocardial infarction. Circ Res. 2012;110:851-856
- Yin L, Ohanyan V, Pung YF, Delucia A, Bailey E, Enrick M, Stevanov K, Kolz CL, Guarini G, Chilian WM. Induction of vascular progenitor cells from endothelial cells stimulates coronary collateral growth. Circ Res. 2012;110:241-252
- Pung YF, Chilian WM. Corruption of coronary collateral growth in metabolic syndrome: Role of oxidative stress. World J Cardiol. 2010;2:421-427
- Belmadani S, Matrougui K, Kolz C, Pung YF, Palen D, Prockop DJ, Chilian WM. Amplification of coronary arteriogenic capacity of multipotent stromal cells by epidermal growth factor. Arterioscler Thromb Vasc Biol. 2009;29:802-808
- Carrao AC, Chilian WM, Yun J, Kolz C, Rocic P, Lehmann K, van den Wijngaard JP, van Horssen P, Spaan JA, Ohanyan V, Pung YF, Buschmann I. Stimulation of coronary collateral growth by granulocyte stimulating factor: Role of reactive oxygen species. Arterioscler Thromb Vasc Biol. 2009;29:1817-1822
- Yun J, Rocic P, Pung YF, Belmadani S, Carrao AC, Ohanyan V, Chilian WM. Redox-dependent mechanisms in coronary collateral growth: The "redox window" hypothesis. Antioxid Redox Signal. 2009;11:1961-1974

REVIEW ARTICLES (2011 to present)

- Deussen A, Ohanyan V, Jannasch A, Yin L, Chilian W. Mechanisms of metabolic coronary flow regulation. J Mol Cell Cardiol. 2011
- Chilian WM, Pung YF, Penn MS, Dong, F, Mayorga M, Yin L. Coronary Collateral Growth—Back to the Future. J Mol Cell Cardiol. 2011 (In Press)

L8

3 月 24 日 (週日) 09:00-10:00
三樓，第 34 教室

GOLGA2/GM130, *cis*-Golgi Matrix Protein, is a Novel Target of Anticancer Gene Therapy

Dr. Myung-Haing Cho
Laboratory of Toxicology College of Veterinary Medicine, Seoul National University

Achievement of long-term survival of patients with lung cancer treated with conventional chemotherapy is still difficult for treatment of metastatic and advanced tumors. Despite recent progress in investigational therapies, survival rates are still disappointingly low and novel adjuvant and systemic therapies are urgently needed. A recently elucidated secretory pathway is attracting considerable interest as a promising anti-cancer target. The *cis*-Golgi matrix protein, GOLGA2/GM130, plays an important role in glycosylation and transport of protein in the secretory pathway. In this study, the effects of short hairpin RNA (shRNA) constructs targeting GOLGA2/GM130 (shGOLGA2) on autophagy and lung cancer growth were evaluated *in vitro* and *in vivo.* Down-regulation of GOLGA2/GM130 led to induction of autophagy and inhibition of glycosylation in A549 cells and in the lungs of K-*ras*^{LA1} mice. Furthermore, down-regulation of GOLGA2/GM130 decreased angiogenesis and cancer cell invasion *in vitro* and suppressed tumorigenesis in lung cancer mice model. The tumor specificity of sequence targeting GOLGA2/GM130 was also demonstrated. Taken together, these results suggest that induction of autophagy by shGOLGA2 may induce cell death rather than cell survival. Therefore, down-regulation of GOLGA2/GM130 may be a potential therapeutic option for lung cancer.

Dr. Myung-Haing Cho
Professor, Laboratory of Toxicology, College of Veterinary Medicine, Seoul National University, Korea
Concurrent Professor, Department of Nanofusion Technology, Graduate School of Convergence Science Technology, Seoul National University, Korea
Concurrent Professor, Graduate Group of Tumor Biology, Seoul National University, Korea
Chairperson, Pesticide Risk Assessment, Rural Development Association, Korea
Fellow, Korean Academy of Science Technology

EDUCATION

1992	Ph.D., Toxicology, University of California, Davis, USA, 1992
1987	M.S., Vet. Toxicology, Seoul National University, Korea, 1987
1985	D.V.M., Seoul National University, Korea, 1985

RESEARCH AND PROFESSIONAL EXPERIENCES

1992-1994	Postdoctoral Researcher, Department of Environmental Science and Engineering, School of Public Health, The University of North Carolina at Chapel Hill, USA
1994-2000	Assistant Professor, Laboratory of Toxicology, College of Veterinary Medicine, Seoul National University, Korea
2000-2005	Associate Professor, Laboratory of Toxicology, College of Veterinary Medicine, Seoul National University, Korea
2005-present	Professor, Laboratory of Toxicology, College of Veterinary Medicine, Seoul National University, Korea
2001-2002	Visiting Fellow, Gene Regulation Section, National Cancer Institute-Frederick Cancer Research and Development Center, Frederick, MD, USA
2007-2009	Director General, National Institute of Toxicological Research, Ministry of Health, Korea
2008-present	Concurrent Professor, Department of Nanofusion Technology, Graduate School of Convergence Science Technology, Seoul National University, Korea
2008-present	Concurrent Professor, Graduate Group of Tumor Biology, Seoul National University, Korea
2009-present	Chairperson, Pesticide Risk Assessment, Rural Development Association, Korea
2009-2011	Concurrent Researcher, Advanced Institutes of Convergence Technology, Seoul National University, Korea,
2010-present	Fellow, Korean Academy of Science Technology

AWARDS

2001	ICC (Union For International Cancer Control) International Scholar Award
2006	CRS-Banner Outstanding Pharmaceutical Paper Award, USA
2007	Baek-Lin Research Award, Seoul National University, Korea
2008	The Best Research Award, Seoul National University, Korea
2008	One of The Best Research Award, Korea Research Foundation
2008	One of the Excellent Research Results, Korea Science and Engineering Foundation, Korea
2009	The Best Research Award, Korean Society of Veterinary Science
2009	Baek-Lin Research Award, College of Veterinary Medicine, Seoul National University
2010	Distinguished Research Award, Seoul National University
2012	Leading Edge in Basic Science Award, SOT, SF, CA, USA

PUBLICATIONS

- Shin JY, Chung YS, Kang B, Jiang HL, Yu DY, Han K, Chae C, Moon JH, Jang G, Cho MH. Co-delivery of LETM1 and CTMP synergistically inhibits tumor growth in H-ras12V liver cancer model mice. Cancer Gene Therapy advance online publication 8 February 2013; doi: 10.1038/cgt.2013.6
- Lee HM, Song SO, Cha SH, Wee SB, Bischoff K, Park SW, Son SW, Kang HG, Cho MH. Development of a monoclonal antibody to deoxynivalenol and application for magnetic nanoparticle-based extraction and enzyme linked immunosorbent assay. J Vet Sci. 2013 Feb 5. [Epub ahead of print]
- Lee HR, Jeung EB, Cho MH, Kim TH, Leung PC, Choi KC. Molecular mechanism(s) of endocrine-disrupting chemicals and their potent oestrogenicity in diverse cells and tissues that express oestrogen receptors. J Cell Mol Med. 2012 Dec 20. doi: 10.1111/j.1582-4934.2012.01649.x. [Epub ahead of print]
- Minai-Tehrani A, Chang SH, Kwon JT, Hwang SK, Kim JE, Shin JY, Yu KN, Park SJ, Jiang HL, Kim JH, Hong SH, Kang B, Kim D, Chae CH, Lee KH, Beck GR Jr, Cho MH. Aerosol delivery of lentivirus-mediated O-glycosylation mutant osteopontin suppresses lung tumorigenesis in K-ras (LA1) mice. Cell Oncol (Dordr). 2012 Oct 16. [Epub ahead of print]
- Islam MA, Shin JY, Firdous J, Park TE, Choi YJ, Cho MH, Yun CH, Cho CS. The role of osmotic polysorbitol-based transporter in RNAi silencing via caveolae-mediated endocytosis and COX-2 expression. Biomaterials. 2012 Sep 10. pii: S0142-9612(12)00952-0. doi: 10.1016/j.biomaterials.2012
- Kim BY, Suh KS, Lee JG, Woo SR, Park IC, Park SH, Han CJ, Kim SB, Jeong SH, Yeom YI, Yang SJ, Kim CM, Cho SJ, Yoo YD, Cho MH, Jang JJ, Choi DW, Lee KH. Integrated analysis of prognostic gene expression profiles from hepatitis B virus-positive hepatocellular carcinoma and adjacent liver tissue. Ann Surg Oncol. Suppl 3:328-38, 2012.
- Park TE, Kang B, Kim YK, Zhang Q, Lee WS, Islam MA, Kang SK, Cho MH, Choi YJ, Cho CS. Selective stimulation of caveolae-mediated endocytosis by an osmotic polymannitol-based gene transporter. Biomaterials. 33(29), 7272-7281, 2012
- Joo HY, Woo SR, Shen YN, Yun MY, Shin HJ, Park ER, Kim SH, Park JE, Ju YJ, Hong SH, Hwang SG, Cho MH, Kim J, Lee KH. SIRT1 Interacts with and Protects Glyceraldehyde-3-Phosphate Dehydrogenase (GAPDH) from Nuclear Translocation: Implications for Cell Survival after Irradiation. Biochem Biophys Res Commun. 424(4), 681-686, 2012
- Chang SH, Hong SH, Jiang HL, Minai-Tehrani A, Yu KN, Lee JH, Kim JE, Shin JY, Kang B, Park S, Han K, Chae C, Cho MH. GOLGA2/GM130, cis-Golgi Matrix Protein, is a Novel Target of Anticancer Gene Therapy. Mol Ther. 2012 Jun 26. doi: 10.1038/mt.2012.125. [Epub ahead of print]
- Luu QP, Shin JY, Kim YK, Islam MA, Kang SK, Cho MH, Choi YJ, Cho CS. High Gene Transfer by the Osmotic Polysorbitol-Mediated Transporter through the Selective Caveolae Endocytic Pathway. Mol Pharm. 2012 Jun 18. [Epub ahead of print]
- Kim JH, Kim YK, Minai-Tehrani A, Hong SH, Lee JH, Kang B, Bang YB, Cho CS, Yu DT, Jiang HL, Cho MH. Galactosylation of chitosan-graft-spermine as a hepatocyte targeting DNA carrier. J Nanosci Nanotech. 12(7), 5178-5184, 2012
- Kim JH, Kim YK, Manai-Tehrani A, Hong SH, Lee JH, Kang B, Bang YB, Cho CS, Yu DY, Jaing HL, Cho MH. J Nanosci Nanotechnol 12, 5178-5184, 2012
- Kim YK, Kwon JT, Jiang HL, Choi YJ, Cho MH, Cho CS. Kidney-specific peptide-conjugated poly(ester amine) for the treatment of kidney fibrosis. J Nanosci Nanotechnol 12, 5149-5154, 2012
- Yoo MK, Park IK, Lim HT, Lee SJ, Jiang HL, Kim YK, Choi YJ, Cho MH, Cho CS. Folate-PEG-superparamagnetic iron oxide nanoparticles for lung cancer imaging. Acta Biomater. 8(8), 3005-3013, 2012
- Shin JY, Lim HT, Minai-Tehrani A, Noh MS, Kim JE, Kim JH, Jiang HL, Arote R, Kim DY, Chae C, Lee KH, Kim MS, Cho MH. Aerosol delivery of beclin1 enhanced the anti-tumor effect of radiation in the lungs of K-rasLA1 mice. J Radiat Res. 53(4), 506-515, 2012
- Chang SH, Minai-Tehrani A, Shin JY, Park S, Kim JE, Yu KN, Hong SH, Hong CM, Lee KH, Beck Jr GR, Cho MH. Beclin1-induced Autophagy Abrogates Radioresistance of Lung Cancer Cells by Suppressing Osteopontin. J Radiat Res. 53(3), 422-432, 2012

- Hong SH, Kim JE, Kim YK, Minai-Tehrani A, Shin JY, Kang B, Kim HJ, Cho CS, Chae C, Jiang HL, Cho MH. Suppression of lung cancer progression by biocompatible glycerol triacrylate-spermine (GT-SPE)-mediated delivery of shAkt1. Int J Nanomed., 7, 2293-2306, 2012.
- Chang SH, Chung YS, Hwang SK, Kwon JT, Minai-Tehrani A, Kim S, Park SB, Kim YS, Cho MH.Lentiviral vector-mediated shRNA against AIMP2-DX2 suppresses lung cancer cell growth through blocking glucose uptake. Mol Cells. 33(6), 553-562, 2012
- Minai-Tehrani A, Jiang HL, Kim YK, Chung YS, Yu KN, Kim JE, Shin JY, Hong SH, Lee JH, Kim HJ, Chang SH, Park SJ, Kang BN, Cho CS, Cho MH. Suppression of tumor growth in xenograft model mice by small interfering RNA targeting osteopontin delivery using biocompatible poly(amino ester). Int J Pharm. 431, 197-203, 2012
- Kim JE, Shin JY, Cho MH. Magnetic nanoparticles: an update of application for drug delivery and possible toxic effects. Arch Toxicol. 86(5), 685-700, 2012.
- Kim JS, Kim YH, Kim JH, Kang KW, Tae EL, Youn H, Kim D, Kim SK, Kwon JT, Cho MH, Lee YS, Jeong JM, Chung JK, Lee DS. Development and in vivo imaging of a PET/MRI nanoprobe with enhanced NIR fluorescence by dye encapsulation. Nanomedicine (Lond). 7(2), 219-229, 2012
- Guo DD, Hong SH, Jiang HL, Kim JH, Minai-Tehrani A, Kim JE, Shin JY, Jiang T, Kim YK, Choi YJ, Cho CS, Cho MH. Synergistic effects of Akt1 shRNA and paclitaxel-incorporated conjugated linoleic acid-coupled poloxamer thermosensitive hydrogel on breast cancer. Biomaterials, 33(7), 2272-2281, 2012.
- Kim JH, Minai-Tehrani A, Kim YK, Shin JY, Hong SH, Kim HJ, Lee HD, Chang SH, Yu KN, Bang YB, Cho CS, Yoon TJ, Yu DY, Jiang HL, Cho MH. Suppression of tumor growth in H-ras12V liver cancer mice by delivery of programmed cell death protein 4 using galactosylated poly(ethylene glycol)-chitosan-graft-spermine. Biomaterials, 33, 1894-1902, 2012.
- Hwang SK, Minai-Tehrani A, Yu KN, Chang SH, Kim JE, Lee KH, Park J, Beck GR Jr, Cho MH. Carboxyl-terminal modulator protein induces apoptosis by regulating mitochondrial function in lung cancer cells. Int J Oncol. 40(5), 1515-1524, 2012.
- Woo SR, Park JE, Juhn KM, Ju YJ, Jeong J, Kang CM, Yun HJ, Yun MY, Shin HJ, Joo HY, Park ER, Park IC, Hong SH, Hwang SG, Kim H, Cho MH, Kim SH, Park GH, Lee KH. Biochem Biophys Res Commun. Cells with dysfunctional telomeres are susceptible to reactive oxygen species hydrogen peroxide via generation of multichromosomal fusions and chromosomal fragments bearing telomeres. BBRC, 417(1), 204-210, 2012.
- Yi BR, Kim SU, Kim YB, Lee HJ, Cho MH, Choi KC. Antitumor effects of genetically engineered stem cells expressing yeast cytosine deaminase in lung cancer brain metastases via their tumor-tropic properties. Oncol Rep 27, 1823-1828, 2012.
- Choi SY, Shen YN, Woo SR, Yun M, Park JE, Ju YJ, Jeong J, Shin HJ, Joo HY, Park ER, Lee JK, Kim SH, Cho MH, Kong IS, Lee KH. Mitomycin C and doxorubicin elicit conflicting signals by causing accumulation of cyclin E prior to p21WAF1/CIP1 elevation in human hepatocellular carcinoma cells. Int J Oncol. 40(1), 277-286, 2012

中國生理學會

研討會轉譯醫學專論：從生理到臨床
時　間：102 年 3 月 23 日 (週六) 09:00-11:15
地　點：一樓，第 2 教室
主持人：樓迎統 教授 / 長庚學校財團法人長庚科技大學

編號	時段	演講者 & 講題
S1	09:10 - 09:50	SPAKling on the Sodium and Blood Pressure Regulation 楊松昇 教授 / 三軍總醫院 內科部腎臟科
S2	09:50 - 10:30	Reactive Oxygen Species Signaling: from Bench to Bedside 鄭劍廷 教授 / 臺灣師範大學 生命科學系
S3	10:30 - 11:10	Hypoxia, epigenetics, and endometriosis 蔡少正 教授 / 國立成功大學 醫學院生理學研究所

中華民國毒物學學會

研討會　The Interplay of Environmental Factors and Estrogen in Cancer
時　間：102 年 3 月 23 日 (週六) 09:00-10:00
地　點：三樓，第 34 教室
主持人：林嬪嬪 研究員 / 國家衛生研究院 環境衛生與職業醫學研究組

編號	時段	演講者 & 講題
S4	09:00 - 09:30	Cigarette sidestream smoke particulates exhibit an estrogenic effect inlung adenocarcinoma cells 李立安 副研究員 / 國家衛生研究院 環境衛生與職業醫學研組
S5	09:30 - 10:00	Association of the cumulative body burden of estrogen-3,4-quinone With body mass index and breast cancer risk using albumin adducts as biomarkers 林伯雄 教授 / 國立中興大學 環境工程所

中華民國細胞及分子生物學學會

研討會 Neuroscience
時　間：102 年 3 月 23 日 (週六) 13:45-15:45
地　點：三樓，第 30 教室
主持人：高閬仙 教授 / 國立陽明大學 生命科學系暨基因體研究所

編號	時段	演講者 & 講題
S6	13:45 - 14:15	Mir-17~92 cluster: a double-edged sword controlling spinal motor neuron generation and degeneration 陳俊安 助研究員 / 中央研究院 分子生物研究所
S7	14:15 - 14:45	Abl kinase at the crossroad of neurodegenerative signaling pathways 莊志立 研究員 / 國家衛生研究院 分子與基因醫學研究所
S8	14:45 - 15:15	Study of the neurodegenerative disease- FTLD-U: from molecular neuroscience to treatment 蔡坤哲 副教授 / 國立成功大學 臨床醫學研究所
S9	15:15 - 15:45	Amyloid-beta (Aβ) D7H mutation on Aβ production and aggregation 鄭菡若 副教授 / 國立陽明大學 腦科學研究所

中華民國臨床生化學會

研討會 Current Trend in Clinical Biochemistry
時　間：102 年 3 月 23 日 (週六) 13:45-15:45
地　點：三樓，第 31 教室
主持人：方偉宏 副教授 / 國立臺灣大學 醫學檢驗暨生物技術學系

編號	時段	演講者 & 講題
S10	13:45 - 14:15	Serum Ferritin - to - iron (F1R) ratio as a hepatocellular carcinoma biomarker complementary to alpha - fetoprotein and as a prognostic predictor of Metastasis 劉燦榮 教授 / 台北醫學大學 癌症中心轉譯研究室
S11	14:15 - 14:45	Simvastatin 對於第二型糖尿病 Ldlr -/- 小鼠具有抑制動脈鈣化之作用 林植培 主任 / 台北榮民總醫院 病理檢驗部生物化學科
S12	14:45 - 15:15	Molecular diagnostics for chromosomal and epigenetic instability in colorectal cancer 楊雅倩 副教授 / 國立臺灣大學 醫學檢驗暨生物技術學系
S13	15:15 - 15:45	Molecular diagnostics for lung cancer multiplex gene testing by MALDI-TOF MS with high sensitivity and flexibility 蘇剛毅 助理教授 / 國立臺灣大學 醫學檢驗暨生物技術學系

中華民國解剖學學會

研討會 Neural Science
時　間：102 年 3 月 23 日 (週六) 13:45-15:45
地　點：三樓，第 32 教室
主持人：郭余民 教授 / 國立成功大學 細胞生物與解剖學研究所

編號	時段	演講者 & 講題
S14	13:45 - 14:15	Surgical Decompression in Small-Fiber Sensory Neuropathy 曾拓榮 助理教授 / 中國醫藥大學 醫學系 解剖科
S15	14:15 - 14:45	The Neuroprotective Effects of Valproic Acid in in vitro Rodent Parkinson's Disease Model 王詔娟 助理教授 / 高雄醫學大學 醫學系 解剖科
S16	14:45 - 15:15	The Potential Roles of Adult Neurogenesis and Maternal Infection in the Etiology of Major Depression 王先逸 助理教授 / 國立陽明大學 解剖學暨細胞生物學研究所
S17	15:15 - 15:45	Running Exercise Prevents Inflammation-induced Dopaminergic Neuron Loss in the Substantia Nigra 郭余民 教授 / 國立成功大學 細胞生物與解剖學研究所

台灣生物化學及分子生物學學會

研討會 Drug discovery
時　間：102 年 3 月 23 日 (週六) 13:45-17:00
地　點：三樓，第 33 教室
主持人：洪慧芝 教授 /　國立中興大學生命科學系
　　特聘教授兼基因體暨生物資訊學研究所所長

編號	時段	演講者 & 講題
S18	13:45 - 14:30	IL-20 antibody is a potential drug for osteoporosis 張明熙 教授 / 國立成功大學 生物化學暨分子生物學研究所
S19	14:30 - 15:15	Trifluoperazine, an Antipsychotic Agent, Inhibits Cancer Stem Cell Growth and Overcomes Drug Resistance of Lung Cancer 黃奇英 教授 / 國立陽明大學 生物藥學研究所
	15:15 - 15:30	休息
S20	15:30 - 16:15	Accelerate your Lead Discovery & BioPharma Development Pipeline Dr. Geraldine Wee/ Senior Field Application Manager
S21	16:15 - 17:00	Lead to Drug Candidate: Discovery of Novel Multiple-Kinase Inhibitors in Cancer Therapy 謝興邦 教授 / 國家衛生研究院 生技與藥物研究所

中國生理學會

研討會 生理學在醫學教育改革中所扮演的角色
時　間：102 年 3 月 24 日 (週日) 09:00-10:00
地　點：一樓，第 2 教室
主持人：蔡美玲 教授 / 國立成功大學 生理所

編號	時段	演講者 & 講題
S22	09:00 - 09:10	國醫學系醫學教育改革現況 蔡美玲 教授 / 國立成功大學 生理所
S23	09:10 - 09:20	一階段教改下高醫生理學整合之經驗 許勤　教授 / 高雄醫學大學 醫學系生理學科
S24	09:20 - 09:30	二階段課程整合下台大生理學之現況 湯志永 教授 / 國立臺灣大學 醫學院生理學研究所
S25	09:30 - 09:40	二階段課程整合下之輔大 PBL 教學特色與分享 卓貴美 教授 / 輔仁大學 醫學系
S26	09:40 - 09:50	生理與國防醫學教育整合之特色 謝博軒 教授 / 國防醫學院 生理學研究所

台灣藥理學會

研討會 Translational Research in Cancers
時　間：102 年 3 月 24 日 (週日) 13:45-15:45
地　點：一樓，第 1 教室
主持人：林滿玉 教授 / 國立陽明大學 藥理學研究所
　　康宏佑 教授 / 長庚大學 臨床醫學研究所

編號	時段	演講者 & 講題
S27	13:45 - 14:15	Role of mitochondrial deacetylase SIRT3 in human cancer progression 李新城 教授 / 國立陽明大學 醫學院藥理學研究所
S28	14:15 - 14:45	Developing new anticancer molecular targeted agents by innovative designs and biomarkers 林家齊 醫師 / 臺大醫院 腫瘤科
S29	14:45 - 15:15	New advances of androgen receptor targeted therapies 康宏佑 教授 / 長庚大學 臨床醫學研究所
S30	15:15 - 15:45	The role of GNMT plays in the liver tumorigenesis and its usefulness in the targeted therapy for hepatocellular carcinoma 陳宜民 教授 / 高雄醫學大學 醫學系微生物學科

中國生理學會

研討會生理學專題研討會
時　間：102 年 3 月 24 日 (週日) 13:45-15:45
地　點：一樓，第 2 教室
主持人：李小媛 教授 / 中央研究院 生醫所

編號	時段	演講者 & 講題
S31	13:45 - 14:15	Differential regulation of adipokine secretion 盧主欽 助理教授 / 長庚大學 生理暨藥理學科
S32	14:15 - 14:45	The role of diosgenin on the male reproductive function in accelerated senescence rat models 余青翰 助理教授 / 中山醫學大學 醫學系 生理學科
S33	14:45 - 15:15	眼框前額葉多巴胺系統與注意力不足過動症抑制功能失調之關係 李季湜 副教授 / 國立中正大學 心理學系
S34	15:15 - 15:45	Synthesis and Characterization of Thermal Responsive HA/Puronic Acid Copolymer and Potential Evaluation on Artificial Vitreous Substitute 林詠凱 副教授 / 中國文化大學 動物科學系

中華民國解剖學學會

研討會 Vascular disorder
時　間：102 年 3 月 24 日 (週日) 13:45-15:45
地　點：三樓，第 32 教室
主持人：葉添順 教授 / 陽明大學 解剖學暨細胞生物學研究所

編號	時段	演講者 & 講題
S35	13:45 - 14:15	Collagen glycosaminoglycan as tissue scaffolds to promote angiogenesis and neurogenesis and to facilitate functional recovery following brain injury 王家儀 教授 / 臺北醫學大學 醫學科學研究所
S36	14:15 - 14:45	Defense against reperfusion injury: From Preconditioning to Postconditioning 賴逸儒 副教授 / 臺灣大學 解剖學暨細胞生物學研究所
S37	14:45 - 15:15	Late outgrowth endothelial cells derived from Wharton's jelly in human umbilical cord reduce neointimal formation after vascular injury: involvement of pigment epithelium-derived factor and its relative mechanism 王淑慧 助理教授 / 臺灣大學 解剖學暨細胞生物學研究所
S38	15:15 - 15:45	The neuroprotective strategies for the immature brain after hypoxia-ischemia 李學德 助理教授 / 陽明大學 解剖學及細胞生物學研究所

S1

3 月 23 日 (週六) 09:10- 09:50
一樓，第 2 教室

SPAKling on the Sodium and Blood Pressure Regulation

楊松昇 副教授
國防醫學院醫學科學研究所暨三軍總醫院腎臟內科

Discovery of genomic mutations in WNK [With-No-Lysine (K)] kinase 1 and 4 responsible for pseudohypoaldosteromisn type II (PHAII; Gordon syndrome) featuring an autosomal-dominant salt-sensitive hypertension with hyperkalemia and metabolic acidosis opens the avenue of the new understanding in renal tubular sodium (Na+) regulation. In mammalian, WNK kinases (WNK1-4) are a group of serine/threonine proteins. In in vitro studies, WNK1 and 4 could enhance the phosphorylation of SPAK [STE20 (sterile 20)/SPS1-related proline/alanine-rich kinase] and OSR1(Oxidative Stress- Response kinase 1) known as the upstream activators of NKCC2 [Na+-K+-2Cl- cotransproter 2] and NCC [Na+-Cl- cotransproter] in the thick ascending limbs and distal convoluted tubules of kidney, respectively. Several genetically-altered mice models have been created to explore the in vivo function of WNK, SPAK/OSR1 and NCC. Mice with altered WNK1 expression also have abnormal blood pressure and disturbed renal Na+ regulation. PHAII-mutant WNK4 transgenic/knock-in mice exhibit typical PHAII phenotype with an increased phosphorylation and function of SPAK/OSR1 and NCC. On the other hand, mice with attenuated WNK4,SPAK and OSR1 expression manifest Gitelman/Bartter-like syndrome, the mirror images of PHAII, with a reduced phosphorylation and function of NCC. Polymorphisms in genes encoding WNK1, WNK4, SPAK and NCC are also associated with essential hypertension and WNK-SPAK/OSR-NCC signaling is also reported to be involved in salt-sensitive hypertension. This talk summarizes the recently reported studies in the molecular pathophysiology of WNK-SPAK/OSR1-N(K)CC signaling in the kidneys from clinical studies to cell and transgenic animal models research.

S2

3 月 23 日 (週六) 09:50- 10:30
一樓，第 2 教室

Reactive Oxygen Species Signaling: from Bench to Bedside

鄭劍廷 特聘教授
國立臺灣師範大學 生命科學系

Reactive oxygen species (ROS) level exerts a detrimental or beneficial effect in our human body. Exacerbated ROS production can be evoked from activated leukocytes or impaired mitochondria in the tissues/organs subjected to ischemia/reperfusion, diabetes, hemodialysis, and bacterial/viral toxin-induced injury. The exaggerated ROS enhance pro-inflammatory cytokines, vascular adhesion molecule expression and non-programmed (necrosis) and programmed cell death (apoptosis, autophagy or pyroptosis). On the other hand, a moderate increase in ROS by preconditioning with hypoxia, hyperthermia or ischemia evokes protective mechanisms against oxidative injury. I have used endogenous antioxidant defense mechanisms induction or the safely administration of exogenous antioxidants as protective and therapeutic strategies to attenuate oxidative injury in the animals and human. For example, in basic studies of the rats, the exogenous antioxidants treatment or endogenous antioxidant attenuates *Helicobacter pylori*–induced gastritis and infection, ischemia/reperfusion injury, hyperactive bladder and delays atherothrombosis formation. In clinical trials, the safely using exogenous antioxidants like vitamin C, green tea extracts, vitamin E-coated dialyzer or antioxidant (low oxidative redox potential) dialysate can ameliorate chronic hemodialysis-induced inflammation, anemia, atherosclerotic risk factor and immune dysfunction in the end-stage renal diseases patients. Taken together, our data support that antioxidant therapies aimed at normalized ROS levels may prove a cost-effective and successful therapeutic strategy to slow down the development of oxidative injury.

S3

3 月 23 日 (週六) 10:30- 11:10
一樓，第 2 教室

Hypoxia, epigenetics, and endometriosis

蔡少正 特聘教授
國立成功大學醫學院生理所

Background:

Hypoxia is an important factor that regulates numerous physiological and pathological processes such as angiogenesis, glucose metabolism, cell cycle regulation, and increased drug resistance. According to the retrograde menstruation hypothesis, endometriotic tissues were originated from shed endometrium.

Hypothesis:

Before the shed endometrium can adhere to peritoneum and attract new blood vessel to grow into, the retrograded tissues are exposed to chronic and persistent hypoxic stress. This notion suggests that hypoxia and/or hypoxia inducible factor-1α (HIF-1α) may be an important factor for the pathogenesis of endometriosis.

Results & discussion:

Elevation of HIF-1α level in endometriotic stromal cells was first reported in 2007. This elevated HIF-1α inhibits the expression of EZH2 and DNA methyltransferase-1 (DNMT1), and upregulates microRNA-20a expression. These data demonstrate that HIF-1α plays important roles in controlling genes involved in epigenetic regulation. Further study reveals that many angiogenic and proliferating genes are regulated by hypoxia in an epigenetic fashion. Results from these studies provide strong evidence to suggest that hypoxia and epigenetic reprogramming are critical pathogenic factors for the development of endometriosis.

S4

3 月 23 日 (週六) 09:00-09:30
三樓，第 34 教室

Cigarette sidestream smoke particulates exhibit an estrogenic effect in lung adenocarcinoma cells

李立安 副研究員
國家衛生研究院 環境衛生與職業醫學研組

Among never smokers, women are more prone to develop lung adenocarcinoma than men. The correlation of circulating estrogen level and in situ aromatase expression with poor prognosis suggests that estrogen plays a role in promoting the development of lung adenocarcinoma. Exposure to exogenous estrogen is expected to increase the risk of the cancer. Environmental cigarette smoke, a major environmental risk factor of lung cancer for never smokers, contains vast amounts of aromatic compounds in the particulate phase. A question is raised whether cigarette sidestream smoke particulates (CSSP) are a source of environmental estrogen. In this study, we examined the effects of a CSSP extract on the transactivation activity, nuclear translocation, phosphorylation, and protein stability of ERα in lung adenocarcinoma cells. Our results demonstrate that the CSSP extract contains a dose-dependent estrogenic effect. In addition, CSSP activates ERα in synergism with 17β-estradiol (E2) in lung adenocarcinoma cells. ICI 182,780 can antagonize CSSP-induced ERα transactivation activity as well as that induced by E2. However, CSSP regulates ERα nuclear translocation, phosphorylation, and degradation similarly but differently from E2. As compared with E2 and ICI 182,780, ERα is rather stable under CSSP treatment, suggesting that CSSP has a long-lasting estrogenic effect.

S5

3 月 23 日 (週六) 09:30-10:00
三樓，第 34 教室

Association of the cumulative body burden of estrogen-3,4-quinone with body mass index and breast cancer risk using albumin adducts as biomarkers

林伯雄 教授
國立中興大學 環境工程所

Both 17β-estradiol-2,3-quinone (E_2-2,3-Q) and 17β-estradiol-3,4-quinone (E_2-3,4-Q)are reactive metabolites of estrogen. Elevation of E_2-3,4-Q to E_2-2,3-Q ratio is thought to be an important indicator of estrogen-induced carcinogenesis. Our current study compared the cumulative body burden of these estrogen quinones in serum samples taken from Taiwanese women with breast cancer (n=152) vs healthy controls (n=75) by using albumin (Alb) adducts as biomarkers. Results clearly demonstrated the presence of cysteinyl adducts of E_2-2,3-Q-4-S-Alb and E_2-3,4-Q-2-S-Alb in all study population at levels ranging from 61.7-1330 and 66.6-1590 pmol/g, respectively. Correlation coefficient between E_2-2,3-Q-4-S-Alb and E_2-3,4-Q-2-S-Alb was 0.610 for controls and 0.767 for breast cancer patients($p<0.001$). We also noticed that in subjects under age 50 with body mass index (BMI) less than 27, background levels of E_2-3,4-Q-2-S-Alb was inversely proportional to BMI with about 25% increase in E_2-3,4-Q-2-S-Alb per 5 kg/m2 decrease in BMI ($p<0.001$). In addition, we confirmed that mean levels of E2-3,4-Q-2-S-Alb in breast cancer patients were ~5 fold greater than in those of controls ($p<0.001$). Overall, this evidence suggests that disparity in estrogen disposition and the subsequent elevation of cumulative body burden of E_2-3,4-Q may play a role in the development of breast cancer.

S6

3 月 23 日 (週六) 13:45-14:15
三樓，第 30 教室

Mir-17~92 cluster: a double-edged sword controlling spinal motor neuron generation and degeneration

陳俊安 助研究員
中央研究院 分子生物研究所

MicroRNAs (miRNAs) are small non-coding RNAs that function during embryonic development and in pathological process such as tumor formation. A representative example is the polycistronic *mir-17~92* cluster known to have dual roles in normal B-cell development and cancerous B-cell lymphomas. Recently we have demonstrated that *mir-17~92* cluster refines ventral spinal cord patterning during neural development, and its loss results in an increase in the number of newborn motor neurons. Here we report that the *mir-17~92* cluster is also strongly expressed by postmitotic motor neurons. Surprisingly, analysis of *mir-17~92* null motor neurons *in vitro* and *in vivo* revealed that its expression is critical for motor neuron survival. Null spinal cord exhibits an overall decrease in the number of motor neurons despite their initial overproduction. Moreover, overexpression of *mir-17~92* in the spinal cord can prevent naturally occurring cell death. Currently we are investigating whether deregulation of *mir-17~92* cluster might contribute to motor neuron loss in degenerative diseases such as ALS or SMA.

S7

3 月 23 日 (週六) 14:15-14:45
三樓，第 30 教室

Abl kinase at the crossroad of neurodegenerative signaling pathways

莊志立 研究員
國家衛生研究院 分子與基因醫學研究所

The Abl kinase, apparently evolutionarily conserved from flies to humans, is involved in the regulation of neuronal development. While the involvement of Abl in neural development is well documented, the pathological role of Abl in neurodegenerative disease is less clear. It has been hypothesized that the $A\beta_{42}$ accumulation induces Cdk5/p25 activation in the Alzheimer's brain, thereby reducing tau's association with microtubules and subsequently resulting in neuronal apoptosis. We used a Drosophila model system to explore how Abl is involved in regulation of Cdk5 during the amyloid-initiated neurodegeneration. We found that the suppression of Abl expression or kinase activity diminished the activation of Cdk5 triggered by $A\beta_{42}$ and reduced Drosophila neuronal cell death. Moreover, $A\beta_{42}$-induced Cdk5 activation and neurodegeneration in mammalian cells were suppressed by an Abl kinase inhibitor, supporting the idea that Abl mediates Cdk5 for $A\beta_{42}$-triggered neurodegeneration. Amazingly, we found that the enterovirus 71 (EV71)-induced neuronal apoptosis is also regulated by Abl-Cdk5 signaling pathway. During the EV71 infection of neuronal cells, we found EV71 could enhance c-Abl kinase activity which subsequently facilitated Cdk5 phosphorylation and kinase activation. Importantly, we showed that by blocking of the activation of either protein kinase, we could effectively ameliorate the neuronal apoptosis, supporting the idea that the modulation of Cdk5 kinase activity by Abl is relevant for EV71 pathogenesis. Together, these findings offer new insights into the regulation of Abl signaling in neurodegenerative diseases.

S8

3 月 23 日 (週六) 14:45-15:15
三樓，第 30 教室

Study of the neurodegenerative disease- FTLD-U: from molecular neuroscience to treatment

蔡坤哲 副教授
國立成功大學 臨床醫學研究所

TDP-43 is a multifunctional DNA/RNA-binding protein that has been identified as the major component of the cytoplasmic ubiquitin (+) inclusions (UBIs) in diseased cells of frontotemporal lobar dementia (FTLD-U) and amyotrophic lateral sclerosis (ALS). Unfortunately, effective drugs for these neurodegenerative diseases are yet to be developed. We have tested the therapeutic potential of rapamycin, an inhibitor of the mammalian target of rapamycin (mTOR) and three other autophagy activators (spermidine, carbamazepine, and tamoxifen) in a FTLD-U mouse model with TDP-43 proteinopathies. Rapamycin treatment has been reported to be beneficial in some animal models of neurodegenerative diseases but not others. Furthermore, the effects of rapamycin treatment in FTLD-U have not been investigated. We show that rapamycin treatment effectively rescues the learning/memory impairment of these mice at 3 month of age, and it significantly slows down the age-dependent loss of their motor function. These behavioral improvements upon rapamycin treatment are accompanied by a decreased level of caspase-3 and a reduction of neuron loss in the forebrain of FTLD-U mice. Furthermore, the number of cells with cytosolic TDP-43 (+) inclusions and the amounts of full-length TDP-43 as well as its cleavage products (35 kDa and 25 kDa) in the urea-soluble fraction of the cellular extract are significantly decreased upon rapamycin treatment. These changes in TDP-43 metabolism are accompanied by rapamycin-induced decreases in mTOR-regulated phospho-p70 S6 kinase (P-p70) and the p62 protein, as well as increases in the autophagic marker LC3. Finally, rapamycin as well as spermidine, carbamazepine, and tamoxifen could also rescue the motor dysfuncion of 7-month-old FTLD-U mice. These data suggest that autophagy activation is a potentially useful route for the therapy of neurodegenerative diseases with TDP-43 proteinopathies.

S9

3 月 23 日 (週六) 15:15-15:45
三樓，第 30 教室

Amyloid-beta (Aβ) D7H mutation on Aβ production and aggregation

鄭菡若 副教授
國立陽明大學 腦科學研究所

Amyloid precursor protein (APP) mutations associated with familial Alzheimer's disease (AD) usually lead to increases in amyloid β-protein (Aβ) levels or aggregation. Here, we identified a novel APP mutation, located within the Aβ sequence ($Aβ_{D7H}$), in a Taiwanese family with early onset AD and explored the pathogenicity of this mutation. Cellular and biochemical analysis reveal that this mutation increased Aβ production, Aβ42/40 ratio and prolonged Aβ42 oligomer state with higher neurotoxicity. Because the D7H mutant Aβ has an additional metal ion-coordinating residue, histidine, we speculate that this mutation may promote susceptibility of Aβ to ion. When co-incubated with Zn^{2+} or Cu^{2+}, AβD7H aggregated into low molecular weight oligomers. Together, the D7H mutation could contribute to AD pathology through a "double punch" effect on elevating both Aβ production and oligomerization. Although the pathogenic nature of this mutation needs further confirmation, our findings suggest that the Aβ N-terminal region potentially modulates APP processing and Aβ aggregation, and further provides a genetic indication of the importance of Zn^{2+} and Cu^{2+} in the etiology of AD.

S10

3 月 23 日 (週六) 13:45-14:15
三樓，第 31 教室

Serum Ferritin-to-iron (FIR) Ratio As A Hepatocellular Carcinoma Marker Complementary to Alpha-fetoprotein and As A Prognostic Predictor of Metastasis

劉燦榮 教授
台北醫學大學癌症中心轉譯研究室

Clinical Utilization of alpha-fetoprotein (AFP) as a single tumor marker for the diagnosis of hepatocellular carcinoma (HCC) has been of limited success, since its

diagnostic sensitivity has been reported to be only in the range of 70-80 %. Along this same line, it has been documented that some pathological conditions, such as chronic hepatitis and liver cirrhosis, can interfere with the accurate diagnosis of small HCC if one uses lower cutoff value of AFP (>25 ng/ml) as a standard. For this reason, an adjunct marker is being sought by us in order to improve the diagnostic sensitivity of AFP for the diagnosis of HCC. First, a panel consisting of AFP and ferritin-to-iron ratio (FIR) was considered and its clinical efficacy was subsequently evaluated. In this study, serum iron, ferritin and AFP levels were simultaneously evaluated in two groups of subjects: Group A (n=60) with histologically proven HCC and Group B (n=112) comprising healthy matched controls without liver diseases (normal liver function tests; HBsAg negative). The results of tests on the HCC group of subjects were tabulated below:

Test item	Abnormality (%)	Diagnostic sensitivity (%)
Iron (1)	42 (25/60)	42
Ferritin (2)	65 (39/60)	65
FIR (3)	68 (41/60)	68
AFP (4)	78 (47/60)	78
(3)+(4)	92 (55/60)	92

Further studies indicated that no correlation was found between tumor sizes and AFP concentrations in these HCC patients. Conversely, a causal correlation was found between tumor size and FIR levels (p=0.67) for these HCC patient with metastasis. In addition, the HCC group was further classified into two subgroups, namely: non-metastatic(C) and metastatic (D) groups. Both FIR values in C (n=40) and D (n=20) groups were 6.34±11.09 and 13.05±16.10, respectively which were substantially higher than normal reference range of 0.9±0.4 (n=112) ($p < 0.001$). In

conclusion, we have established that serum FIR value can serve as a marker complementary to AFP and as a prognostic predictor of metastasis.

S11

3 月 23 日 (週六) 14:15-14:45
三樓，第 31 教室

Simvastatin have artery calcification inhibitory effects in type II DM *Ldlr* $^{-/-}$ mice

林植培 主任
台北榮民總醫院 病理檢驗部 生物化學科

Background:

Inflammation stress triggered vascular media-layer calcification in diabetes. We studied the anti-inflammation effect of simvastatin in vascular calcification.

Materials and Methods:

In animal study, we used *Ldlr* $^{-/-}$ mice, an arterial calcification animal model of type 2 DM, and vascular smooth muscle cell to study the mechanism of vascular cell calcification. The molecular signature of vascular calcification is strikingly by low-grade arterial inflammation levels of tumor necrosis factor-alpha (TNF-α) had analyzed. The protection effects of simvastatin also clarified.

Results:

High-fat diet significantly induced *Ldlr* $^{-/}$ mice vascular calcification formation as well as increased circulating TNF-α level for six months feeding. *Ldlr* $^{-/-}$ mice treatment with simvastatin (10 mg/kg/day) attenuated both vascular calcification and circulating TNF-α level. In cell culture study, TNF-α induces the osteogenic bone morphogenetic protein-2 (BMP-2), Msx2mRNAs, and calcium accumulation in HASMCs. TNF-α R1 receptor siRNA or simvastatin suppressed TNF-α-mediated osteogenic effect in HASMC. In addition, simvastatin suppressed TNF-α-mediated NADPH oxidase generation superoxide in HASMC. Similar results also could find in apocynin (antioxidant agent, NADPH oxidase inhibitor) treatment group. Furthermore, TNF-α-mediated redox-sensitive p65 activation was also suppressed by simvastatin.

Conclusion:

In vivo study demonstrated chronic vascular inflammation involved vascular calcification. Simvastatin attenuated high-fat diet-induced vascular inflammation and calcification. In vitro study showed antioxidant effect involved simvastatin suppressed TNF-α-mediated calcium deposition in HASMC. These results suggested chronic inflammation and oxidative stress involved vascular calcification. Antioxidant effect plays crucial role in simvastatin-suppressed calcium deposition in HASMC.

S12

3 月 23 日 (週六) 14:45-15:15
三樓，第 31 教室

Molecular diagnostics for chromosomal and epigenetic instability in colorectal cancer

楊雅倩 副教授
國立臺灣大學 醫學檢驗暨生物技術學系

Colorectal cancer is probably the type of cancer for which the most is known about the genes affected by cancer-causing mutations. Approximately 6% of colorectal cancer can be attributed to recognizable heritable germline mutations, while 75-80% of the cancer is sporadic. Current models suggest that the initiation and progression of colorectal cancer are as a consequence of the accumulation of genetic and epigenetic alterations that result in the loss-of-function of tumor suppressor genes and the activation of oncogenes. Chromosomal instability is a hallmark of cancer and is markedly prevalent in colorectal cancer. Substantial studies have demonstrated that appreciable numbers of chromosome aberrations are frequently determined in sporadic colorectal cancer, most notably loss of chromosomes 4, 8p, 17p and 18q. These chromosomal alternations are associated with stage progression, shorter survival times and tumor metastasis. In addition, epigenetic instability results in the aberrant methylation of tumor suppressor genes that are involved in the transformation of colonic epithelium and promote tumor progression. Identification of the specific chromosomal regions that are lost or epigenetically modified in conjunction with the development of invasiveness and tumor metastatic ability, and a search for the tumor suppressor genes localized to these respective regions, may lead to a more accurate prediction of prognosis and cancer progression.

S13

3 月 23 日 (週六) 15:15-15:45
三樓，第 31 教室

Molecular diagnostics for lung cancer multiplex gene testing by MALDI-TOF MS with high sensitivity and flexibility

蘇剛毅 助理教授
國立臺灣大學 醫學檢驗暨生物技術學系

In the field of cancer therapy, molecular diagnostics has supported accurate and appropriate treatment selection. While the incidence of cancer and the deaths due to cancer still remain high, novel cancer molecular diagnostics are allowing physicians and pathologists to identify predisposition and decide targeted and personalized therapeutic administration. We established multiplex nucleotide MALDI-TOF mass spectrometry (MS) with high sensitivity to perform quantitative gene testing in patients with lung adenocarcinoma for pioneering concept proof. EGFR is a well-known target for molecular target therapy and inhibition of EGFR kinase activities by EGFR tyrosine kinase inhibitors (TKIs) such as gefitinib and erlotinib results in effective treatment for patients with lung adenocarcinoma. In addition, patients with EGFR-activating mutations in exon19 and exon21 had benefit for TKIs response and prolonged progression-free survival (PFS) while with EGFR-resistant mutation had poor treatment efficacy. The MALDI-TOF MS we set up had ~1% mutation frequency detection limitation among wild-type background. In addition to 30% more detection rate of EGFR-activating mutation, we also confirmed EGFR-resistant mutation may be more prevalent than expected before TKIs treatment. These patients with detected mutations also revealed impact in clinical outcome such as PFS and TKIs responsiveness. Furthermore, MALDI-TOF MS is quantifiable in mutation frequency among heterogeneous tumor mass. With this uniqueness, we also found the quantitative mutation frequency was correlated to tumor size outcome. The regression modeling exhibited patients with more EGFR–activating mutation and less EGFR-resistant mutation had reduced tumorodiameter. In conclusion, the achievement of this platform provides not only a novel molecular diagnostics choice but also a flexible methodology for personalized therapy. We can apply it to any other gene testing related to human diseases in the future.

S14

3 月 23 日 (週六) 13:45-14:15
三樓，第 32 教室

Surgical Decompression in Small-Fiber Sensory Neuropathy

曾拓榮 助理教授
中國醫藥大學醫學系 解剖科

Peripheral nerve injury from compression is the foundation for establishing animal models of Chronic Constriction Injury (CCI) with neuropathic pain. Clinically, surgical decompression is an important therapeutic strategy; however, there is lack of an animal model to evaluate the potential mechanisms. To address the temporal course of neuropathic pain (thermal hyperalgesia and mechanical allodynia), corresponding effects on skin reinnervation and synaptic reorganization in the dorsal horn of the spinal cord, we established a model of surgical decompression on Sprague–Dawley rats with CCI. Animals were divided into a decompression group and a CCI group at postoperative week 4 (POW 4). At POW 8, neuropathic pain had completely disappeared in the decompression group, which had a higher skin innervation index of substance P (SP) than the CCI group ($p<0.05$). At POW 12, skin innervation index of SP of the CCI group had returned to the same value as that of the decompression group with normalized thermal hyperalgesia but not the mechanical allodynia. These indexes were similar in both groups for protein gene product 9.5 (PGP 9.5) ($p>0.05$) and calcitonin gene-related peptide (CGRP) ($p>0.05$) throughout the entire period. At POW 8, in the decompression group with significant reversal of the dorsal horn indexes of SP and delta-opioid receptor (DOR) compared with the CCI group ($p<0.05$). In the CCI group, dorsal horn indexes for both SP and DOR at POW 12 with similar changes to those of the decompression group. In contrast, changes in the dorsal horn indexes of CGRP were similar in both groups throughout the entire period. These findings demonstrate the temporal course of neuropathic pain after surgical decompression, and suggest that different peptidergic patterns of skin reinnervation and plasticity of DOR in the dorsal horn of the spinal cord.

S15

3 月 23 日 (週六) 14:15-14:45
三樓，第 32 教室

The Neuroprotective Effects of Valproic Acid in *in vitro* Rodent Parkinson's Disease Model

王詔絹 助理教授
高醫大學醫學系 解剖科

Parkinson's disease (PD) is characterized by the selective and progressive loss of dopaminergic (DA) neurons in the midbrain substantia nigra. Currently, available treatment is unable to alter PD progression. Valproate (VPA), one of the mood stabilizers and antiepileptic drugs, was recently found to inhibit histone deacetylases (HDAC). Increasing reports demonstrate that VPA has neurotrophic effects in diverse cell types including midbrain dopaminergic (DA) neurons. However, the origin and nature of the mediator of the neurotrophic effects are unclear. Using the lipopolysaccharide (LPS)-treated neuron-glia cultures, Professor Hong's lab members discovered that VPA prolongs the survival of midbrain DA neurons in lipopolysaccharide (LPS)-treated neuron-glia cultures through reducing neurotoxicity activated by microglia and increasing the release of neurotrophic factors from astrocyte. Further, the neuroprotection action of VPA including the induction of microglial apoptosis and the upregulation of BDNF and GDNF gene expressions associated with its histone acetylation was demonstrated. These studies indicate that VPA could be considered as a utility of this drug for treating neurodegenerative disorders including PD.

S16

3 月 23 日 (週六) 14:45-15:15
三樓，第 32 教室

The Potential Roles of Adult Neurogenesis and Maternal Infection in the Etiology of Major Depression

王先逸 助理教授
國立陽明大學 解剖學暨細胞生物學研究所

Major depression is a serious mental disorder with high prevalence and instigates formidable strain on social economical resources. It had been shown that prefrontal cortex and hippocampal formation have reduced volume in depression patients. In view of the fact that the dentate gyrus of the hippocampal formation is one of the brain areas capable of continuously generating new neurons in adulthood, the reduction in the hippocampal volume could be caused not only by the atrophy of existing neurons but also by a reduction in adult neurogenesis. Thus, adult neurogenesis in the dentate gyrus might be implicated in the pathophysiology of major depression. We use a “learned helplessness” animal model of depression to test this hypothesis. Specifically, we examined the neurogenesis rate and the survival rate of young neurons in the dentate gyrus of animals displaying depression-like behaviors. In addition, the synaptic responses in dentate gyrus during the manifestations of depressive behaviors were examined by electrophysiological recordings. We found that the adult neurogenesis was significantly reduced in the dorsal hippocampus of rats displaying learned helplessness depressive behavior and their synaptic transmission was also reduced, suggesting a role of adult neurogenesis in depression pathophysiology. The etiology of major depression is currently unknown but ample studies have shown that mild infection during pregnancy may have profound effects on the developing nervous system and as a consequence affect the behavior of the offspring later in life. Among the neurotransmitters dopamine and serotonin play major roles in mood regulation in the brain. Disturbance in either system may result in serious mental disorder. We used low dose lipopolysaccharide (LPS) exposure to mimic mild maternal infection and examined its effects on embryonic dopaminergic and serotonergic neuronal development and the behavioral outcome in the affected offspring. We found that prenatal LPS exposure in a critical developmental window caused reductions of dopaminergic neurons in the substantia nigra and serotonergic neurons in the dorsal raphe nucleus. The behavioral phenotype of the affected offspring will be discussed. By studying the neurochemical, anatomical, and behavior abnormality in the offspring exposed to LPS during neurodevelopment we can have a better understanding of the potential harms of maternal infection in increasing the vulnerability in mood-related mental disorders in offspring later in life.

S17

3 月 23 日 (週六) 15:15-15:45
三樓，第 32 教室

Running Exercise Prevents Inflammation-induced Dopaminergic Neuron Loss in the Substantia Nigra

郭余民 教授
國立成功大學 細胞生物與解剖學研究所

Parkinson's disease (PD) is characterized by a progressive and selective loss of dopaminergic (DA) neurons in the substantia nigra (SN). Although the etiology of PD remains unclear, neuroinflammation has been implicated in the development of PD. Running exercise (Ex) enhances neuroplasticity and promotes neuronal survival. Thus, we hypothesize that Ex protects the DA neurons against inflammation-induced injury in the SN. We found that the SN had the highest microglia density in the brain. The degree of microglia activation increased sharply in middle age and negatively correlated to the number of DA neurons. Systemic injection of LPS induced 1) microglia activation, 2) dopaminergic neuron loss and reduced levels of dopamine, 3) motor coordination dysfunction, and 4) reduced levels of the BDNF in the SN. Four weeks of Ex before LPS treatment prevented the LPS-induced loss of DA neurons, reduction of dopamine levels and dysfunction of motor movement. Ex did not change the LPS-induced status of microglia activation or the levels of cytokines/chemokines, but restored the levels of LPS-reduced BDNF-TrkB signaling molecules. TrkB antagonist, K252a, abolished the Ex-induced protection against LPS-induced DA neuron loss; whereas, perfusion of BDNF counteracted the LPS-induced DA neuron loss. In summary, our results show that Ex protects DA neurons against inflammation-induced insults. The neuroprotective effects of Ex are not due to the modulation of inflammation status, but rather to the activation of the BDNF-TrkB signaling pathway.

S18

3 月 23 日 (週六) 13:45-14:30
三樓，第 33 教室

IL-20 antibody is a potential drug for osteoporosis

張明熙 教授
國立成功大學 生物化學暨分子生物學研究所

IL-20 is a proinflammatory cytokine of the IL-10 family that is involved in psoriasis, rheumatoid arthritis, atherosclerosis, and stroke. However, little is known about the role of IL-20 in bone destruction. We explored the function of IL-20 in osteoclastogenesis and the therapeutic potential of IL-20 monoclonal antibody 7E for treating osteoporosis. Higher serum IL-20 levels were detected in patients with osteopenia and osteoporosis and in mice with ovariectomy-induced osteoporosis (OVX). IL-20 mediates osteoclastogenesis by upregulating the receptor activator of NF-κB (RANK) expression in osteoclast precursor cells and RANK ligand (RANKL) in osteoblasts. 7E treatment completely inhibited osteoclast differentiation induced by macrophage colony-stimulating factor (M-CSF) and RANKL *in vitro*, and protected mice from OVX-induced bone loss *in vivo*. Furthermore, IL-20R1-deficient mice had significantly higher bone mineral density (BMD) than did wild-type controls. IL-20R1-deficiency also abolished IL-20-induced osteoclastogenesis and increased BMD in OVX mice. We have identified a pivotal role of IL-20 in osteoclast differentiation, and we conclude that IL-20 monoclonal antibody is a potential therapeutic for protecting against osteoporotic bone loss.

S19

3 月 23 日 (週六) 14:30-15:15
三樓，第 33 教室

Trifluoperazine, an Antipsychotic Agent, Inhibits Cancer Stem Cell Growth and Overcomes Drug Resistance of Lung Cancer

黃奇英 教授
國立陽明大學 生物藥學研究所

Objectives:

To screen drugs that target CSCs to improve the current treatment outcome and overcome drug resistance in patients with lung cancer.

Methods:

We used publicly available embryonic stem cell and CSCassociated gene signatures to query the Connectivity Map for potential drugs that can, at least in part, reverse the gene expression profile of CSCs. High scores were noted for several phenothiazine-like antipsychotic drugs, including trifluoperazine. We then treated lung CSCs with different EGFR mutation status with trifluoperazine to examine its anti-CSC properties. Lung CSCs resistant to epidermal growth factor receptor–tyrosine kinase inhibitor or cisplatin were treated with trifluoperazine plus gefitinib or trifluoperazine plus cisplatin. Animal models were used for in vivo validation of the anti-CSC effect and synergistic effect of trifluoperazine with gefitinib.

Measurements and Main Results:

We demonstrated that trifluoperazine inhibited CSC tumor spheroid formation and down-regulated the expression of CSC markers (CD44/CD133). Trifluoperazine inhibited Wnt/b-catenin signaling in gefitinib-resistant lung cancer spheroids. The combination of trifluoperazine with either gefitinib or cisplatin overcame drug resistance in lung CSCs. Trifluoperazine inhibited the tumor growth and enhanced the inhibitory activity of gefitinib in lung cancermetastatic and orthotopic CSC animalmodels.

Conclusions:

Usingin silicodrug screening by Connectivity Map followed by empirical validations, we repurposed an existing phenothiazine-like antipsychotic drug, trifluoperazine, as a potential anti-CSC agent that could overcome epidermal growth factor receptor–tyrosine kinase inhibitor and chemotherapy resistance.

Keywords:

Trifluoperazine; lung cancer; cancer stem cell; gefitinib; connectivity map

S20

3 月 23 日 (週六) 15:30-16:15
三樓，第 33 教室

Accelerate your Lead Discovery & BioPharma Development Pipeline

Dr. Geraldine Wee
Senior Field Application Manager

An introduction to Merck Millipore products and services to provide a complete picture of all your compounds and biologics against key drug discovery target classes. The talk will focus on GPCRs, Ion Channels, Kinases, Phosphatases and invitro tox, and will end with service capabilities for biologics investigation.

S21

3 月 23 日 (週六) 16:15-17:00
三樓，第 33 教室

Lead to Drug Candidate: Discovery of Novel Multiple-Kinase Inhibitors in Cancer Therapy

謝興邦 教授
國家衛生研究院 生技與藥物研究所

Cancer is a leading cause of death worldwide, accounting for 13% of all deaths in 2007, and the World Health Organization (WHO) projects that by 2030 the death toll from cancer will reach 12 million. In particular, cancer has been a leading cause of death in Taiwan for the past twenty years. Traditional approaches to cancer chemotherapy using cytotoxic drugs are hindered by lack of efficacy, severe toxicity, and development of drug resistance. These limitations have fueled interest in developing molecular targeted therapies to minimize toxicity to healthy tissues.Currently there are only 13 small molecule targeted anti-cancer drugs in the market. It is estimated that the market for targeted therapy will reach 60 billion US dollars in sales by 2025. Compared to 2005, there will be over 10 times growth in the markets in the next 20 years, presenting good market and growth opportunity. Therefore, development of novel small molecule targeted therapy for cancer, will present a significant opportunity and huge benefit in the markets.

Aurora kinases A, B, and C, members of sereine/threonine kinase, are key mitotic regulators involved in maintaining the genomic integrity of daughter cells. Because over-expression of Aurora A and Aurora B is frequently associated with tumorigenesis, these molecules have been targeted for cancer therapy. Based on the structural analysis of the known Aurora kinase inhibitors and pharmacophore screening from in-house HTS compound library, we developed BPR1K0724 as the 4th generation of lead compound. BPR1K0724 first not only showed significant inhibitory activity against aurora-A kinase assay (IC_{50} = 7 nM), but also exhibited tumor growth effect in HCT-116, Colo 205 and MiaPaca2 xenograft models. Furthermore, by utilizing three lead optimization strategies, over 500 compounds were synthesized and evaluated for their structural-property relationships. We identified BPR000A that that displayed multiple-targeted kinase inhibitory activity against a panel of cancer-related kinases and exhibited excellent in vivo efficacy in MOLM-13, MV4-11, MiaPaca2 xenograft models. Currently, those compounds are under preclinical development evaluation and two patents (one US and one ROC) were granted in 2012 among 6 patents (2 of US, 2 of TW and 2 of PCT) filed before.

1.Hsieh, H. P.; Chang, J. Y. et al. Expert Opin. Ther. Pat. 2009, 19, 321-356.
2.Hsieh, H. P.; Chang, J. Y. et al. Expert Opin. Investig. Drugs 2009, 18, 379-398.
3.Hsieh, H. P.; Chang, J. Y. et al. Expert Opin. Ther. Pat. 2011, 21, 857-884.
4.Hsieh, H. P.; Coumar, M. S. et al "Fast-forwarding Hit to Lead: Aurora and Epidermal Growth Factor Receptor Kinase Inhibitor Lead Identification", J. Med. Chem. 2010, 53, 4980-4988.

S22-S26

3 月 24 日 (週日) 09:00-10:00
一樓，第 2 教室

S22 蔡美玲 教授
國立成功大學 生理所

S23 許　勤 教授
高雄醫學大學 醫學系生理學科

S24 湯志永 教授
國立臺灣大學 醫學院生理學研究所

S25 卓貴美 教授
輔仁大學 醫學系

S26 謝博軒 教授
國防醫學院 生理學研究所

※ 醫學教育改革下，　國醫學系整合課程之規劃 ※

學校	整合方式	整合課程安排
台大	二階段 (學科成績)	三年級： 大體解剖、組織、胚胎、生理整合。大體解剖、組織、胚胎上課時間沒固定，但生理學因合班上課固定於星期五上課。 微免和寄生蟲獨立上課，但也會排在課表裡供學生參考。
陽明	二階段 (學科成績)	三年級： 1.Introduction to Human Biology、Host defenses (Blood & Immune)、Musculoskeletal System、Cardiovascular System、Pulmonary System 2.FERGU (Fluid, electrolytes, renal and genitourinary system)、Gastrointestinal System、Endocrine & Metabolism、Brain & Behaviors、Reproduction System、Growth & Development 四年級： 1.Introduction to Clinical Medicine、Cardiovascular、Pulmonary、Endocrine & Metabolism、Gastrointestinal、Brain & Behavior 2.Musculoskeletal、Integument、Host Defense & Infection、FERGU、Hematology & Oncology
高醫	基礎 + 臨床整合 (block 成績)	三年級：基礎醫學、血液及腫瘤學、心臟血管系統、呼吸系統、感染與宿主免疫反應、神經系統、肌肉骨骼關節學 四年級：腎臟泌尿系統、消化系統、內分泌新陳代謝學、預防醫學與社區醫學、精神健康與精神醫學、特殊感官系統、生殖醫學
北醫	二階段 block 成績	三年級： 1. 人體結構與功能概論、骨骼肌肉系統結構與功能、呼吸循環系統結構與功能、消化系統結構與功能、泌尿生殖內分泌系統結構與功能、神經系統結構與功能 2. 免疫及傳染病學、公共衛生與預防醫學、疾病與治療 四年級： 1. 臨床醫學概論、一般醫學概論、呼吸系統疾病、消化系統疾病、循環系統疾病、血液及淋巴系統疾病 2. 骨骼肌肉系統疾病、神經系統疾病、內分泌系統疾病、女性生殖系統疾病、腎臟泌尿及男性生殖系統疾病
馬偕	二階段 (block 成績)	三年級： Introduction to Human Structure（3 週）、Musculoskeletal System（3 週）、Pulmonary System（1.5 週）、Cardiovascular System（3 週）、Gastrointestinal System（2 週）、Fluid, Electrolytes, Renal and Genitourinary System（2 週）、Host defense (Blood & Immune)（5.5 週）、Reproduction System 及 Growth & Development（4 週）Endocrine and Metabolism（3.5 週）、Brain & Behaviors（4 週） 四年級： Introduction to Clinical Medicine（1 週）、Cardiovascular System（3 週）、Pulmonary System（2 週）、Endocrine and Metabolism（2 週）、Gastrointestinal System（3 週）、Brain & Behaviors（5 週）、Musculoskeletal System（4 週）、Integument System（1 週）、Host defense and Infection（4 週）、Fluid, Electrolytes, Renal and Genitourinary System（4 週）、Hematology and Oncology（4 週）
長庚		還未開始作整合課程，目前正在協調各課程能儘量互相配合。
慈濟		1. 還未開始作整合課程。 2. 三下、四上有整合課程 (一) (二) (三) (四)，以 PBL 形式上課，Case 以系統為主，內容融合生理、病理、藥理，因此這些課程會儘量於 PBL 前上課，如未能先上課則會修改 case。

<table>
<tr><td>輔仁</td><td>基礎 + 臨床整合
(block 成績)</td><td>三年級:
1. 基礎臨床醫學整合課程入門單元、心臟血管單元、呼吸及循環單元、資源學習、醫院工作體驗、基礎醫學實驗 (一)、臨床技術學 (一)
2. 胃腸單元、內分泌及生殖單元、泌尿單元、資源學習、、基礎醫學實驗 (一)、臨床技術學 (一)
四年級:
1. 婦產及小兒單元、神經運動單元 (一)、神經運動單元 (二)、大體解剖學實驗、社區醫學、基礎醫學實驗 (二)、
2. 臨床技術學 (二)、感染及免疫單元、血液單元、精神行為及重症單元、生死學、實驗診斷學、流行病學、基礎醫學實驗 (二)、臨床技術學 (二)</td></tr>
<tr><td>中山</td><td>基礎 + 臨床整合
(block 成績)</td><td>三年級:
1. 基礎解剖學、解剖學實驗、人類遺傳學、病理學實驗、藥理學實驗、基礎生理學、基礎生理學實驗、基礎病理學、基礎藥理學
2. 神經科學模組、骨骼關節與肌肉學模組、大體解剖學實驗
四年級:
心臟循環學模組、免疫、防禦與感染學模組、呼吸科學模組、內分泌與新陳代謝學模組、消化科學模組、血液與腫瘤學模組、腎臟泌尿學模組、生殖學模組、家庭與社區醫學模組</td></tr>
<tr><td>中國</td><td>基礎整合
(臨床沒有)
(學科成績)</td><td>三年級:基礎醫學導論、骨骼肌肉系統、肺臟呼吸系統、神經科學
四年級:
1. 胃腸暨營養系統、腎臟泌尿系統、內分泌系統、男女生殖暨生長發育系統、血液腫瘤學
2. 器官模組含大體解剖學、胚胎學、神經解剖學、組織學、組織學實驗、生理學、生理學實驗、微生物學暨免疫學、微生物學暨免疫學實驗、寄生蟲學、寄生蟲學實驗、藥理學、藥理學實驗、病理學、病理學實驗</td></tr>
<tr><td>國防</td><td>二階段
(block 成績)</td><td>基礎與臨床整合科目:
1. 三年級:人　生物學導論、宿主防禦 (I)、骨骼肌肉系統 (I)、呼吸系統 (I)、腦科學及行為科學 (神經科學) (I)、心臟血管系統 (I)、胃腸系統、腎臟和泌尿系統、生殖系統、內分泌與新陳代謝 (I)、生長發育、造血及淋巴系統
2. 四年級:區段課程導論、骨骼肌肉系統 (II)、呼吸系統 (II)、感染與免疫 (II)、腦科學及行為科學 (神經科學) (II)、心臟血管系統 (II)、消化系統、內分泌與新陳代謝 (II)、皮膚系統、血液學與腫瘤學、腎臟與泌尿學
 
</td></tr>
<tr><td>成大</td><td>二階段
Year 3:
學科成績
Year 4:
block 成績</td><td>三年級:因合班上課固定
1. 基礎整合科目 - 上學期 : 解剖,胚胎,組織,生理
下學期 : 生理,神解,組織,胚胎,微免與寄生蟲
2. 區段課程導論、骨骼肌肉系統 (I)、造血及淋巴系統、心臟血管系統呼吸系統、胃腸系統、腎臟和泌尿系統、內分泌與新陳代謝、生長發育與生殖系統、神經科學
四年級:
區段課程導論、感染與免疫、呼吸系統、心臟血管系統、腎臟與泌尿學、骨骼肌肉系統、消化系統、內分泌與新陳代謝、神經科學、皮膚系統、血液學與腫瘤學。</td></tr>
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S27

3 月 24 日 (週日) 13:45-14:15
一樓，第 1 教室

Role of Mitochondrial Deacetylase SIRT3 in Human Gastric Cancer Progression

李新城 教授
陽明大學醫學院藥理學研究所

Background:

Mitochondrial NAD-dependent deacetylase sirtuin-3 (SIRT3) plays an important role in regulating cell metabolism. However, its role in carcinogenesis is still controversial. We previously found that somatic mutation and a decrease of copy number in mitochondrial DNA (mtDNA) frequently occur in human gastric cancer specimens. The decreased mtDNA copy number was associated with ill-defined tumors. Down-regulation of SIRT3 was proposed to result in a decreased integrity of mtDNA in animal cells. Thus, we were exploring the roles of SIRT3 in mtDNA maintenance and in gastric cancer progression.

Materials and Methods:

Gastric cancer patients who underwent curative surgery were enrolled at the Department of Surgery, Taipei Veterans General Hospital. SIRT3 expression in gastric tissue and tumors were examined using immunohistochemical stains. Clinicopathological characteristics and survival were analyzed and compared in gastric cancer patients with or without SIRT3 expression. In addition, human gastric cancer cells with stable knockdown or overexpression of SIRT3 were investigated for the changes of mtDNA copy number, energy metabolism, and cancer phenotypes.

Results:

We found that the patients without SIRT3 expression in gastric cancer have a poorer overall 5-year survival rate. There is poorer cell differentiation in gastric cancer without SIRT3 expression. Multivariate analysis with overall survival as an end point showed that TNM stage is significantly correlated with gastric cancer in relation to SIRT3 expression. In addition, knockdown of SIRT3 lead to decreases in mtDNA copy number and in intracellular ATP content, but not promoting malignant phenotypes of gastric cancer cells.

Conclusion:

Our results indicated that patients without SIRT3 expression in gastric cancer have poorer prognosis than those with SIRT3 expression. The mechanism for SIRT3 regulating gastric cancer progression needs to be further investigated.

S28

3 月 24 日 (週日) 14:15-14:45
一樓，第 1 教室

Developing Molecularly Targeted Anticancer Agents by Innovative Trial Designs and Biomarkers

林家齊 醫師
臺大醫院 腫瘤科

Driver mutations render cancer cells addicted to the constitutive activation (mutation or overexpression) of oncogenes that are responsible for sustaining the malignant phenotype. Pharmacological blockade of oncogenic events, to which cancer cells are reliant, often leads to cell death or the blockade of cell growth. The 'addiction paradigm' has been pharmacologically exploited and drugs designed to specifically inhibit mutated proteins have led to what is commonly known as personalized cancer medicine. For example, imatinib is used to treat gastrointestinal stromal tumors carrying activating mutations in two tyrosine kinase receptors, *KIT* and *PDGFR*. Trastuzumab can be prescribed to patients with breast cancer with amplification or overexpression of *HER2*. Gefitinib is administered to patients with lung adenocarcinoma whose tumors harbor mutations *in EGFR* and crizotinib to those with lung adenocarcinoma whose tumors had *ALK* rearrangement. Moreover, the monoclonal antibodies cetuximab should not be administered to patients with *KRAS*-mutant colorectal cancer. Vamurafenib should be administered to patients with *BRAF*-mutated malignant melanoma

Novel designs have been applied in the clinical trials of molecularly targeted anticancer agents. For example, the development of crizotinib in lung adenocarcinoma and vamurafenib in malignant melanoma has been facilitated by the phase I trials with molecularly preselected patient populations. Without the randomized discontinuation phase II trial, the development of sorafenib in renal cell carcinoma would not be so successful.

S29

3 月 24 日 (週日) 14:45-15:15
一樓，第 1 教室

New Advances of Androgen Receptor Targeted Therapies

康宏佑 教授
長庚大學 臨床醫學研究所

The androgen receptor (AR), a member of the steroid hormone receptor superfamily, functions as a ligand-inducible transcription factor that mediates the expression of target genes in response to androgens. Androgen/AR-mediated signaling in a variety of tissues is critical to development, aging, and malignant transformation. The transcriptional activity of AR is regulated by AR co-regulators, which influence the AR translocation, ligand selectivity and DNA binding capacity of AR. Aberrant AR function due to genetic/somatic mutations, conformational changes of proteins or altered expression levels may be a contributing factor in the progression of AR-mediated diseases such as prostate cancer, androgenic alopecia and spinal and bulbar muscular atrophy/Kennedy disease. While androgen deprivation therapy has remains the main therapeutic option for patients with prostate cancer, advanced prostate tumors are refractory to available AR antagonists. Recent work exploring the molecular structure and evolution of AR in response to hormonal therapies has revealed novel mechanisms of AR-mediated diseases and yielded new targets for drug development. Here we focuses on understanding the mechanisms of persistent AR signaling, and highlights new therapies targeting the AR axis that are either currently experimental promising or in clinical trials including inhibitors of androgen synthesis, inhibitors for transcriptional AR co-regulators and novel direct AR inhibitors.

S30

3 月 24 日 (週日) 15:15-15:45
一樓，第 1 教室

The role of GNMT plays in the liver tumorigenesis and its translational research in preventive medicine

陳宜民 教授
高雄醫學大學 醫學系微生物學科

Although glycine N-methyltransferase (GNMT) has been discovered for five decades, its function was not elucidated until recently. In this presentation, I will discuss the multiple roles of GNMT in toxicology and cancer and elaborate its potential usage in the target therapy for hepatocellular carcinoma. Besides catalyzing the production of methylglycine (sarcosine) in one carbon metabolism pathway, GNMT was found to be able to bind a number of polycyclic aromatic hydrocarbons and inhibit DNA adducts formation. Moreover, GNMT exerts protective effects against the cytotoxicity and carcinogenicity of benzo(a)pyrene and aflatoxin

B1 in vitro and in vivo. Occupational study showed that workers who had genotypes with higher GNMT promoter activity may have lower content of oxidative damaged DNA products in their urine. In terms of cancer, recent studies using GNMT knockout mouse models demonstrated that GNMT deficiency has high penetrance in inducing the development of steatohepatitis and hepatocellular carcinoma. In terms of the mechanism, besides dysregulation of epigenetic modification, insights have been provided by recent identification of two novel proteins interacting with GNMT-DEPTOR and NPC2. These studies suggest that GNMT not only is involved in mTOR signaling pathway, but also plays an important role in the intracellular trafficking of cholesterol. The implication of these findings to the preventive medicine and translational research will be discussed.

S31

3 月 24 日 (週日) 13:45-14:15
一樓，第 2 教室

Differential regulation of adipokine secretion

盧主欽 助理教授
長庚大學生理暨藥理學科

The adipose tissue is recognized as an endocrine organ due to its active secretion of many peptide hormones, collectively named adipokines, which regulate many important physiological functions. Despite the discovery of many adipokines in the past decades, the secretory mechanism of adipocytes remains poorly understood. SNARE (soluble N-ethylmaleimide-sensitive factor attachment protein receptors) proteins, including VAMPs, syntaxins and SNAPs, are known to mediate exocytosis in neuronal and endocrine cells. However whether SNARE proteins mediate the secretion of adipokines has not been studied. We depleted SNARE proteins in 3T3-L1 adipocytes to investigate their roles in adipokine secretion. We found that depletion of VAMP2 or VAMP8, but not syntaxin 4, SNAP23 or VAMP3, suppressed insulin-stimulated leptin secretion. In contrast, depletion of these SNARE proteins minimally affected secretion of chemokine monocyte chemoattractant protein-1 (MCP-1), suggesting differentially regulatory secretion of these two adipokines. To gain an idea of the intracellular pathways of leptin and MCP-1, pharmacological inhibitors of cellular trafficking were used. Brefeldin A and monensin, inhibitors of trafficking from endoplasmic reticulum to Golgi and *cis*-to-*trans* Golgi, respectively, blocked secretion of both leptin and MCP-1, suggesting a common trafficking route for both adipokines. Interestingly, protein kinase D inhibitor, which blocks the trafficking from *trans*-Golgi to the plasma membrane, increased insulin-stimulated leptin secretion but suppressed MCP-1 secretion. Further experiments will be required to elucidate detailed mechanism underlying these regulations. This study may provide insight to the general secretory mechanism of adipocytes, and point to potential therapeutic targets for the diseases in the future.

S32

3 月 24 日 (週日) 14:15-14:45
一樓，第 2 教室

The role of diosgenin on the male reproductive function in accelerated senescence rat models

余青翰 助理教授
中山醫學大學醫學系生理學科

Diosgenin is the bioactive compound from dioscorea. It has been found that diosgenin shows anticancer and antioxidative activities. D-galactose injection has been proved to induce brain aging in rodents by oxidative stress. Moreover, D-galactose-induced neurotoxicity is related to the unbalance of calcium and dysfunction of mitochondria. The strain of OXYS rat is bred from Wistar rat and genetically defined accelerated senescence. Lipoxidation is higher in OXYS rats than the parental strain. Oxidative stress produced from lipoxidation might cause the testicular dysfunction. Mitochondria are the center of steroidogenesis, and the production of testosterone by Leydig cells is critical for the testicular function. Thus, the rescued effects of diosgenin on the testis structure, testosterone production and sperm motility of accelerated senescence rat models were investigated. Male Wistar rats were separated in four groups and treated as following for 8 weeks, (1) control, (2) D-galactose (150 mg/kg/day), (3) D-galactose + diosgenin (10 mg/kg/day), and (4) D-galactose + diosgenin (50 mg/kg/day). OXYS rats were divided into three groups, including control, diosgenin 10 mg and 50 mg/kg/day. Accelerated senescence rat models showed impairments of reproductive function, such as decreasing sperm motility, down-regulating testosterone secretion, increasing spermatogonia apoptosis, and decreasing CD31 expression in penis. After the treatment of diosgenin, most of these impairments were partially or fully recovered, except testosterone secretion. The above results suggested that diosgenin might have protective effects for the reproductive system on accelerated senescence rats which had higher oxidative stress even with its anti-androgen secretion property.

S33

3 月 24 日 (週日) 14:45-15:15
一樓，第 2 教室

眼框前額葉多巴胺系統與注意力不足過動症抑制功能失調之關係

李季湜 副教授
國立中正大學心理學系

注意力不足過動症（ADHD）有三個主要症狀：衝動、過動、與注意力不足，有學者指出其背後成因可能是抑制控制這項認知功能缺損。臨床研究發現：在注意力轉換作業中，ADHD 患者的表現較差。以 ADHD 動物模式自發性高血壓大鼠（SHR）為實驗對象之研究也有類似發現。然而過去研究並未針對特定腦區，故我們對於抑制功能失調之機制仍無徹底瞭解。針對此點，我們在 SHR 大鼠上周邊注射利他能和另外一種 ADHD 臨床藥物 Atomoxetine，搭配在眼框前額葉施予多巴胺拮抗劑 Haloperidol，觀察動物在注意力轉換作業之表現。實驗結果顯示：1. SHR 之反向學習較慢且錯誤較多，顯示抑制控制能力不足；2. 利他能或 Atomoxetine 都能改善動物在反向學習的缺損；3. 在眼框前額葉施予 Haloperidol 會消除利他能的效果，而不會消除 Atomoxetine 的效果，意味著眼框前額葉之多巴胺系統可能與 ADHD 的抑制控制能力有關，至於 Atomoxetine 的效果可能並非透過多巴胺，而是去甲腎上腺素（Norepinephrine）。

S34

3 月 24 日 (週日) 15:15-15:45
一樓，第 2 教室

Synthesis and Characterization of Thermal Responsive HA/Puronic Acid Copolymer and Potential Evaluation on Artificial Vitreous Substitute

林詠凱 副教授
中國文化大學動物科學系

Vitreouretinal pathological complications, such as cataracts, are still a major cause of blindness. Silicone oil has been used in vitreoretinal surgery since the 1960s because of its stability, transparency and because it causes a tamponade effect in the ocular cavity. The hydrophobic and low-density properties of silicone oil result in poor contact with the retinal and vitreous humor, which can induce life-threatening complications over long periods of implantation. This study synthesizes a smart *in-situ* polymerizable artificial vitreous substitute (AVS) through copolymerization of HA and pluronic F-127, which results in a unique solution-gel transition at different temperatures. The liquid is injected at room temperature and forms a hydrogel at physiological temperatures, within the vitreous cavity. The chemical, rheological and optical properties and the biodegradability and biocompatibility are studied to determine the optimum formulation for the hydrogel. H1F20 hydrogel also exhibits similar optical properties to those of vitreous humor. The rheological properties demonstrate that the H1F20 hydrogel demonstrates suitable, thermally responsive polymerization. Furthermore, analysis of the biodegradability indicates that H1F20 hydrogel still accounts for 60% of the mass in 10000 U/ml lysozyme solution, after 7 days. The biocompatibility assay shows that the H1F20 hydrogel demonstrates the highest ARPE-19 cell viability and is significantly higher than that of the control ($p<0.01$). In summary, the H1F20 is a suitable artificial vitreous substitute.

S35

3 月 24 日 (週日) 13:45-14:15
三樓，第 32 教室

Collagen glycosaminoglycan as tissue scaffolds to promote angiogenesis and neurogenesis and to facilitate functional recovery following brain injury

王家儀 教授
北醫 醫學科學研究所

Surgical brain injury (SBI) is unavoidable during many neurosurgical procedures intrinsically linked to postoperative neurological deficits. There is as yet no clinically effective strategy for neural regeneration. The purpose of this study was to evaluate the effects of collagen-glycosaminoglycan (CG) matrix scaffolds in a rat model of SBI. A rodent model of SBI in which a part of the right frontal-parietal cortex was resected. Sprague-Dawley male rates (weighting 300-350 g) were randomly divided into three groups: 1. Sham 2. SBI 3. SBI with CG matrix implantation . Implantation of porous biodegradable CG matrix after SBI improved sensorimotor functional outcomes as shown by mNSS scores at various time points. The numbers of proliferative (Ki67 positive) and differentiated migratory (DCX positive) cells time-dependently increased after surgery both in the intra-matrix zone (IMZ) and lesion boundary zone (LBZ). Therefore, CG scaffold facilitated proliferation, differentiation and migration of endogenous neural precursor cells.

Immunohistochemical staining for smooth muscle actin (SMA) and CD31 also indicated neovascularization after implantation of CG scaffolds in lesion-boundary zone and intra-matrix zone following implantation of CG scaffolds. In addition, the tissue concentrations of vascular endothelial growth factor (VEGF), platelet-derived growth factor (PDGF) and basic fibroblast growth factor (bFGF) revealed a sustained increase in both zones up to 28 days following implantation of CG scaffold.

We conclude that CG scaffolds provides a microenvironment to facilitate neovascularization and neurogenesis after surgical brain trauma.

S36

3 月 24 日 (週日) 14:15-14:45
三樓，第 32 教室

Defense against reperfusion injury: From Preconditioning to Postconditioning

賴逸儒 副教授
台大 解剖學暨細胞生物學研究所

Ischemia-reperfusion (IR) injury occurs in clinical practices including organ transplantation, and resuscitation of hypovolemic shock. The pathogenesis of IR injury involves complex signaling pathways. New strategies to mitigate the IR injury, include the use of preconditioning and postconditioning, are to intervene the progress of vicious cycle of IR injury at the decisive time windows. Ischemic preconditioning (IPreC) uses intermittent, non-lethal ischemia-reperfusion stimulation prior to the occurrence of index ischemia. Ischemic postconditioning (iPoC) refers to a controlled reperfusion maneuver performed at the early reperfusion period. Both principles are shown protective against IR injury in various models.

In our previous studies, we found that hypoxia, hind limb ischemia and simvastatin preconditioning could mitigate IR injury of the liver, and heme oxygenase-1 played an important role in the protective mechanisms of the three models of preconditioning. In this presentation, we would like to show the protective effects of ischemic postconditioning on reducing the IR injury of liver and intestines, and the protective mechanism of iPoC was associated with the modulation of mitochondrial permeability transition.

S37

3 月 24 日 (週日) 14:45-15:15
三樓，第 32 教室

Late outgrowth endothelial cells derived from Wharton's jelly in human umbilical cord reduce neointimal formation after vascular injury: involvement of pigment epithelium-derived factor and its relative mechanism

王淑慧 助理教授
台大 解剖學暨細胞生物學研究所

Disruption of the anatomic and functional integrity of the endothelium has been postulated as the major mechanism for the initiation of atherosclerosis and restenosis. The number of endothelial progenitor cells (EPCs) that can be obtained from adult bone marrow and peripheral blood to treat cardiovascular diseases is limited. We demonstrated the cell population within Wharton's jelly in human umbilical cord (WJC) that has the potential to differentiate into outgrowth endothelial cells (OECs). Transplantation of WJC-OECs into injured vessels reduced significantly the neointimal hyperplasia by reestablishing endothelial integrity to prevent the furthermore injury progression and pigment epithelium-derived factor (PEDF) significantly expressed in the injury site. PEDF plays an important role in the proliferation and migration of human aortic smooth muscle cells (HASMCs). In *In vitro* assays, the high amount of PEDF was detected in the WJC-OECs and the cultured medium (CM) of WJC-OECs. After the treatment of CM on HASMCs, migration and proliferation of HASMCs were inhibited. The inhibitory mechanism of PEDF on HASMCs arrested cell in G0/G1 phase through regulating the cell cycle proteins expression. The antiproliferative and antimigratory effects of PEDF were partially blocked by the PPARγ antagonist GW9662. In *in vivo* studies, the neointimal hyperplasia of endothelial-denuded artery of C57BL/6 mice was reduced by PEDF treatment and the effect was inhibited by GW9662 pretreatment. Our data show that WJC has potential to differentiate into OECs and has the therapeutic effect on the vascular injury. The effect was regulated by PEDF increasing PPARγ expression and activation, preventing entry of HASMCs into the cell cycle *in vitro*, reducing the neointimal area and cell proliferation in the neointima *in vivo*. These findings have implications for a novel and practical cell-based therapy for vascular diseases.

S38

3 月 24 日 (週日) 15:15-15:45
三樓，第 32 教室

The neuroprotective strategies for the immature brain after hypoxia-ischemia

李學德 助理教授
陽明 解剖學及細胞生物學研究所

Hypoxic-ischemic (HI) encephalopathy is a major cause of neonatal mortality and neurological disabilities in childhood. Although scientific understanding of the pathogenesis of neonatal HI brain injury has increased considerably, there is still no effective treatment until now. We use an approach to study the therapy of neonatal HI encephalopathy that allows for neuroprotection is to investigate the states of tolerance to HI. Tolerance is attained by preconditioning tissue to sublethal stress, which causes the tissue to augment endogenous defense mechanisms and become more tolerant of subsequent lethal insult 24 hours carotid-artery ligation preconditioning established by delaying the onset of hypoxia for 24 hours after permanent unilateral carotid ligation rats markedly diminished the cerebral injury. Preconditioning protects endothelial cells as well as neurons from ischemic injury. In immature rat pups, the protective effect of the 24 h artery ligation preconditioning model requires the activation of cAMP response element-binding protein (CREB). We tested the hypothesis that vascular endothelial growth factor (VEGF)-A/VEGF receptor-2 (VEGFR-2) signaling that leads to CREB activation is the shared pathway underlying the protective effect of preconditioning in neurons and endothelial cells. VEGF-A, VEGFR-1, or VEGFR-2 was inhibited in vivo and in vitro. The pCREB and VEGF-A and VEGFR-2 expression were increased and colocalized in vascular endothelial cells and neurons in the ipsilateral cerebral cortex 24 h after ligation. The antisense ODN blockades of VEGF-A and VEGFR-2 decreased pCREB and reduced the protection of 24 h ligation preconditioning. Furthermore, oxygen-glucose deprivation (OGD) preconditioning upregulated VEGF-A, VEGFR-2, and pCREB levels and protected immortalized H19-7 neuronal cells and b.End3 vascular endothelial cells against 24 h OGD cell death. Blocking VEGF-A or VEGFR-2 reduced CREB activation and the effects of OGD preconditioning in neuronal cells and endothelial cells. Transfecting a serine-133 phosphorylation mutant CREB also inhibited the protective effect of OGD preconditioning. We concluded that VEGF-A/ VEGFR-2 signaling leading to CREB phosphorylation is the shared pathway underlying the preconditioning-induced protective effect in neurons and vascular endothelial cells in the developing brain.

T1 科技新知研討會

時間：102 年 3 月 23 日 (週六) 12:00-13:00
地點：一樓，第 1 教室
單位：美商沃斯特國際股份有限公司台灣分公司

演講（一）
Structural Comparability Assessment of Innovator and Biosimilar Rituximab Using the Biopharmaceutical System Solution with UNIFI.

Speaker:
陳順莉
現職 : 美商沃特斯國際 (股) 公司台灣分公司 技術應用專員

內容摘要：

Waters 為了幫助生物製藥企業解決採用高分辨分析技術來應對藥物開發過程中的挑戰，專門設計一套分析平台系統來滿足分析實驗室現在及未來發展的需求。

利用高解析度質譜儀 SYNAPT G2 HDMS 搭配分析平台 UNIFI 的使用，可對 Rituximab 進行廣泛性之結構鑑定，並且進一步與生物相似藥物作一自動且快速的生物相似性分析比較，其中包括一級結構鑑定 (Peptide Mapping)、完整蛋白質 (Intact Protein) 分析及醣基化 (glycosylation) 分析等。

演講（二）
最新層析技術應用於生技製藥的分析

Speaker:
黃筠華 博士
現職 : 美商沃特斯國際 (股) 公司台灣分公司化學產品經理

內容摘要：

Waters 一直領先在提供創新及符合應用的解決方案給生技製藥及製藥產業，讓實驗室作有信心的決定並有效的縮短產品的上市的時間。我們將介紹 Waters 最新的層析技術應用於生技製藥的分析，內容包括應用最新的層析顆粒技術來解決 Peptide, Protein, Glycan, Amino Acids 等分析的挑戰。

T2

科技新知研討會

時間：102 年 3 月 23 日 (週六) 12:00-13:00
地點：一樓，第 2 教室
單位：基龍米克斯生物科技股份有限公司

Pico-Liter Droplet Technology Enables Revolutionary Breakthrough High Resolution Digital PCR and Single Plex PCR Based NGS Target Enrichment

Speaker:

Chen Gen-Der (陳根德)
1999-2005 Ph.D. Institute of Biochemistry, National Yang-Ming University, Taiwan
2005-2011 postdoctor fellow, Institute of Biochemistry, Academia sinica, R.O.C
2011~ Chief Technical Officer, Genomics BioSci. & Tech.

Moderator:

Liu Chun Hao(劉君豪)
Vice General Manager, Genomics BioSci. & Tech.

RainDance Technologies have developed its core technology by using pico-liter droplet based chemsitry for over 8 years. In order to help NGS users to enrich target sequencing regions, we have launced TunderStorm platform to enable highly paralleled, singplex PCR amplifiation within picoliter droplets. Such enrichment delivers unique performance benefits, such as >99% coverage, high uniformity and specificty. The NGS target enrichment technology has been widely adopted by key customers across the world, and is considered the Gold Standard for Critical Gene Sequencing. In collaboration Genomics BioSci & Tech, we plan to establish ThunderStorm service laboratory in March 2013, so that Asia NGS customers will gain immediate access to our technologies. Very recently, the company has announced the commercial launch of the revolutionary RainDrop digital PCR platform, which is expected to deliver the highest possible resolution and sensitivity for digital profiling of genetic variants. Detailed technology details, as well as customer success stories, will be discussed at the presentation.

T3

科技新知研討會

時間：102 年 3 月 23 日 (週六) 12:00-13:00
地點：三樓，第 30 教室
單位：金萬林企業股份有限公司

Golden Helix 與 DNAStar 在 NGS 數據上的應用

Speaker:

陳宣甫
金萬林企業股份有限公司 研究員
(UCLA 博士 ,UCSF 博士後 , 中研院統計所博士後)

Moderator:

隨著次世代基因定序時代的來臨 , 以往用 common variants 來探索疾病的策略逐漸轉向到以 rare variants 為目標 , 我們將介紹 Golden Helix 在這方面的應用 , 如何使用 Golden Helix 根據 population MAF, functional classification 等資料庫來篩選出 rare variants, 並將結果與疾病作關聯性分析 ; 另外 , 我們將介紹 DNAStar 在 NGS 數據方面的應用 , 重點會放在多個 sample 彼此間 SNP 的互相比較 , 以及若干性能與速度上的優勢

T4

科技新知研討會

時間：102 年 3 月 23 日 (週六) 12:00-13:00
地點：三樓，第 31 教室
單位：萊富生命科技股份有限公司

Semi-conductor sequencing transforms translational medicine revolutionizing patient and health care

Speaker:

Pat Brooks

Vice President of International Sales, Ion Torrent, a Division of Life Technologies.

CV:

Pat Brooks is currently Vice President of International Sales, Ion Torrent, a Division of Life Technologies. Involved in Next Generation Sequencing technologies for four years, part of this as the founding commercial member of a start-up organization. Before this he managed a global sales and support business in microarrays for over eight years. Previous experiences also included managing global sales and support divisions for over nine years in Amersham and then Amersham Pharmacia.

The rapid adoption of semi-conductor based sequencing technology by Ion Torrent and Life Technologies is revolutionizing translational research and molecular medicine. By dramatically reducing the cost of sequencing while increasing throughput and simplicity, now thousands of labs worldwide are engaged in active pursuit of applying the cutting edge sequencing technology to the clinic. Genetic traits linked to prediction of diseases or treatment outcome can be analyzed within hours and this brings true personalized medicine within our reach.

T5

科技新知研討會

時間：102 年 3 月 23 日 (週六) 12:00-13:00
地點：三樓，第 32 教室
單位：諾貝爾生物有限公司

The Easiest Way to Nucleic Acid Extraction – New Generation Membrane Column Automated System – LabTurbo 24 / 48 Compact System

Speaker:
閔相儒 先生 諾貝爾生物有限公司 產品應用經理

全功能 LabTurbo Compact System 為全球核酸應用市場重新定義了簡便、安全、高產值的高自動化標準，並成功取得各項國際認證。

LabTurbo 24 / 48 Compact System 具備嶄新的設計：高通量快速的能力，解決持續性或臨時性的大檢體量；最佳化程式能處理各類型的檢體；檢體大體積上機容量，符合各式各樣的核酸應用。

全功能 LabTurbo Compact System 已使用於包括病原檢測、產前篩檢、遺傳分析、癌症篩檢、基因表現研究、流行病學研究、次世代定序、法醫鑑定等應用，可有效節省人力、時間，獲得最大的核酸純化效益，搭配 Biometra 高階光纖即時定量 PCR - TOptical Realtime Thermocycler，提供最完整純化到分析解決方案，歡迎您前來體驗。

T6

科技新知研討會

時間：102 年 3 月 23 日 (週六) 12:00-13:00
地點：三樓，第 33 教室
單位：世翔國際有限公司

Non-invasive microRNA biomarkers for therapy monitoring and drug development

Speaker:

Dr. Matthias Scheffler
VP Business Development & Sales of Comprehensive Biomarker Center GmbH Heidelberg, Germany.
經歷 :
1.Vice President of Operations, Febit
2.Biochip Development, Team Manager, Febit.

Moderator:

王梓明
世翔國際有限公司，總經理
經歷 :
1. 勁因科技有限公司 , 資深業務專員
2. 臺大醫院，研究助理
3. 陽明大學臨床醫學研究所，碩士

microRNAs are small non-coding RNAs controlling gene expression either by degradation or by translational silencing of mRNA. These small RNAs have been shown to contribute to the control of many biological processes microRNAs cannot only be detected in tissue samples but also in 12 different human body fluids. This qualifies microRNAs as high potential non-invasive biomarkers.

During the past 3 years we have analyzed more than 4000 whole blood samples in hypothesis-free microRNA screenings collaborating with numerous clinical centers of excellence. We have successfully discovered non-invasive microRNA biomarker signatures for more than 40 cancer types as well as for autoimmune and inflammatory diseases as in the following examples.

We showed that miRNA blood signatures are capable to differentiate Chronic obstructive pulmonary disease from lung cancer with a specificity of 89.2% and a sensitivity of 91.7%.

Likewise, we have identified a multiple sclerosis specific microRNA biomarker signature from whole blood which could discriminate relapsing-remitting multiple sclerosis from healthy controls with a specificity of 95% and a sensitivity of 97.6%. More results of these studies have been published in 18 peer reviewed journal articles (including Nature Methods, Sept 2011,Toward the blood-borne miRNome of human diseases).

Most of our discovered signatures have diagnostic, differential diagnostic or prognostic value. We will present recent evidence on the high potential of microRNAs as therapy monitoring biomarker for non-invasive surveillance of drug response. Preliminary results from a longitudinal and cross-sectional study show that a microRNA signature from blood is correlating with positive therapy response. Furthermore, the signature of treated patients correlates well with the signature of an independent healthy control group. Case study will be presented to demonstrate the above potential of microRNAs as biomarkers for monitoring of disease response to therapy.

T7

科技新知研討會

時間：102 年 3 月 23 日 (週六) 12:00-13:00
地點：三樓，第 34 教室
單位：均泰生物科技有限公司 GeneTech Biotech Co., Ltd.

Next Generation Sequencing: Driving Improved Clinical Outcomes

Speaker:

Sujin Kim
Sequencing Segment Manager, Illumina

Moderator:

Lee Chee Koon 李知勳
Territory Account Manager, Illumina

As research advances, new discoveries may lead to the development of novel tools for use in clinical laboratories, aiding clinicians in their quest to provide patients with optimized treatment plans. Illumina is at the forefront of this movement, collaborating with researchers and healthcare experts in an effort to enable all laboratories to realize the benefits of next-generation sequencing.

The TruSight content sets are the first realization of Illumina's efforts in this area. Designed with recognized healthcare experts at leading institutions, the TruSight content sets comprise oligo probes targeting genes and regions thought to be relevant for particular diseases or conditions.

Researchers are rapidly advancing our understanding of disease-causing mutations and genetic dispositions. Illumina is committed to helping our customers deploy these new discoveries on next-generation sequencing technologies, and leverage them in a clinical environment. The ultimate goal is to make genomic information readily accessible for more informed, and hopefully better, patient care.

T8

科技新知研討會

時間：102 年 3 月 24 日 (週日) 12:00-13:00
地點：一樓，第 1 教室
單位：財團法人國家實驗研究院國家實驗動物中心

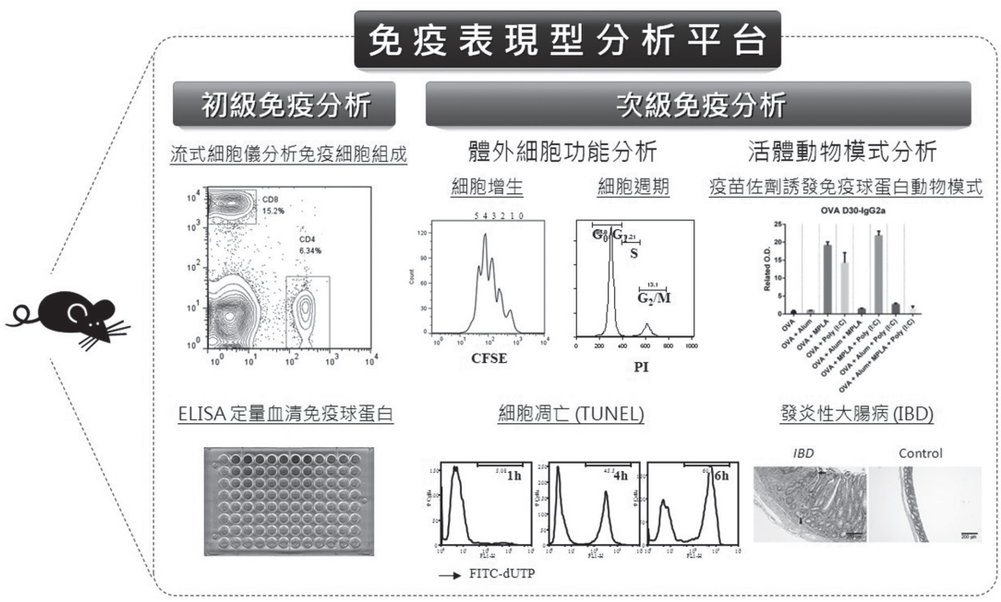
常見近親品系小鼠免疫細胞相分析與免疫球蛋白亞群定量

Speaker:
蘇裕家 博士
國研院動物中心 助理研究員
國立台灣大學免疫學研究所 博士

Moderator:
秦咸靜 博士
國研院動物中心 副研究員
美國康乃狄克大學醫學院遺傳與發育生物學 博士

近親品系小鼠是利用兄妹或父母子女連續交配 20 代 (或以上) 所得，因此每一隻相同近親品系小鼠的基因序列有 99.99% 以上是相同的。全世界有許多的近親品系小鼠應用於多種不同的動物實驗，其中較常見的包括 C57BL/6、BALB/c、C3H……等等。但由於每一個近親品系都是經過長時間近親交配，不同的近親品系間有著相當大的差異，因此利用國家實驗動物中心今年開放的免疫表現型分析平台的服務，比較各個近親品系間的免疫表現型間是否有重大差異。

本中心以國際小鼠表現型分析聯盟 (International Mouse Phenotyping Consortium) 所建立的標準與建議，首先在台灣建立初級免疫表現型分析平台，分析血液與淋巴組織中免疫細胞的組成，同時亦監測免疫球蛋白亞群的表現，並評比不同近親品系間的差異。除了上述兩種小鼠免疫力的初步篩檢，本平台亦提供次級免疫力測試平台，包括免疫細胞功能測試平台 (體外測試) 與小鼠疫苗佐劑的刺激試驗平台 (活體測試)。期望在小鼠免疫力表現型分析服務，不論廣度 (初級) 與深度 (次級) 上提供更全面性的服務。



T8

科技新知研討會

時間：102 年 3 月 24 日 (週日) 12:00-13:00
地點：一樓，第 1 教室
單位：財團法人國家實驗研究院國家實驗動物中心

隔離操作箱技術之現況與未來

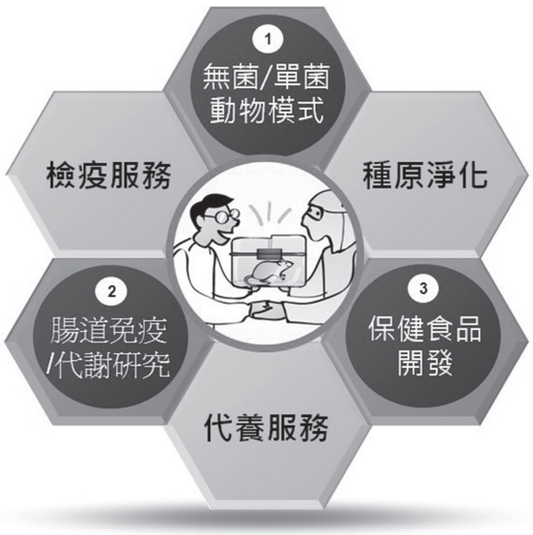
Speaker:
莊曉莉 博士
國研院動物中心 助理研究員
國立中興大學獸醫學系 博士

Moderator:
秦咸靜 博士
國研院動物中心 副研究員
美國康乃狄克大學醫學院遺傳與發育生物學 博士

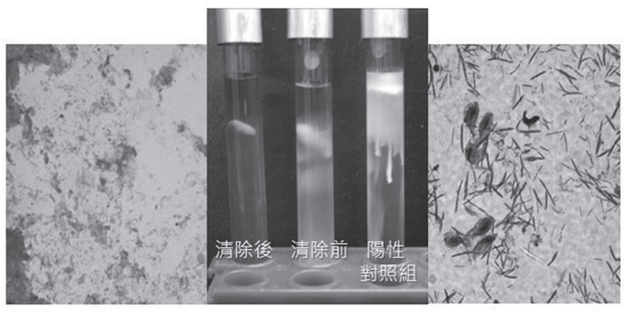
近年來，隔離操作箱在國際學術上之應用已是不可或缺的技術平台，根據跨庫分析資料庫 SCOPUS 進行查詢，isolator、germ free mice、gnobiotic mice 等名詞查詢所得研究論文有逐年攀升的趨勢，可知此平台已經受到矚目。而我國則於 2003 年 8 月起，由本中心建立國內的無菌鼠族群及無菌隔離操作箱技術平台，目前可應用於 (1) 病原清除、種原復育及提升實驗動物的品質。(2) 探討微生物對先天性或後天性免疫反應之調控。(3) 基因轉殖或基因剃除鼠處於不同微生物狀態下，對其表現型 (phenotyping) 的影響。

本服務除了可以提供學術單位或醫藥業界進一步探討微生物對代謝性疾病、癌症的發生和老化等疾病動物模式的影響，並可以協助國內推動前瞻性研究，包含基因體醫學、生技製藥、農業生物技術等國家型計畫之研發平台，對於提升我國技術研發、科學發展為不可或缺之角色。

隔離操作箱技術之應用



病原清除前和清除後的糞便檢體微生物培養



病原清除後　　病原清除前

T9

科技新知研討會

時間：102 年 3 月 24 日 (週日) 12:00-13:00
地點：一樓，第 2 教室
單位：弘晉有限公司

細胞面面觀 - 用螢光看細胞
CELLestial Assay Kits for Live Cell Analysis

Speaker:

Adrian Rea
Technical marketing and sales manager for global distributors
2012-Present
Technical marketing and sales manager for global distributors
Enzo Life Sciences
2009-2012
Technical marketing and sales manager for the United Kingdom
Enzo Life Sciences
2008-2009
Lecturer in Pharmacology and Biomedical Science
Glasgow Caledonian University
2003-2007
Ph.D. in Pharmacology/Biochemistry
Glasgow Caledonian University
1999-2003
B.Sc. in Pharmacology
University of Glasgow

Moderator:

楊春茂 教授
長庚大學醫學院生理暨藥理學科
曾任藥理學科主任和天然藥物研究所所長

NOVEL FLUORESCENT PROBES & REPORTER ASSAYS

The CELLestial® range provides high-specificity, next-generation fluorescent dyes for visualizing cellular responses.

The use of fluorescent dyes to identify cell structural components and monitor cytotoxicity or cellular responses to growth signals is well established. In addition to a wide selection of gold standard labeling dyes such as DAPI, Hoechst, and JC-1, Enzo Life Sciences has translated its expertise in fluorescent probe chemistry and cellular analysis into our CELLestial® portfolio of unique probe-based assays and reagents to meet the emerging needs of the life sciences and drug discovery markets. From simple organelle specific dyes for imaging cell structure and determining cell viability, to more complex dyes and reporter assays for monitoring cell signaling, death pathways, and toxicity, every product is developed and reliably manufactured to provide sensitivity, specificity, and convenience.

Key Features of the CELLestial® product line:

- Increased photostability reduces photobleaching
- Reduce false positives by eliminating non-specific dye-associated artifacts
- Compatible with common dyes and fluorescent markers (i.e., GFP) for multiplex analysis
- Optimized for reproducibility on microplate, flow cytometry, or fluorescent imaging platforms
- Widely published in peer-reviewed literature

The CELLestial® product line provides a variety of tools to help pharmaceutical and biotech companies optimize their pre-clinical and clinical drug development programs through early lead drug identification, lead candidate selection, predictive toxicology and compound characterization. Overall, these assays may be broadly classified into six main categories:

Death pathway assays

Cell-based assays for monitoring compound effects on apoptosis, autophagy and necrosis. Includes monitoring of annexin V redistribution, nuclear condensation, autophagosome generation and loss of plasma membrane integrity.

Cell cycle and transcriptional arrest assays

Cell-based assays for monitoring compound effects on cell cycle dynamics, ribosome biogenesis, inhibition of transcription

Oxidative stress, antioxidants & scavenger assays

Cell-based assays for monitoring compound effects on reactive oxygen species, superoxide, nitric oxide and peroxynitrite.

Toxicology assays

Cell-based assays for monitoring compound effects on the function and viability of human cell lines. Includes monitoring cell viability, cell proliferation/cytotoxicity, lysosome expansion, aggresome formation and mitochondrial activity.

Organelle Detection

One of the most comprehensive selections of multi-color organelle-specific dyes for co-localization studies and monitoring structural changes in response to chemical or environmental stress.

Gold Standard Dyes

Enzo Life Sciences offers conventional fluorescent dyes for organelle detection & function including DAPI, Hoechst, JC-1, and more.

T10

科技新知研討會

時間：102 年 3 月 24 日 (週日) 12:00-13:00
地點：三樓，第 30 教室
單位：承洺科技有限公司

仿生理動態刺激細胞培養系統於生物醫學之應用

Speaker:

國立嘉義大學生物機電工程學系 艾群 特聘教授
台灣生物機電學會 監事主席 (2009 年 7 月 ~2012 年 7 月)
台灣生物機電學會理事長 (2006 年 5 月 ~2009 年 7 月)
國立嘉義大學教務長 (2005 年 2 月 ~2007 年 7 月)
國立嘉義大學理工學院院長 (2000 年 8 月 ~2006 年 7 月)

Moderator:

國立成功大學生物科技研究所 黃玲惠 教授
國立成功大學醫學院臨床醫學研究所 合聘教授
國立成功大學再生醫學卓越研究中心 主任
國際生醫材料科學及工程學會之聯盟國會議 台灣代表
台灣再生醫學學會 理事
台灣幹細胞學會 監事

從胚胎發育到嬰兒誕生，從幹細胞分化到組織再生，生物體本就處於動態的環境，於生理狀況下細胞不斷地接受到「力」的刺激，包含了血管脈動、肺部呼吸、肌肉皮膚延展、關節骨骼壓縮、胃腸蠕動及泌尿系統過濾等，細胞無時無刻都處於動態的環境。這些力的刺激不只改變細胞骨架形狀及型態，並且對細胞增生、分化、凋亡、遷移、細胞外基質的重塑及基因表現等都會產生很大的影響。

仿生理動態刺激細胞培養系統 -【ATMS】，有別於以往「傳統靜置細胞培養」的方法，可模擬細胞在生物體內生理情況下的受力情形，並能夠依實驗需求調整拉伸 / 壓縮頻率、應變量、及流體對細胞造成的剪應力，更能符合實際生理運動狀況，重現體內的微觀動態環境，改善傳統靜置培養無法真實呈現的研究結果。進化的【仿生理動態刺激細胞培養系統】源自於對生命科學的無限渴望！探索生醫科學的奧妙，需要您用不同角度看事物！

該系統具有下列五大運用功能：
一、【仿生理機械力伸拉】刺激細胞培養之研究。
二、【生醫材料】與【細胞】同時整合伸拉刺激之研究
三、【植體】、【生醫材料】、【細胞】同時整合之擠壓刺激之研究。
四、【活體組織培養】與機械力壓縮刺激之研究。
五、【恆溫流體剪應力】於細胞培養系統之研究。

T11

科技新知研討會

時間：102 年 3 月 24 日 (週日) 12:00-13:00
地點：三樓，第 31 教室
單位：卓昇有限公司

Western Blot and Optiblot Products Introduction

Speaker:

Mr. Wong Sze Ki (MPhil, CUHK)
Scientific Support Specialist of Abcam (Hong Kong) Ltd. Research interest in Vibrio virulence factors inducing apoptosis. Mr. Wong is experienced in various laboratory techniques, especially in Western blot.

Moderator:

呂侑侖 (Ada Lu)
Technical Support Specialist of Interlab Company

Western blot (WB), also called immunoblot, uses specific antibodies to analyze one protein in a sample containing multiple proteins. Proteins are separated from each other by size using gel electrophoresis, then transferred to a membrane and detected with a specific antibody. This technique is widely used in biological research, as it provides information about the molecular weight of a protein as well as relative differences in expression between samples. This talk aims to introduce WB procedure including the process of sample preparation, gel electrophoresis, transfer from gel to membrane, and immunostaining for protein detection. Troubleshooting tips for common problems in the procedure are also included. Optiblot products are specially designed for improving performance in WB. By using Optiblot products, researchers are able to perform protein electrophoresis or blotting rapidly and conveniently, generate high quality of experimental results.

T12

科技新知研討會

時間：102 年 3 月 24 日 (週日) 12:00-13:00
地點：三樓，第 32 教室
單位：百律有限公司

自動化多功能液體工作站與應用

Speaker:
梁洞泉 博士
Aurora Biomed 執行長
中科院聯合生命科學實驗室研究員

Moderator:
林益民 先生
百律有限公司 業務部經理

在日以繼夜的研究當中，許多繁瑣且重復的實驗流程佔據了大部分研究員的時間。慢慢的，科技發展了自動化設備來簡化許多流程。而 Auora Biomed 更是進一步將許多簡化流程整合在一台全自動的工作站。不但可以施行複雜的樣品純化，如 DNA Purification, SPE, LLE。甚至可以迅速製備分析前的冗長步驟，如 NGS, PCR, ELISA。提升實驗效率，精准度，與重現性，降低重工與錯誤率。讓研究員把心力放在更重要的地方：data 分析。

T13

科技新知研討會

時間：102 年 3 月 24 日 (週日) 12:00-13:00
地點：三樓，第 33 教室
單位：Promega Corporation

Deducing the Mechanism of Toxicity- the Cell Based Approach

Drug discovery is a highly knowledge oriented, rapidly advancing field. The process of drug discovery involves multiple stages beginning with basic research to identify targets, validation of the targets, screening of candidates, identification of leads and lead optimisation. Understanding the necessity for sensitive and robust assays to increase the success rate, compatible technologies to streamline workflows, and simple solutions to enable efficiency and time reductions, Promega has developed a wide spectrum of bioluminescent assays for the various processes involved in drug discovery. High-throughput screening assays and multiplexed viability and cytotoxicity analysis to screen for candidates; mechanistic assays to understand the MOA of therapeutic candidates and to map the signalling regulation that they orchestrate, kinase assays to screen for possible inhibitors of kinase activity, powerful tools for ADME-Tox screens, technologies to assess the cell health, etc offer the researchers with a bouquet of highly sensitive and easy-to-use tools to support the drug discovery workflow. With a strong pipeline of new technologies, we also offer customisable solutions to suit specific needs.

Moderator:

Dr. Xin Chen

Investigator, Institute of Biotechnology and Pharmaceutical Research, National Health Research Institutes, Miaoli, Taiwan

Dr. Chen was involved in several drug discovery projects in the Institute targeting metabolic diseases and SARS coronavirus from 2002 to 2011. The drug targets her lab worked on were DPP4 (a prolyl dipetidase) and papain-like protease 2 (PLP2) of SARS coronavirus. Dr. Chen's lab provided the biological assays, including setting up in vitro screening platforms starting from enzyme expression, purification and characterization, and various cellular screening platforms with intact mammalian cells. Her lab also characterized the biochemical properties of several other prolyl enzymes and PLP2, whose biochemical properties were largely unknown. The DPP4 inhibitor discovered and developed is in human phase I clinical trial in Taiwan.

Currently her group focuses on the development of assay systems for endothelin-1 receptors to discover the antagonists for the treatment of pulmonary hypertension (PAH), and possibly chronic kidney disease (CKD) too. Specifically, she is interested to understand the mechanism of action for various existing drugs/antagonists so that the cause for the toxicity associated with this class of GPCR can be elucidated for the development of better and safer drugs in the future.

Speaker:

Karthik Narasimhan, Ph.D., Promega Corporation

Dr. Karthik Narasimhan is the Field Application Specialist for the Asia Pacific at Promega Corporation. He is responsible for forging strategic collaborations in Asia. Prior to joining Promega in 2010, Karthik was researching the mechanism of action of novel therapeutics in Acute Myeloid Leukemia using high-throughput technologies at the National University of Singapore, from where he obtained his PhD. Karthik has been travelling extensively, delivering talks at scientific meetings and networking with key opinion leaders in the field of drug discovery and development.

T14 科技新知研討會

時間：102 年 3 月 24 日 (週日) 12:00-13:00
地點：三樓，第 34 教室
單位：凱杰生物科技有限公司 QIAGEN Taiwan

Get the most from NGS – the solution to challenging sample prep, library QC and post NGS validation

Speaker:

Dr. Gerald Schock
Associate Director, Pyrosequencing, QIAGEN GmbH

Moderator:

Dr. Annie Chan
Manager , Marketing LS Asia Pacific

The development of sequencing technology has greatly expanded our understanding of how biological information is coded in the sequence of nucleotides of DNA. In this seminar, we will address the challenge in next-generation sequencing (NGS) from sample preparation, quality control to data validation. The high detection sensitivity provided by the QIAxcel Advanced instrument enables robust results even with low concentrations of nucleic acid to enhance a greater confidence in data interpretation. PyroMark Q24 Advanced with software that handles allele frequency quantification, genotyping, and methylation analysis, provides a platform to validate the data generated from NGS technology.

口頭論文分類、時間、地點

102 年 3 月 23 日 (週六)

學會別	地 點	時 間	編 號
台灣藥理學會	第 1 教室	10:10-11:10	O1-O5
		16:00-17:00	O6-O10
中國生理學會	第 2 教室	16:00-17:00	O11-O16
中華民國細胞及分子生物學學會	第 30 教室	09:00-10:00	O17-O20
		16:00-17:00	O21-O24
中華民國解剖學學會	第 32 教室	16:00-17:00	O37-O39
中華民國毒物學學會	第 34 教室	14:00-15:45	O52-O59

102 年 3 月 24 日 (週日)

學會別	地 點	時 間	編 號
中華民國細胞及分子生物學學會	第 30 教室	09:00-10:00	O25-O28
		13:45-15:45	O29-O36
中華民國解剖學學會	第 32 教室	09:00-10:00	O40-O42
台灣生物化學及分子生物學學會	第 33 教室	13:45-14:45	O43-O45
		14:55-15:55	O46-O48
		16:05-17:05	O49-O51

台灣藥理學會

時　間：102 年 3 月 23 日 (週六) 10:10-11:10
地　點：一樓，第 1 教室
主持人：林琬琬 教授 / 臺大藥理所
　　陳炯東教授 / 國衛院 生技與藥物研究所

編號	時段	演講者 & 講題
O1	10:10-10:20	Nutrient deprivation induces the Warburg effect through ROS/AMPK-dependent activation of pyruvate dehydrogenase kinase. 巫清安 [a], 趙毅 [b], 夏興國 [c], 林琬琬 [a,d] [a] 台大醫學院藥理所 ,[b] 台北榮總癌症中心 [c] 國家衛生研究院癌症研究所 ,[d] 台北醫學大學醫學科學研究所
O2	10:20-10:30	Autophagy Is Involved in The Cell Migration of Gefitinib-Resistant NSCLC Cells 唐美娟 , 張雅婷 , 林滿玉 , 楊志新 台灣大學癌症研究中心
O3	10:30-10:40	Establishment of Gefitinib and BIBW2992-Resistant Non-Small Cell Lung Cancer Cells 鍾政達 [1, 2], 葉凱嘉 [1], 李家惠 [3], 黎耀基 [2], 陳炯東 [1] 財團法人國家衛生研究院 , 生物技術與藥物研究所
O4	10:40-10:50	To Investigate the Alterations of Histone Deacetylase 8 (HDAC8) in Breast Tumorigenesis and Its Application in Cancer Therapeutics 謝昌霖 [1], 黃偉展 [2], 林若凱 [2*] [1] 臺北醫學大學藥學院生技製藥產業碩士專班 , [2] 臺北醫學大學生藥學研究所
O5	10:50-11:00	A Novel DNA Methyltransferase Inhibitor, D-Antroquinonol, Inhibits The DNMT-1 Activity and Induces Anticancer Effects on Human Breast Cancer Cells 王昇超 [1] , 李宗徽 [1] , 徐駿森 [2] , 張育嘉 [3] , 王憶卿 [4] , 溫武哲 [5] , 林若凱 [1*] [1] 臺北醫學大學生藥學研究所 , [2] 國立臺灣大學農業化學系 , [3] 臺北醫學大學醫學院臨床醫學研究所 , [4] 國立成功大學基礎醫學研究所藥理所 , [5] 國鼎生物科技股份有限公司
	11:00-11:10	Discussion

台灣藥理學會

時　間：102 年 3 月 23 日 (週六) 16:00-17:00
地　點：一樓，第 1 教室
主持人：顧記華 教授 / 臺大藥學系
　　石宜銘 教授 / 陽明醫學系

編號	時段	演講者 & 講題
O6	16:00-16:10	Calanquinone A Displays Anticancer Activity through Depletion of Cellular Glutathione in Human Glioblastoma 劉凡綸 [1], 李衍彰 [2], 顧記華 [1], 孔繁璐 [1],* [1] 國立臺灣大學醫學院藥學系暨研究所 [2] 國立彰化師範大學化學系
O7	16:10-16:20	The Anticancer Effect of Extracts from Mycelium of Antrodia camphorate in Non-Small Cell Lung Cancer Cell Line. 顏怡婷 [1] , 李宗徽 [1] , 徐駿森 [2], 溫武哲 [5], 林若凱 [1]* [1] 臺北醫學大學生技製藥產業碩士專班 [2] 國立臺灣大學農業化學系 [5] 國鼎生物科技股份有限公司
O8	16:20~16:30	In vitro and in vivo Effects of Xanthorrhizol on Human Breast Cancer MCF-7 cells treated with Tamoxifen 許文欣 , 張君如 , 陳俊良 , 邱仁輝 , 曾令民 , 石宜銘 陽明大學傳醫所 , 海洋大學時科所 , 長庚醫院中醫部 , 榮總一般外科 , 北榮傳醫中心
O9	16:30-16:40	Effects of Chinese Herbal Extracts on ERBB2 and ESR1 Gene Expression in Human Breast Cancer MCF-7 Cell Line. 劉蕙如 , 張君如 , 陳俊良 , 邱仁輝 , 黃威棨 , 黃玉慈 , 曾令民 , 石宜銘 [1] 陽明大學傳統醫藥研究所 ,[2] 海洋大學食科所 ,[3] 長庚醫院中醫部 ,[4] 台北榮總一般外科 , [5] 北榮傳醫中心
O10	16:40-16:50	CC-36, an asymmetrical 1,2-disubstituted amide-linked anthraquinone derivative, inhibits proliferation of hormone-refractory prostate cancer cells through LKB1-AMPK-mTOR pathway 徐瑞苓 [1], 黃旭山 [2], 顧記華 [1] [1] 台灣大學藥學系 , 國防醫學院藥學系
	16:50-17:00	Discussion

中國生理學會

時　間：102 年 3 月 23 日 (週六) 16:00-17:00
地　點：一樓，第 2 教室
主持人：童吉士 教授 / 國防醫學院生理學科
　　陳景宗 教授 / 長庚大學生理藥理科主任

編號	時段	演講者 & 講題
O11	16:00-16:15	Angiotensin II Type I Receptor-Mediated Oxidative Stress in Rostral Ventrolateral Medulla Underlies the Elevated Blood Pressure after Stroke 李佳欣 , 張雅雯 高雄長庚紀念醫院 生物醫學轉譯研究中心
O12	16:15-16:30	Gabapentin Enhanced Periaqueductal Gray and Suppressed Insular Cortex Glucose Metabolism in Conscious Rats with Neuropathic Pain: a PET Study 林校群 [1], 孫維仁 [2], 嚴震東 [1] [1] 國立台灣大學動物學研究所 ,[2] 國立台灣大學醫學院附設醫院麻醉部
O13	16:30-16:45	Alcohol Consumption Aggravates Hematomal Hemolyses and Inflammations in Brain Injuries Caused by Intracerebral Hemorrhage in Rats 廖學健 [1], 鄭弘裕 [2,6], 黃麗娟 [3,6], 李國瑋 [1], 林伯謙 [1,5], 彭筱芬 [1], 楊蕙怡 [1], 陳新源 [4], 郭重雄 [4,6] 馮清榮 [1,6] 花蓮慈濟醫院 研究部 [1], 復健科 [2], 影像醫學部 [3], 神經醫學科學中心 [4], 花蓮慈濟大學 醫學檢驗生物技術學系 [5], 醫學科學研究所 [6]
O14	16:45-17:00	Molecular Mechanism of Curcumin on the Suppression of Cholesterol Accumulation in Macrophage Foam Cells and Atherosclerosis 趙錦鳳 [1], 井立捷 [1], 黃御筑 [1], 陳建宇 [1], 姜安娜 [2], 高毓儒 [1], 徐松錕 [3], 李宗玄 [1,4] [1] 陽明大學 生理所 ,[2] 生化所 ,[3] 中研院生醫所 ,[4] 陽明大學 腦科學研究中心
O15	17:00-17:15	Differential Nociceptive Coding Ability of Medial and Lateral Thalamus during Different Brain States 魯本立 [1], 嚴震東 [1] [1] 台灣大學動物所
O16	17:15-17:30	The functional role of TYRO3 in colorectal cancer progression and metastasis 簡郡緯 [1], 賴嬿羽 [2], 林博文 [3], 林劭潔 [3], 李政昌 [3], 蔡少正 [1, 2] [1] 成功大學基礎醫學研究所 , [2] 生理學研究所 , [3] 成功大學附設醫院外科

中華民國細胞及分子生物學學會

時　間：102 年 3 月 23 日 (週六) 09:00-10:00
地　點：三樓，第 30 教室
主持人：王廷方副研究員 / 中央研究院分子生物研究

編號	時段	演講者 & 講題
O17	09:00-09:15	The Novel Tubulin Inhibitor, MPT0B098, Inhibits Stat3 Pathway and Induces Apoptosis via up-regulation of SOCS3 in Oral Cancer Cells 彭軒鈺 [1]*, 劉景平 [2], 金秀蓮 [3], 張俊彥 [1#], 夏興國 [1#] [1] 國家衛生研究院癌症研究所 , [2] 臺北醫學大學 藥學系 , [3] 中央大學生命科學系
O18	09:15-09:30	PKC412, an Oral Small-molecule Multi-kinase Inhibitor, Induces a Unique Cell Death Mode in Human Oral Squamous Carcinoma Cells [1] 蘇迺文 ,[2] 曾文瑟 ,[2] 許敏玲 ,[2,3] 陳裕仁 [1] 馬偕紀念醫院血液腫瘤科 ,[2] 醫學研究部 ,[3] 放射腫瘤科
O19	09:30-09:45	Characterization of the Putative Oncogene UBE1C and Its Relationship with p53 in Lung Cancer 施詠馨 [1], 任婕羽 [2], 王憶卿 [1, 2*] [1] 國立成功大學藥理學研究所 , [2] 基礎醫學研究所
O20	09:45-10:00	Role of thymidine phosphorylase and Rad51 in HSP90 inhibition induced cytotoxic effect in non-small-cell lung cancer cells 曾聖捷 , 黃羽淨 , 陳煌仁 , 翁紹婬 , 林芸薇 * 嘉義大學生化科技學系分子癌病學實驗室

中華民國細胞及分子生物學學會

時　間：102 年 3 月 23 日 (週六) 16:00-17:00
地　點：三樓，第 30 教室
主持人：楊昀良教授 / 交通大學生物科技系

編號	時段	演講者 & 講題
O21	16:00-16:15	The quantitative analysis for a synthetic autoregulatory circuit 李柏翰 , Zhongge Zhang , Tom Kuhlman and Terence Hwa [1] 敏通健康生技股份有限公司 ,[2] 美國加州聖地牙哥大學物理系與生物物理理論中心
O22	16:15-16:30	Effect of Low Intensity Pulsed Ultrasound (LIPUS) on Ex Vivo Expansion of Hematopoietic Stem Cells 溫政浩 [1], Jie Chen[2], James Xing[3], 黃效民 [1] [1] 食品工業發展研究所 , [2] 加拿大亞伯達大學生醫工程學系 [3] 加拿大亞伯達大學實驗醫學與病理學系
O23	16:30-16:45	Characterizing the interaction of neuron and glia by electroretinogram 葉柏安 , 孫以瀚 中央研究院 分子生物研究所
O24	16:45-17:00	The Application of Curcumin-loaded Liposomes on Osteoporosis Treatment 蘇鈺涵 [1], 吳志龍 [1], 葉致昌 [2], 張心怡 [1] [1] 國立嘉義大學生化科技系 , [2] 台中榮民醫院嘉義分院

中華民國細胞及分子生物學學會

時　間：102 年 3 月 24 日 (週日) 09:00-10:00
地　點：三樓，第 30 教室
主持人：楊瑞彬研究員 / 中央研究院生物醫學科學研究所

編號	時段	演講者 & 講題
O25	09:00-09:15	Deficiency of plasma SCUBE1, a novel platelet adhesive protein, impairs thrombus stabilization and protects mice against thrombosis 吳孟縈 ‡§, 林育嬋 ‡§, 廖偉如 ‡§, 楊瑞彬 § ‡ 國防醫學院生命科學研究所 , § 中央研究院生物醫學研究所 ¶ 國立陽明大學藥理學科暨研究所
O26	09:15-09:30	Domain Analysis and Functional Study of a Novel Platelet-Endothelial Surface Glycoprotein SCUBE1 廖偉如 [1,2] , 楊瑞彬 [1,2,3] [1] 中央研究院生物醫學研究所 , [2] 國防醫學院生命科學研究所 [3] 國立陽明大學藥理學科暨研究所
O27	09:30-09:45	GSK3beta-Mediated Drp1 Phosphorylation Induced Elongated Mitochondrial Morphology against Oxidative Stress 周佳樺 [1,2], 林敬智 [1], 楊明昌 [1,2,3], 許清玫 [2], 洪義人 [1,2,4 *] [1] 高雄醫學大學醫學系生化科 , [2] 中山大學生物科學系 , [3] 高雄國軍總醫院 [4] 高雄醫學大學醫學研究所
O28	09:45-10:00	Beta-nodavirus B2 Can Induce ROS Production that Affect the Mitochondrial Fragmentation and Necrotic Cell Death 蘇郁清 [1], 陳博榕 [1*], 吳金洌 [2], 洪健睿 [1] [1] 國立成功大學生物科技研究所 分子病毒與生物技術研究室 [2] 中央研究院細胞與個體生物學研究所 分子病毒與生物技術研究室

中華民國細胞及分子生物學學會

時　間：102 年 3 月 24 日 (週日) 13:45-15:45
地　點：三樓，第 30 教室
主持人：陳紀如副教授 / 陽明大學微生物及免疫學研究所
　　李心予教授 / 台灣大學動物所

編號	時段	演講者 & 講題
O29	13:45-14:00	Anterior Gradient 2: a Novel Tumor Marker Overexpressed in Metastatic Oral Carcinoma 陳怡婷 [1], 何中良 [1,2,3], 陳柏谷 [1], 陳玉玲 [1,4], 張權發 [*,1,3,5] [1] 國立成功大學基礎醫學研究所 , [2] 成大醫院病理部 , [3] 國立成功大學醫學檢驗生物技術學系 , [4] 國立成功大學口腔醫學研究所 , [5] 國立成功大學傳染性疾病及訊息研究中心
O30	14:00-14:15	Androgen Accumulation and Androgen Receptor Activation Involve in Aromatase Inhibitor-Suppressed Proliferation in Breast Cancer Cells 白家明 [1], 黃寶萱 [1], 黃振權 [1], 連傳岳 [1], 于家珩 [1,2], 李岳聰 [1,3], 林赫 [1*] [1] 台中中興大學生命科學系 , [2] 童綜合醫院 , [3] 彰化彰濱秀傳紀念醫院
O31	14:15-14:30	Cdk5 Regulates Cytoskeleton Organization and Src Activity and Affects Cancer Cell Motility 周敬唐 [1], 連傳岳 [1], 林育慶 [1,2], 林赫 [1#] [1] 中興大學生命科學系 , [2] 彰濱秀傳紀念醫院泌尿科
O32	14:30-14:45	The functional role of haptoglobin subunits on tumor metastasis in non-small cell lung cancer 林佳煒 , 陰冠言 , 黃薏寧 , 秦儷慈 , 陳文亮 國立交通大學生物科技學系
O33	14:45-15:00	Identification of A Small Molecule Enhancing Autophagic Clearance of Polyglutamine Aggregation 謝長亨 [1], 李麗卿 [1], 遊逸如 [1], 楊采禎 [1], 梁偉賢 [1], 李惠芳 [1], 姚清發 [2], 方剛 [1] [1.] 國立臺灣師範大學生命科學學系 , [2.] 國立臺灣師範大學化學學系
O34	15:00-15:15	Upregulation of Immune-related Genes during Luminal Clearance of the Mammary Gland 杜軍毅 , 李宜儒 中山醫學大學微生物免疫研究所
O35	15:15-15:30	Generation of Tolerogenic CD4+ T Cells by Bone Marrow-Derived IL-15Rα-/- Dendritic Cells 吳宗舜 , 吳甯甯 , 林士傑 長庚大學生物醫學系
O36	15:30-15:45	The Role of KLF2 in Autoimmune Crescentic Glomerulonephritis Model 李煜嬋* [1], 賈淑敏 [2], 花國鋒 [3], 張嘉銘 [4], 陳安 [1,5#] [1] 國防醫學院病理及寄生蟲研究所 , [2] 國防醫學院醫學系航太及海底醫學研究所 , [3] 國立宜蘭大學生物技術研究所 , [4] 財團法人生物技術開發中心 , [5] 三軍總醫院病理部

中華民國解剖學學會

時　間：102 年 3 月 23 日 (週六) 16:00-17:00
地　點：三樓，第 32 教室
主持人：龔秀妮 助理教授 / 台灣大學解剖學暨細胞生物學研究所

編號	時段	演講者 & 講題
O37	16:00-16:15	Cordycepin Shows in vitro and in vivo Potent Anticancer Activity on Testicular Cancer by Regulating Caspase, MAPK/ERK/JNK and p53 Signaling Pathways 潘博雄 [1,2], 黃步敏 [2] 國立成功大學 醫學院 基礎醫學研究所 [1] 國立成功大學 醫學院 細胞生物與解剖學研究所 [2]
O38	16:15-16:30	Extracellular Matrix Protein CCN1 Regulates Cardiomyocyte Apoptosis in Mice with Stress-induced Cardiac Injury 許佩玲 [*,1,2], 蘇柏全 [*,1,2], 郭倩妤 [2], 莫凡毅 [1,2] [1] 國立成功大學基礎醫學研究所 , [2] 國立成功大學細胞生物與解剖學研究所 , *
O39	16:30-16:45	C1GALT1 Promotes Invasiveness and Metastasis of Hepatocellular Carcinoma Cells via Integrin β1 Pathway 劉炯輝 , 吳耀銘 , 黃敏銓 國立台灣大學醫學院解剖學暨細胞生物學研究所
	16:45-17:00	Discussion

中華民國解剖學學會

時　間：102 年 3 月 24 日 (週日) 09:00-10:00
地　點：三樓，第 32 教室
主持人：龔秀妮 助理教授 / 台灣大學解剖學暨細胞生物學研究所

編號	時段	演講者 & 講題
O40		從缺
O41	09:00-09:15	Low-dose of Bisphenol A (BPA) Affects Steroidogenic genes in Placental JEG-3 Cell 楊智傑 , 林怡妏 , 藍心婕 國防醫學院生物及解剖學科
O42	09:15-09:30	LHX2 drives neural differentiation via transcriptional regulation of PAX6 and CER1 in hESCs 侯珮珊 [1], 莊靜玉 [2], 高承福 [3], 周申如 [3], 石力 [3], 何弘能 [4], 郭紘志 [2], 錢宗良 [1] [1] 臺大醫學院解剖所 , [2] 中央研究院基因體中心 , [3] 中央研究院細胞與生物研究所 , [2] 臺大醫院生殖與內分泌科
	09:30-10:00	Discussion

台灣生物化學及分子生物學學會

時　間：102 年 3 月 24 日 (週日) 13:45-17:05
地　點：三樓，第 33 教室
主持人：高銘欽 教授 / 中國醫藥大學生物科技系暨碩士班
　　李明學 副教授 / 國立台灣大學醫學院生物化學暨分子生物學研究所
　　陳佩燁 副研究員 / 中央研究院生物化學研究所

編號	時段	演講者 & 講題
O43	13:45-14:05	A novel cell-penetrating peptide derived from human eosinophil cationic protein 方韶瓏 [1], 范丹琪 [2], 傅化文 [1,3], 陳建榮 [1], 黃啟訓 [1,4], 洪達任 [1], 林立元 [1,3], 張大慈 [1,5] 清華大學 ,[1]分子與細胞科學研究所 , [3] 生命科學系 , [5] 醫學科學系 , 中研院 ,[2] 基因體中心北市聯合醫院忠孝院區 , [4] 神經內科
O44	14:05-14:25	SCUBE2, an Epigenetically Silenced Tumor Suppressor, inhibits Breast Cancer Invasion and Metastasis through Reversal of Epithelial-Mesenchymal Transition 林育嬋 [1,2], 鄭建睿 [3], 李宜靜 [4], 楊瑞彬 [1,2,5,*] [1] 國防醫學院生命科學研究所 , [2] 中央研究院生物醫學科學研究所 , [3] 臺北醫學大學附設醫院病理科 , [4] 國立清華大學分子醫學研究所 , [5] 國立陽明大學藥理學研究所
O45	14:25-14:45	Antibody Prophylaxis and Therapeutic Against Herpes Simplex Virus Infection in Wild-type and Immunodeficient Mice 艾麗霜 , 曾婉瑩 , 李岳錡 , 李世偉 , 蕭瑞綺 , 尤曉莉 , 賴建勳 財團法人生物技術開發中心
	14:45-14:55	Break 休息
O46	14:55-15:15	Targeting β-tubulin:CCT-β complexes incurs Hsp90 and VCP-related protein degradation and induces ER stress-related cell apoptosis via triggering capacitative Ca2+-entry, mitochondrial perturbation and caspase over-activation 林源峰 [1], 李亞菲 [2], 梁博煌 [1,2*] [1] 中央研究院 生物化學研究所 , [2] 國立台灣大學 生化科學所
O47	15:15-15:35	Myrciaria cauliflora extracts attenuate diabetic nephropathy in type II DM mice 施懿宸 [1], 黃惠珮 [1,2] [1] 中山醫學大學 生化暨生物科技研究所 , [2] 中山醫學大學 醫學院生物化學系
O48	15:35-15:55	Identification of DNA Methylation Biomarkers for Concurrent Chemoradiation Therapy Prediction and Development of DNMT Inhibitor in Esophageal Squamous Cell Carcinoma 黃鈺琳 [1], 郭懿瑩 [2], 王憶卿 [1,2*] [1] 國立成功大學藥理學研究所 , [2] 基礎醫學研究所
	15:55-16:05	Break 休息

O49 16:05-16:25 Disabled-2 is Required for Efficient Haemostasis and Platelet Activation by Thrombin in Mouse

蔡蕙如 [1], 黃千凌 [2], 黃鼎元 [2], 林忠慶 [2], 鄭如茜 [3], 曾慶平 [1,2,4]
[1] 長庚大學生物醫學研究所 , [2] 長庚大學醫學生物技術暨檢驗學系 , [3] 中國醫藥大學醫學檢驗生物技術學系所 , [4] 長庚大學分子醫學研究中心

O50 16:25-16:45 Zebrafish scube1 Is Involved in Primitive Hematopoiesis by Modulating Bone Morphogenetic Protein (BMP) Signaling

曹古驥 [1], 涂瀞芬 [1,2,3], 李士傑 [4], 楊瑞彬 [1,2,3]
[1] 中央研究院 生物醫學研究所 , [2] 中央研究院 生物醫學研究所 國際研究生學程 分子醫學學程 , [3] 國立陽明大學 生物化學與分子生物學研究所 , [4] 國立台灣大學

O51 16:45-17:05 An analysis of protein-protein interactions in cross-talk pathways reveals CRKL as a novel prognostic marker in hepatocellular carcinoma

劉家宏 [1], 陳咨錡 [2], 周嘉揚 [3], 冉毅驊 [4], 陳君厚 [5], 許鈞南 [6,7], 林冠廷 [8], 莊育棡 [9], 呂佩融 [10], 鄭惠娟 [10], 陳明晃 [2], 張佳棻 [11], 丁郁珊 [12], 高成炎 [1], 蕭宏昇 [4], 黃奇英 [2,8,11 *]
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中華民國毒物學學會

時　間：102 年 3 月 23 日 (週六) 14:00-15:45
地　點：三樓，第 34 教室
主持人：張正琪 副教授 / 國立台灣大學醫學院口腔生物科學研究所

編號	時段	演講者 & 講題
O52	14:00-14:15	Cholinergic-mediated Inflammation in Amygdala Underlies Organophosphate-induced Seizure in Rats 吳嘉琦 , 張雅雯 高雄長庚紀念醫院生物醫學轉譯研究中心
O53	14:15-14:30	Overexpression of Manganese Superoxide Dismutase and Glutathione Reductase Prevent Thioacetamide induced Edema in Pericardial Sac and Correlate with Mast Cell Activation during Zebrafish Development 劉雅菁 , 江柏蓉 , 耿全福 國立彰化師範大學生物技術研究所
O54		從缺
O55	14:30-14:45	Gold Nanoparticles Increases Blood-Brain Barrier Disruption through Down-Regulation of Tight Junction Proteins 詹晟 , 李青澔 , 廖伯霖 , 劉振偉 , 蔡季濠 , 康照洲 國立台灣大學醫學院毒理學研究所 , 台北醫學大學醫學院醫學系生理學科 台北醫學大學藥學院藥學系
O56	14:45-15:00	Hibiscus Sabdariffa Leaf Polyphenolic Extract Induces Apoptosis and Autophagy of Human Prostate Cancer Cells 林佳良 [1], 陳璟賢 [2], 黃貞榕 [1], 徐英華 [1], 林慧萱 [1] [1] 中山醫學大學醫學檢驗暨生物技術學系 , [2] 中山醫學大學營養學系
O57	15:00-15:15	Oct4-Mediated Transcription Deregulation in Lung Tumorigenesis and Drug Resistance 陳其欣 [1], 湯硯安 [2], 王憶卿 [1,2*] [1] 國立成功大學藥理學研究所 ,[2] 基礎醫學研究所
O58	15:15-15:30	Eugenol suppresses gastric tumor growth and peritoneal dissemination by increasing ER stress in an orthotopic model. 賴德偉 [1], 阿必勝 [3], 潘宏川 [1,4], 許美鈴 [1,2*] [1] 國立中興大學生物醫學研究所 ,[2] 台中榮民總醫院 ,[3] 艾默里大學醫學院 , [4] 國立陽明大學醫學院醫學系
O59	15:30-15:45	YYEI Motif Is Critical to Oncogenicity of 14-3-3 Proteins 張文馨 [1, 2] , 陳靜嫻 [2] , 洪啟盛 [1, 2], 陳健尉 [3] , 俞松良 [1, 2] [1] 台灣大學醫事檢驗暨生物科技學所 , [2] 台大基因體醫學研究中心 [3] 中興大學生物醫學所

O01

Nutrient deprivation induces the Warburg effect through ROS/AMPK-dependent activation of pyruvate dehydrogenase kinase.

Ching-An Wu[1]
Department of Pharmacology, College of Medicine, National Taiwan University

The Warburg effect is known to be crucial for cancer cells to acquire energy. Nutrient deficiencies are an important phenomenon in solid tumors, but the effect on cancer cell metabolism is not yet clear. In this study, we demonstrate that starvation of HeLa cells by incubation with Hank's buffered salt solution (HBSS) induced cell apoptosis, which was accompanied by the induction of reactive oxygen species (ROS) production and AMP-activated protein kinase (AMPK) phosphorylation. Notably, HBSS starvation increased lactate production, cytoplasmic pyruvate content and decreased oxygen consumption, but failed to change the lactate dehydrogenase (LDH) activity or the glucose uptake. We found that HBSS starvation rapidly induced pyruvate dehydrogenase kinase (PDK) activation and pyruvate dehydrogenase (PDH) phosphorylation, both of which were inhibited by compound C (an AMPK inhibitor), NAC (a ROS scavenger), and the dominant negative mutant of AMPK. Our data further revealed the involvement of ROS production in AMPK activation. Moreover, DCA (a PDK inhibitor), NAC, and compound C all significantly decreased HBSS starvation-induced lactate production accompanied by enhancement of HBSS starvation-induced cell apoptosis. Not only in HeLa cells, HBSS-induced lactate production and PDH phosphorylation were also observed in CL1.5, A431 and human umbilical vein endothelial cells. Taken together, we for the first time demonstrated that a low-nutrient condition drives cancer cells to utilize glycolysis to produce ATP, and this increases the Warburg effect through a novel mechanism involving ROS/AMPK-dependent activation of PDK. Such an event contributes to protecting cells from apoptosis upon nutrient deprivation.

O02

Autophagy Is Involved in The Cell Migration of Gefitinib-Resistant NSCLC Cells

Mei-Chuan Tang[a], **Ya-Ting Chang**[b], **Anya Maan-Yuh Lin**[b, c], **James Chih-Hsin Yang**[a,d]
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[b] Institute of Pharmacology, National Yang-Ming University, Taipei, Taiwan, ROC
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[d] Graduate Institute of Oncology, National Taiwan University, Taipei, Taiwan, ROC

Epidermal growth factor receptor-tyrosine kinase inhibitors (EGFR-TKIs) such as gefitinib and erlotinib are recommended as first-line treatment for nonsmall cell lung cancer (NSCLC) with EGFR mutations including deletions in exon 19 or L858R mutation but not wild type EGFR. However, most if not all NSCLC patients who responded to EGFR-TKI eventually develop acquired resistance after a median duration of 8-14 months. To study the mechanism of acquired resistance, gefitinib-resistant PC-9 (PC-9/gef) cells were established and these cells were 230-fold resistant to gefitinib than PC-9 lung adenocarcinoma cells (EGFR exon 19 deletion). The present study focused on the correlation of migration ability and autophagy activity in gefitinib-resistant cells. Migration of PC-9 and PC-9/gef cells was measured by wound healing and modified Boyden chambers. The LC3-II expression of PC-9 and PC-9/gef cells was detected by Western blotting. And the effects of autophagy inhibitors on the cell migration and LC3-II expression were also measured. Our data shows that PC-9/gef cells have higher migration ability and LC3-II levels, indicating elevated autophagy in PC-9/gef cells than PC-9 cells. Both si-RNAs and autophagy inhibitors decreased cell migration while RAD001, an mTOR inhibitor, increased cell migration of PC-9/gef cells, indicating that autophagy is involved in cell migration of PC-9/gef cells. Moreover, autophagy inhibitors and si-Atg7 RNA reduced cell migration induced by hypoxia. In vivo study is undergoing. These data indicate that autophagy may contribute to the metastasis of NSCLC cells and autophagy inhibitors may be therapeutically useful in the treatment of gefitinib resistant NSCLC cells.

Keywords: EGFR-TKI, autophagy, cell migration

O03

Establishment of Gefitinib and BIBW2992-Resistant Non-Small Cell Lung Cancer Cells

Cheng-Ta Chung[1, 2], **Kia-Chia Yeh**[1], **Chia-Huei Lee**[3], **Yiu-Kay Lai**[2], **Chiung-Tong Chen**[1]
[1]Institute of Biotechnology and Pharmaceutical Research, National Health Research Institutes
[2]Graduate Institute of Biotechnology, National Tsing-Hua University
[3]National Institute of Cancer Research, National Health Research Institutes

Lung cancer is the leading cause of cancer deaths worldwide and in Taiwan with a 5-year survival rate of approximately 15%. Epidermal growth factor receptor (EGFR) targeting is a valid and vital approach in development of therapeutics for patient with advance non-small cell lung cancer (NSCLC). Tyrosine kinase inhibitors, gefitinib and BIBW2992, are used to treat patients who harbor mutated EGFR leading to hyperactivation of down-stream MAPKs and ERKs signaling pathways. However, patients treated with gefitinib develop drug resistance over time through T790M mutation or MET amplification. Recent clinical trials indicated that BIBW2992 did not improve overall survival of patients previously treated with gefitinib. Therefore, to probe novel molecular targets and to search for new therapeutics for tacking NSCLC are warranted. We have established gefitinib and BIBW2992-resistant human lung cancer cell lines. Real-time PCR assay showed that the drug-resistant cells exhibit different degrees of c-MET amplification and loss of EGFR gene copy number. Combination of gefitinib or BIBW2992 with c-MET inhibitors remarkably increased their cell killing activity against the drug-resistant cancer cells. DNA microarray and protein profile analyses showed that a number of receptor tyrosine kinases were activated in these drug-resistant cells. A therapy using combined multiple kinase inhibitors is likely a promising regimen option as one of the first-line as well as second-line treatments for both naïve and kinase inhibitors-resistant lung cancers.

O04

To Investigate the Alterations of Histone Deacetylase 8 (HDAC8) in Breast Tumorigenesis and Its Application in Cancer Therapeutics

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[2] Graduate Institute of Pharmacognosy, Taipei Medical University, Taipei, Taiwan, R. O. C.

Backgrounds:
The overexpression of HDACs was considered to be a key factor contributing to tumorigenesis. We evaluated the functions and targets of HDAC8 and its association with clinical parameters.
Materials and Methods:
A novel semi-synthetic compound exhibiting HDAC inhibitory activity, along with HDAC8 siRNA, was used to evaluate the role HDAC8 in different breast cancer cell lines. RNA microarray was used to identify possible downstream targets of HDAC8, and results were later confirmed by real-time PCR and Western blotting. Cell migrations were measured by xCELLigence biosensor system, wound-healing, transwell assays. Cell apoptosis, DNA damages, and proliferation were evaluated by flow cytometry. Clinical samples from breast cancer patients were used to investigate correlations between HDAC8 abnormity, its downstream gene expressions, and clinical parameters.
Results:
Among all the semi-synthetic lovastatin derivatives, D compound exhibited the most promising inhibitory effect on HDAC8 activity and cell viabilities. D compound and HDAC8 siRNA inhibited the migration ability of MDA-MB-231 breast cancer cells by about 80% and 30% respectively. Analytical results from flow cytometry indicated that D compound had a potency of inducing apoptosis, DNA damage, and anti-proliferation in breast cancer cells by increasing cleaved PARP, H2AX, and decreasing BrdU signals respectively. Targets of D compound were elucidated by performing mRNA microarray, and the most elevated genes, such as IL-24, ULK1, and ATF3, were further confirmed by real-time PCR and Western blotting. The confirmation of interested genes, including HDAC8, in breast cancer patient tissues is now undergoing to conclude the correlations between gene expressions and clinical parameters.
Conclusion:
Our research revealed that HDAC8 expression level might be related to abnormal regulation of tumor-associated genes, and lovastatin derivatives may offer an additional opportunity in breast cancer therapeutics.

O05

A Novel DNA Methyltransferase Inhibitor, D-Antroquinonol, Inhibits The DNMT-1 Activity and Induces Anticancer Effects on Human Breast Cancer Cells

Sheng-Chao Wang[1], Tzong-Huei Lee Ph.D.[1], Chun-Hua Hsu Ph.D.[2], Yu-Jia Chang Ph.D.[3], Yi-Ching Wang Ph.D.[4], Wu-Che Wen Ph.D.[5] and Ruo-Kai Lin Ph.D.[1*]

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Backgrounds:

D-Antroquinonol is a novel compound isolated from Antrodia camphorate. To investigate whether the D-Antroquinonol is potent to inhibit the DNA methyltransferase-1 (DNMT-1) enzyme activity and reactivate the tumor suppressor genes (TSGs) by downregulating the promoter hypermethylation of TSG-associated CpG islands, and result in suppression of breast cancer cells growth and migration.

Materials and Methods:

D-Antroquinonol (3-Demethoxyl Antroquinonol) was identified by nuclear magnetic resonance. The drug targeting and anticancer effects of D-Antroquinonol to breast cancer cells (MDA-MB-231) were determined by the DNMT-1 enzyme activity assay, molecular modeling and docking, the Illumina Methylation 450K array-based assay, pyrosequencing, real-time RT-PCR, Western blotting. Cell cytotoxicity, growth inhibition and migration ability were also analyzed.

Results:

The D-Antroquinonol inhibited DNMT-1 in a dose-dependent manner. Molecular docking revealed that D-Antroquinonol was bound at catalytic domain of DNMT-1. The D-Antroquinonol decreased the methylation level of multiple TSGs, including the *FANCC* and *CACNA1A* genes, in MDA-MB-231 breast cancer cells. Western blot and RT-PCR analysis showed that D-Antroquinonol increased *FANCC, CACNA1A* mRNA and protein expression levels.

The SRB assay result indicated that D-Antroquinonol inhibits the growth of breast cancer cells (MDA-MB-231, MCF-7, T-47D, ZR-75-1) but not normal cells (H184B5F5/M10). The results of wound-healing assay and transwell assays suggested that D-Antroquinonol inhibits the migration of MDA-MB-231 breast cancer cells.

Conclusion:

We identified a novel DNMT inhibitor, D-Antroquinonol, which induced DNA demethylation, recovered the expression of multiple tumor suppressor genes, and inhibited cancer cell growth and metastasis.

O06

Calanquinone A Displays Anticancer Activity through Depletion of Cellular Glutathione in Human Glioblastoma

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Glioblastoma, also called grade IV astrocytoma, is the most common malignant primary brain tumor. Calanquinone A, a hydrophobic nature product derived from *Calanthe arisanensis*, has been reported to display antiproliferative activity in several cancer cell lines including human non-small cell lung cancer A549, hormone-refractory prostate cancer PC-3 and DU145, colorectal adenocarcinoma HCT-8, breast cancer MCF-7 and oral squamous carcinoma KB cell lines. However, the anticancer mechanism has not been identified. In this study, cell growth of three glioblastoma cell lines, A-172, T-98, and U-87, was inhibited by Calanquinone A. After releasing from thymidine block, the progression of cell cycle from synchronized cells was detected. As a result, calanquinone A induced S-phase arrest of the cell cycle. A short-term exposure to calanquinone A (1 h) triggered the production of reactive oxygen species (ROS) and induction of DNA damage. Interestingly, N-acetyl-cysteine (NAC) but not trolox inhibited ROS production and DNA damage. Further identification showed that calanquinone A significantly reduced the level of cellular glutathione. Western blot analysis showed that Chk-1, a DNA damage related protein, was activated after calanquinone A treatment, confirming the DNA damage activity. *In vivo* complex of enzyme (ICE) assay revealed that calanquinone A showed low topoisomerase poison ability. Taken together, the data suggest that calanquinone A is a potential anticancer agent against glioblastoma through the reduction of cellular glutathione, leading to DNA damage response and an arrest of cell cycle at S phase. The data also reveal that manipulation of cellular glutathione may be a new strategy for anticancer drug development.

O07

The Anticancer Effect of Extracts from Mycelium of Antrodia camphorate in Non-Small Cell Lung Cancer Cell Line.

Yi-Ting Yen[1], Tzong-Huei Lee Ph.D.[1], Chun-Hua Hsu Ph.D.[2], Wu-Che Wen Ph.D.[5]and Ruo-Kai Lin Ph.D.[1*]

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Backgrounds: Lung cancer is the leading cause of mortality in both men and women worldwide. Lung cancer can be divided into two major histopathological group : small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC). About 80% of patients are non-small cell lung cancer. Antroquinonol and D-antroquinonol were isolated from Antrodia camphorate, and antroquinonol has been reported to have antitumor effects against various cancer cells. The aim of this study was to investigate the mRNA expression level of multiple tumor suppressor genes in non-small cell lung cancer cell lines and to analyze them associated with cell viability and migration ability after treated with D-antroquinonol or antroquinonol.

Materials and Methods: The cell viability was assessed in lung cancer cells CL1-5, H1299 and A549 and normal lung call IMR90 by SRB assay. The cell migration ability was performed by wound-healing assay and transwell assay. Cell proliferation assay was performed by BrdU staining and analyzed by Flow Cytometry assay. The mRNA expression level was measured by a real-time quantitative PCR system using the *GAPDH* gene as an internal control in lung cancer cell line.

Results: The mRNA expression level of tumor suppressor genes, *CCND2* and *FOXN3* genes was up-regulated after treating with the extracts. The *CCND2* gene showed 20 fold increase in expression level after treated with D-antroquinonol in CL1-5, and in H1299 cell line, this gene showed 7 fold increase in expression level after treated with antroquinonol. The *FOXN3* gene showed 2.7 fold increase in expression level after treated with Antroquinonol in CL1-5, and in H1299, this gene showed 1.7 fold increase in expression level after treated with Antroquinonol. The transwell assay indicated that, CL1-5 cell migrated to the lower side of the filter was decreased about 90% and 70% after treated with D-antroquinonol and antroquinonol respectively. The extracts-treated wounds were found to heal slower than the control group. The index for BrdU-labeled cells decreased 18% and 15% after treating with D-antroquinonol and antroquinonol respectively.

Conclusion: Both D-antroquinonol and antroquinonol have abilities of inhibiting cancer cell growth, metastasis and recovered the expression of multiple tumor suppressor genes.

O08

In vitro and *in vivo* Effects of Xanthorrhizol on Human Breast Cancer MCF-7 cells treated with Tamoxifen

Nattanant Noomhorm[1], Chun-Ju Chang[2], Jiun-Liang Chen[1,3], Jen-Hwey Chiu[1,4,5], Ling-Ming Tseng[4], Yi-Ming Shyr[4]

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[5]Research Center for Traditional Medicine, Taipei Veterans General Hospital;

Aim of study:

The aim of this study was to investigate the herb-drug interaction of xanthorrhizol on human breast cancer MCF-7 cells treated with tamoxifen.

Materials and Methods:

By using human breast cancer MCF-7 cell line (ER+, HER2 low) as *in vitro* model, the herb-drug interaction between xanthorrhizol and tamoxifen were measured by MTT, Trypan Blue dye exclusion assay, luciferase reporter assay and cell cycle analysis. The effects of xanthorrhizol on growth related and autophagy-related signaling were determined by Western blot and real time RT-PCR and Immunostain, respectively. Moreover, effects of xanthorrhizol on MCF-7 implanted athymic nude mice treated with tamoxifen were also evaluated.

Results:

The results showed that xanthorrhizol concentration-dependently (0.3μM ~ 3μM) stimulated the cell growth of MCF-7 cells, while there was no significant changes, in terms of cell number by MTT, luciferase activity, percentage of S+G2M fraction by cell cycle analysis, growth related signaling by Western blot and real-time PCR, when cells were co-treated with tamoxifen and xanthorrhizol, compared to treatment with tamoxifen alone. However, in MCF-7 implanted nude mice model, there was an increased tumor volume and tumor weight in Xanthorrhizol + Tamoxifen group compared to Tamoxifen alone group. The effects of xanthorrhizol on tamoxifen-induced autophagy will be discussed.

Conclusion:

We conclude that there was no evidence of xanthorrhizol-tamoxifen interaction in cell culture system, but growth interference could be noticed in chronic use of xanthorrhizol in tamoxifen-treated MCF-7 implanted nude mice, which provide important information when treating patients with receptors positive breast cancers.

Key words:

breast cancer, tamoxifen, xanthorrhizol, interaction, herbs

O09

Effects of Chinese Herbal Extracts on *ERBB2* and *ESR1* Gene Expression in Human Breast Cancer MCF-7 Cell Line.

Hui-Ju Liu[1], Chun-Ju Chang[2], Jiun-Liang Chen[1,3],Jen-Hwey Chiu[1,4,5], Wei-Chi Huang[3], Yu-Tzu Huang[4], Ling-Ming Tseng[6], Yi-Ming Shyr[6].
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Aim of study:
The aim of this study was to establish a rapid screening platform to screen Chinese medicine herbs on *ERBB2* and *ESR1* gene expression in MCF-7 cells.
Materials and Methods:
Using MCF-7 human breast cancer cell line, luciferase reporter assay was established by transient transfection of plasmids containing *ERBB2* or *ESR1* promoter region and luciferase gene. Effects of Chinese herbal extracts (CME), including 27 single herbs and 5 compound recipes, were treated 48 h after transfection, followed by detection of luciferase activity. The screened results were verified by Western blot and real-time PCR for ERBB2 and ESR1 gene expression, respectively. Antibodies against HER2, ERα, P27KIP1, ERK, AKT and P38 were used to detect the effects of Chinese medicinal herbs on growth-related proteins expression in MCF-7 cell line
Results:
Under little cytotoxicity of CHE treatments, 13 single herbal extracts (dose ranges from 0.1μg/mL to 10μg/mL) and 1 compound recipe (dose range from 0.1μg/mL - 1μg/mL) were demonstrated to increase the *ERBB2* or *ESR1* luciferase activities. Analyzed by Western blot, extracts of Si-Wu-Tang, Jia-Wei-Xiao-Yao-San, K'uan-Hsin-Yin, and Suan-Zao-Ren-Tang increased HER2 but not ERα protein expression. The effects of CHE on growth-related signal pathway will be discussed.
Conclusion:
We conclude that a rapid screening system for investigation of effects of CME on ERBB2 and ESR1 gene expression has been established and the results provide important information for clinical treatment strategy in breast cancer patients receiving hormonal- or target therapy
Key words:
breast cancer, luciferase reporter, ERBB2, ESR1, herbs

O10

CC-36, an asymmetrical 1,2-disubstituted amide-linked anthraquinone derivative, inhibits proliferation of hormone-refractory prostate cancer cells through LKB1-AMPK-mTOR pathway

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[2]Graduate Institute of Life Sciences, National Defense Medical Center, Taiwan.

Hormone-refractory prostate cancer (HRPC), which is metastatic and resistant to hormone therapy, is an intractable problem in clinical treatment. CC-36, N-(2-(2-(((1,3-dioxolan-2-yl)methyl)(methyl)amino)acetamido)-9,10-dioxo-9,10-dihydroanthracen-1-yl)-4-methylbenzamide, displayed antiproliferative activity in PC-3, a metastatic HRPC cell line, with a GI_{50} value of 8.64 μM and presented a ten-fold higher potency in PC-3 than that in H9c2 cardiomyoblasts and in normal prostate cells. CC-36 treatment caused G1 arrest of cell cycle, supported by up-regulation of p21 and down-regulation of cyclin D1 and E expression. Co-immunoprecipitation assay showed that CC-36 enhanced the level of TSC1/TSC2 association, leading to inhibition of protein phosphorylation including mTOR (Ser2448), p70S6K (Thr421/Ser424 and Thr389) and 4E-BP1 (Thr37/Thr46 and Thr70), and subsequently affected the initiation and elongation of protein translation by ribosomal profiling analysis. Furthermore, CC-36 quickly induced LKB1 (Liver kinase B1) phosphorylation at Ser428, which caused LKB1 translocated from nucleus to cytosol for AMPK activation. Moreover, compound C (a selective AMPK inhibitor) significantly inhibited CC-36-mediated inhibition of mTOR signaling, suggesting the central role of LKB1-AMPK pathway to CC-36 action. In spite of anticancer potential, CC-36 also simultaneously triggered an increase of Akt activity which might counteract the anticancer effect. Accordingly, a combination treatment of MK226 (a specific AKT inhibitor) with CC-36 was used and the data demonstrated a dramatic apoptosis. Taken together, the data suggested CC-36 displayed anticancer activity through the activation of LKB1-AMPK pathway, leading to inhibition of mTOR signaling and the induction of G1 arrest of the cell cycle. Furthermore, the combination use of CC-36 and Akt inhibitors may be a potential strategy for HRPC treatment.

O11

Angiotensin II Type I Receptor-Mediated Oxidative Stress in Rostral Ventrolateral Medulla Underlies the Elevated Blood Pressure after Stroke

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Center for Translational Research in Biomedical Sciences, Kaohsiung Chang Gung Memorial Hospital

Background:
Stroke is a major health problem throughout the world and the elevated blood pressure (BP) after stroke is a common complication associated with poor outcome. The underlying mechanism of elevated BP after stroke is less understood. Concerning the incredible roles of angiotensin II (Ang II) and rostral ventrolateral medulla (RVLM) in central regulation of BP, the present study delineated the role of Ang II type I receptor (AT1R) in RVLM contributing to the elevated BP after transient stroke.
Materials and Methods:
The stroked Sprague-Dawley rats received 2-hours left middle cerebral artery occlusion (MCAO) processes under anesthesia and the BP were measured by tail-cuff in conscious conditions before and 24-hours after stroke. The levels of Ang II, AT1R mRNA or protein and superoxide and the activities of NADPH oxidase (Nox) and mitochondria in RVLM were determined by ELISA, RT-PCR or chemiluminence method.
Results:
The stroked rats with elevated BP was observed at 24 hours after MCAO, accompanied by an increase of the amount of Ang II and the mRNA or protein levels of AT1R in RVLM. Moreover, the elevated BP, increased superoxide levels, augmented Nox activity or decreased mitochondrial activities in RVLM at 24 hours after stroke were significantly reduced by bilateral microinjection of AT1R antagonist candesartan (5 nmol), Nox inhibitor apocynin (10 nmol) or mitochondrial superoxide anion scavenger mitoTEMPO (500 pmol) into RVLM immediately after MCAO.
Conclusion:
We concluded that the AT1R-mediated oxidative stress in the RVLM plays a critical role in the elevated BP after stroke.

O12

Gabapentin Enhanced Periaqueductal Gray and Suppressed Insular Cortex Glucose Metabolism in Conscious Rats with Neuropathic Pain: a PET Study

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[2]Department of Anesthesiology, National Taiwan University Hospital, Taipei, Taiwan

Backgrounds:
Gabapentin is known to suppress neuropathic pain on primary afferents and spinal cord dorsal horn. However, its supra-spinal mappings are lacking. Positron emission tomography (PET) allows a freely movable period when behavioral parameters could be measured followed by scanning under anesthesia. This study is designed to identify various brain region where gabapentin suppresses the neuropathic pain, especially the allodynia condition.
Materials & Methods:
Spared nerve injury (SNI) of the sciatic nerve of the rat was used as the neuropathic pain model. Mechanical allodynia was verified using von Frey filaments test. Fluoro-deoxyglucose-positron emission tomography (FDG-PET) scanning was performed to measure the change of glucose metabolism in the rat brain before and after gabapentin (100 mg/kg, i.p.) treatment. The PET imaging data were analyzed by statistical parametric mapping. The significant results were displayed on t-value maps.
Results:
Three days after SNI surgery, the rats showed apparent and sustained neuropathic pain behavior. For PET scanning, during the FDG uptake period, mechanical stimulation caused enhanced hindpaw withdrawal frequency, and gabapentin treatment reversed the behavioral sensitization. Comparing the PET imaging data before and after the gabapentin treatment, contralateral insular cortex (IC) showed decreased glucose metabolic rate, and periaqueductal gray (PAG) exhibited increased glucose metabolic rate. Immunostaining of pERK in the IC showed similar decrease by gabapentin.
Conclusion:
Our results indicate that gabapentin analgesia may be produced by an activation of the PAG descending pain modulation system and a suppression of nociceptive IC area.

O13

Alcohol Consumption Aggravates Hematomal Hemolyses and Inflammations in Brain Injuries Caused by Intracerebral Hemorrhage in Rats

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Purpose: To investigate whether alcohol consumption may aggravate hematomal hemolyses and neural inflammations in brain injuries induced by intracerebral hemorrhage (ICH) in rats.
Materials & Methods: Rats were subjected to ICH (intrastriatal infusion of collagenase, 0.23 U in 1 μl saline over 5 minutes) at 1 hour after intraperitoneal injection of ethanol (3 g/kg) or normal saline. Accumulative mortality rate, body weight changes, and motor-sensory and neurological deficits were evaluated. The hemorrhagic, hematoma, and brain edema volumes were determined with Drabkin's assay, morphometric and water content measurement on day 1 after ICH, respectively. The magnetic resonance imaging technique was used to evaluate the cerebral perfusion volume. Immunohistochemical staining for glutathione peroxidase, malondialdehyde, and in situ O2- production were used to evaluate the oxidative stress. The OX-42 immunohistochemical staining was done to assess the neuroinflammation.
Results: As compared with the saline injection, alcohol injection resulted in increases of mortality rate and motor sensory deficits in ICH rats. These increases were accompanied with more enlarged hemorrhagic, hematoma and cerebral edema volumes. Alcohol injection in addition caused more activated microglia cells around hematoma lesions, and increased production of reactive oxygen species (ROS) and activities of glutathione peroxidase around perihematomal brain tissue. Further immunohistochemical staining implicated ROS accumulated in neuronal, microglia, and vascular endothelial cells. The alcohol injected ICH rats exhibited more reduction of cerebral perfusion in perihematomal brain tissue after ICH.
Conclusion: Alcohol consumption aggravated the severity of brain injury by inducing excessive oxidative stress and neuroinflammation after ICH. Targeting on anti-ROS production and neuroinflammation can be a novel preventive approach to reduce the alcohol-exacerbation ICH injury.

O14

Molecular Mechanism of Curcumin on the Suppression of Cholesterol Accumulation in Macrophage Foam Cells and Atherosclerosis

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Purpose:
Curcumin, a potent antioxidant extracted from Curcuma longa, confers protection against atherosclerosis, yet the detailed mechanisms are not fully understood. In this study, we examined the effect of curcumin on lipid accumulation and the underlying molecular mechanisms in macrophages and apolipoprotein E-deficient (apoE$^{-/-}$) mice.
Materials and Methods:
J774.1 macrophage and apoE$^{-/-}$ mice were used as our *in vitro* and *in vivo* experimental models, respectively.
Results:
Treatment with curcumin markedly ameliorated oxidized low-density lipoprotein (oxLDL)-induced cholesterol accumulation in macrophages, which was due to decreased oxLDL uptake and increased cholesterol efflux. In addition, curcumin decreased the protein expression of scavenger receptor class A (SR-A) but increased that of ATP-binding cassette transporter (ABC) A1 and had no effect on the protein expression of CD36, class B receptor type I (SR-BI), or ATP-binding cassette transporter G1 (ABCG1). The downregulation of SR-A by curcumin was via ubiquitin–proteasome–calpain-mediated proteolysis. Furthermore, the curcumin-induced upregulation of ABCA1 was mainly through calmodulin-liver X receptoraα (LXR α)-dependent transcriptional regulation. Curcumin administration modulated the expression of SR-A, ABCA1, ABCG1, and SR-BI in aortas and retarded atherosclerosis in apoE$^{-/-}$ mice.
Conclusion:
Our findings suggest that inhibition of SR-A-mediated oxLDL uptake and promotion of ABCA1-dependent cholesterol efflux are two crucial events in suppression of cholesterol accumulation by curcumin in the transformation of macrophage foam cells.

O15

Differential Nociceptive Coding Ability of Medial and Lateral Thalamus during Different Brain States

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Backgrounds:
Pain sensation under different brain states, such as wake and drowsy, may differ. Thalamic nuclei lied in medial and lateral pain pathways have been reported could encode laser intensities. However, little is known about their coding ability changes between wake and drowsy states.
Materials and Methods:
We used ten rats implanted at both medial and lateral thalamus. We used 4 laser intensities, from non-painful to painful, to evaluate stimulus-response function (SRF) of thalamic neurons. Coding ability was defined as linear slope of the SRF. Brain states were identified by frontal EEG.
Results:
We first identified laser-evoked responses under light isoflurane anesthesia. Lateral thalamus had fast and slow responses with latency of 0.02-0.1 s and 0.25-0.6 s after laser pulse, respectively. Medial thalamus had one slow response with latency of 0.3-1 s. During wake condition, the fast response of lateral thalamus was less obvious. The slow response of lateral and medial thalamus became dominated and prolonged. The slow response of either lateral or medial thalamus encoded laser intensities. The coding ability of lateral thalamus was greater than that of medial thalamus. During drowsy condition, lateral thalamic neurons remained the same coding ability. In contrast, medial thalamic neurons showed enhanced coding ability.
Conclusion:
The differential coding ability of lateral and medial thalamus implies more flexibility of the medial pain pathway during different brain states. The enhanced response of medial thalamus also implies an alarm function.
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O16

The functional role of TYRO3 in colorectal cancer progression and metastasis

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Colon cancer is a multiple-step disease with less 10% survival rate at late stage. To achieve improvement of colon cancer therapy, we aim to find novel oncogenes that may contribute to colon cancer progression. By our in-house bioinformatic tool prediction, we identified TYRO3 to be a potential oncogene. TYRO3, a receptor tyrosine kinase, was reported to be overexpressed in melanoma via genomic screening; however, its role in cancer initiation, progression, and malignancy remains largely unknown. Herein, we showed that compared to normal colon tissue, TYRO3 is overexpressed in polyps and colon cancer tissue. The expression level in colon cancer is significantly associated with cancer malignancy. In immunofluorescence staining results, we demonstrated that the central region and C-terminal domain of TYRO3 can translocate to the nucleus. Mutating nuclear localization signal of TYRO3 inhibited TYRO3 translocation to nucleus and induced cell apoptosis, suggesting that TYRO3 performs important biological function in nucleus. We further demonstrated that overexpression of TYRO3 increased cell proliferation, motility, and anchorage-independent colony formation *in vitro*. Furthermore, we confirmed TYRO3 tumorigenic potential by xenograft model and metastatic assay *in vivo*. To verify novel mechanism mediated by TYRO3, we performed next generation sequencing to identify genes that were upregulated under TYRO3 overexpression. Results showed that TYRO3 significantly enriched genes involved in epithelial-mesenchymal transition and tumorigenesis, which is consistent with our hypothesis and finding. Taken together, these data provide strong evidence to support that TYRO3 plays an important role in malignant process of colon cancer progression likely through its novel functions in the nucleus.

O17

The Novel Tubulin Inhibitor, MPT0B098, Inhibits Stat3 Pathway and Induces Apoptosis via up-regulation of SOCS3 in Oral Cancer Cells

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MPT0B098 is a novel synthetic compound that was identified as a tubulin inhibitor in tumor cell lines. Disruption of tubulin-microtubule equilibrium can induce cell cycle arrest and ultimately lead to apoptosis. However, a major disadvantage of these type of anticancer drug is the loss of efficacy eventually because of the development of drug-resistant. Therefore, it is urgent to develop new drugs or combination therapies to combat drug-resistant. Stat3 is one of the transcription factors that play an important role in tumor cell growth, survival, proliferation, differentiation, apoptosis, metastasis, angiogenesis and drug resistance. In our preliminary results, we found that MPT0B098 inhibited cell proliferation in a dose- and time course-dependent manner in oral cancer cell lines (OEC-M1 and HSC-3). In addition, treatment with MPT0B098 induced growth inhibition, cell cycle arrest in G2/M phase and apoptosis in oral cancer cell lines. We are found MPT0B 098 induced apoptosis with cleavage of caspases 3 and down-regulate anti-apoptosis protein (Mcl-1, Bcl-2, Bcl-x, Survivin). We uses confocal microscopic investigation of tubulin, confirm the truth of MPT0B098 inhibits the polymerization of microtubules. Importantly, we also found MPT0B 098 reduced JAK/Stat3 pathway via regulate SOCS3. Collectively, we found that MPT0B098 inhibits JAK/Stat3 via SOCS3 promoting ubiquitination and degradation of TYK2 and JAK2. SOCS3 may be a potential therapeutic target for MPT0B098 treatment. Upon these results, we demonstrate this tubulin inhibitor, MPT0B098, may represent a potential therapeutic drug for the treatment of cancer disease.

O18

PKC412, an Oral Small-molecule Multi-kinase Inhibitor, Induces a Unique Cell Death Mode in Human Oral Squamous Carcinoma Cells

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Background:
PKC412 is an oral small-molecule multi-targeted tyrosine kinase inhibitor targeting PKC, VEGFR2, FLT3, PDGFR and KIT. We previously reported that PKC412 induced megakaryocytic differentiation of chronic myeloid leukemia cells and deviated dendritic cell maturation toward tolerogenic phenotype. This study was to investigate the effect of PKC412 on human oral squamous cell carcinoma (OSCC) cells.
Methods:
Human OSCC SAS and OECM-1 cells kept in exponential growth were treated with PKC412. Experimental assays included MTT for viability, BrdU uptake for cell proliferation, Liu stain for morphological observation, immunofluorescence for mitotic spindle polarization and centrosome amplification, DNA histogram for cell cycle and ploidy analysis, Western blotting for signaling molecules.
Results:
PKC412 inhibited the viability of SAS cells in a dose- and time-dependent manner with estimated IC_{50} at 1 nM. Cell proliferation was also suppressed. PKC412 induced development of giant multi-nucleated cells accompanied with multiple polarization of mitotic spindles and amplification of centrosomes. DNA histogram showed increase in populations of hypoploid (sub-G1), G2/M arrest and hyperploid of SAS cells, suggesting a unique and combinatory mode of cell death. Expression of signaling molecules involving both intrinsic and extrinsic apoptotic pathways was modulated by PKC412, such as downregulation of Bax, activation of caspases 3, 8 and 9 as well as cleavage of PARP.
Conclusion:
PKC412 inhibited viability and proliferation of human OSCC cells. Combination of cell-cell fusion, mitotic arrest, aneuploid development and apoptosis was postulated as a unique mode of cell death induced by PKC412.

O19

Characterization of the Putative Oncogene *UBE1C* and Its Relationship with p53 in Lung Cancer

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Backgrounds:
NEDDylation is one of posttranslational modifications. Our previous array-comparative genomic hybridization study showed that *UBE1C*, which encodes NEDDylation E1 enzyme, is highly amplified in both Taiwanese and Caucasian lung cancer patients. To date, there are just a few proteins, including the tumor suppressor p53, had been reported as NEDDylation substrates. However, the effects of NEDDylation of 53 remain largely unknown.
Materials and Methods:
The mRNA expression and mutation of *UBE1C* gene was examined in patients. Expression of p53 downstream genes in cells manipulated for *UBE1C* expression was examined by qRT-PCR. The cell proliferation was examined by trypan blue exclusion and colony formation assays. The NEDDylated p53 was investigated by western blot analysis.
Results:
Our results showed that *UBE1C* mRNA was overexpressed in 46.8% (44/94) lung cancer patients. Some mutations were also found in patients. Accordingly, protein level of UBE1C was higher in lung cancer cells than that of normal lung cells. Knockdown of UBE1C in lung cancer cell H460 showed that p53 regulated genes, such as cell cycle controller p21 and apoptosis protein Fas, were activated both in mRNA and protein levels, thus leading to poor cell proliferation. In contrast, overexpression of UBE1C resulted in down-regulation of p53 regulated genes, which in part was mediated by an increase of acetylation level of lysine 382 at p53 C-terminal region.
Conclusion:
Our findings suggest that *UBE1C* is a novel oncogene in lung cancer and overexpression of NEDDylation E1 enzyme-UBE1C downregulates p53 transcriptional activity through acetylation of p53 on lysine 382 residue.

O20

Role of thymidine phosphorylase and Rad51 in HSP90 inhibition induced cytotoxic effect in non-small-cell lung cancer cells

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Elevated expression of thymidine phosphorylase (TP), a key enzyme in the pyrimidine nucleoside salvage pathway, are associated with an aggressive disease phenotype and poor prognoses. Repair protein Rad51 is involved in protecting non-small lung cancer (NSCLC) cell lines against chemotherapeutic agent-induced cytotoxicity. This study investigated the role of TP and Rad51 expression in heat shock protein 90 (HSP90) inhibitor 17-allylamino-17-demethoxygeldanamycin (17-AAG)-induced cytotoxicity in NSCLC cell line, A549. The 17-AAG treatment decreased cellular TP and Rad51 protein and mRNA levels and phosphorylated MKK1/2-ERK1/2 and AKT protein levels. Specific inhibition of TP and Rad51 expression by siRNA further enhanced 17-AAG-induced cytotoxicity and growth inhibition. Furthermore, enhancement of ERK1/2 or AKT activation by transfecting the cancer cells with constitutively active MKK1/2 or AKT expression vectors significantly restored the 17-AAG-reduced TP protein levels as well as cell viability. The 17-AAG treatment disrupted the interaction between HSP90 and TP or HSP90 and Rad51, and triggered these two proteins degradation through the ubiquitin-26S proteasome pathway. The U0126 (a MKK1/2 inhibitor) or LY294002 (a PI3K inhibitor) treatment decreased the TP expression and cell viability induced by 17-AAG. Moreover, 17-AAG enhanced the cisplatin-induced cytotoxic effect through downregulation of the cisplatin-induced TP expression and ERK1/2 and AKT activation. Our results suggested that the down-regulation of TP and Rad51 protein by 17-AAG represents a key factor in enhancing the cytotoxic effects in NSCLC cells.
Key words:
HSP90; thymidine phosphorylase; Rad51; cytotoxicity; non-small cell lung cancer.

O21

The quantitative analysis for a synthetic autoregulatory circuit

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Graded tunable expression is often required for quantitatively characterizing the roles of a gene in microbial physiology and metabolism. One devious limitation of current available gene expression systems is that they respond to the inducers in a narrow range, often in nearly all-or-none fashion. Our theoretical modeling suggests that the all-or-none response may be converted to a graded rheostat-like response by negative autoregulation. To test this prediction, we developed a tunable autorepression circuit, using a synthetic *tet* promoter driving expression of *tetR* (encoding the *tet* repressor protein) and expression of a reporter gene. The system was shown to respond in a graded-manner (Hill coeff = 1) to a wide-range of the inducer chloro-tetracycline (cTc) in Escherichia *coli*, compared to a very abrupt response (Hill coeff > 4) in a control strain in which tetR was constitutivly expressed. As one application, we used this regulatory system to control expression of *gdhA* encoding glutamate dehydrogenase (GDH). In a strain deleted of Glutamate Synthase (GOGAT) so that GDH provides the only pathway to assimilate ammonia, we showed that the growth rate of the strain could indeed be tuned continuously over a wide range by varying cTc levels in media with ammonia as the sole nitrogen source. Our construct provides a simple mock chemostat which allows us to probe various aspects of the nitrogen metabolic pathway. It also sheds light on possible functional roles of the negative autoregulatory feedback motifs controlling a large number of biosynthetic operons in bacteria.

O22

Effect of Low Intensity Pulsed Ultrasound (LIPUS) *on Ex Vivo* Expansion of Hematopoietic Stem Cells

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Backgrounds:
Low intensity pulsed ultrasound (LIPUS) is a form of mechanical wave that has been commonly used to enhance bone regeneration for therapeutic applications. To evaluate the effects of LIPUS on HSCs, we have applied multiple ultrasound intensities on cord blood-derived hematopoietic stem cells (HSCs) in serum (BGS-containing) and serum-free system (SF-HSC).
Materials and Methods:
The LIPUS intensities range from 30~80 mW/cm2 were applied on the HSCs culture for 4 days. The cells were then continuously cultured for another 3 days. The stimulation frequency was 10 minutes per day. The expanded cells were analyzed by FACS using flow cytometry and methylcellulose-based colony forming medium to evaluate the hematopoietic potency.
Results:
The results showed that hematopoietic CD34+ cells were increased 140% with the optimal intensity of 60 mW/cm2 in BGS-containing expansion medium compared to the untreated control. However, there was no further enhanced effect in SF-HSC system. Interestingly, the methocult analysis showed both positive effects with LIPUS stimulation compared to the untreated control. Based on the FACS analysis, most cells cultured in SF-HSC system were the long-term HSCs, which expressed the surface antigen CD34+/CD38-; however the cells in BGS-containing culture system were presumed as short-term HSCs, which expressed CD34+/CD38+.
Conclusion:
LIPUS stimulation can enhance the CB-HSCs proliferation and promote the hematopoietic potency. The novel LIPUS stimulation approach on HSCs may enhance the efficacy of clinical transplantation and cellular therapies in the future.

O23

Characterizing the interaction of neuron and glia by electroretinogram

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Neurodegenerative diseases have been intensively studied. An increasing body of evidence shows that glia played an important role in the progression or propagation of neurodegeneration pathology. Nonetheless, the molecular mechanism of the crosstalk between neuron and glia is still unclear or under debate. Fly retina, a very regular and well organized structure, has been utilized to study neural diseases. In addition, electroretinogram (ERG) can diagnose very subtle deficit before the photoreceptor neurons completely lose their function or die. Taking advantage of this system, we attempted to investigate the interaction between neuron and glia. We found that expression of several polyglutamine-expanded proteins exclusively in glial cell resulted in reverse ERG signal without apparent morphological and anatomical deficit. Conversely, expressing these in retina did not cause acute neuronal deficit, suggesting that glia cells, instead of neurons, are more vulnerable to these polyglutamine-expanded proteins. These data gives a new vista to explore the effect on neuronal function by manipulating the surrounding glia. This tool will facilitate us into underlining the pathological mechanism of human neurodegenerative disorders.

O24

The Application of Curcumin-loaded Liposomes on Osteoporosis Treatment

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Curcumin(diferuloylmethane) is a non-water-soluble polyphenol compound that has anti-inflammatory potential. Recent studies found that curcumin can reduce the osteoclastogenic activity for preventing bone loss.

Osteoporosis is a skeletal disease due to an imbalance between bone resorption and bone formation. Osteoprotegerin (OPG) and RANKL have been shown to play important roles in bone remodeling.

To increase cellular uptake of curcumin, we used soybean phosphatidylcholine to encapsulate curcumin for liposome formation. In this study, curcumin-loaded liposomes have been characterized in particle size, encapsulation efficiency, liposome stability and cellular uptake. To study the effect of curcumin-loaded liposomes in vitro, lipopolysaccharide and RANKL were added to induce osteoclastogenesis in rat macrophage (RAW264.7) and 50 μg/ml ascorbic acid and 10 mM β-glycerol phosphate were added to stimulate mouse osteoblast-like cells (7F2) differentiation. Besides, we used IL-1β to induce 7F2 cell inflammation to investigate the anti-inflammatory activities of curcumin-loaded liposomes.

The results show that there are about 70% entrapment efficiency of curcumin in liposomes and particle sizes are stable after liposome formation. Curcumin-loaded liposomes can inhibit macrophage inflammation and differential activities. In comparison with curcumin only, curcumin-loaded liposomes have no significant cytotoxicity and can remain the osteoblast differential functions. With IL-1β stimulation, curcumin-loaded liposomes can successfully down-regulate the expression of inflammation markers on osteoblasts and showed high OPG/RANKL ratio to prevent osteoclastogenesis.

In this study, we observed that curcumin can be encapsulated in liposomes successfully and which can reduce osteoclast activity and maintain osteoblast functions. Therefore, Curcumin-loaded liposomes can provide a potential application in osteoporosis treatment.

O25

Deficiency of plasma SCUBE1, a novel platelet adhesive protein, impairs thrombus stabilization and protects mice against thrombosis

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SCUBE1 (signal peptide-**CUB**-**E**GF domain-containing protein **1**) is a novel secreted, membrane-associated protein expressed in platelet and endothelial cells. Our previous studies demonstrated that surface-expressed SCUBE1 functions as a novel adhesive molecule and its plasma level is a potential biomarker of platelet activation in acute coronary syndrome and ischemic stroke. To elucidate the precise pathophysiological role of plasma SCUBE1 in platelet biology, we generated a mutant mouse with a targeted deletion of the spacer region and cysteine-rich motifs of the Scube1 gene (named Δ allele) defected in producing secreted SCUBE1 protein. At baseline, wild-type (WT) mice actively produced secreted SCUBE1 in plasma at concentration of 146 ng/ml; however, secretion of SCUBE1 was defected and plasma SCUBE1 level was undetectable in the Δ/Δ mutant mice. Interestingly, lack of secreted SCUBE1 significantly affected the platelet aggregation induced by ADP using platelet-rich plasma (PRP) from the Δ/Δ mutant mice. Furthermore, addition of the purified recombinant SCUBE1 protein could restore aggregation in the ADP-stimulated Δ/Δ PRP or further stabilize platelet aggregation in the wild-type PRP. Importantly, the Δ/Δ mice are significantly protected from $FeCl_2$-induced arterial thrombosis but have only a mild prolonged tail-cut bleeding time. Consistently, injection of anti-SCUBE1 antibody could protect mice against collagen/epinephrine-induced fatal pulmonary thromboembolism. Together, our results demonstrate that the secreted SCUBE1 is a key factor in acute thrombotic events by promoting platelet aggregation and thrombus formation, and suggest that plasma SCUBE1 may serve as a novel anti-thrombotic target.

O26

Domain Analysis and Functional Study of a Novel Platelet-Endothelial Surface Glycoprotein SCUBE1

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Signal peptide-CUB-EGF domain-containing protein 1 (SCUBE1) is a cell-surface expressed and secreted glycoprotein in human platelet and endothelial cells. SCUBE1 is composed of an NH2-terminal signal peptide sequence followed by 9 EGF-like repeats, a spacer-region, 3 cycteine-rich (CR) repeat motifs, and one CUB domain at COOH terminus. Our previous data suggested that the NH2-terminal EGF-like repeats acts as a homophilic adhesive module in a Ca2+-dependent manner, whereas the COOH-terminal CUB domain can directly bind and antagonize the bone morphogenetic protein activity. This study specifically aims to further elucidate the molecular mechanism and function of the membrane-anchoring activity of the spacer region and the CR repeats of SCUBE1. By a series of comprehensive deletion analysis, we identified a short stretch of amino acids (residues 534 to 550) contribute to the membrane-binding activity mediated by the spacer region. With respect to the membrane-binding activity of the CR repeats which contain 4 N-linked glycosylation sites, we found that each N-linked glycan alone is capable of conferring the membrane-binding ability, suggesting a yet-unidentyified lectin-like molecule acting as surface receptor for SCUBE1. In the future, we plan to identify and elucidate the molecular structure and functions for each N-linked glycan and the lectin-like receptor for SCUBE1. In addition, a new genetically modified mouse model carrying the null allele Scube1D2 deleting exons 2 to 18 has been created. This new knockout mouse is a valuable tool to further investigate the physiological or pathological role of SCUBE1 in the future.

O27

GSK3beta-Mediated Drp1 Phosphorylation Induced Elongated Mitochondrial Morphology against Oxidative Stress

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Multiple phosphorylation sites of Drp1 have been characterized for their functional importance. However, the functional consequence of GSK3beta-mediated phosphorylation of Drp1 remains unclear. In this report, we pinpointed 11 Serine/ Threonine sites spanning from residue 634~736 of the GED domain and robustly confirmed Drp1 Ser693 as a novel GSK3beta phosphorylation site. Our results suggest that GSK3beta-mediated phosphorylation at Ser693 does cause a dramatic decrease of GTPase activity; in contrast, it appears not to affect Drp1inter-/intra-molecular interactions. After identifying Ser693 as a GSK3beta phosphorylation site, we also determined that K679 is crucial for GSK3beta-binding, which strongly suggests that Drp1 is a novel substrate for GSK3beta. Thereafter, we found that overexpressed S693D, but not S693A mutant, caused an elongated mitochondrial morphology which is similar to that of K38A, S637D and K679A mutants. Interestedly, using H89 and LiCl to inhibit PKA and GSK3beta signaling, respectively, it appears that a portion of the elongated mitochondria switched to a fragmented phenotype. In investigating the biofunctionality of phosphorylation sites, cells overexpressing Drp1 S693D and S637D, but not S693A, showed an acquired resistance to H_2O_2-induced mitochondrial fragmentation and ensuing apoptosis, which affected cytochrome c, capase-3, -7, and PARP, but not LC3B, Atg-5, Beclin-1 and Bcl2 expressions. These results also showed that the S693D group is more effective in protecting both non-neuronal and neuronal cells from apoptotic death than the S637D group. Altogether, our data suggest that GSK3beta-mediated phosphorylation at Ser693 of Drp1 may be associated with mitochondrial elongation via down-regulating apoptosis, but not autophagy upon H_2O_2 insult.

O28

Beta-nodavirus B2 Can Induce ROS Production that Affect the Mitochondrial Fragmentation and Necrotic Cell Death

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The roles of non-structural protein B2 in the pathogenesis of RNA nervous necrosis virus infection is still few known. The present study demonstrated that non-structural protein B2 can induce oxidative stress-mediated necrotic cell death via mitochondrial targeting. We found that B2 mitochondrial targeting signal peptide (^{41}RTFVISAHAA^{50}) was correlated to free radical species (ROS) production and necrotic cell death in fish cell, and zebrafish. Then, in blockade of oxidative stress assays, anti-oxidant drug N-acetylcysteine (NAC) and antioxidant genes zfCu/Zn SOD and zfCatalase were used. We found that NAC, zfCu/Zn SOD and zfCatalase can also reduce ROS production and cell death ratio that correlated to superoxide (O_2-) and H_2O_2 metabolism. Furthermore, in vivo assay, B2 injected into zebrafish embryos at one stage for test its cytotoxicity with ROS production. Finally, in B2 induced mitochondrial fragmentation that can be reversed by antioxidant (NAC) and dynamin-related protein 1(Drp1) inhibitor (mdivi) in GF-1 cells. Taken together, betanodavirus B2 directly targeting into mitochondria and induction of ROS production is required for mitochondrial breakdown and necrosis cell death *in vitro* and in vivo. It provides new insight into RNA virus pathogenesis and treatment.

Key words:
nervous necrosis virus, ROS production, oxidative stress, anti-oxidants, viral protein, cell death, mitochondrial breakdown

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O29

Anterior Gradient 2: a Novel Tumor Marker Overexpressed in Metastatic Oral Carcinoma

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Background:

The incidence and mortality of oral cancer is increasing in eastern and western countries. Averagely, the 5-year survival rate of distant metastasis of oral carcinoma is only 30-40%. To increase the survival rate for oral cancer patients, it is urgent to identify new metastatic tumor markers for early detection.

Materials and methods:

Transwell invasion assay was applied to isolate sub-populations of HSC-3 cells. The tumorigenic and metastatic characteristics of isolated cells were assessed *in vitro* and *in vivo*. Microarray-based gene expression of parental/isolated cells and their corresponded xenografts were performed and compared. The protein expression of the most up-regulated gene was verified in human oral cancer tissue arrays.

Results:

HSC-3-5 cells exhibited higher metastatic capacities due to cytoskeletal rearrangement accompanied with epithelial mesenchymal transition. They also showed tumorigenic and metastatic characteristics in spontaneous and experimental metastasis experiments. In addition, Anterior gradient 2 (*AGR2*) was the most significantly up-regulated gene in HSC-3-5 cells. Overexpression of AGR2 was confirmed in HSC-3-5 cells, xenografts, and the late-stages oral cancer tissues.

Conclusion:

A highly metastatic subpopulation was isolated and well characterized *in vitro* and *in vivo*. According to microarray analysis and immunohistochemistry staining, AGR2 was identified and confirmed to be a potential novel biomarker for metastatic oral cancer.

O30

Androgen Accumulation and Androgen Receptor Activation Involve in Aromatase Inhibitor-Suppressed Proliferation in Breast Cancer Cells

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Breast cancer is the most prevalent cancer in women. Estrogen plays an important role in the growth and development of breast cancer. Therefore, reducing estrogen level will be helpful in treating breast cancer. The aromatase inhibitors (AI) inhibit the conversion of androgen to estrogen and cause the drop of estrogen level and the accumulation of androgens. Several lines of evidence indicate that androgens exert a direct inhibitory effect on the proliferation of human breast cancer cells. Our hypothesis is that androgen might be accumulated after AI (Anastrozole) treatment and decreasing cell proliferation of breast cancer cells. Our results showed that Anastrozole decreased the cell proliferation of estrogen receptor positive T-47D cells but not estrogen receptor negative MDA-MB-231 cells. In addition, we found that synthetic androgen R1881 decreased cell proliferation of T-47D cells and the levels of androgen receptor protein and S81 phosphorylation were increased. Furthermore, Anastrozole promoted AR translocation into the nucleus of T-47D cells evaluating by fractionation of cellular proteins. In summary, our data indicate that Anastrozole might inhibit proliferation of breast cancer cells through AR activation. This finding provides a new mechanism by which aromatase inhibitor reduces breast cancer cell growth.

O31

Cdk5 Regulates Cytoskeleton Organization and Src Activity and Affects Cancer Cell Motility

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Cyclin-dependent kinase 5 (Cdk5), which belongs to Cdk family but not involve cell cycle regulation, plays roles ubiquitously in proliferation, apoptosis, cytoskeleton organization and motility of many cell types. Previous study show that Cdk5 promotes metastasis of prostate cancer, glioblastoma, and pancreatic cancer, which suggest that Cdk5 regulates cancer metastasis across cancer types. In this study, we scan several cancer types to identify roles of Cdk5 and detailed mechanisms during cancer migration. Reduction of migration rate by Cdk5 inhibitor, roscovitine, and increase of the rate by Cdk5 overexpression were found in breast, lung and bladder cancer cells. In addition, we found Cdk5 was located at lamellipodia and might be disrupted by roscovitine in migrating breast and lung cancer cells, which reflects the important role of Cdk5 during cancer cells migration. According to the finding in corneal epithelial cells, we also found the relationship between Cdk5 and Src in breast and lung cancer cells, in which Cdk5 interacted and co-localized with Src determined by immunoprecipitation and immunostaining. Roscovitine treatment reduced Src protein levels and the distribution of Src at lamellipodia. Moreover, we examined whether Rho/ROCK pathway, the controller of motility commonly regulated by Src, was regulated by Cdk5. The data showed that the up-regulated migration rate by Cdk5 overexpression was reversed while treating ROCK inhibitor Y27632. Taken together, our findings suggest that Cdk5 locates in the leading edge of migrating cells and regulates lamellipodia organization to promote cancer cell motility through Src-related regulation.

O32

The functional role of haptoglobin subunits on tumor metastasis in non-small cell lung cancer

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Haptoglobin (Hp) is acute phase protein and highly expressed in several malignant diseases. Previous study reported that Hp phenotypes was correlated with pathological outcomes in non-small cell lung cancer cancers(NSCLC), in which indicated Hp phenotypes may play a potential role in NSCLC, such as tumor metastasis. However, the difference and effect of Hp phenotypes on tumor metastasis is still not clear. In this study, we analyzed correlation between characteristics of NSCLC cell lines (H2126, CL1-1, H1437, H23, H838, CL1-5, and H2009) and Hp phenotypes on migration/invasion ability by RT-PCR, Western blot, and immunocytochemistry. We found Hp significantly expressed in highly migration/invasion cell (H838, CL1-5, and H2009). Meanwhile, Hp subunit genes were cloned (α1, α2, β) and transfected into low migration/invasion NSCLC cells (CL1-1). We demonstrated Hp subunits could enhance migration, invasion, proliferation, and wound healing ability of NSCLC CL1-1 cells (α2>β>α1) after transfected Hp subunit genes. We also found that Hp subunits effected cancer migration/invasion via EMT marker regulation. Furthermore, our result showed that Hp α2 subunit was significantly enhanced on cancer migration/invasion via regulating EMT markers such as E-cadherin, N-cadherin and twist. We thus concluded that NSCLC patients of Hp2-2 phenotypes may determine worse outcomes since high risk of metastasis relatively.

O33
Identification of A Small Molecule Enhancing Autophagic Clearance of Polyglutamine Aggregation

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The expansion of CAG trinucleotide repeats in the coding region of polyglutamine (polyQ) disease genes causes neuropathogenesis, such as the Huntington disease (HD). Strategies that enhance autophagic clearance of polyQ accumulation without affecting cell survival have attracted a great attention.

In this study, we have identified a small molecule that enhances autophagic clearance of polyglutamine aggregation in neuroblastoma cells. First, we established stable clones expressing TBP-conjugated enhanced green fluorescent with different polyQ length protein (TBP-polyQ-EGFP). Second, by screening a series of synthetic oxazoline derivative, a small molecule compound p-11 was identified capable of eradicating more than 50% polyQ accumulations in TBP-polyQ-EGFP cells at concentrations at 10 μM. The progression was achieved through increased autophagy without reducing cell viabilities and causing cytotoxicity. In addition, autophagosome marker LC3 was increased in the stable cell lines with expanded polyQ tracts, but not in the parental cells as shown in the confocal microscopy. The enhanced autophagy was also confirmed by fluorescence microscopy with elevated intracellular acidic vesicles by staining with Lysotracker and acridine orange., In Western blotting the increased Beclin-1 and conversion of LC3-I to LC3-II formed autophagosome and compound induced autophagy could inhibited by 3MA,a autophagy inhibitor. Durg-induced autophagy eliminating insoluble polyQ protein by dose-dependent manner. And, confirm autophagic pathway was a JNK-dependent pathway in western boltting. The identified small molecular compound capable of enhancing autophagic clearance of insoluble polyQ aggregation without influencing toxicity of the cells of polyQ accumulation provides new revenue in alleviating toxic effect of polyQ disease.

O34
Upregulation of Immune-related Genes during Luminal Clearance of the Mammary Gland

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A fully developed alveolus which consists of a single layer of polarized luminal epithelial cells surrounding a hollow lumen is formed during gestation. Lumen formation of the mammary gland is a complex process of controlled apoptosis and clearance of centrally localized cells. Extracellular matrix (ECM) provides crucial biochemical and biomechanical cues for mammary morphogenesis. *In vitro* cultures of mammary epithelial cells on a reconstituted basement membrane (BM) matrix recapitulates the acinar morphology, whereas cells cultured on plastic or thin-layer of collagen I form monolayers. Comparing gene expression in cells cultured different matrices by microarray analysis reveals a group of genes that are upregulated in cells cultured on BM. These genes are involved in innate immune response or clearance of apoptotic cells. We are thus of interest to examine the expression and the role of these genes in luminal clearance. Our results show that the expression levels of complement 3 (C3), LPS-binding protein (LBP), CD14, milk fat globule-EGF factor 8 (MFG-E8) and growth arrest-specific 6 (GAS6) are greater in cells cultured on BM than those in cells cultured on collagen I. Upregulation of immune-related genes precedes lumen formation, suggesting that they might have a role in luminal clearance of the mammary gland. Moreover, expression of immune-related genes is inhibited by the RhoA-Rok-myosin II pathway which is highly activated in cells cultured on collagen I, and are demonstrated to hampers prolactin and insulin signaling. We are currently exploring the mechanisms for upregulation of immune-related genes during morphogenesis of the mammary acinus.

O35
Generation of Tolerogenic CD4+ T Cells by Bone Marrow-Derived IL-15Rα-/- Dendritic Cells

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We have previously demonstrated that compared with their counterparts primed by wild type dendritic cells (DCs), $CD4^+$ T cells primed by IL-15Rα deficient spleen DCs were restimulated into IL-10 over-production. In addition, the excess production of IL-10 by IL-15Rα$^{-/-}$ DC-primed $CD4^+$ T cells was partially attributed to the enhanced IL-10 production by stimulated IL-15Rα$^{-/-}$ DCs. In this report, we further demonstrated that bone marrow-derived DCs (BM-DCs) exhibited the similar activities. The generation of IL-10 by wild type BM-DCs could be enhanced by blocking IL-15 transpresentation upon DC activation, indicating that the overproduction of IL-10 by IL-15Rα$^{-/-}$ BM-DCs is not an epigenetic effects resulting from gene ablation. We also showed that the IL-15Rα$^{-/-}$ BM-DCs primed $CD4^+$ T cells inhibited the activation of naïve $CD4^+$ T cells in an *in vitro* experiment.

O36
The Role of KLF2 in Autoimmune Crescentic Glomerulonephritis Model

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Autoimmune crescentic glomerulonephritis (ACGN) is a progressive form of glomerulonephritis, in which extensive glomerular crescents and macrophages/lymphocytes infiltrations are formed. However, the current therapy for ACGN is still poor, and many patients require dialysis or renal transplantation. Recent studies have demonstrated that transcription factor Kruppel-Like Factor 2 (KLF2) regulates the expression of genes involved in regulation of vascular tone, inflammation, migration and morphology. Meanwhile, KLF2 is greatly increased in glomerular endothelial cell in response to laminar shear stress, and also is as a negative regulator of monocytic activation through inhibiting the activation of NF-KB pathway. In the present study, we tested the hypothesis that KLF2 gene therapy might prevent the progression of ACGN mice by enhancing the KLF2 pathway, inhibiting renal T cell/macrophage infiltration, and blocking the NF-κB mediated inflammatory pathway. We delivered KLF2 plasmids into the kidney of ACGN mice, using a kidney-targeting ultrasound-mediated microbubble inducible gene transfer. The results showed that KLF2 gene therapy significantly inhibited renal injury including: (1) proteinuria and renal function impairment; (2) renal fibrosis such as glomerular sclerosis, tubulointerstitial collagen matrix expression, and renal macrophage infiltration. Further study demonstrated that improved ACGN renal injury by overexpression of KLF2 was associated with a significant activation of KLF2 signaling pathway, and inhibition of NF-κB signaling pathways locally in the kidney.

Keywords:
Autoimmune crescentic glomerulonephritis; Kruppel-like factor 2; NF-κB; Fibrosis; Ultrasound-mediated microbubble inducible gene transfer.

O37

Cordycepin Shows i*n vitro and in vivo* Potent Anticancer Activity on Testicular Cancer by Regulating Caspase, MAPK/ERK/JNK and p53 Signaling Pathways

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The present study was designed to determine the vitro and *in vivo* apoptotic effects of cordycepin, 3'-deoxyadenosine, with the underlying mechanisms investigation in testicular tumor cells. Testicular cancer highly occurs between 15 and 35 years in man, and radical orchidectomy combined with chemotherapy is the common protocol for clinical treatment. However, these chemotherapy drugs could cause resistance, side effects and serious impacts on life quality. To explore better alternative chemotherapy strategy, the *in vitro* anticancer effect of cordycepin in MA-10 mouse Leydig tumor cells were examined. Also, the in vivo xenograft tumor growth in male SCID mice with cordycepin treatment was evaluated. Results showed that cordycepin could significantly induce cell apoptosis by Annexin V/PI staining cytometric analysis in MA-10 cells. Mechanistic studies revealed that cordycepin significantly stimulated the cleavage of caspase-8, -9, -3, -6, -7 and PARP proteins, the phosphorylation of MAPK/ERK/JNK signaling proteins, the generation of ROS, and the activation of p53 signaling pathway, but inhibited the PI3K/Akt pathway in MA-10 cells. Moreover, cordycepin significantly inhibited xenograft tumor growth on SCID mice. Taken together, cordycepin exhibited significant anticancer activity against testicular tumor cells, which could facilitate the development of therapeutic drugs for the treatment of testicular cancer.

Keywords:
cordycepin; MAPK/ERK/JNK; ROS; p53; in vivo; apoptosis; MA-10 mouse Leydig tumor cells; TM4 Sertoli tumor cells

O38

Extracellular Matrix Protein CCN1 Regulates Cardiomyocyte Apoptosis in Mice with Stress-induced Cardiac Injury

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Backgrounds:
Expression of extracellular matrix protein CCN1 is induced in end-stage ischemic cardiomyopathy in humans, and after cardiac ischemia and reperfusion in experimental animal models. Despite its well-documented angiogenic activities, CCN1 increases the cytotoxicities of the tumor necrosis factor family cytokines, which promotes apoptosis in fibroblasts. We aimed to determine the physiological function of CCN1 in an injured heart.
Materials and Methods:
Knock-in mice carrying the apoptosis-defective mutant allele *Ccn1-dm* were tested in an isoproterenol (ISO)-induced myocardial injury model (100 mg/kg/day of subcutaneously injected ISO for 5 days). Tissue sections from mouse hearts were subjected to TUNEL staining, or H&E, Masson's trichrome, and immunohistochemical stainings following standard procedures. Neonatal rat ventricular myocytes were isolated from Sprague-Dawley rats and cultured for 2 days before the western blotting, and flow cytometry.
Results:
We employed an ISO-induced myocardial injury model to test the role of CCN1 in cardiac injury in mice. Compared with wild-type mice, $Ccn1^{dm/dm}$ mice were remarkably resistant to ISO-induced cardiac injury: They showed no post-treatment cardiomyocyte apoptosis or myocardial tissue damage. ISO cardiotoxicity was dependent on Fas ligand (FasL) and its downstream signaling. Using primary cultures of cardiomyocytes isolated from rats, we demonstrated that CCN1 sensitized FasL-mediated apoptosis by engaging its cell surface receptor integrin $\alpha_6\beta_1$ and upregulating intracellular reactive oxygen species (ROS), which activated mitogen-activated protein kinase p38, and increased cell-surface Fas expression.
Conclusion:
CCN1 is a critical pathophysiological regulator that mediates cardiomyocyte apoptosis during work-overload-induced cardiac injury. CCN1 increases cellular susceptibility to Fas-induced apoptosis by increasing ROS and cell-surface Fas expression.

O39

C1GALT1 Promotes Invasiveness and Metastasis of Hepatocellular Carcinoma Cells via Integrin β1 Pathway

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Hepatocellular carcinomas (HCC) express abnormal mucin type O-glycans. However, their roles in HCC development remain unclear. The core 1 β1,3-galactosyltransferase (C1GALT1) is a critical O-glycosyltransferase to control the formation of mucin-type O-glycans. We therefore investigated the expression and roles of C1GALT1 in HCC

In the present study, human HCC tissues and tissue microarrays were used to analyze C1GALT1 expression. Effects of C1GALT1 on HCC cells, including HCC36, Sk-Hep1, HepG2, and HA22T, were assessed by *in vitro* studies and *in vivo* tumor metastasis analysis in mice. Changes in glycosylation and cell signaling were analyzed by Western blotting.

Results showed that C1GALT1 mRNA and protein were frequently overexpressed in HCC tumors compared with non-tumor tissues. C1GALT1 expression correlated with higher histological grade, vascular invasion, and metastasis. Overexpression of C1GALT1 promoted HCC cell migration, invasion, and adhesion to extracellur matrix

(ECM) *in vitro*. Conversely, knockdown of C1GALT1 suppressed these malignant phenotypes *in vitro*. Importantly, blocking an ECM receptor, integrin β1, can suppress C1GALT1-induced HCC cell migration, invasion, and adhesion. We found that C1GALT1 can modify O-glycosylation on integrin β1, and consequently regulate integrin β1 activity and cell adhesion signaling. Moreover, knockdown of C1GALT1 inhibits HCC cancer cell metastasis in immunodeficiency mice.

Our study identifies a previously unknown role of C1GALT1 in promoting HCC malignancy via modifying integrin β1 O-glycosylation. C1GALT1 could be an attractive target for therapeutic treatment of HCC.

O41

Low-dose of Bisphenol A (BPA) Affects Steroidogenic genes in Placental JEG-3 Cell

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Backgrounds:
The widespread industrial material Bisphenol A (BPA) is a well-known endocrine disruption chemical (EDC). In this study, we investigate the BPA effects on JEG-3 cells survival and transcriptional activities of steroidogenic genes (*StAR, CYP11A1, CYP19*). These steroidogenic genes encode important enzymes that control cholesterol transport or conversion to different steroid hormones. The productions of steroid hormones are critical for placenta development and pregnancy.
Materials and Methods:
We used the human placenta choriocarcinoma cell line JEG-3 as the cell model. Perform MTT assay to exam the cell survival in different dose/time of BPA treatment. For steroidogenic genes analysis, reporter assay was used to detect the transcriptional activities and western blot was used in protein level measurement.
Results:
We found that JEG-3 cells still has normal viability with 1μM BPA for long-time treatment, and viability was significantly reduced only over 100μM. However, P450scc (CYP11A1) protein was down regulated in low dose of BPA (1nM). We also found that BPA certainly reduce *CYP11A1* and *CYP19* promoter activities no matter in the basal condition or cAMP stimulation.
Conclusion:
Our data demonstrated that after low dose of BPA treatment (1nM to 1μM), JEG-3 cells were survived but the gene expressions of steroidogenic enzymes were altered. In recent work, certain signal molecules that participate in the gene regulation were further investigated. These results provide more understandings of BPA effects and mechanisms in placenta.

O42

LHX2 drives neural differentiation via transcriptional regulation of PAX6 and CER1 in hESCs

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Background:

LIM homeobox 2, LHX2, a transcription factor, is found highly expressed at very early stage of *in vitro* neural induction from hESCs. In murine models, Lhx2 plays roles in hippocampal specification and regional fate of dorsal telencephalon. However, the role of LHX2 in human neural differentiation is still elusive.

Materials and Methods:

To examine the spatial and temporal expression pattern of LHX2 during neural differentiation, hESC-derived neural cells were assayed by RT-PCR and immunocytochemistry. To explore the role of LHX2 in neural fate determination, the gain- and loss-of-function studies were performed with transgenic hESCs. To understand the target genes of LHX2 in neural cells, chromatin immunoprecipitation assays were performed.

Results:

Using hESCs, the expression of LHX2 was prior to PAX6 and SOX1, and LHX2 was co-expressed with early neural markers. Conditional LHX2 overexpression promoted the formation of neural rosette-like structure and, conversely, disruption of LHX2 in hESCs impaired neural differentiation. By ChIP and reporter analysis, LHX2 was found targeting to critical neurogenic gene PAX6 enhancers to activate downstream neural gene expressions. Also, LHX2 was found to inhibit non-neural differentiation by augmenting the expression of BMP and WNT antagonist, Cerberus 1(CER1), by targeting to CER1 enhancers.

Conclusions:

In our study, we found LHX2 regulates neural differentiation in two levels. First, LHX2 regulates PAX6 expression to promote neural fate acquisition. Second, LHX2 controls CER1 expression to inhibit non-neural differentiation.

O43

A novel cell-penetrating peptide derived from human eosinophil cationic protein

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Cell-penetrating peptides (CPPs) are short peptides which can carry various types of molecules into cells; however, although most CPPs rapidly penetrate cells *in vitro*, their *in vivo* tissue-targeting specificities are low. Herein, we describe cell-binding, internalization, and targeting characteristics of a newly identified 10-residue CPP, denoted $ECP^{32–41}$, derived from the core heparin-binding motif of human eosinophil cationic protein. Besides traditional emphasis on positively charged residues, the presence of cysteine and tryptophan residues was demonstrated to be essential for internalization. $ECP^{32–41}$ entered Beas-2B and wild-type CHO-K1 cells, but not CHO cells lacking of cell-surface glycosaminoglycans (GAGs), indicating that binding of $ECP^{32–41}$ to cell-surface GAGs was required for internalization. When cells were cultured with GAGs or pre-treated with GAG-digesting enzymes, significant decreases in $ECP^{32–41}$ internalization were observed, suggesting that cell-surface GAGs, especially heparan sulfate proteoglycans (HSPGs) were necessary for $ECP^{32–41}$ attachment and penetration. Furthermore, treatment with pharmacological agents identified two forms of energy-dependent endocytosis, lipid-raft endocytosis and macropinocytosis, as the major $ECP^{32–41}$ internalization routes. $ECP^{32–41}$ was demonstrated to transport various cargoes including fluorescent chemical, fluorescent protein, and peptidomimetic drug into cultured Beas-2B cells *in vitro*, and targeted broncho-epithelial and intestinal villi tissues *in vivo*. Hence this CPP has the potential to serve as a novel vehicle for intracellular delivery of biomolecules or medicines, especially for the treatment of pulmonary or gastrointestinal diseases.

O44

SCUBE2, an Epigenetically Silenced Tumor Suppressor, inhibits Breast Cancer Invasion and Metastasis through Reversal of Epithelial-Mesenchymal Transition

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Signal peptide-complement protein C1r/C1s, Uegf, and Bmp1 (CUB)-epidermal growth factor (EGF) domain-containing protein 2 (SCUBE2) belongs to a secreted and membrane-associated multidomain SCUBE protein family. We previously demonstrated that SCUBE2 was a breast-tumor suppressor and could be a useful prognostic marker. However, the role of SCUBE2 in breast-cancer cell migration, invasion, and metastasis and how it is regulated in breast-cancer cells during epithelial–mesenchymal transition (EMT) remain undefined. In this study, we demonstrated that SCUBE2 was co-expressed and formed a stable complex with β-catenin and E-cadherin, a master tumor-invasion/metastasis-suppressor gene. Ectopic expression of SCUBE2 resulted in epithelial transition and inhibited migration, invasion, and metastasis of invasive, mesenchyme-like MDA-MB-231 breast-cancer cells. Quantitative DNA methylation and methylation-specific PCR analyses revealed that SCUBE2 expression was inactivated by DNA hypermethylation at the CpG islands downstream of exon 1 in breast-cancer cells undergoing transforming growth factor β (TGF-β)–induced EMT. Furthermore, Western blot and chromation immunoprecipitation assays showed that DNA methyltransferase 1 was upregulated and recruited to the regulatory CpG sites at the SCUBE2 locus during TGF-β–induced EMT. Thus, SCUBE2 plays an important role in modulating breast tumor invasion and metastasis, possibly by stabilizing the E-cadherin–β-catenin adhesive complex to promote the epithelial transition and drive the reversal of EMT.

O45

Antibody Prophylaxis and Therapeutic Against Herpes Simplex Virus Infection in Wild-type and Immunodeficient Mice

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Herpes simplex virus type 1 (HSV-1) and type 2 (HSV-2) are common human pathogens that include primary and recurrent infections of mucous membranes (genital and orofacial herpes), neonatal HSV infection, visceral HSV infections in immunocompromised hosts, HSV encephalitis, and an association with erythema multiforme. However, infections in the eye, central nervous system, and brain can be life-threatening. Several approaches are currently available for treating HSV infection, including antiviral medication and vaccine. However, these approaches do not prevent or cure HSV infection and only reduce viral reproduction or alleviate complications associated with HSV infection. In this study we used scFv phage displayed human libraries to screen specific antibodies against HSV. We have identified three glycoprotein D (gD)-specific monoclonal antibodies (E317, E425, Y571), but not glycoprotein B, which show equal potency of HSV-1 and HSV-2-neutralizing activity *in vitro* and demonstrated that MAb E317 had prophylactic and therapeutic efficacy in SCID mice challenged with lethal dose of HSV-1. We, furthermore demonstrate that MAb E317 appeared to be more effective than acyclovir (ACV) suitable as therapeutic tools in clinical applications. When SCID mice were treated intraperitoneally with a single dosage of 15 mg per kg of E317 at 24 hours after HSV-1 challenge, the antibody protected 100% of mice from death compared to 0% survival rate with ten consecutive days of ACV treatment. These studies define the complexity of epitopes on gD of HSV-1 and HSV-2 that is recognized by highly protective antibodies with therapeutic potential.

O46

Targeting β-tubulin:CCT-β complexes incurs Hsp90 and VCP-related protein degradation and induces ER stress-related cell apoptosis via triggering capacitative Ca2+-entry, mitochondrial perturbation and caspase over-activation

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We have previously demonstrated that interrupting the protein-protein interaction (PPI) of β-tubulin:chaperonin-containing TCP-1β (CCT-β) induces the selective killing of multidrug-resistant (MDR) cancer cells due to CCT-β overexpression. However, the molecular mechanism has not yet been identified. In this study, we found that CCT-β interacts with a myriad of intracellular proteins involved in the cellular functions of the endoplasmic reticulum (ER), mitochondria, cytoskeleton, proteasome and apoptosome. Our data show that the targeted cells activate both the heat-shock protein 90 (Hsp90)-associated protein ubiquitination/degradation pathway to eliminate misfolded proteins in the cytoplasm and the valosin-containing protein (VCP)-centered ER-associated protein degradation (ERAD) pathway to reduce the excessive levels of unfolded polypeptides from the ER, thereby mitigating ER stress, at the onset of β-tubulin:CCT-β complex disruption. Once ER stress is expanded, ER stress-associated apoptotic signaling is enforced, as exhibited by cellular vacuolization and intracellular Ca^{2+} release. Furthermore, the elevated intracellular Ca^{2+} levels resulting from capacitative Ca^{2+} entry augments apoptotic signaling by provoking mitochondrial perturbation and caspase overactivation in the targeted cells. These findings not only provide a detailed picture of the apoptotic signaling cascades evoked by targeting the β-tubulin:CCT-β complex but also demonstrate a strategy to combat malignancies with chemoresistance to Hsp90 and VCP-related anti-cancer agents.

O47

Myrciaria cauliflora extracts attenuate diabetic nephropathy in type II DM mice

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Diabetic nephropathy (DN) is a major cause of end-stage renal disease (ESRD) and the mortality rate due to this disease is continuously progressing worldwide. Previously studies indicate that reactive oxygen species play an important role in high glucose-induced renal injury. *Myrciaria cauliflora* has been reported as a functional food rich in anthocyanins possessing anti-oxidative and anti-inflammative properties. This study examined whether *Myrciaria cauliflora* extracts (MCE) can attenuate diabetic nephropathy progression in type II DM mice. First, the composition anthocyanins and polyphenols of MCE were determined by HLPC and spectrophotometer. 100mg/Kg streptozotocin and 240mg/Kg nicotinamide were administered to C57BL/6J mice with high fat diet and variant concentrations of MCE. The plasma glucose concentration, body weight, oral glucose tolerance, insulin tolerance and renal echo were monitored every two weeks. The results showed that MCE decreased the plasma glucose and improved the insulin sensitivity in type II mice. In addition, diabetes-caused glomerular atrophy was recovered under treatment with MCE in diabetic mice. Our results indicate that MCE has beneficial effects in early diabetic nephropathy and detailed mechanism has been confirmed in vitro.

O48

Identification of DNA Methylation Biomarkers for Concurrent Chemoradiation Therapy Prediction and Development of DNMT Inhibitor in Esophageal Squamous Cell Carcinoma

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Backgrounds:
Esophageal squamous cell carcinoma (ESCC) is the sixth cause of cancer death in Taiwanese male. The concurrent chemoradiation therapy (CCRT) composed of cisplatin-based chemotherapy and radiotherapy is applied on ESCC, but often failed due to resistance. DNA methylation has been shown to serve as treatment response biomarker. Moreover, DNA methyltransferase (DNMT) inhibitors are implicated as efficient chemoradio-sensitizers in solid tumors. Therefore, we aim to identify DNA methylation biomarkers for CCRT response prediction and develop DNMT inhibitor as a sensitizer in ESCC.
Materials and Methods:
We performed DNA methylation array for ESCC patients with known CCRT response. In addition, DNMT inhibitor 5-aza-2'-deoxycytidine (5-aza-dC) was evaluated for sensitization ability in ESCC cells treated with chemoradiation.
Results:
Top 30 differential methylated genes were identified between CCRT responding and non-responding ESCC patients. Among the validated hypermethylated genes, *SOX17* mRNA low expression correlated with poor CCRT response (70%) of endoscopic specimen from 43 ESCC patients. In addition, radio-resistant KYSE510 and CE48T cell lines showed *SOX17* mRNA low expression with DNA hypermethylation. Note that overexpression of *SOX17* sensitized radio-resistant KYSE510 cells to chemotherapy agent cisplatin. We further confirmed that combination of 5-aza-dC with low dose CCRT treatment or combination of 5-aza-dC with low dose HDAC inhibitor SAHA treatment showed significant cytotoxicity in ESCC cells along with increased expression of tumor suppressive genes.
Conclusion:
Our findings suggest that *SOX17* hypermethylation is a biomarker for CCRT response prediction in ESCC patients. In addition, overexpression of SOX17 or treatment with DNMT inhibitors sensitizes ESCC cells to chemoradiation.

O49

Disabled-2 is Required for Efficient Haemostasis and Platelet Activation by Thrombin in Mouse

Hui-Ju Tsai, M.S.[1] Chien-Ling Huang, Ph.D.[2] Ding-Yuan Huang, B.S.[2] Chung-Ching Lin, M.S.[2] Ju-Chien Cheng, Ph.D.[3] and Ching-Ping Tseng, Ph.D.[1,2,4]
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Backgrounds:
The essential role of platelet activation in haemostasis and thrombotic diseases focuses attention on unveiling the underlying intracellular signals of platelet activation. Disabled-2 (Dab2) has been implicated in platelet aggregation and in the control of clotting responses. Nevertheless, there is not yet any *in vivo* study to provide a direct evidence for the role of Dab2 in haemostasis and thrombosis.
Materials and Methods:
In this study, megakaryocyte/platelet lineage-restricted Dab2 knockout ($Dab2^{-/-}$) mice were generated by using the PF4-Cre transgenic system. Bleeding time and thrombus formation assays was performed to explore DAB2 function in primary haemostasis and thrombosis. Further, platelet aggregation, spreading, clot retraction, integrin αIIbβ3 activation assays and platelet signaling protein activation were analyzed to delineate the intrinsic properties of $Dab2^{-/-}$ platelets.
Results:
$Dab2^{-/-}$ mice appeared normal in size and platelet production but bleeding time was prolonged and thrombus formation was impaired. Analyses of the intrinsic properties of $Dab2^{-/-}$ platelets revealed a decrease in fibrinogen content and selective defects in platelet aggregation, spreading on immobilized fibrinogen, and clot retraction in response to low concentrations of thrombin. Investigation of the role of Dab2 in thrombin signaling showed decreased thrombin-induced Akt-Ser473 and mTOR-Ser2448 phosphorylations and integrin αIIbβ3 activation in $Dab2^{-/-}$ platelets. In contrast, basal expression of CD41 and thrombin receptors (PAR3 and PAR4) and thrombin-induced CD62P expression and PDK1-Ser241 phosphorylation were not affected.
Conclusion:
These data indicate that Dab2 is a key regulator of haemostasis and thrombosis by playing a selective role in cytoskeleton reorganization and mTORC2-Akt-mTORC1 pathway underlying thrombin-stimulated signaling.

O50

Zebrafish *scube1* Is Involved in Primitive Hematopoiesis by Modulating Bone Morphogenetic Protein (BMP) Signaling

Ku-Chi Tsao[1], Cheng-Fen Tu[1,2,3], Shyh-Jye Lee[4], Ruey-Bing Yang[1,2,3]
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SCUBE1 (signal peptide-CUB-EGF domain-containing protein 1) is the founding member of a novel secreted, cell-surface SCUBE protein family. To date, 3 different isoforms have been identified and named SCUBE1 to 3. The mouse *Scube1* gene has been shown to be expressed predominantly in a variety of developing tissues, including gonads, the central nervous system, dermomyotome, digital mesenchyme, and limb buds during early embryogenesis. Recently, we demonstrated that targeted disruption of the COOH-terminal CUB region resulted in brain malformation in the *Scube1*$^{\Delta cub/\Delta cub}$ mouse embryos (*J. Biol. Chem*., 283: 12478, 2008). However, the full range of its expression and function is probably beyond brain development and not completely understood. In this study, we identified and characterized zebrafish scube1 and analyzed its function by injection of antisense morpholino (MO) oligonucleotide into the embryos (*Scube1*-morphants). Whole-mount *in situ* hybridization revealed that zebrafish scube1 mRNA is maternally expressed and widely distributed during early embryonic development. From 24 hpf onward, *Scube1*-morphant embryos showed reduced numbers of viable circulating blood cells, compared to control embryos. Furthermore, injection of scube1 MO down-regulated marker genes associated with hematopoietic stem cells (*scl*), erythroid (*gata1* and β-embryonic hemoglobin) as well as well early (*pu.1*) and late (*mpo and l-plastin*) myelomonocytic lineages, whereas an endothelial marker fli1 expression or the vasculature structure in *Tg*(*kdr:*GFP) remained unaffected. Furthermore, biochemical and molecular analysis revealed that Scube1 can form complexes with bone morphogenetic protein (BMP) type I and type II receptor and regulates BMP signaling activity. Our results demonstrated for the first time that *Scube1* regulates primitive hematopoiesis, possible through modulating BMP activity during zebrafish embryogenesis.

O51

An analysis of protein-protein interactions in cross-talk pathways reveals CRKL as a novel prognostic marker in hepatocellular carcinoma

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Summary:

Deciphering the network of signaling pathways in cancer via protein-protein interactions (PPIs) at the cellular level is a promising approach but remains incomplete. We used an *in situ* proximity ligation assay to identify and quantify 67 endogenous PPIs among 21 interlinked pathways in two hepatocellular carcinoma (HCC) cells, Huh7 (minimally migratory cells) and Mahlavu (highly migratory cells). We then applied a differential network biology analysis and determined that the novel interaction, CRKL-FLT1, has a high centrality ranking, and the expression of this interaction is strongly correlated with the migratory ability of HCC and other cancer cell lines. Knockdown of CRKL and FLT1 in HCC cells leads to a decrease in cell migration via ERK signaling and the epithelial-mesenchymal transition (EMT) process. Our immunohistochemical analysis shows high expression levels of CRKL and CRKL-FLT1 pair that strongly correlate with reduced disease-free and overall survival in HCC patient samples and a multivariate analysis further established CRKL and the CRKL-FLT1 as novel prognosis markers. This study demonstrated that functional exploration of a disease network with interlinked pathways via PPIs can be used to discover novel biomarkers.

O52

Cholinergic-mediated Inflammation in Amygdala Underlies Organophosphate-induced Seizure in Rats

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Background:

Seizure is a common clinical complication in organophosphate intoxication followed by fatality. However, much less studies are devoted to its detailed mechanisms. The amygdala (AMG) is one of the most seizure-prone brain structures. The present study delineated whether AMG is the main target for organophosphate mevinphos (Mev)-induced seizures and whether inflammation mediates the underlying mechanism.

Materials and Methods:

Seizure was determined by the EEG signals recorded from the somatosensory cortex and amygdala of Sprague-Dawley rats maintained under propofol anesthesia and received Mev via i.v. (0.64 mg/kg) or local application (100 nmol) into the basolateral (BLA) or central nucleus (CeA) of AMG. The level of acetylcholinesterase (AChE), acetylcholine (ACh), IL-2, IL-4, IL-6, IL-10 and IL-13 in AMG were determined by ELISA and the mRNA levels of inflammatory mediators were determined by RT-PCR.

Results:

Seizure-like EEG signals were elicited by Mev administered by i.v. or microinjecting into BLA, accompanied by a decrease of AChE level, an increase of ACh level and an increase of mRNA or protein levels of IL-2, IL-4, IL-6, IL-10 and IL-13 in AMG. Both Mev-induced seizure and inflammation in AMG were antagonized by local application into BLA of atropine (a muscarinic receptor antagonist) or pentoxyphylline (an inhibitor of inflammatory synthesis). On the other hand, microinjection of Mev into CeA did not elicit seizure nor inflammation in AMG.

Conclusion:

These results suggested that BLA is the main target contributing to Mev-induced seizure, which is mediated by a cholinergic-mediated inflammation in AMG.

O53

Overexpression of Manganese Superoxide Dismutase and Glutathione Reductase Prevent Thioacetamide induced Edema in Pericardial Sac and Correlate with Mast Cell Activation during Zebrafish Development

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Backgrounds:

Thioacetamide (TAA) is a hepatotoxin and it can cause hepatocellular carcinoma in mice. In the previous study, we have showed TAA can down-regulate mef2cb and nrp2b genes expression, and induced the edema in pericardial sac (eps) formation, but the cellular mechanism was still unclear. In this study, we try to identify the cells which involved in TAA induced eps formation, and overexpress antioxidant enzymes to reduce eps formation in TAA treatment.

Materials and Methods:

Zebrafish (Danio *rerio*) AB strain were used in the following experiments. Eps was induced in zebrafish embryos after 0-32 mM TAA treatment for 0-96 h, ROS was detected by DCFH-DA staining, the embryos were used for histopathological study and mast cell activation was detected by toluidine blue staining. The mast cells inhibitor cromolyn was used to inhibit mast cell degranulation. Mn-Superoxide dismutase (SOD2) and glutathione reductase (GR) were overexpress in transgenic fish by *Tol2* transposon system. Transgenic F1 were used for reduce the eps formation under TAA treatment.

Results:

The eps was observed in embryos after 8-32 mM TAA treatment for 24-96 h. The level of intracellular ROS and oxidative damage were significantly increased to about 6 and 2.6 fold. The mast cells were congregate and degranulation at the pericardial sac by toluidine blue staining. The eps formation was significantly reduced when embryos were co-treated with 0.2-5 mM cromolyn and TAA. Overexpress SOD2 and GR transgenic fish were generated and confirmed by RT-PCR, western blotting and enzyme activity assay. The transgenic F1 were treated with TAA for 48-72 h, the ROS and oxidative damages were inhibited and the eps formation rate was reduced to about 10-20%.

Conclusion:

Our results showed TAA induced eps formation was due to enhanced ROS generation and induced mast cells activation during embryonic development. To inhibit mast cell activation and overexpress SOD2 and GR can down-regulate intracellular ROS and oxidative damages, increase the embryos survival rate, and can rescue TAA induced eps formation.

O55
Gold Nanoparticles Increases Blood-Brain Barrier Disruption through Down-Regulation of Tight Junction Proteins

Cheng Jhan[1], Ching-Hao Li[2], Po-Lin Liao[3], Chen-Wei Liu[1], Chi-Hao Tsai[1], Jaw-Jou Kang[1]
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[2]Department of Physiology, School of Medicine, College of Medicine, Taipei Medicine University,
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Nanoparticles (NPs) have smaller size and different physical-chemical characteristics, so the absorption, distribution and toxicity may differ from its bulk material in the human body. Therefore, nanoparticles may cause health risks which are different from those of similar materials in micro or macro form. The blood-brain barrier (BBB) formed by endothelial cells is lining the cerebral microvessels, and has impermeability structure that regulates molecular traffic. Since nanoparticles are so small that possibly cross the BBB or destroy the impermeability structure, in this study, we investigated whether three commonly used metal particles including gold, silver and zinc oxide, could disrupt BBB and increase permeability. Human umbilical vein endothelial cells (HUVECs) were treated with gold, silver, zinc oxide nanoparticles and non-nanoparticles. Cells permeability was increased when treated with gold nanoparticles by *in vitro* permeability assay, while silver and zinc oxide nanoparticles did not. Previous reports indicated that the cells permeability was related to cell junctions containing adherens and tight junctions. We found that gold nanoparticles reduce tight junction proteins expression such as occludin, cluadin-5 and JAM-1, but had no effect on adherens junction proteins such as VE-cadherin. However, the mRNA of tight junctions was not affected by gold nanoparticles. Furthermore, we used *in vivo* BBB permeability assay and found that injection of gold nanoparticles into mice through tail vein injection, had more permeability compare with non-nanoparticles in the brain, indicating the BBB disruption. Our results showed that the gold nanoparticles could cause BBB permeability increase via protein level regulation of tight junctions.

O56
Hibiscus Sabdariffa Leaf Polyphenolic Extract Induces Apoptosis and Autophagy of Human Prostate Cancer Cells

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[2]School of Nutrition, Chung Shan Medical University.

Background:
Many studies have shown that polyphenols can inhibit cancer cell growth and metastasis. In previous study, *Hibiscus sabdariffa* leaf extract (HLE) was demonstrated be rich in flavonoids, and induce apoptosis of human prostate cancer LNCaP cells. Therefore, the object of the study was to examine the anti-cancer potential and molecular mechanism of *H.* sabdariffa leaf polyphenolic extract (HLP) on LNCaP cells.
Materials and Methods:
We used trypan blue assay and BrdU assay to analyse the effects of HLP, its main compound epicatechin gallate (ECG) and β-sitosterol, a plant sterol, on the cell viability and proliferation. Using a set of cell death detection assays, including Flow cytometric analysis, TUNEL assay, and AVO stain, the effects of these agents on the cell cycle distribution, apoptosis, and autophagy were defined *in vitro*. The expressions of molecular proteins were measured by Western blotting.
Results:
HLP, ECG and β-sitosterol inhibited the LNCaP cell growth. Our results also revealed the cells presented TUNEL-positive morphology, and had an increase in the distribution of hypodiploid phase after a 48-h treatment with HLP. This effect of HLP in LNCaP cells might be mediated via the death receptor (FasL-mediated caspase-8) and/or partially mitochondria (Bax-mediated caspase-3) pathways. In addition, HLP and β-sitosterol could induce cellular autophagy via ATG signaling.
Conclusion:
Our data imply that HLP induced LNCaP cell apoptosis and autophagy. These results suggested that HLP potentially could be developed as an anti-cancer agent, and may open interesting perspectives to the strategy in human prostate cancer treatment.

O57
Oct4-Mediated Transcription Deregulation in Lung Tumorigenesis and Drug Resistance

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Background:
Transcription factor Oct4 is critical in pluripotency regulation of human embryonic stem cells. However, the precise transcriptional control especially in drug resistance remains largely unclear. Therefore, we aim to identify and correlate Oct4 transcriptional target genes with drug resistance and lung tumorigenesis.
Materials and Methods:
A total of 98 lung cancer patients were recruited. Protein expression was assessed by immunohistochemistry. Oct4 binding sites and putative transcriptional targets were identified via ChIP-sequencing analysis of stably Oct4-overexpressed lung cancer cell line A549. Expression of target genes was verified by quantitative RT-PCR.
Results:
Clinical studies showed high Oct4 protein expression in 67.25% lung cancer patients, which correlated with poor prognosis (p=0.023). Oct4 overexpressed lung cancer cells demonstrated increased proliferation, migration, and drug-resistance. Validation of 30 putative target genes showed that Oct4 repressed expression of tumor suppressor-like genes, whereas transactivated oncogenic genes. Among them, we identified for the first time that Oct4 downregulated tumor suppressor gene *PTEN*, which is involved in drug-resistance. We further discovered that Oct4 downregulation of PTEN resulted in drug resistance to epi-drug SAHA, which could be diminished after cotreatment with LY294002, a PI3K inhibitor. Moreover, clinical PTEN protein expression had an inverse correlation with Oct4 ($p=0.006$), and patients overexpressing Oct4 and PTEN low expression had poor prognosis ($p=0.035$).
Conclusion:
Our results suggest that Oct4 is an oncogenic transcription factor that regulates expressions of critical genes promoting lung tumorigenesis. Transcriptional repression of PTEN by Oct4 leading to activation of AKT signal mediates the observed resistance of SAHA in Oct4 overexpressing cells.

O58
Eugenol suppresses gastric tumor growth and peritoneal dissemination by increasing ER stress in an orthotopic model.

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Eugenol (4-allyl-2-methoxyphenol) is known to suppress the inflammation; however, its anti-tumor growth, anti-peritoneal dissemination effects have not been studied so far in orthotopic mouse model. In the present study, we aimed to evaluate the anti-tumor growth and anti-metastatic potential of Eugenol in vivo and in vitro. Our results demonstrate that tumor growth, peritoneal dissemination and liver/lung metastasis of orthotopically implanted MKN45 cells were significantly reduced in Eugenol-treated mice along with the induction of apoptosis. Furthermore, Eugenol-treated tumors showed increased ER stress signature such as increased expression of IRE1a, GADD153, p-PERK, p-elf2a, Caspase7. The aryl hydrocarbon receptor (AhR) and COX-2 is an environmental carcinogen-activated transcription factor associated with tumorigenesis and metastasis. Simultaneously, Eugenol-treated also decreased cooperation of AhR/NF-kB/RelA and COX-2 expression. Similar observations were made when SCM-1, AGS and N87 cells were treated *in vitro*. Eugeno-induced upregulation of death receptor 5 by increase GADD153(CHOP)/DR5 binding activity but not death receptor 4. Moreover, AhR was down-regulated and cleavaged in the ER fraction of Eugenol-treated cells, as indicated by increased interaction of specific Calpain-10, but not Calpain-1 or Calpain-2. Silence Calpain-10 was abrogated by Eugenol treatment biological effects. In addition, Eugenol inhibited AhR/NF-kB/RelA interaction, nuclear translocation and DNA binding activity in cancer cells in time course and dose-dependent manner by Calpain-10 activation. Taken together, our results suggest that Eugenol suppresses both gastric tumor growth and peritoneal dissemination by inducing apoptosis and activating ER stress.

O59
YYEI Motif Is Critical to Oncogenicity of 14-3-3 Proteins

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1Department of Clinical Laboratory Sciences and Medical Biotechnology, College of Medicine, National Taiwan University
2NTU Center for Genomic Medicine, National Taiwan University College of Medicine
3Institute of Biomedical Sciences, National Chung Hsing University

Backgrounds:
14-3-3 family consists of seven highly conserved isoforms and most of them are identified as oncogenes in various types of cancer except for 14-3-3sigma, a well-known tumor suppressor.
Materials and Methods:
pcDNA3.1-V5 and various pcDNA3.1-V5-14-3-3 wild type and mutants were transiently or stably expressed in CL1-0 cells. Then these cells were subjected into transwell chamber for invasion assay or into 96-well plate for MTT assay. The in vivo interaction of 14-3-3 and Src was examined by immunoprecipitation.
Results:
In non-small cell lung cancer, 14-3-3 proteins increased cell growth besides 14-3-3sigma, which inhibited cancer cell viability. To clarify the suppressor characteristic of 14-3-3sigma divergent from others, we found that the major difference between the other oncogenic members and 14-3-3sigma by protein alignment was an amino acid substitution (Y180H) by which the SH2-binding motif (YYEI) is disrupted and cannot be phosphorylation. Thus, we generated a H180Y 14-3-3sigma mutant and investigated the impact of the acquired YYEI motif on the tumor suppression. First, we found that 14-3-3sigma decreased cancer invasion. Surprisingly, the H180Y mutant not only enhanced cell invasion but increased cell viability. Meanwhile, the interaction between H180Y mutant and Src was higher than wild type. It indicates one amino acid substitution switches 14-3-3sigma from tumor suppressor to oncogene. Hence, the YYEI motif might be important for the oncogenicity of other 14-3-3 proteins. Indeed, we demonstrated that 14-3-3zeta interacted with Src through Y178 phosphorylation, which is crucial for the binding of 14-3-3zeta with Src-SH2 domain. Owing to the importance of Y178 phosphorylation in the 14-3-3zeta/Src interaction, we introduced the Y178F 14-3-3zeta mutant to lung cancer cells and confirmed that Y178 phosphorylation is important for the increase of invasion and viability.
Conclusion:
YYEI motif is essential for 14-3-3 proteins to interact with Src and to regulate Src-mediated cell functions.

中國生理學會
The Chinese Physiological Society

- **會員大會 歡迎蒞臨出席**

時間：102 年 3 月 23 日（星期六） 14:45-15:45
地點：國防醫學院 第二教室

- **2013 年生物醫學聯合年會 歡迎踴躍參加**

（一）、轉譯醫學專論：從生理到臨床

時間/地點：3 月 23 日 09:00- 11:15 /第二教室
主講者人：楊松昇、鄭劍廷、蔡少正 教授

（二）、生理學會特別演講：

時間/地點：3 月 23 日 13:45-14:45 /第二教室
主講者：Prof. William Chilian
Department of Integrative Medical Sciences, Northeast Ohio Medical University
題目：Regulation of Blood Flow to the Heart: A feed-forward process that is regulated by H_2O_2-dependent redox signaling

（三）、生理學在醫學教育改革中所扮演的角色

時間/地點：3 月 24 日 09:00-10:00 /第二教室
主講者：蔡美玲、許勤、湯志永、卓貴美、謝博軒 教授

（四）、生理學專題研討會

時間/地點：3 月 24 日 13:45-15:45 /第二教室
主講者：盧主欽、余青翰、李季湜、林詠凱 教授

（五）、論文競賽：

口頭發表競賽 時間/地點：3 月 23 日 16:00-17:00 /第二教室
海報競賽 3 月 23 日 13:00-13:45 /1 樓 海報區

- **歡迎申請入會** 請下載入會申請表(http://www.cps.org.tw)，填妥後寄給學會幹事洪櫻慈小姐(apple123104@hotmail.com)或秘書長**何應瑞**(yjho@csmu.edu.tw)。

中華民國毒物學學會

The Toxicology Society of Taiwan

http://ge-orz.com/toxicology/index.php

本會宗旨: 本會以促進毒物學及相關科學之研究與發展及應用為宗旨。

本會之任務為:

一、促進毒物學之研究與應用。

二、舉辦有關毒物學學術演講及討論會。

三、參加國際有關毒物學各項會議，並經常與國外毒物學會連繫。

四、出版有關毒物學刊物。

五、辦理其他有關毒物學事項。

本會第八屆理監事名錄:

理 事 長 郭明良 (國立臺灣大學 生命科學院院長)

理　　事 李　輝、李德章、林榮耀、林嬪嬪、柯俊良、洪東榮、翁祖輝、戚謹文、陳慧誠、黃登福、楊振昌、劉宗榮、劉興華、鄧昭芳

監　　事 何英剛、吳金洌、蕭水銀、王榮德、周昌弘

秘 書 長 張正琪

➢ 會員大會

時間：102 年 3 月 23 日（星期六）　9:00-10:00

地點：國防醫學院 第 34 教室

➢ 毒物學會特別演講 歡迎踴躍參加

I.時間/地點：3 月 23 日 10:15- 11:15 /第二教

演講者：羅浩 院士

主持人：郭明良 教授

II.時間/地點：3 月 23 日 13:45-14:45 /第二教室

演講者：Dr. Myung-Haing Cho

主持人：郭明良 教授

➢ 歡迎申請入會

請下載入會申請表(http://ge-orz.com/toxicology/explor.php?id=18)，並至郵局劃撥或銀行匯款繳交會費後，將申請表和收據一併傳真或寄給學會秘書范家睿先生(傳真：02-23820785；toxology.kuo@gmail.com)

郵政劃撥帳戶

戶名：中華民國毒物學學會郭明良

帳號：11600004

會費：

一般會員：入會費 200 元，年費 400 元；

永久會員：入會費 200 元，會費 4000 元。

學生會員：免入會費，年費 200 元。

中華民國細胞及分子生物學學會

THE CHINESE SOCIETY OF CELL AND MOLECULAR BIOLOGY

「中華民國細胞及分子生物學學會」於1989年經先進們促成，於行政院國科會生物處的支持下籌畫成立，24年來在細胞及分子生物學領域之研究推動與學術交流上努力耕耘，對長期推動生命科學教育，及提升學子對生命科學之認知等基礎紮根工作，成果豐碩。

學會每年固定舉辦之主要活動包括：1.「細胞及分子生物新知研討會」，本研討會舉辦至今已有21屆歷史，每年會中均邀請細胞及分子生物學相關領域之優秀學者進行專題演講，另舉辦碩、博士班學生口頭以及壁報論文競賽，鼓勵研究生發表研究心得，並對優秀論文予以獎勵。除可提供研究者學術交流機會，也鼓勵青年學子投入相關領域之研究，落實基礎紮根；2.「生物醫學聯合學術年會」，學會每年與其它六個基礎醫學相關學會共同合作舉辦；以及3.「海峽兩岸細胞生物學學術研討會」由本學會及中國細胞生物學學會輪流辦理，與會者可藉此機會彼此交流與砌磋最新研究成果。

另外，為鼓勵年輕優秀之研究人員踴躍參加學術活動，吸收生物科技新知並拓展視野，本學會每年皆辦理兩次之學生、助理及博士後研究員出席國際學術會議補助。

經歷任理事長吳成文院士、沈哲鯤院士、張仲明特聘研究員、吳妍華院士、伍焜玉院士及現任理事長王陸海院士的努力不懈，加上各屆的理事與監事大力護持與指導，本會得以在穩定中成長與茁壯。

《第十一屆理監事名單》(依姓名筆劃順序)

理 事 長：王陸海

常務理事：吳華林、魏耀揮

理　　事：王惠鈞、王憶卿、伍焜玉、吳益群、周玉山、施修明、唐　堂、孫以瀚、郭明良、陳瑞華、陳鴻震、湯銘哲、楊泮池、賴明宗、謝世良、鍾邦柱、簡伯武、蘇益仁

常務監事：張文昌

監　　事：吳成文、吳妍華、沈哲鯤、林榮耀、張仲明、賴明詔

今年學會已邁入第24年，目前所累積的會員人數共計有6,656人，其中普通會員為1,280位，學生會員為5,376位。展望未來除秉持創會宗旨，亦將力圖與世界的細胞生物學界接軌，更上層樓。

http://www.cscmb.org.tw

中華民國解剖學學會

特別演講及會員大會

日期： 2013 年 3 月 23 日　9:30-11:10

地點： 國防醫學大學 32 教室

研討會：32 教室

(一) **Neural Science**　3/23 星期六 13:45-15:45

(二) **Vascular disorder**　3/24 星期日 13:45-15:45

本會宗旨：本會以聯絡國內外人士，共同發展解剖科學之研究及應用

本會任務：

(一)促進解剖科學之研究與發展。

(二)聯繫國內外解剖科學機構及學術團體交換有關資訊，以供各學術研究團體之參考。

(三)舉辦有關解剖科學之學術演講及研討會。

(四)審議有關解剖科學之名詞。

(五)發行有關解剖科學之雜誌及刊物。

(六)參加或舉辦國際解剖學學術活動及其他有關解剖學之技術研究事項。

第十三屆理監事名錄

理 事 長　錢宗良 (台灣大學解剖學暨細胞生物學研究所教授)

常務理事　劉鴻文 王順德 謝松蒼 馬國興

理　　事　陳玉怜 呂俊宏 馮琮涵 徐佳福 傅毓秀
王懷詩 吳建春 鄭授德 鄭瓊娟 柯妙華

常務監事　劉江川

監　　事　盧國賢 曾國藩 吳慶祥 歐陽品

秘 書 長　龔秀妮

本會網址：http://anatomy.org.tw/index.html

入會費用：個人會費 -- 入會費 500 元，常年會費 500 元
學生會員 -- 入會費 100 元，常年會費 100 元

中華民國臨床生化學會

本會以聯絡國內外人士共同促進臨床生化之研究、發展及應用，並加強對國際臨床生化組織之交流，增進國民之健康為宗旨。認同本會宗旨者，誠摯邀請入會共圖發展。

會址：台北市常德街一號　國立臺灣大學醫學院醫學檢驗暨生物技術系
核准立案：內政部台(71)內社字第 92662 號
統一編號：00966410
電話：02-27049977 轉 563
傳真：02-23711574
信箱：office@cacb.org.tw
網址：http://www.cacb.org.tw/

第十一屆理監事名錄

理事長　方偉宏
常務理事　蔡麗玉、謝淑珠
理事　林淑萍、林聰義、徐慧貞、陳秋霞、甯孝真、葉振聲、劉俊仁、歐月星
常務監事　毛小薇
監事　高照村、賴明龍
秘書長　張雅雯
秘書　鐘明義、李承光

郵局劃撥帳號：
戶名：中華民國臨床生化學會
帳號：05664401
ATM 轉帳：
合作金庫銀行：006
帳號：1346 717 034896
常年會費 NT$800，請記得繳納常年會費，您的奉獻推動了中華民國臨床生化學會會務的發展。

本會將在 2016 年主辦第十四屆亞太臨床生化暨檢驗醫學會大會（14th APFCB CONBRESS 2016），敬請踴躍參與。

歡迎踴躍入會

台灣生物化學及分子生物學學會
The Taiwan Society for Biochemistry and Molecular Biology

102 年度會員大會

日期：102 年 3 月 23 日星期六上午 10 點

地點：國防醫學院第 33 教室

1. 繳費通知：請普通會員及學生會員撥冗前往學會報到處繳納 102 年度常年會費，亦可撥冗前往郵局劃撥或親至國立中興大學生命科學系 703 室洽陳小姐繳交，依據本學會章程及理監事會議決議，凡普通(學生)會員連續兩年未繳交會費，暫列入不活躍會員，暫停其會員各項權益。
2. 本年度將展示本學會新版網頁，歡迎會員蒞臨指導。
3. 本學會將發送創刊號會訊，敬請踴躍參加本年度會員大會。

劃撥帳戶：00170375
戶名：台灣生物化學及分子生物學學會
地址：(402)台中市南區國光路 250 號國立中興大學生命科學院
電話：(04)2284-0416 轉 616(劉奕良) or 704(陳貞如)
網址：http://www.tsbmb.org.tw/
電子郵件：sgl0220@gmail.com

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學生會員： 入會費 100 元　常年會費 100 元

歡迎踴躍入會

臺灣生物化學及分子生物學學會
台中市南區 402 國光路 250 號　國立中興大學生命科學院
National Chung Hsing University, College of Life Science　250 Kuo-Kuang road, Taichung 402, Taiwan
TEL: 886-4-22840370; FAX: 886-4-22860164; E-MAIL: sgl0220@gmail.com
http:www.tsbmb.org.tw

台灣藥理學會

The Pharmacological Society in Taiwan

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常務監事	顏茂雄
監　　事	李哲夫、張文昌、陳慶鏗、鄧哲明
常務理事	符文美、陳青周、曾清俊、簡伯武、蘇銘嘉
理　　事	吳錦楨、吳炳男、林琬琬、林滿玉、許桂森、許準榕、黃德富、楊春茂、華　瑜、陶寶綠
秘　書　長	陳文彬

◎台灣藥理學會網站：http://www.pharmacology.org.tw/index.php

◎ 入會辦法：

請至本會下載入會申請書，填妥後以郵寄或傳真方式傳至本會。
申請書下載網址：http://www.pharmacology.org.tw/memberlist_index.php

◎台灣藥理學會會址：

10051 台北市仁愛路一段 1 號 國立台灣大學藥理學科
學會信箱：tpharmacol@gmail.com
學會電話：(02)2312-3456 轉 88319 傳真：(02)2341-7930

2013 The 28th Joint Annual Conference of Biomedical Science
第 28 屆生物醫學聯合學術年會

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