NTU Center of Genomic Medicine

臺大基因體醫學研究中心

主持人：楊泮池　教授
陳明豐　教授
陳為堅　教授
執行長：錢宗良　教授

NTU Center of Genomic Medicine (NTU-CGM)

- 2002/10/30 教育部正式通過計畫
- 2003/03/25 通過設置**臺大基因體醫學研究中心** (NTU-CGM)
- 2003/04/02 協助臺大SARS團隊相關研究支援
- 2004/04/01 臺大基因體醫學研究中心正式啟用
- 2005/12/01 更名為**臺大醫學卓越研究中心** (NTU-RCME)
- 2007/07/27 生醫分子影像核心實驗室正式落成啟用
- 2008/09/12 幹細胞核心實驗室正式啟用
- 2009/09/09 永齡基金會捐贈共軛焦顯微鏡等貴重儀器
- 2009/12/15 美商應用生命系統(ABI)捐贈新一代核酸定序儀
- 2010/03/19 代謝體核心實驗室成立
- 2010/08/01 校方通過變更回為「**臺大基因體醫學研究中心**」
- 2010/11/20 與臺灣大學/醫院/醫學院合作，推動轉譯醫學研究

NTU Center of Genomic Medicine

Mission

To establish state-of-the-art core facilities, support cutting edge genomic research for scientists in NTU

Our Focus

Disease-based translation research, emphasize on cancer and infectious diseases

Bench Mark

Top-ranking university in Asia-Pacific area

Osaka University, Melbourne University

臺大基因體醫學研究中心
NTU Center of Genomic Medicine

主持人: 楊泮池 院長　陳明豐 院長　陳為堅 院長

Genomic Medicine Cores
執行長：錢宗良教授

Cancer Division
楊泮池教授

Infectious Disease Division
陳培哲教授

Administration Office & Teaching Resource Center

- **Proteomics** 周綠蘋
- **Microbial Genomic** 陳培哲、王錦堂等
- **Microarray** 楊泮池、俞松良等
- **Tissue Bank** 林中梧
- **Transgenic & Knockout Mouse** 蘇銘嘉、林淑華
- **Genetic Epidemiology** 陳為堅、簡國龍等
- **Bioinformatics Biostatistics** 莊曜宇、蕭朱杏等
- **Stem Cell** 何弘能 錢宗良
- **Metabolomics** 郭明良、曾宇鳳、郭錦樺

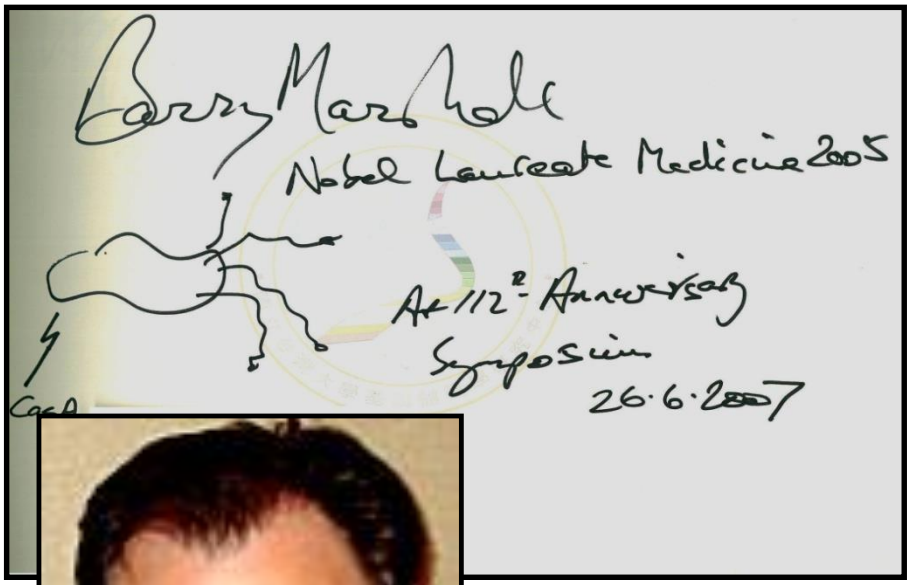
任務目標

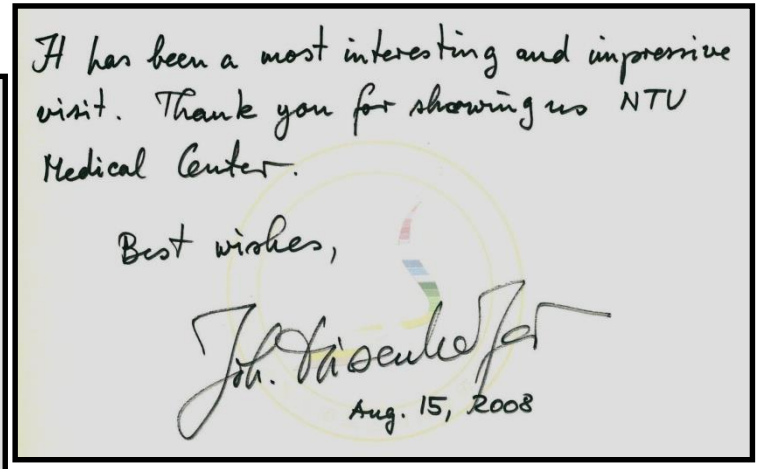
- 基因醫學研究領域設置10個設備完善之核心實驗室整合跨領域、跨院校研究交流
- 每年支持計畫主持人發表50篇以上之國際學術論文期刊，及超過2項專利申請案
- 每年舉辦20個以上之教育訓練課程
- 每年舉辦暑期研習營，培訓學生超過30人次
- 促進國際學術交流及合作

Milestone Achieved

- Fully function core facilities in genomic research
- Facilitate multidisciplinary collaborations in NTU
- Support NTU PI publish high ranking research papers > 50/year, patent > 2/year
- Educational programs and workshops > 20/year
- NTU students summer research program
- International credibility and collaboration

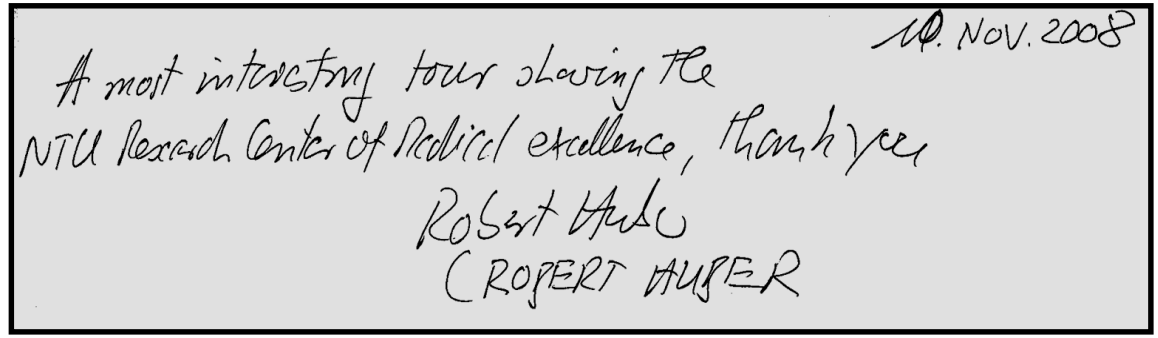
國際學術交流：諾貝爾獎得主參訪研究中心

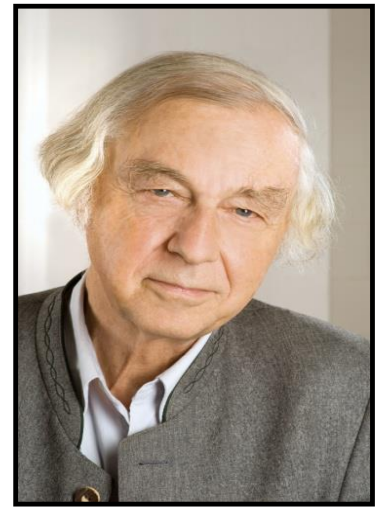




Dr. Johann Deisenhofer
The 1988 in Chemistry

Dr. Barry Marshall
The 2005 in Medicine





Dr. Robert Huber
The 1988 in Chemistry

醫學研究中心暑期研習營
(2006-2011)

臺灣大學






量化研究成果 (2011/04-2011/12)

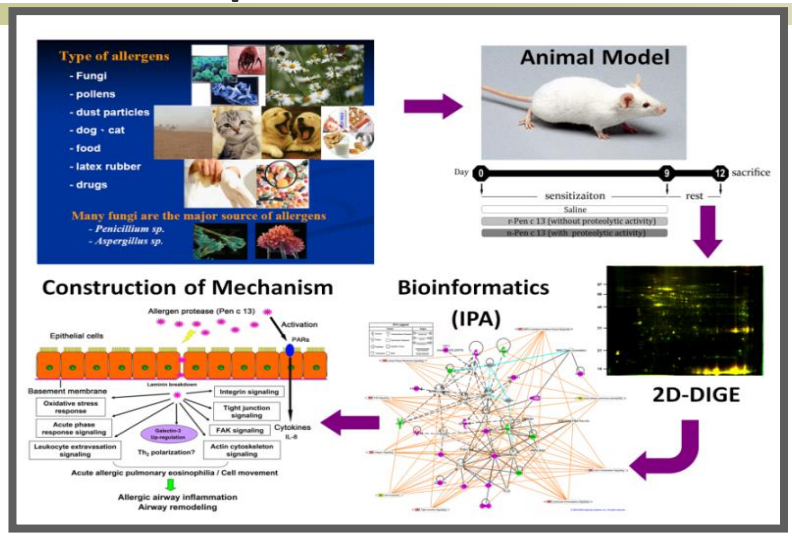
Listing		Total	Significant
Published Articles	Journals	196	96
	Conferences	61	27
	Technology Reports		
Patents	Pending	8	
	Granted	3	
Personal Achievements	Honors Awards	15	4
	Keynotes Given by PIs	24	4
	Editor for Journals	29	18

量化研究成果 (2011/04-2011/12)臺灣大學

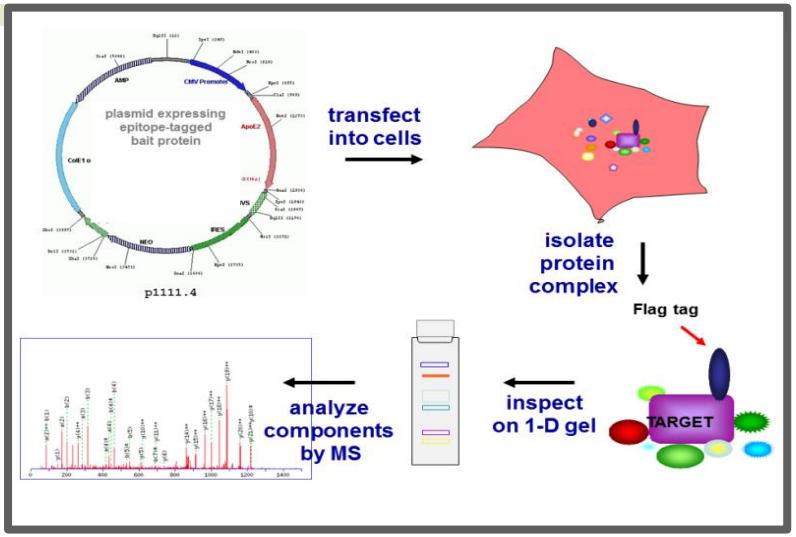
Listing		Total	Significant
Workshops Conferences	Item	20	4
	Participants	2679	1200
International Cooperation Activities	Item		
	Participants		
Training Courses	Hours	1453	120
	Participants	345	210
Technological Services	Item	2459	
	Service Fee	1,842,280	

Proteomics strategies for clinical research

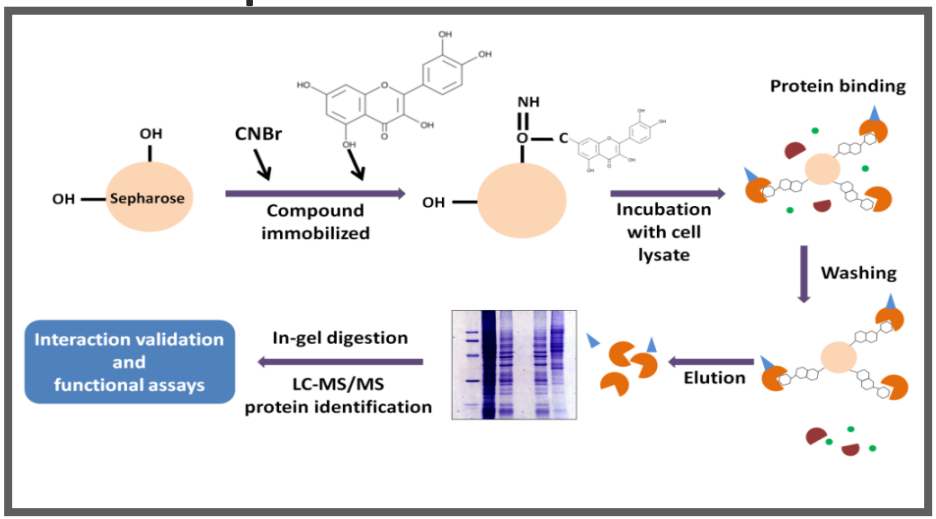
Differential proteome in murine model



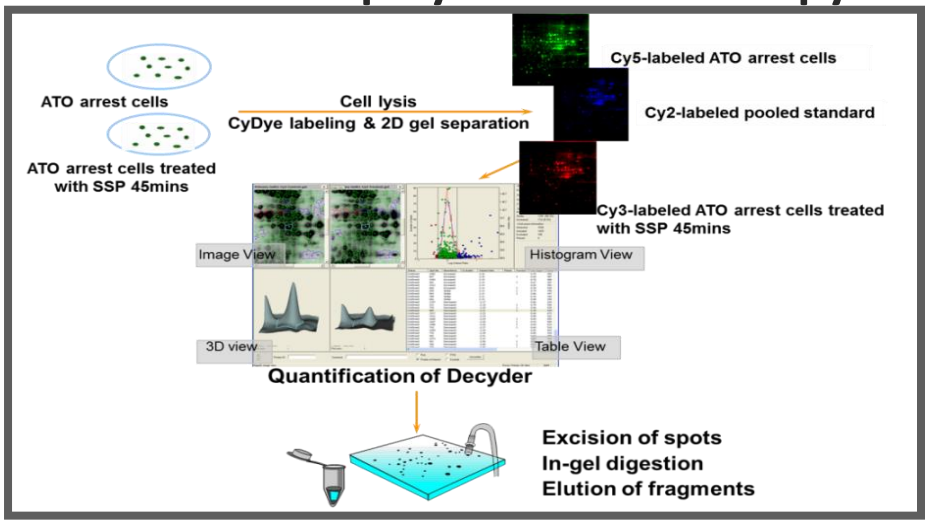
Protein interactome



Chemical proteomics



Differential display of cancer therapy



ARTICLE

Associations Between Hepatitis B Virus Genotype and Mutants and the Risk of Hepatocellular Carcinoma

Hwai-I Yang, Shiou-Hwei Yeh, Pei-Jer Chen, Uchenna H. Iloeje, Chin-Lan Jen, Jun Su, Li-Yu Wang, Sheng-Nan Lu, San-Lin You, Ding-Shinn Chen, Yun-Fan Liaw, Chien-Jen Chen

For the REVEAL-HBV Study Group

(A successful collaboration between Microbial Genomics Core Laboratory and Academia Sinica)

HBV genotype	Precore 1896 variant	BCP 1762/1764 variant	No. of participants	Person-years of follow-up	No. of HCC cases	HCC incidence (per 100 000 person-years)	Adjusted HR† (95% CI)	*P*‡
B	Wild type	Wild type	198	2404.8	14	582.2	1.0 (referent)	
B	Wild type	A1762T/G1764A	82	950.1	9	947.3	1.35 (0.58 to 3.12)	.48
B	G1896A	Wild type	413	5175.0	9	173.9	0.20 (0.09 to 0.46)†	<.001
B	G1896A	A1762T/G1764A	110	1319.9	7	530.3	0.62 (0.25 to 1.54)	.30
C	Wild type	Wild type	129	1633.2	6	367.4	0.73 (0.28 to 1.89)	.51
C	Wild type	A1762T/G1764A	115	1242.1	28	2254.2	2.99 (1.57 to 5.70)†	<.001
C	G1896A	Wild type	41	497.3	4	804.3	1.38 (0.45 to 4.20)	.57
C	G1896A	A1762T/G1764A	73	911.2	2	219.5	0.36 (0.08 to 1.59)	.18

* HCC = hepatocellular carcinoma; HBV = hepatitis B virus; BCP = basal core promoter; HR = hazard ratio; CI = confidence interval.

† Adjusted for sex and age at recruitment.

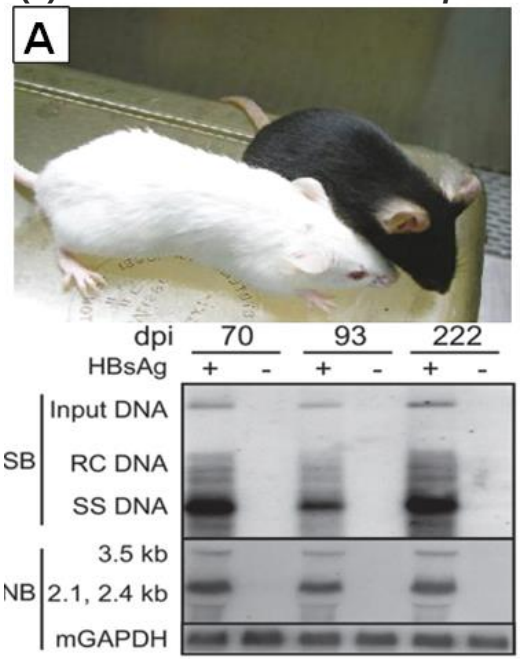
‡ *P* values (two-sided) were from Cox proportional hazards models.

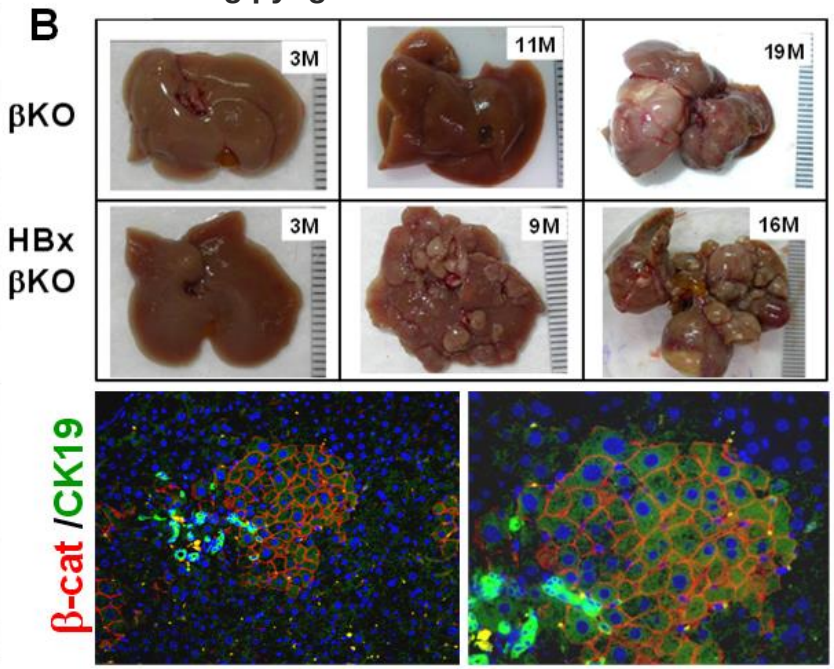
(Yang HI, et al. J Natl Cancer Inst. 2008)

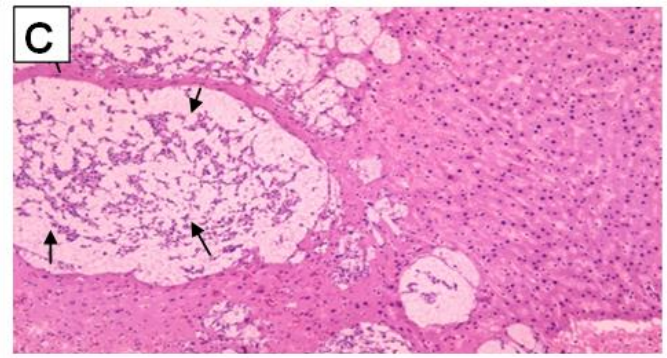
Microbial Genomics Core

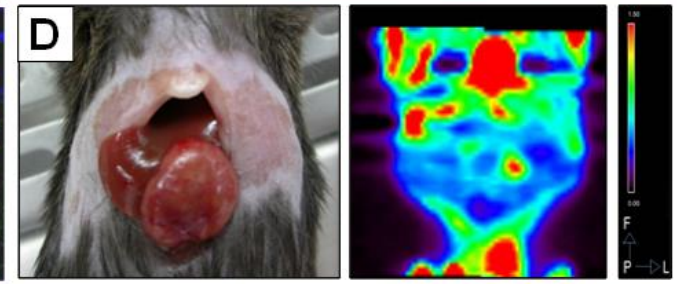
Establish the animal models for Infectious diseases

(1) Immunocompetent mouse model for chronic HBV infection
(2) Orthotopic HCC mouse model → Gene therapy and drug development
(3) The knockout mouse model for viral protein induced HCC from progenitor cells
(4) Woodchuck models for hepatitis virus infection and HCC
(5) The mice model for *K. pneumoniae* causing pyogenic liver abscess





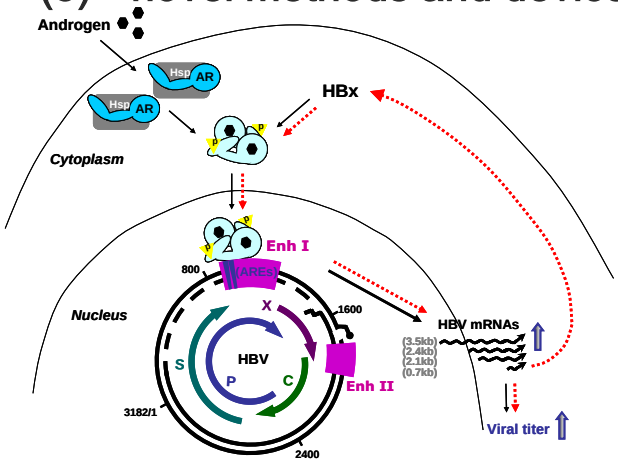


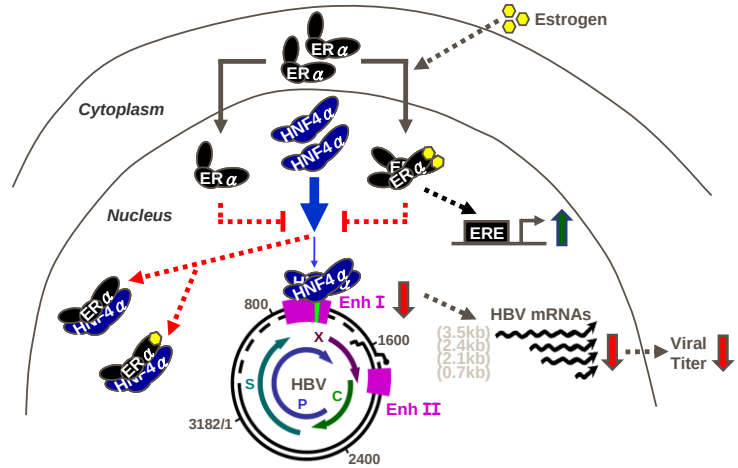


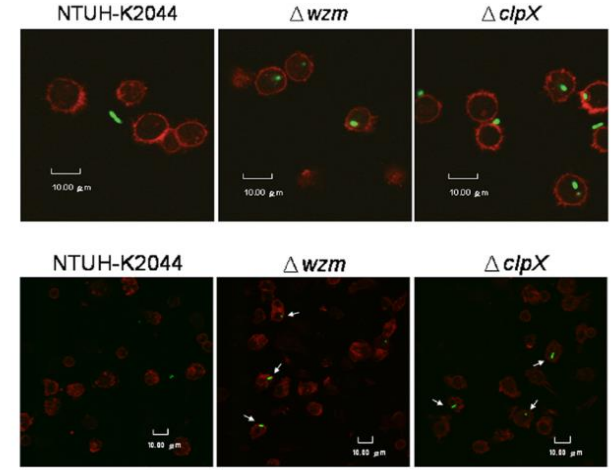
Lin YJ, et al. Proc. Natl. Acad. Sci. USA. 2010
Fang CT, et al. J. Exp. Med. 2004
Huang KW, et al. Proc. Natl. Acad. Sci. USA. 2010
Wang EY, et al. Proc. Natl. Acad. Sci. USA. 2011

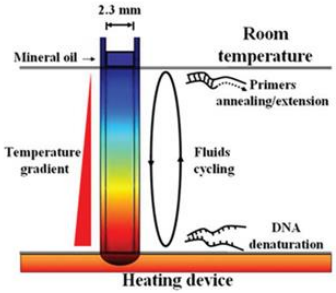
Identify novel mechanisms for infectious diseases

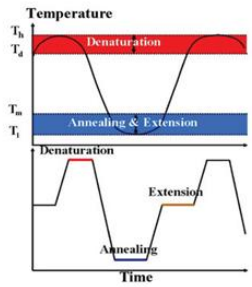
(1) the sex steroids in regulating virus infection and liver carcinogenesis
(2) the genetic loci for *K. pneumoniae* pathogenesis
(3) the factors in determining the persistence of viral infection
(4) the genome evolution in liver cancer development
(5) novel methods and devices for microbial detection

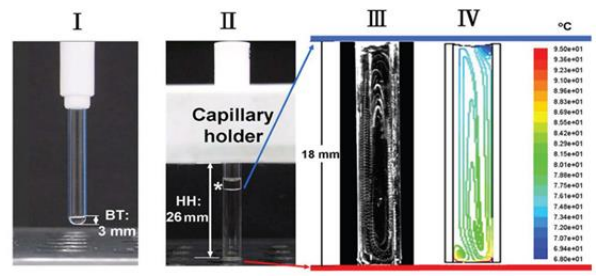








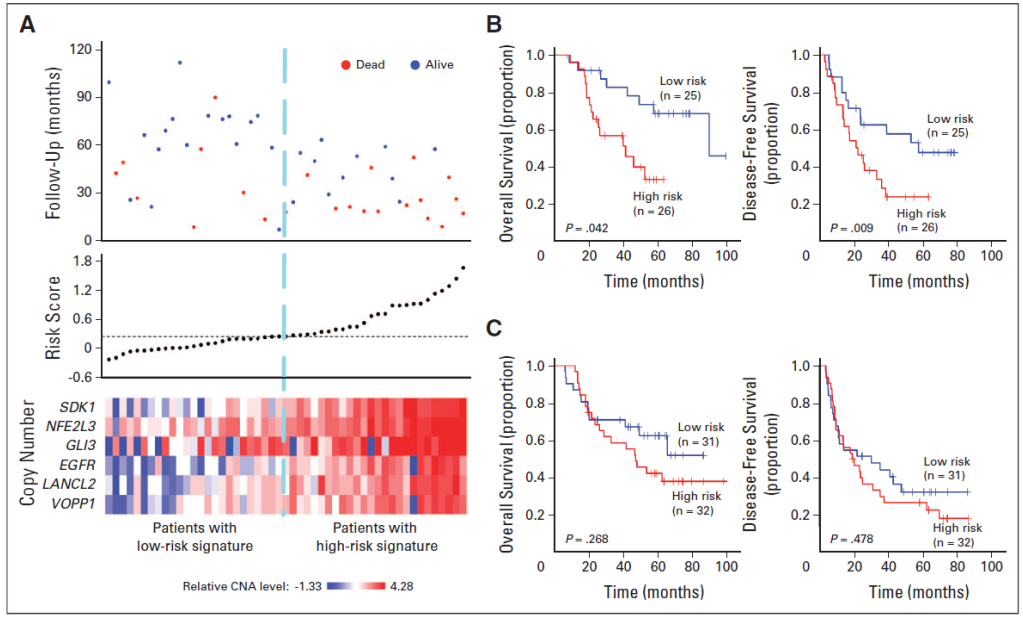


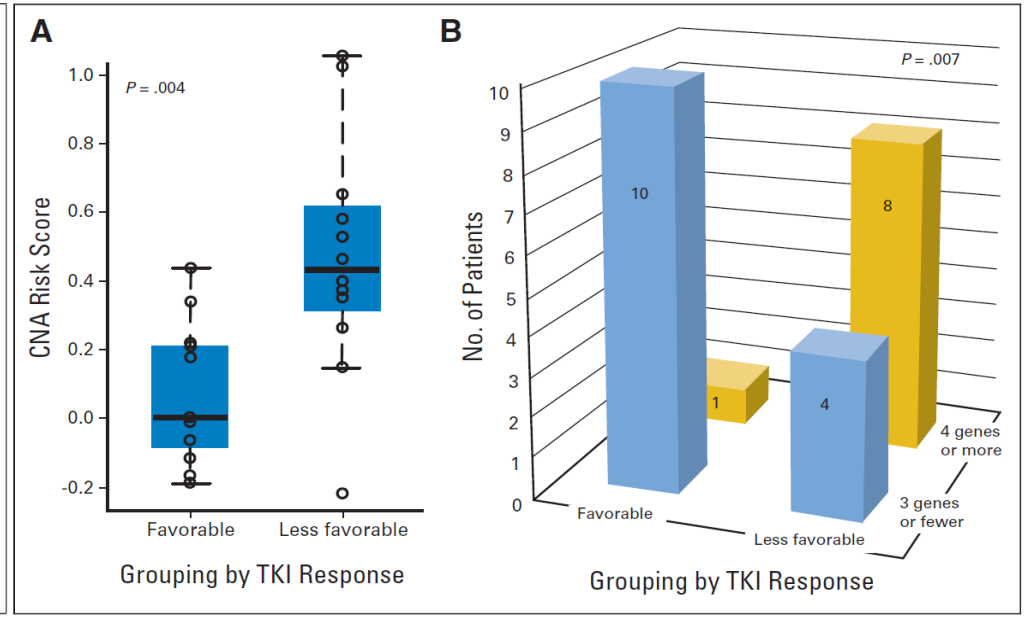


Wang SH, et al. Gastroenterology. 2012
Tao Y, et al. Proc. Natl. Acad. Sci. USA. 2011
Pan YJ, et al., Infect Immun. 2011
Chou WP, et al. Biotechniques . 2011
Wang SH, et al. Hepatology. 2009
Liu WH, et al. Gastroenterology. 2009

Predicting Therapeutic Response of Lung Adenocarcinoma with EGFR Mutations

30% of lung adenocarcinoma patients with EGFR-activating mutation are non-responders in epidermal growth factor receptor tyrosine kinase inhibitors (EGFR-TKIs) treatment. We identify a prognostic signature unique to the EGFR-activating mutant patients. Our finding may lead to a better patient management for EGFR-mutant patients.



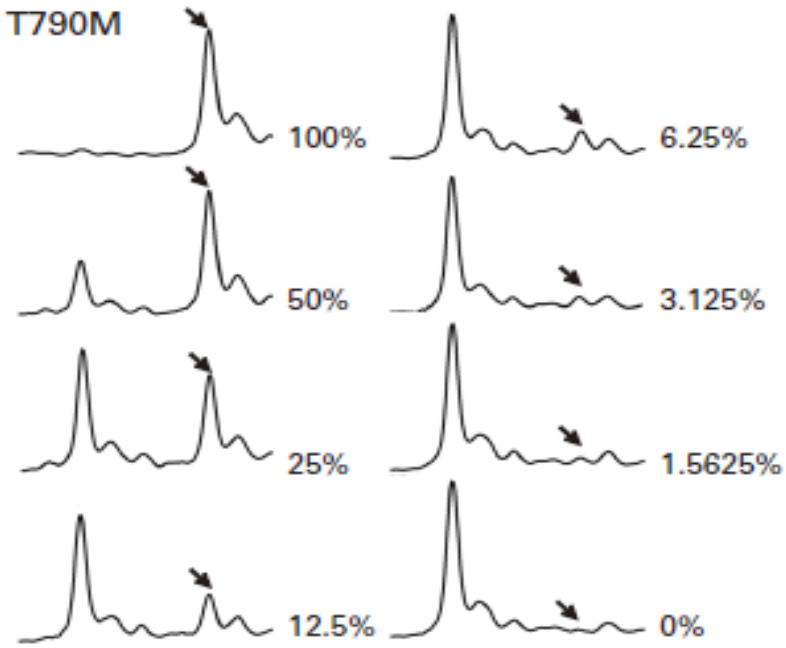


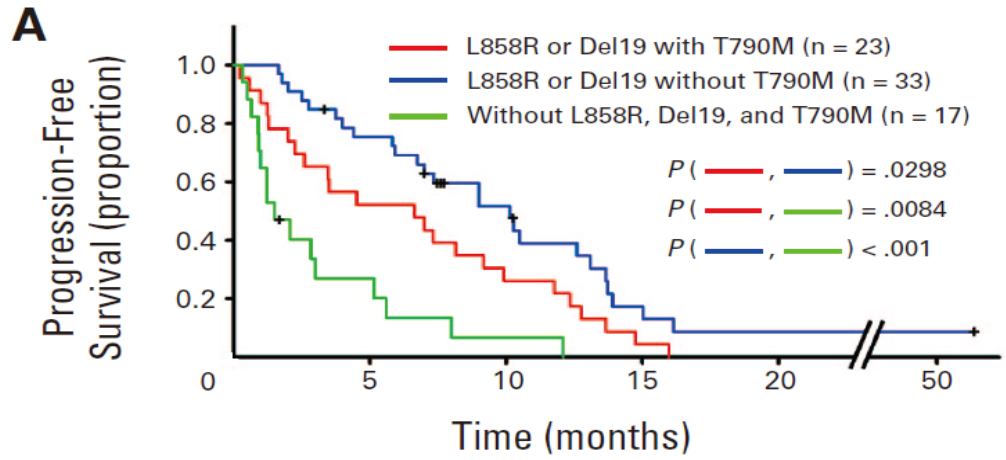
Microarray Core

Publications: Journal of Clinical Oncology 2011, 29:3435-42.
Patent Application: US US1975-2011.7.4, PCT

Pre-treatment EGFR T790M Mutation Predicts Shorter EGFR-TKI Response in Lung Cancer

- Non-small cell lung cancer (NSCLC) patients with EGFR-activating mutations have excellent response to EGFR-tyrosine-kinase-inhibitors (EGFR-TKIs) but T790M mutation accounts for most TKI drug resistance. This study used highly sensitive methods to detect T790M before and after TKI therapy and found the pre-treatment T790M mutation was associated with shorter PFS of EGFR TKI therapy in NSCLC patients.





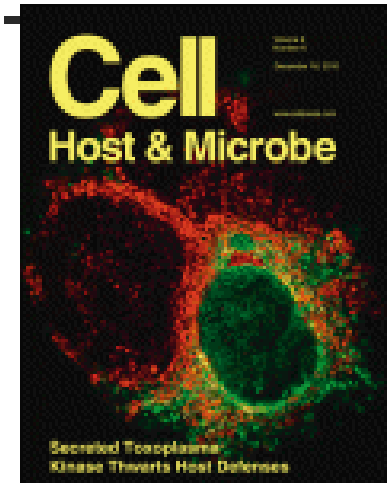
Cox Regression Model

Variable	Hazard Ratio	95% CI	*P*
L858R or Del19 without T790M	1.000		
L858R or Del19 with T790M	1.854	1.044 to 3.292	.035
Without L858R, Del19, and T790M	4.965	2.524 to 9.765	< .001

Publications: **Journal of Clinical Oncology 2012 Jan 3.**

Enterovirus vs. microRNA

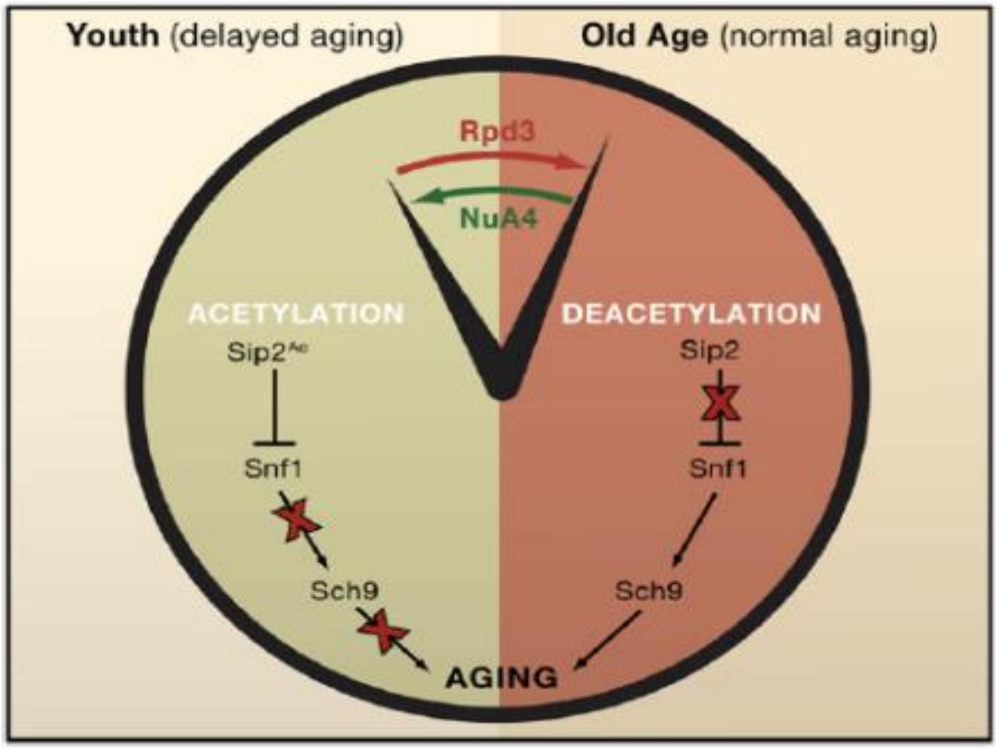
- Enterovirus can up-regulate microRNA-141 to shutdown host protein synthesis and start to make viral proteins and promote viral replication (**Cell Host & Microbe,** January issue of 2011).
- This work demonstrated that microRNA-141 will be a novel therapeutic target.



Acetylation of Yeast AMPK Controls Intrinsic Aging Independently of Caloric Restriction

Cell

Jin-Ying Lu,[1,2] Yu-Yi Lin,[3] Jin-Chuan Sheu,[4] June-Tai Wu,[5] Fang-Jen Lee,[5] Yue Chen,[6] Min-I Lin,[1] Fu-Tien Chiang,[1,] Tong-Yuan Tai,[4] Shelley L. Berger,[7] Yingming Zhao,[6] Keh-Sung Tsai,[1,2,4] Heng Zhu,[8,10,*] Lee-Ming Chuang,[2,4,*] and Jef D. Boeke[9,10,*]



Acetylation and The Elixir of Life

在Yeast模式，限制卡路里可延緩老化，然而細胞內生性的老化仍然受到 *Acetylation* 調控！

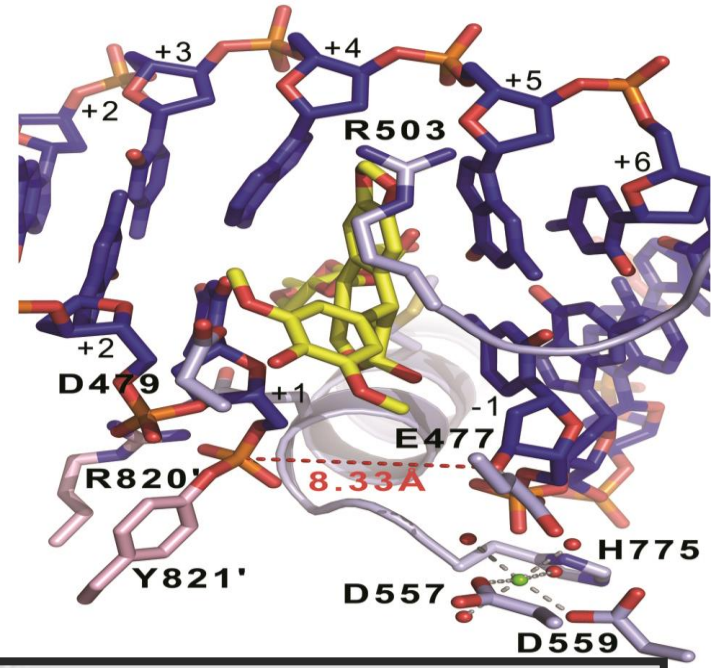
[1]Department of Laboratory Medicine, National Taiwan University Hospital
[2]Graduate Institute of Clinical Medicine, College of Medicine
[3]Institute of Biochemistry and Molecular Biology, College of Medicine

Lu JY et al, Cell 146:969 -79, 2011

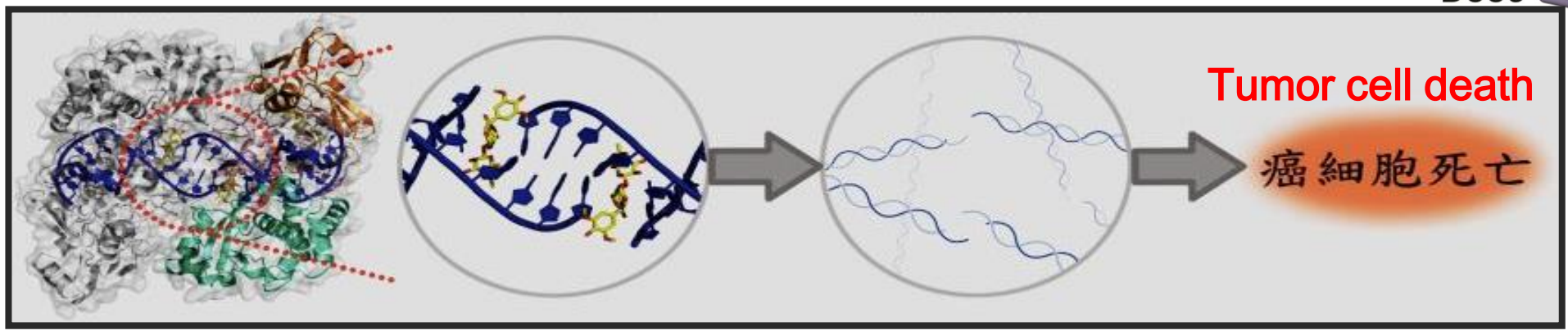
SCIENCE Vol. 333, 22 JULY 2011, 459-462

Structural Basis of Type II Topoisomerase Inhibition by the Anticancer Drug Etoposide

Chyuan-Chuan Wu,[1] Tsai-Kun Li,[2,3] Lynn Farh,[4] Li-Ying Lin,[1,5] Te-Sheng Lin,[1,5] Yu-Jen Yu,[1] Tien-Jui Yen,[1] Chia-Wang Chiang,[1,5] Nei-Li Chan[1,5]*
[1]台大醫學院生物化學暨分子生物學研究所



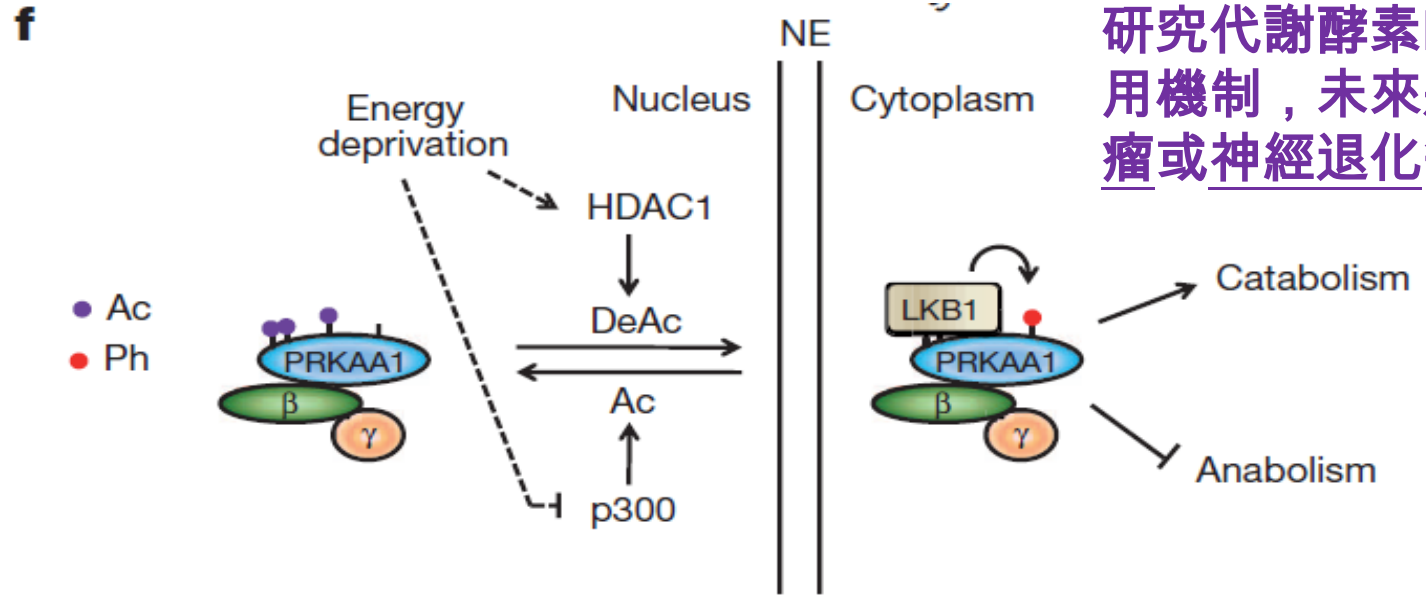
研究闡明抗癌藥etoposide引發DNA斷裂，導致癌細胞死亡結構基礎，可用於開發低副作用的新型抗癌藥物。



LETTER Volume: 482, Pages: 251–255 (09 February, 2012)
doi:10.1038/nature10804

Functional dissection of lysine deacetylases reveals that HDAC1 and p300 regulate AMPK

Yu-yi Lin[1,2,3], Samara Kiihl[4]*, Yasir Suhail[5]*, Shang-Yun Liu[1], Yi-hsuan Chou[1], Zheng Kuang[6,7], Jin-ying Lu[2,8], Chin Ni Khor[9], Chi-Long Lin[9], Joel S. Bader[5], Rafael Irizarry[4] & Jef D. Boeke[6,7]

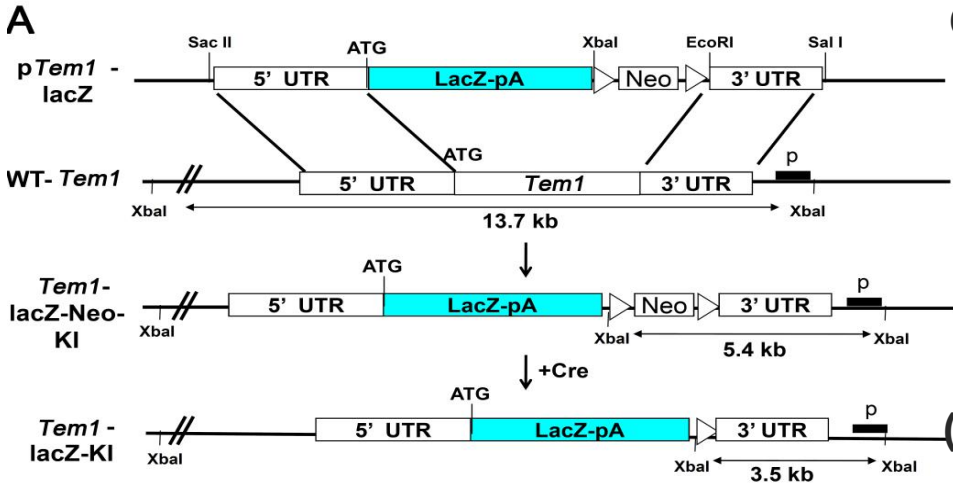


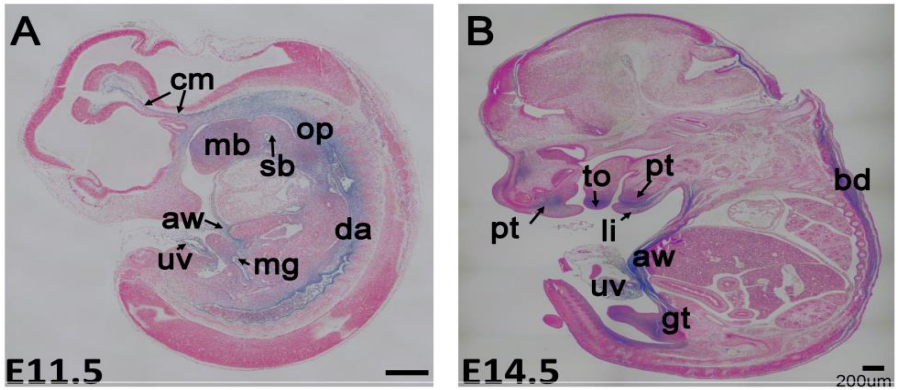
研究代謝酵素Lysine deacetylases 作用機制，未來將可能運用在治療新生腫瘤或神經退化等之疾病。

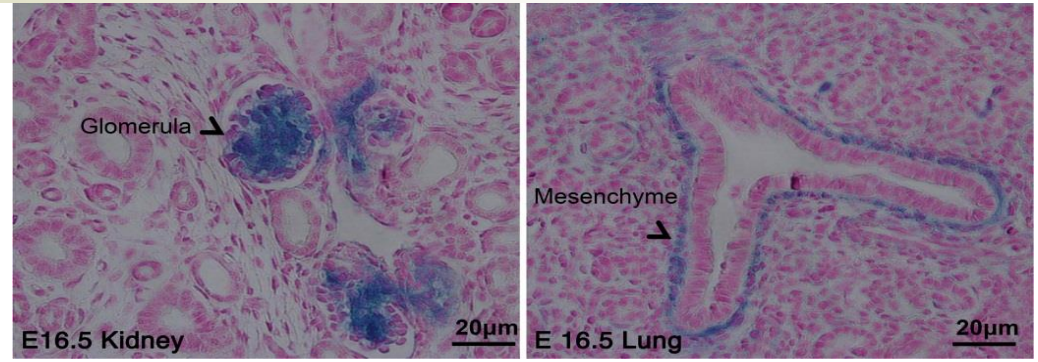
Figure 4 | Deacetylation of PRKAA1 specifically enhances its physical interaction with LKB1 kinase. **a**, Phosphorylation of endogenous PRKAA1 is reduced and unresponsive to acetylation status upon knockdown of *LKB1*.

Gene Knockout Mouse Core Laboratory

Gene targeting and expression analysis of mouse protein using the lacZ reporter







(A) Maps of wild-type Tem1 allele, recombinant allele with the single exon of the Tem1 gene replaced by the lacZ/neo gene, and final recombinant allele with lacZ but without neo.

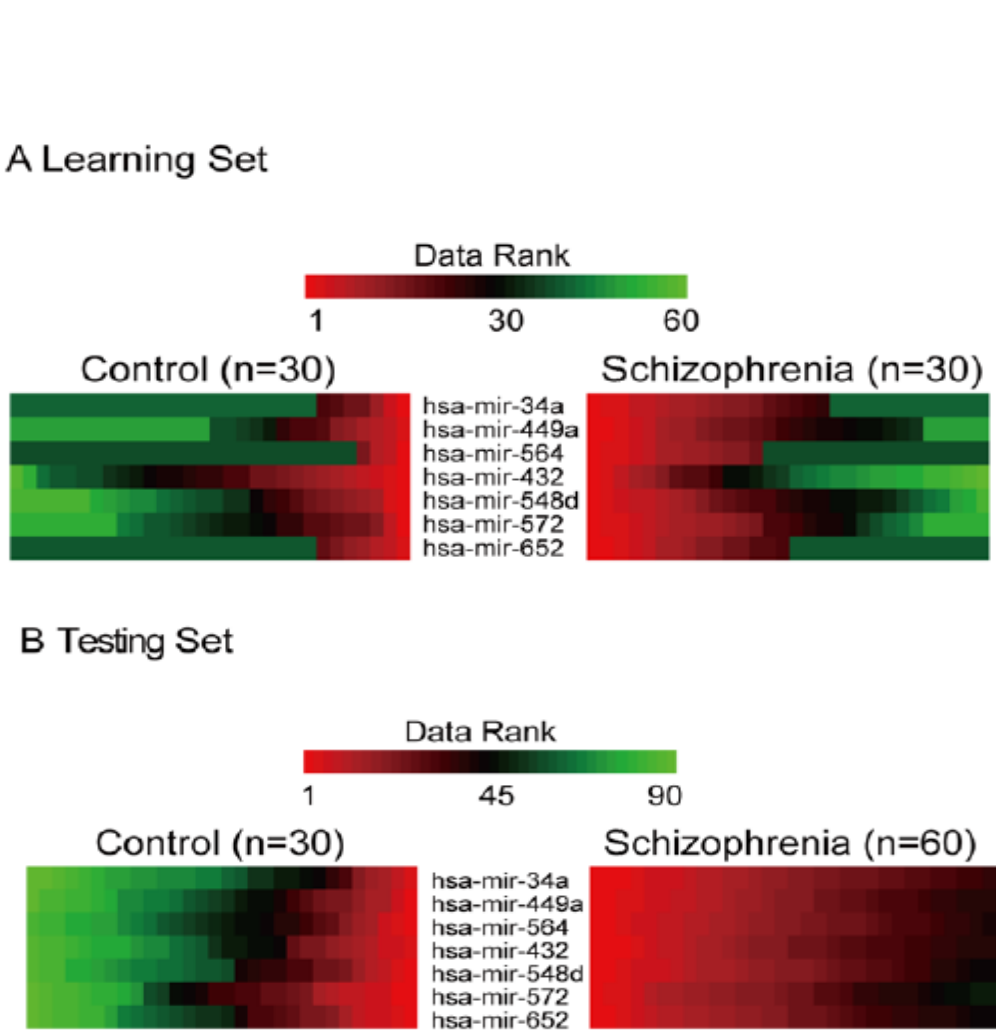
(B) Whole-mount Bluo-Gal staining followed by sagittal sectioning showing Tem1-lacZ expression in E11.5 and E14.5 mouse embryos.

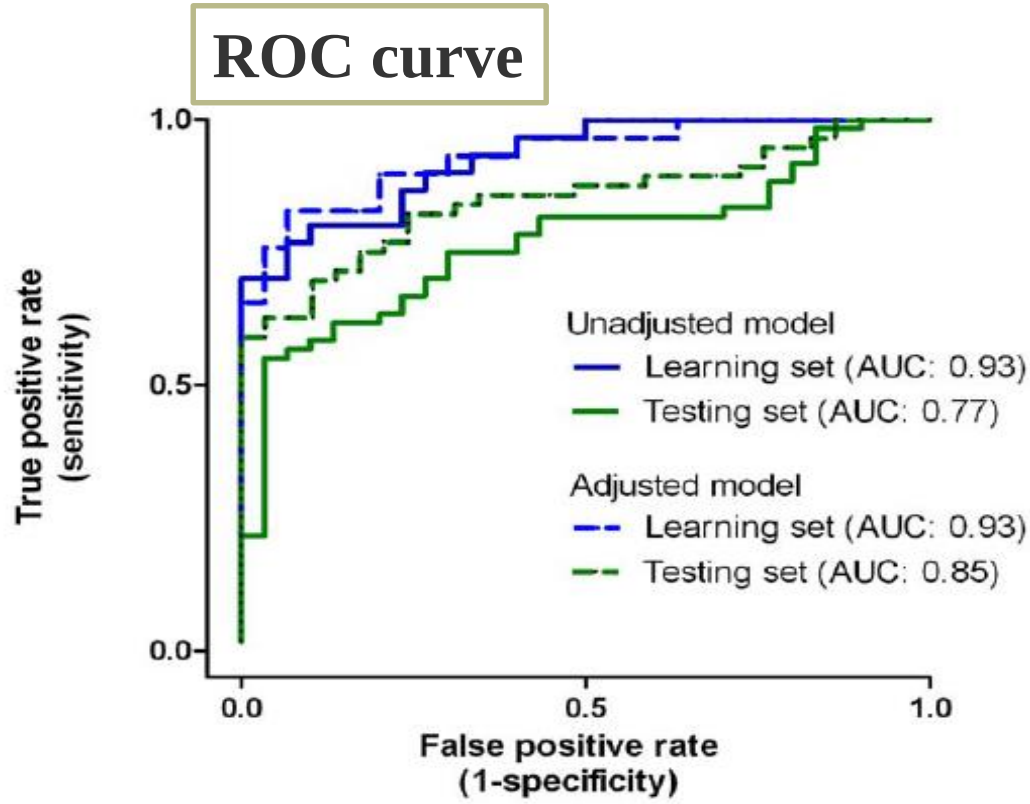
(C) At E16.5, strong Tem1-lacZ expression emerges in the glomeruli of the kidney and the mesenchymal cells or mesenchymal-like cells or around the bronchial epithelial cells of the lung.

(ref. Huang et al., Gene Expression Patterns, 2011)

週邊血液之7種微小核醣核酸 (microRNA)表現偏差作為精神分裂症生物標記的可能性

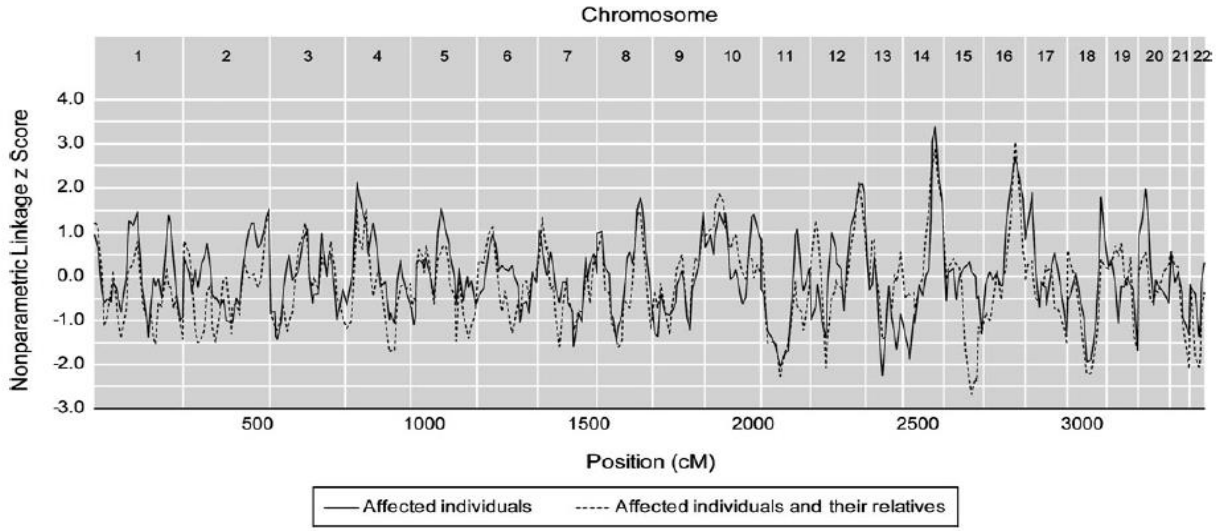
(Lai et al., 2011, *PLoS ONE* 6: e21635)





針對病人及其家屬之菸鹼酸貼片皮膚紅腫反應進行QTL全基因體掃描，尋獲新的精神分裂症遺傳連鎖標誌14q32.12

(Lien et al., 2011, *Schizophrenia Bulletin*: doi: 10.1093/schbul/sbr054)



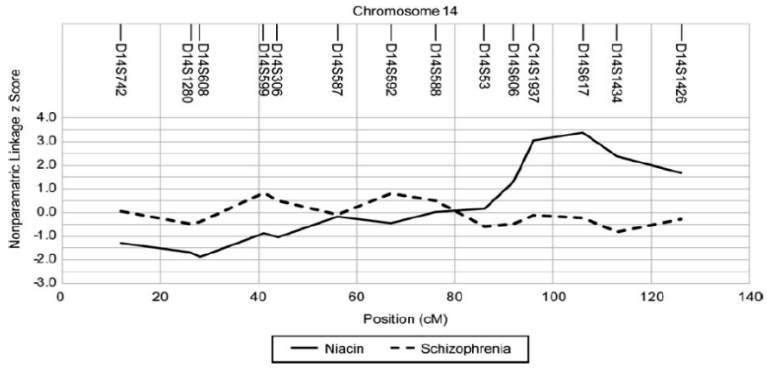
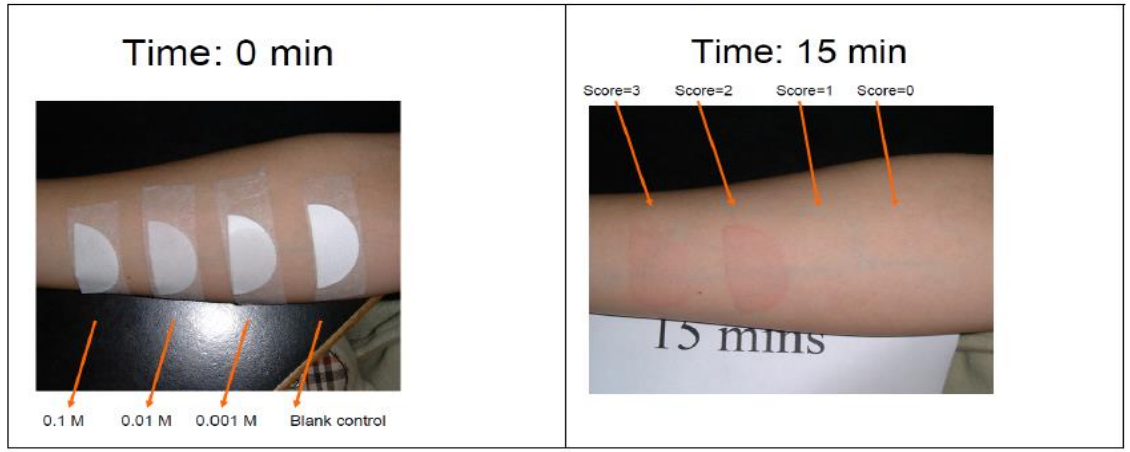
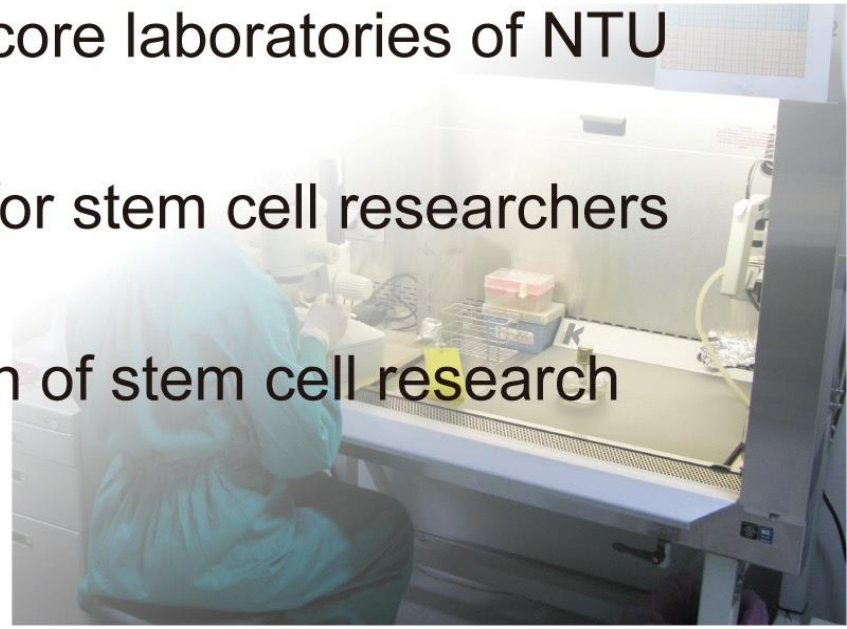


Figure S1. Implementation of the niacin skin patch and the scoring for the flush response.



Stem Cell Core

- To supply hESC for **the researchers within NTU medical campus**
- To provide the techniques and routines for characterization of hESC
- To integrate the service provided by the core laboratories of NTU **Center of Genomic Medicine**
- To supply hESC and technical supports for stem cell researchers nationwide
- To promote the international collaboration of stem cell research



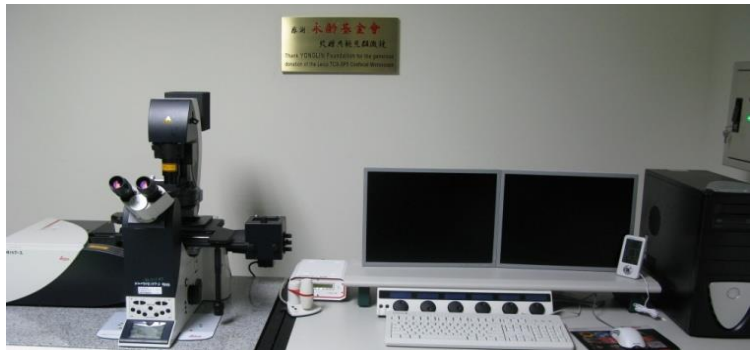
6F, No. 2, Syu-jhou Road, Taipei 10055, Taiwan, R.O.C.
Phone:+886-2-2312-3456 ext 88637 E-mail: stemcell@ntu.edu.tw

Human ES cell and feeder cell supply
(2008/10/31-2011/06/15)

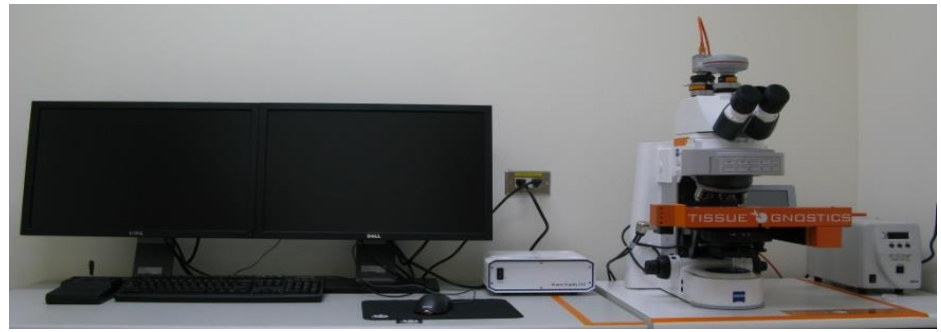
Applicant Units	PI	Dish	Research subject
NTU, IOB	李宣書	318	Generation of insulin-producing cells
NTU, Dept. of Food Science and Technology	蔣丙煌	61	The effect of Ginkgo extract on dopaminergic neuron differentiation
NTUH, Dept. of Surgery	吳耀銘	86	Hepatic differentiation of ES cell
NTU, Dept. of Pharmacology	郭明良	52	Cancer stem cell study
NTU, Institute of Microbiology	鄧述諄	275	Telomerase capacity of ES cell differentiation
NTU, Institute of Clinical Genomics	陳佑宗	60	Genetic manipulation of ES by PiggyBac transposon
NTU, Dept. of Pharmacology	陳青周	20	Hepatic differentiation of ES cell
NTU, Biomedical Engineering	林峰輝	192	Expansion ES cell by bioreactor
NTUH, Dept.of Obs/Gyn	何弘能	70	Establish new ES cell line
NTUH, Dept. of Ophthalmology	楊長豪	184	The oxidative stress of ES cells induced by paraquat

Core Facilities

Confocal (Leica TCS SP5)



Tissue FAXS



Laser-Enabled Analysis and Processing System (LEAP™)

Cell Sorter (BD FACS Aria II)

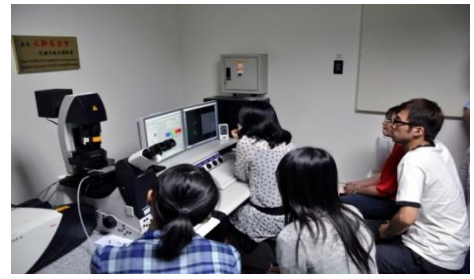
Stem Cell Core Workshop

Introducing Stem Cell Core service and its core facilities on 2010/05/26

NTU participants		Non-NTU participants	
Professors	11	Students	1
Students	27	Industrial	5
Research Assistants	22	YongLin Healthcare Foundation	2
Postdoctoral Research Fellow	8		
Medical Doctors	2		
Medical Laboratory Scientist	1		
Subtotal	71	**Subtotal**	8
Total		79	

Core PI, Prof. Ho gave a brief introduction.

Core Co-PI, Prof. Chien introduced core service and instruments



Instrument Demonstration: Confocal microscope

Instrument Demonstration: IVIS, Xonogen

Education

International Students		
Year	Nationality	Subtotal
2008	Thailand、Spain(2)、Poland、Slovenia、Serbia(2)	7
2009	Spain、Portugal、Hungary、Italy	4
2010	Thailand、the Netherlands(2)、Spain、Italy、Italy、Austria、Hungary	8
2011	Thailand、Slovenia(2)、Hungary、Italy、USA	6
Total		**25**

Summer Camp Students		
Year	Grade	Subtotal
2008	3rd grade、4th grade	2
2009	1st grade、2nd grade、5th grade (2)	4
2010	2nd grade	3
2011	1st grade、2nd grade (2)、3rd grade	4
Total		**13**

代謝體核心實驗室
Metabolomics Core Laboratory

臺灣大學

- **代謝體研究服務**: 樣品處理、樣品分析、代謝體諮詢服務、生物標的確效(biomarker verification)、代謝圖譜分析
- **代謝體分析方法開發**:開發並改良LC-MS與GC-MS分析方法
- **數值分析方法開發**: run order analysis, outlier detection, peak detection, baseline correction, alignment
- **代謝體研究**: 包括臨床及營養代謝體研究以達到轉譯醫學之個人化醫療。

代謝體核心實驗室

Metabolomics Core Lab.

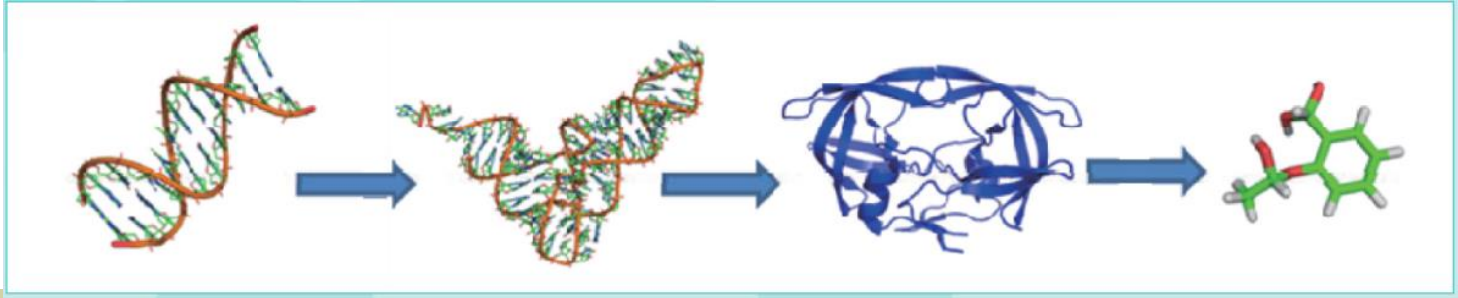


Figure 1. Central Dogma of Molecular Biology with Metabolome

Honors Awards

MetaPick, a denoising and peak picking algorithm for extracting single compound from complex mixtures in liquid chromatography/mass spectrometry (LC/MS) metabolomics data, Metabolomics 2011, Best informatics presentation award.

Services

- 代謝體服務包括代謝體研究與實驗設計諮詢、樣品處理、儀器分析質譜圖譜分析；服務申請者包括臨床醫師與基礎學術研究者，樣品種類包括血液、尿液、細胞萃取液及呼出氣體等。
- 100年度已完成之服務共計21案，總計樣品數量1124個，進樣針數4496針，品管針數540針。收樣中及預計進行之服務共計25案，總計樣品數量2380個。

Future Directions

- Backup new research Institutes:
  Cancer, Genomics, IBMS (Neurosciences)
- Multidisciplinary translational research
- International collaborations (MD Anderson, Terry Fox, Peking University, etc.)
- New area and facility:
  Metabolomics
  High throughput sequencer
  Novel drug design for target therapy
  Molecular Imaging & Medical devices, etc.

校內跨中心合作

針對 系統生物學研究中心、分子生醫影像研究中心兩大研究領域之合作，將以人才交流共同提升國際化為目標。

每年將規劃暑期研習營培訓大學部同學，栽培未來跨領域研究新秀。

共同舉辦國際學術研討會，為臺灣大學與英、美、日及歐盟等大學建構學術合作平臺。

中心已獲得或申請中之其他計畫/經費說明

99年度教育部補助之邁向頂尖大學經費佔中心實際經費資源約30%，校務基金及中心核心服務收入約10%，向外爭取之經費包含貴重儀器與其他經常費用超過60%，教育部補助本中心之效益比超過兩倍以上。

100年度中心已獲得之其他計畫包括:

- 教育部顧問室轉譯醫學人才培育計畫
- 生技醫藥國家型科技計畫：通過多項計畫
- 國科會100年幹細胞及再生醫學前瞻計畫
- 跨國頂尖中心計畫 (MD Anderson)

中心100年度核定經費 (單位：千元)

補助項目	核定金額
研究人力費	21,040
業務費 (耗材、物品及雜項費用)	8,960
儀器設備費	10,000
合　　計	**40,000**

中心101年度期經費規劃說明

年次	研究人力費	耗材及雜項費用	研究設備費	國外或大陸地區差旅費	出席國際學術會議差旅費	小計
101	42,417	12,598	20,455	1,280	3,327	80,077
102	43,536	12,602	21,623	1,280	3,327	82,368
103	44,422	12,600	20,513	1,280	3,327	83,142
104	45,173	12,604	20,149	1,280	3,327	82,533

中心5年期經費規劃說明

- 研究人力費：(核心實驗室基本服務人力; 規劃聘用10位專案助理教授 ，儲備具國際競爭力人才):

  ~ NT$ 43,000,000/year

- 耗材及雜項費 (實驗室耗材及研究中心基本維護費)：

  ~ NT$ 13,000,000/year

- 研究設備費 (汰舊換新設備、大型儀器組件維護)：

  ~ NT$ 21,000,000/year

- 國際交流經費 (邀請國外學者及出席國際會議差旅費)：

  ~ NT$ 5,000,000/year

Total: ~ NT$ 82,000,000/year

敬請
委員們支持與指正