研 究 之 美
--傳承與志業

2013年05月02日
佛教慈濟綜合醫院
劉鴻文

教學目標：

一、瞭解研究本質

二、激發研究興趣

三、享受研究樂趣

四、促進本院研究

DEFINITION OF RESEARCH

- In the broadest sense of the word, the definition of research includes any gathering of data, information and facts for the advancement of knowledge.

DEFINITION OF RESEARCH

- It is an creative, cumulative and often long-term activity conducted by people with specialist' knowledge about the theories, methods and information concerning their field of enquiry. Its findings must be open to scrutiny and formal evaluation by others in the field, and this may be achieved through publication or public presentation.

研 究 本 質

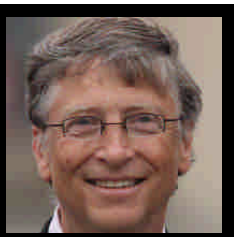
Who

What

Why

Where

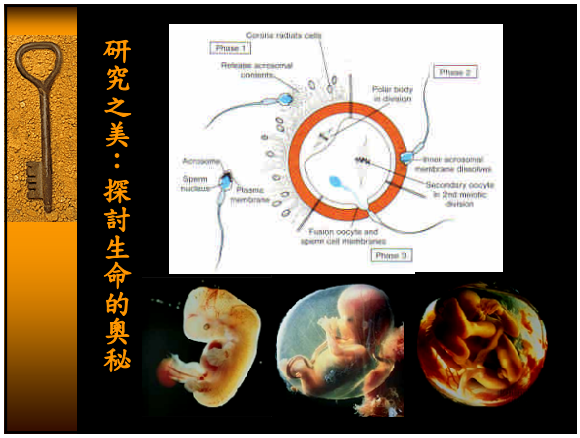
How

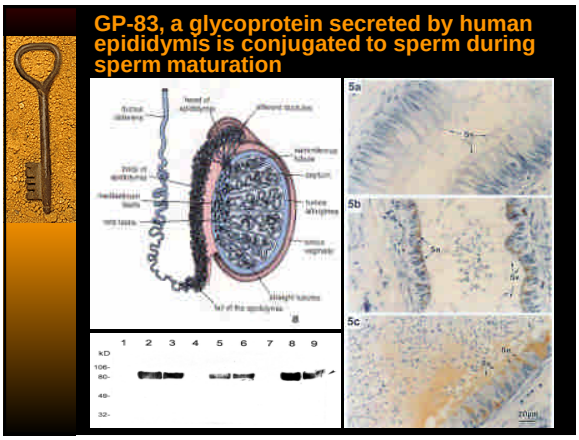


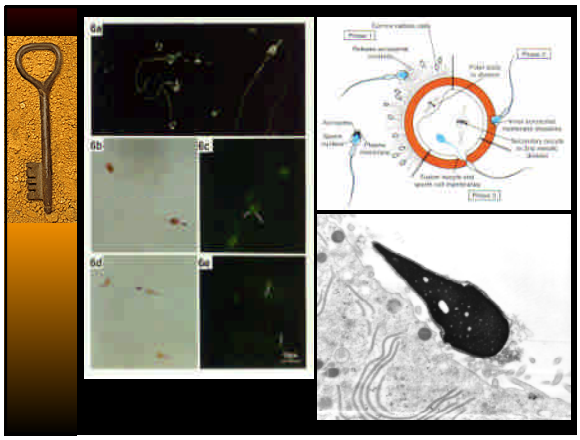
At age 14, Bill Gates started a venture, Traf-O-Data with Allen to make traffic counters using Intel 8008 processor. That first year he made $20,000. In 1975, Gates took a leave of absence from Harvard to work with Allen at MITS, dubbing their partnership "Micro-soft" (microcomputer and software)

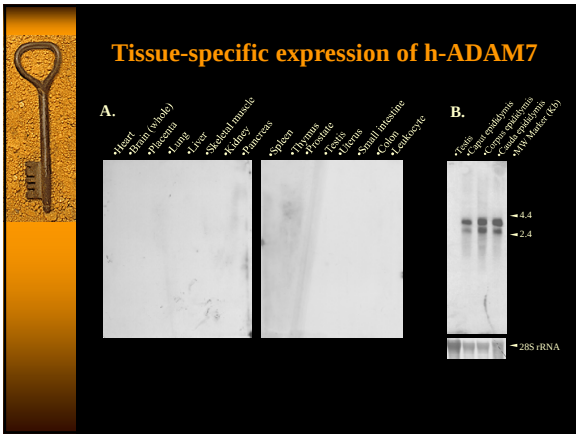
5/1/2013 6

傳承
傳道、授業、解惑
真如本性
一生追求的志業


研究之美：探討生命的奧秘


GP-83, a glycoprotein secreted by human epididymis is conjugated to sperm during sperm maturation




Tissue-specific expression of h-ADAM7

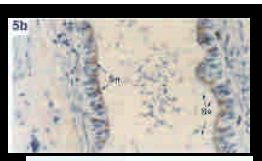
Human ADAM7
prodomain
Metalloprotease
Disintegrin
Cysteine-rich
EGF-like
Transmembrane & Cytoplasmic

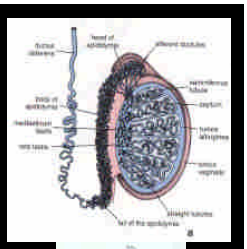
GeneBank

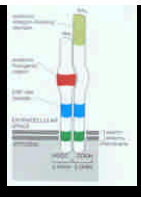
LOCUS AF215824 2583 bp mRNA linear PRI
02-JAN-2001
DEFINITION Homo sapiens a disintegrin and metalloproteinase 7 (ADAM7) mRNA, complete cds.
ACCESSION AF215824
VERSION AF215824.1 GI:12004291
KEYWORDS .
SOURCE Homo sapiens (human)
ORGANISM Homo sapiens
Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Primates; Haplorrhini; Catarrhini; Hominidae; Homo.
REFERENCE 1 (bases 1 to 2583)
AUTHORS Lin,Y.C., Lee,Y.M., Sun,G.H. and Liu,H.W.
TITLE Expression of human ADAM7 (GP-83)

Chromosome localization

- Human ADAM7 is located at chromosome 8p22 according to the DNA sequence elucidated in "Human Genome Project (completed in April 2003)".

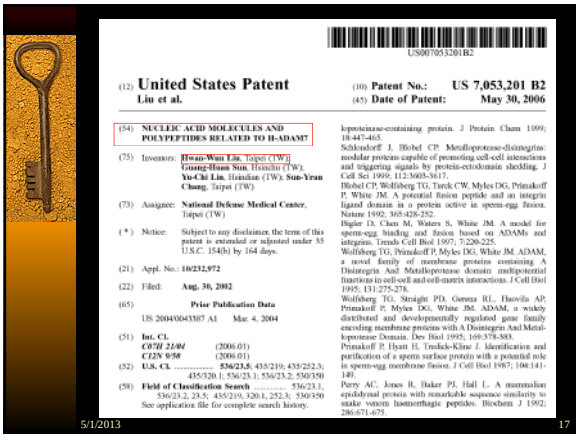






Cloning and Characterization of a Complementary DNA Encoding a Human Epididymis-Associated Disintegrin and Metalloprotease 7 Protein1

Received: 22 March 2001.
First decision: 18 April 2001.
Accepted: 3 May 2001.
© 2001 by the Society for the Study of Reproduction, Inc.
ISSN: 0006-3363. http://www.biolreprod.org



US007053201B2

(12) United States Patent
Liu et al.

(10) Patent No.: US 7,053,201 B2
(45) Date of Patent: May 30, 2006

(54) NUCLEIC ACID MOLECULES AND POLYPEPTIDES RELATED TO H-ADAM7

(75) Inventors: Hwan-Wun Liu, Taipei (TW); Giang-Huan Sun, Hsinchu (TW); Yu-Chi Lin, Hsinchu (TW); Sun-Yuan Chang, Taipei (TW)

(73) Assignee: National Defense Medical Center, Taipei (TW)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 164 days.

(21) Appl. No.: 10/232,972

(22) Filed: Aug. 30, 2002

(65) Prior Publication Data

US 2004/0043387 A1 Mar. 4, 2004

(51) Int. Cl.
C07H 21/04 (2006.01)
C12N 9/50 (2006.01)

(52) U.S. Cl. 536/23.5; 435/219; 435/252.3; 435/320.1; 536/23.1; 536/23.2; 530/350

(58) Field of Classification Search 536/23.1, 536/23.2, 23.5; 435/219, 320.1, 252.3; 530/350
See application file for complete search history.

lopoteinase-containing protein. J Protein Chem 1999; 18:447-465.
Schlondorff J, Blobel CP. Metalloprotease-disintegrins: modular proteins capable of promoting cell-cell interactions and triggering signals by protein-ectodomain shedding. J Cell Sci 1999; 112:3603-3617.
Blobel CP, Wolfsberg TG, Turck CW, Myles DG, Primakoff P, White JM. A potential fusion peptide and an integrin ligand domain in a protein active in sperm-egg fusion. Nature 1992; 356:428-252.
Bigler D, Cham M, Waters S, White JM. A model for sperm-egg binding and fusion based on ADAMs and integrins. Trends Cell Biol 1997; 7:220-225.
Wolfsberg TG, Primakoff P, Myles DG, White JM. ADAM, a novel family of membrane proteins containing A Disintegrin And Metalloprotease domain: multipotential functions in cell-cell and cell-matrix interactions. J Cell Biol 1995; 131:275-278.
Wolfsberg TG, Straight PD, Gerena RL, Huovila AP, Primakoff P, Myles DG, White JM. ADAM, a widely distributed and developmentally regulated gene family encoding membrane proteins with A Disintegrin And Metalloprotease Domain. Dev Biol 1995; 169:378-383.
Primakoff P, Hyatt H, Tredick-Kline J. Identification and purification of a sperm surface protein with a potential role in sperm-egg membrane fusion. J Cell Biol 1987; 104:141-149.
Perry AC, Jones R, Baker PJ, Hall L. A mammalian epididymal protein with remarkable sequence similarity to snake venom haemorrhagic peptides. Biochem J 1992; 286:671-675.

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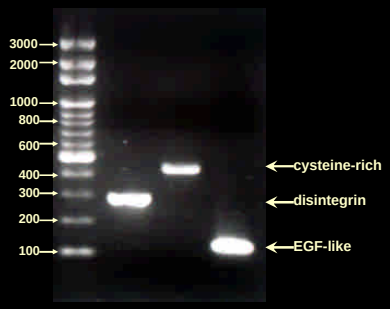
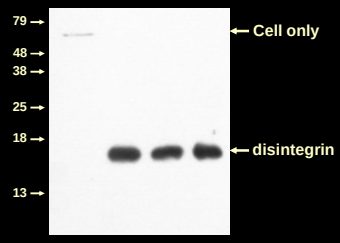
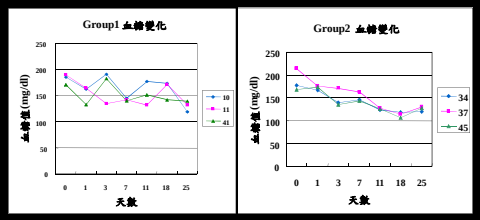
PCR amplification



Ex vivo expression of the disintegrin domain recombinant protein in the BHK-21 cells.





圖二、SD公鼠在施打人類ADAM7去整合素重組蛋白後血糖變化情形；Group 1的劑量為0.45mg/100g， Group 2的劑量為0.9mg/100g 。

結合教學、服務之研究

賴春生

Chung-Sheng Lai, M.D., EMBA, Ph.D.

- 整形外科醫學會 理事長
  President, Plastic Surgical Association, ROC
- 高雄醫學大學 醫學院院長
  Dean, College of Medicine, Kaohsiung Medical University
- 高醫附院 整形外科主任
  Director, Department of Plastic Surgery, Kaohsiung Medical University Hospital

病人健康照護矩陣 (Patient Healthcare Matrix: Care of Patient with...)

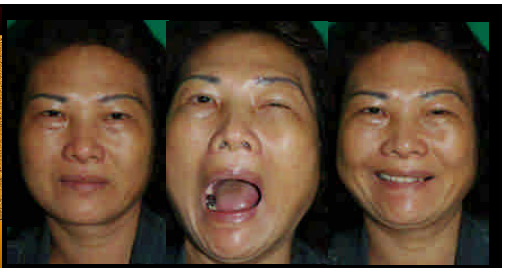
目標 / 能力	病人安全 SAFE[7] (Injury or potential for injury)	及時醫療 TIMELY[8] (Delay in Hrs, Days, week)	醫療成效 EFFECTIVE[9] (Evidence-based care and outcomes)	醫療效率 EFFICIENT[6] (Waste of resources)	平權對待 EQUITABLE[5] (Gender, ethnicity, race, SEC)	病人中心 PATIENT-CENTERED[4] (Preference, needs, values)
病人照護 PATIENT CARE[1] (Overall Assessment) Yes/No						
醫學知能 MEDICAL KNOWLEDGE AND SKILLS[2] (What must we know?)						
人際溝通 INTERPERSONAL AND COMMUNICATION SKILLS[3] (What must we say?)						
專業醫德 PROFESSIONALISM[10] (How must we behave?)						
制度醫療 SYSTEM-BASED PRACTICE[11] (What is the process? On whom do we depend? Who depends on us?)						
實證學習 PRACTICE-BASED LEARNING AND IMPROVEMENT[12] (What have we learned? What will we improve?)						

Doris C. Quinn & John W. Bingham
Journal of Quality & Patient Safety, 2005

病人健康照護矩陣（Taiwanese version of Healthcare Matrix)

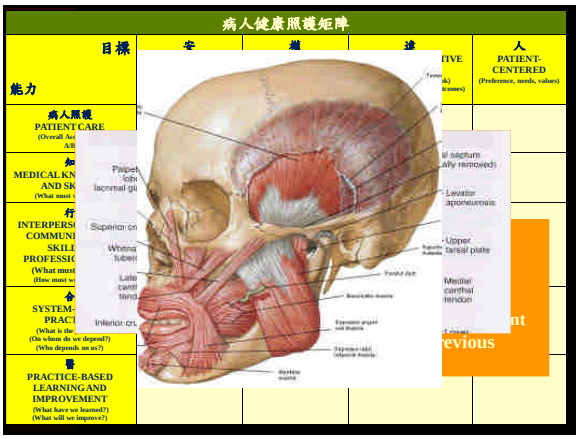
目標 / 能力	安 SAFE (Injury or potential for injury)	權 EQUITABLE (Gender, ethnicity, race, SEX)	速 TIMELY & EFFECTIVE & EFFICIENT (Delay in Hrs, Days, week) (Evidence-based care and outcomes) (Waste of resources)	人 PATIENT-CENTERED (Preference, needs, values)
病人照護 PATIENT CARE (Overall Assessment) A/B	A: yes; B: no			
知 MEDICAL KNOWLEDGE AND SKILLS (What must we know?)				
行 INTERPERSONAL AND COMMUNICATION SKILLS & PROFESSIONALISM (What must we say?) (How must we behave?)				
合 SYSTEM-BASED PRACTICE (What is the process?) (On whom do we depend?) (Who depends on us?)				
學 PRACTICE-BASED LEARNING AND IMPROVEMENT (What have we learned?) (What will we improve?)				

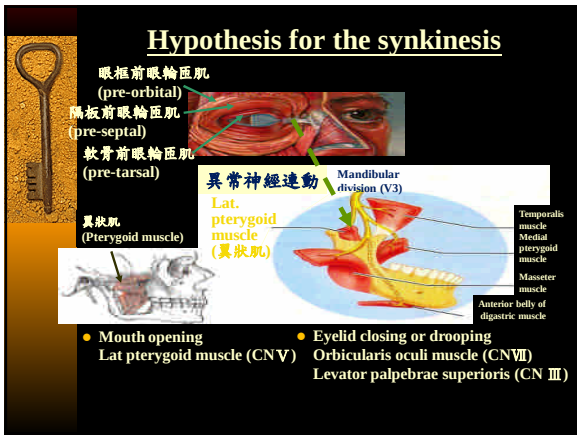
Lee SS, Chiang HC, Chen MC, Chen LS, Hsu PL, Sun IF, *Lai CS.** Experiences of interprofessional implementation of a healthcare matrix. Kaohsiung J. Med. Sci. 24(12):634-9, 2008.

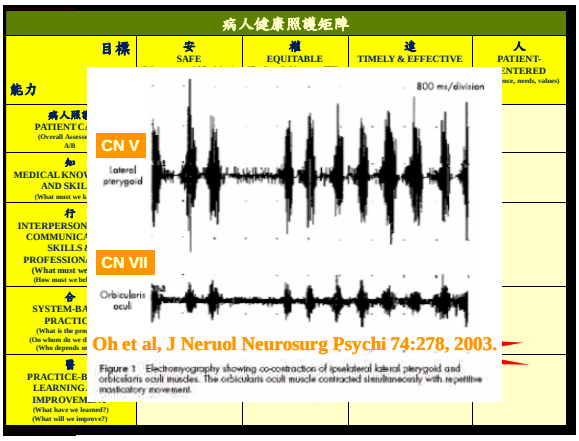


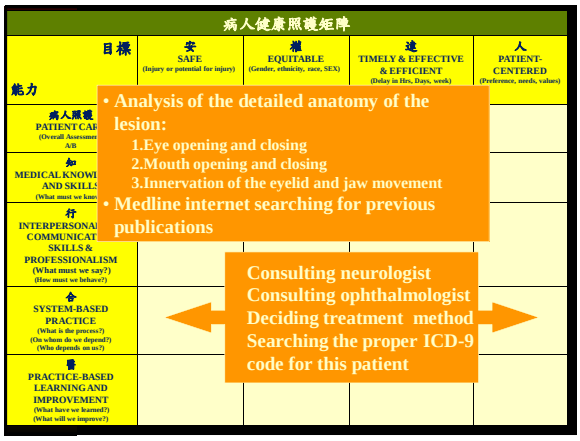
Synkinetic downward closure of her left upper lid when she opened her mouth, chewed, or moved the jaw laterally, especially to the right side (contralateral side)

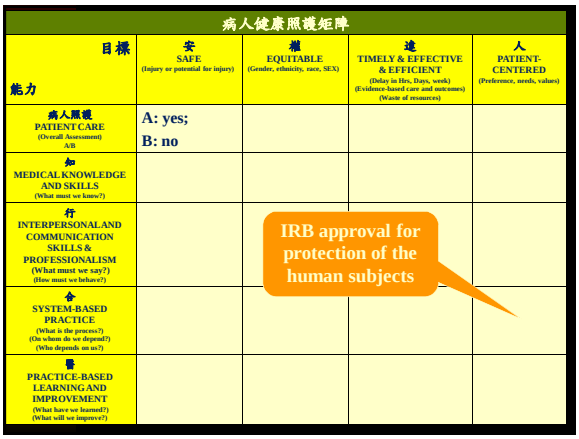
Keywords: facial synkinesia, eyelid, mouth

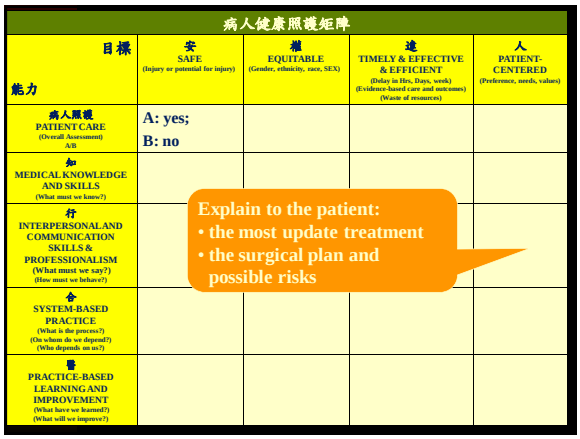

病人健康照護矩陣
目標
能力
安
權
達
人
PATIENT-CENTERED
(Preference, needs, values)
病人照護
PATIENT CARE
MEDICAL KN
AND SK
INTERPERS
COMMUNI
SKILL
PROFESSIO
SYSTEM-
PRACT
PRACTICE-BASED LEARNING AND IMPROVEMENT
(What have we learned?)
(What will we improve?)
Levator aponeurosis
Upper tarsal plate
Medial canthal tendon
Superior cr
Inferior cr
nt
evious


Hypothesis for the synkinesis
眼框前眼輪匝肌
(pre-orbital)
隔板前眼輪匝肌
(pre-septal)
軟骨前眼輪匝肌
(pre-tarsal)
異常神經連動
Mandibular division (V3)
Lat. pterygoid muscle
(翼狀肌)
翼狀肌
(Pterygoid muscle)
Temporalis muscle
Medial pterygoid muscle
Masseter muscle
Anterior belly of digastric muscle
• Mouth opening
Lat pterygoid muscle (CNⅤ)
• Eyelid closing or drooping
Orbicularis oculi muscle (CNⅦ)
Levator palpebrae superioris (CN Ⅲ)


病人健康照護矩陣
目標
能力
安
SAFE
權
EQUITABLE
達
TIMELY & EFFECTIVE
人
PATIENT-CENTERED
800 ms/division
CN V
Lateral pterygoid
CN VII
Orbicularis oculi
Oh et al, J Neruol Neurosurg Psychi 74:278, 2003.
Figure 1 Electromyography showing co-contraction of ipsilateral lateral pterygoid and orbicularis oculi muscles. The orbicularis oculi muscle contracted simultaneously with repetitive masticatory movement.


病人健康照護矩陣
目標
能力
安
SAFE
(Injury or potential for injury)
權
EQUITABLE
(Gender, ethnicity, race, SEX)
達
TIMELY & EFFECTIVE & EFFICIENT
(Delay in Hrs, Days, week)
人
PATIENT-CENTERED
(Preference, needs, values)
• Analysis of the detailed anatomy of the lesion:
1.Eye opening and closing
2.Mouth opening and closing
3.Innervation of the eyelid and jaw movement
• Medline internet searching for previous publications
Consulting neurologist
Consulting ophthalmologist
Deciding treatment method
Searching the proper ICD-9 code for this patient
SYSTEM-BASED PRACTICE
PRACTICE-BASED LEARNING AND IMPROVEMENT


病人健康照護矩陣
目標
能力
安
SAFE
(Injury or potential for injury)
權
EQUITABLE
(Gender, ethnicity, race, SEX)
達
TIMELY & EFFECTIVE & EFFICIENT
(Delay in Hrs, Days, week)
(Evidence-based care and outcomes)
(Waste of resources)
人
PATIENT-CENTERED
(Preference, needs, values)
病人照護
PATIENT CARE
(Overall Assessment)
A/B
A: yes;
B: no
知
MEDICAL KNOWLEDGE AND SKILLS
(What must we know?)
行
INTERPERSONAL AND COMMUNICATION SKILLS & PROFESSIONALISM
(What must we say?)
(How must we behave?)
IRB approval for protection of the human subjects
合
SYSTEM-BASED PRACTICE
(What is the process?)
(On whom do we depend?)
(Who depends on us?)
醫
PRACTICE-BASED LEARNING AND IMPROVEMENT
(What have we learned?)
(What will we improve?)


病人健康照護矩陣
目標
能力
安
SAFE
(Injury or potential for injury)
權
EQUITABLE
(Gender, ethnicity, race, SEX)
達
TIMELY & EFFECTIVE & EFFICIENT
(Delay in Hrs, Days, week)
(Evidence-based care and outcomes)
(Waste of resources)
人
PATIENT-CENTERED
(Preference, needs, values)
病人照護
PATIENT CARE
(Overall Assessment)
A/B
A: yes;
B: no
知
MEDICAL KNOWLEDGE AND SKILLS
(What must we know?)
行
INTERPERSONAL AND COMMUNICATION SKILLS & PROFESSIONALISM
(What must we say?)
(How must we behave?)
Explain to the patient:
• the most update treatment
• the surgical plan and possible risks
合
SYSTEM-BASED PRACTICE
(What is the process?)
(On whom do we depend?)
(Who depends on us?)
醫
PRACTICE-BASED LEARNING AND IMPROVEMENT
(What have we learned?)
(What will we improve?)

Before and after surgery

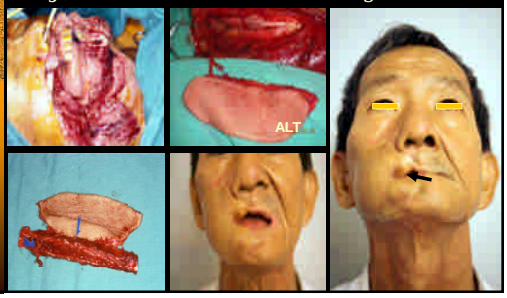
術前 (Sep. 12 2007)　術後3個半月 (Dec. 24 2007)　術後1年半 (Mar. 16 2009)

臨床醫療與基礎研究結合
--醫生科學家
(Physician Scientist)

郭耀仁
Yur-Ren Kuo, MD, PhD, FACS
高雄長庚醫院外科部部長

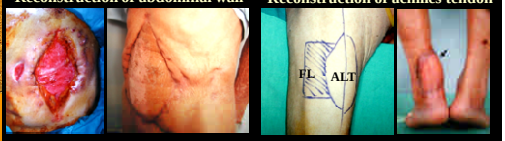
臨床技巧的躍進

Composite Mandibular Defect Including Oral Commissure Reconstructed with A Fibula Osteoseptocutaneous Flap and An ALT Flap Including Vascularized Fascia
Jeng SF/Kuo YR et al. Plast. Reconstr. Surg. 2005



Challenge the boundary
Versatility of ALT flap
- with inclusion of vascularized fascia lata

Reconstruction of abdominal wall　Reconstruction of achilles tendon



Reconstruction of patella

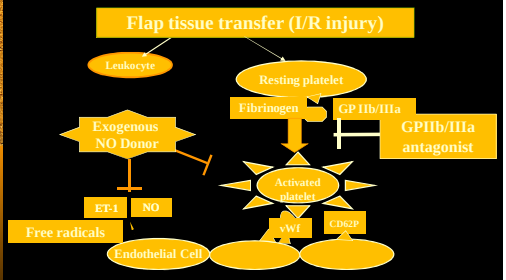
Kuo YR, et al . Ann Plast Surg, 2003
Kuo YR, et al. Ann Surg, 2004
Kuo YR. J Plast Reconstr Anesthet Surg, 2008
Kuo YR et al. Plast Reconstr Surg, 2009

失敗的痛苦
Microsurgical Adversaries
Failure of microsurgical reconstruction

- Perfusion
  - Thrombosis
  - Ischemia / reperfusion injury
- Rejection

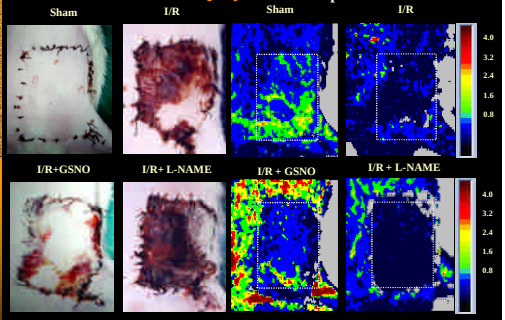
From bedside to bench, from bench to bedside

Clinical-related 臨床醫師以臨床問題為導向研究調控血小板活化及血管內皮對皮瓣組織缺氧再灌注影響



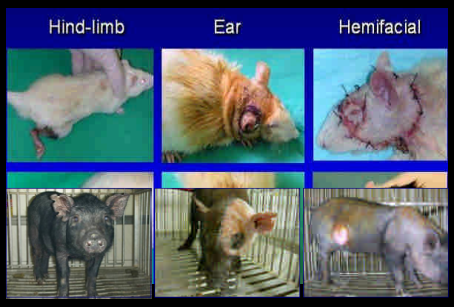
Kuo YR. Plast Reconstr Surg, 2002.
Kuo YR *et al.* Ann Plast Surg, 2003.
Kuo YR *et al.* J Surg Res, 2004.
Kuo YR *et al.* J Surg Res, 2002.
Kuo YR *et al.* Surgery, 2004.
Kuo YR *et al.* J Trauma, 2004.

GSNO (Nitrosoglutathione) 促進皮瓣組織缺氧再灌注存活 Free radicals and I/R injury



Kuo YR et al. J Surg, 2004.
Kuo YR et al. J Trauma, 2004.

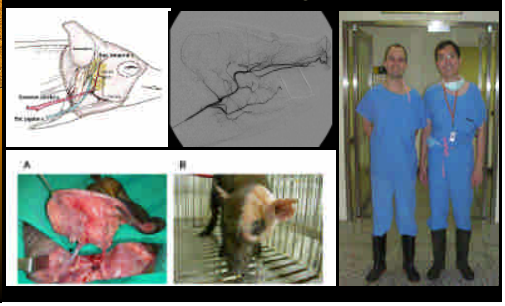
Stable Composite Tissue Allo-transplantation (CTA) Animal Models



大動物變臉移植模型：迷你豬世界文獻首例

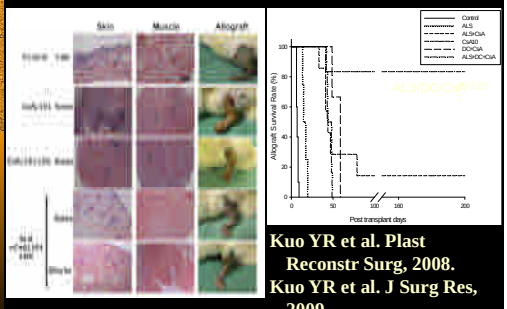
Swine Hemi-facial Composite Tissue Allotransplantation: A Model to Study Immune Rejection

J Surg Res153:268-273, 2009.



不成熟樹突細胞誘發複合性組織移植免疫耐受性

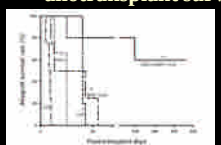
Alloantigen-Pulsed Host Dendritic Cells Induce T-Cell Regulation and Prolong Allograft Survival in a Rat Model of Hindlimb Allotransplantation



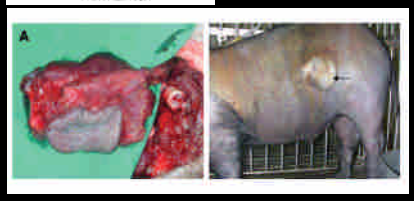
Kuo YR et al. Plast Reconstr Surg, 2008.
Kuo YR et al. J Surg Res, 2009.

間質幹細胞增加複合性組織異體移植成功率

Mesenchymal stem cells prolong composite tissue allotransplant survival in a swine model



Kuo YR et al, Transplantation, 2009



- International Guest Scholarship of American College of Surgeons (ACS)
- Godina Lecture Award (Jan. 12, 2010), American Society for Reconstructive Microsurgery (ASRM)

Incoming President Peter Neligan, MD, with Godina Lecturer Yun-Ren Kuo, MD

郭箴言：

一、如何找研究題目

From bedside to bench, from bench to bedside

臨床問題　　基礎研究

結論：

一、研究必須有明確的目標、具體可行的方法、具學術或臨床參考價值的結果；

二、基礎醫學和臨床醫學的結合；

三、臨床服務、教學和研究的結合；

四、Paper 、 patten 、product 的產出。

感 恩 聆 聽

恭 請 指 教