行政院及所屬各機關出國報告
（出國類別：研　究）

幹細胞（stem cell）研究及排尿功能障礙（voiding dysfunction）研究

服務機關：台北榮民總醫院
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出國地區：美國
出國期間：89.8.16.－91.8.12.
報告日期：91.年 9.月 19.日

系統識別號:C08904067

公 務 出 國 報 告 提 要

頁數: 15　含附件: 是

報告名稱:

幹細胞(stem cell) 研究及排尿功能障礙(voiding dysfunction)研究

主辦機關:

行政院輔導會臺北榮民總醫院

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出國類別: 進修　研究

出國地區: 美國

出國期間: 民國 89 年 08 月 16 日 -民國 91 年 08 月 12 日

報告日期: 民國 91 年 09 月 19 日

分類號/目: J3／醫療　J3／醫療

關鍵詞:　幹細胞(stem cell) 研究及排尿功能障礙(voiding dysfunction)研究

內容摘要: 此次赴美進修主要內容爲幹細胞相關之研究以及排尿功能障礙之生理及藥理之研究。職於美國進修期間有幸承蒙美國賓州匹茲堡大學肌肉衍生幹細胞之先趨大師Dr. Chancellor教授及Dr. Huard 教授之指導並提供幹細胞研究之良好環境; 職同時承蒙藥理學大師Dr. de Groat 教授親自指導排尿功能障礙之生理及藥理學研究，獲益良多。職於進修期間兢兢業業，全力以赴，今年5月於美國泌尿科年會暨國際學術大會中發表5篇論文，並獲得年度最佳論文獎之榮譽，另有二篇論文獲選爲該領域前三名之論文。撰寫論文方面，目前已發表SCI論文1篇，另有數篇論文投稿SCI雜誌審查中。幹細胞之研究目前爲極熱門而先進之題材，全球醫學中心及著名研究機構均將此項目列爲重點計畫，在泌尿科的應用方面，幹細胞可應用於尿道及膀胱之重建，用於治療尿失禁及膀胱肌肉收縮之障礙，並有修補其它泌尿生殖器官之潛能。 膀胱功能障礙及尿失禁的病人有日漸增多的趨勢，若能加強幹細胞研究工作之發展，並結合膀胱功能障礙之研究，將有助於治療此一現代人之痼疾，此一研究方向極具發展潛力及臨床應用價值，值得有關單位大力支持。

本文電子檔已上傳至出國報告資訊網

摘　要

此次赴美進修主要內容為幹細胞相關之研究以及排尿功能障礙之生理及藥理之研究。

職於美國進修期間有幸承蒙美國賓州匹茲堡大學肌肉衍生幹細胞之先趨大師 Dr. Chancellor 教授及 Dr. Huard 教授之指導並提供幹細胞研究之良好環境; 職同時承蒙藥理學大師 Dr. de Groat 教授親自指導排尿功能障礙之生理及藥理學研究，獲益良多。

職於進修期間兢兢業業，全力以赴，今年 5 月於美國泌尿科年會暨國際學術大會中發表 5 篇論文，並獲得年度最佳論文獎之榮譽，另有二篇論文獲選為該領域前三名之論文。撰寫論文方面，目前已發表 SCI 論文 1 篇，另有數篇論文投稿 SCI 雜誌審查中。

幹細胞之研究目前為極熱門而先進之題材，全球醫學中心及著名研究機構均將此項目列為重點計畫，在泌尿科的應用方面，幹細胞可應用於尿道及膀胱之重建，用於治療尿失禁及膀胱肌肉收縮之障礙，並有修補其它泌尿生殖器官之潛能。

膀胱功能障礙及尿失禁的病人有日漸增多的趨勢，若能加強幹細胞研究工作之發展，並結合膀胱功能障礙之研究，將有助於治療此一現代人之痼疾，此一研究方向極具發展潛力及臨床應用價值，值得有關單位大力支持。

目　次

正　文

目的:

此次赴美進修主要內容為幹細胞相關之研究以及排尿功能障礙之生理及藥理之研究。

過程:

職於美國進修期間有幸承蒙美國匹茲堡大學肌肉衍生幹細胞之先趨大師 Dr. Chancellor 教授及 Dr. Huard 教授之指導及提供幹細胞研究之良好環境，於第一年研究期間即有良好之初步成果，進而邀請職繼續從事第二年之研究工作，並提供獎學金，以期有更深入之研究成果，並承蒙輔導會及台北榮總各級長官之支持並同意以留職停薪方式延長進修一年。

Dr. de Groat 教授為美國 NIH 膀胱功能研究發展會議之主持人，治學嚴謹，於學界頗負盛名，職同時承蒙藥理學大師 Dr. de Groat 教授親自指導排尿功能障礙之生理及藥理學研究，獲益良多。

職於進修期間全力以赴，不敢稍有懈怠，深恐時間不足所幸不負長官期望，已完成以下研究主題:

(一) 由肌肉衍生幹細胞能否使小腸黏膜下組織 (small intestinal

submucosa) 更具包容性而更適用於膀胱及尿道重建術。

(二) 肌肉衍生幹細胞長入小腸黏膜下組織後的生理特性及收縮能力之探討。

(三) 肌肉衍生幹細胞於體外 acetylcholine receptor 表現之研究。

(四) 新型 C 纖維傳入神經抑制劑對於老鼠膀胱功能的影響。

(五) 脊髓損傷之老鼠排尿功能障礙及其藥理研究。

(六) Vallinoid receptor 於排尿功能障礙所扮演之角色。

職於今年 5 月於美國泌尿科醫學會(American Urological Association)年會暨國際學術大會中發表 5 篇論文，並獲得年度最佳論文獎之榮譽，另有二篇論文獲選為該領域前三名之論文；另於去年 11 月參加美國神經科學學會(Neuroscience Society)年會，並於去年及今年 9 月美國下肢癱瘓學會(American Paraplegia Society)年會，分別發表論文。

撰寫論文方面，職於美國進修兩年期間已發表 SCI 論文 1 篇，另有數篇論文投稿 SCI 雜誌審查中，內容均為幹細胞及膀胱功能障礙有關之題材。

心得：

幹細胞之研究目前為極熱門而先進之題材，全球醫學中心

及著名研究機構均將此項目列為重點計畫，幹細胞之來源有由骨骼肌、胚胎及骨髓衍生而來；胚胎來源之幹細胞受限於道德考量及法律規範，未來有研發限制及困難，骨髓來源之幹細胞取得時頗具侵犯性，臨床應用上亦有其限制，唯肌肉衍生之幹細胞不受上述條件之限制，頗具發展潛力，目前已越來越受到重視。

幹細胞具備多重分化潛能、自我更新及增殖之特性，臨床上之應用極為廣泛，可用於各類器官損傷之修補及功能障礙之調整，在泌尿科的應用方面，幹細胞可應用於尿道及膀胱之重建，用於治療尿失禁及膀胱肌肉收縮之障礙，並有修補其它泌尿生殖器官之潛能。此外，由於幹細胞之來源為自體本身，若用於器官的重建不會產生排斥作用，值得吾人全力研發。

建議:

由於社會及生活型態的變遷以及諱疾忌醫觀念之逐漸破除，膀胱功能障礙及尿失禁的病人有日漸增多的趨勢，若能加強幹細胞研究工作之發展，並結合膀胱功能障礙之研究，將有助於治療此一現代人之痼疾，嘉惠病患並增進其生活品質，此一研究方向極具發展潛力及臨床應用價值，值得有關單位大力支持。

2002 Poster Presentation Award

Presented By

SOCIETY FOR
URODYNAMICS &
FEMALE UROLOGY

TO

Shing-Hwa Lu, M.D. Ph.D.

For The Presentation Of

"CONTRACTILE ACTIVITY OF MUSCLE-DERIVED STEM CELLS INCORPORATED INTO SMALL INTESTINAL SUBMUCOSA SCAFFOLDS"

23rd Annual Meeting of the Society of Urodymanics and Female Urology
May 26, 2002
Orlando, Florida

University of Pittsburgh

School of Medicine
Department of Pharmacology

13th Floor Biomedical Science Tower
Pittsburgh, Pennsylvania 15261
Fax 412-648-1945

September 6, 2002

To Whom It May Concern:

This letter is written in support of Shing-Hwa Lu, M.D., Ph.D. He has worked in my laboratory at the University of Pittsburgh, Department of Pharmacology as Visiting Assistant Professor from August 2000 to September 2002.

Dr. Lu has done an excellent job during his stay in Pittsburgh. He has successfully completed seven projects. He has published one manuscript and has three other manuscripts submitted for publication. He received a poster presentation award from the Society for Urodynamic and Female Urology during the 2002 annual meeting in Orlando, Florida. He also presented four papers including one podium and three moderated posters at the American Urological Association annual meeting in Orlando, Florida in May, 2002. Two of his posters received special recognition as one of the top three posters in each session. He also presented papers at the Neuroscience Society annual meeting in San Diego in November, 2001, American Paraplegia Society annual meeting in Las Vegas in September, 2001 and 2002. Another poster will be presented at the Neuroscience Society annual meeting in Orlando in November, 2002.

Dr. Lu is a very skilled and imaginative investigator in the laboratory. In addition, he interacted very effectively with coworkers and organized several important collaborative research projects with scientists in other departments at the University. He speaks and writes very well in English and has excellent interpersonal skills. In summary, I can gave Dr. Lu my highest recommendation. I would be pleased to have him return to work in my laboratory in the future.

Best regards,

William C. de Groat

William C. de Groat, Ph.D.
Professor
Department of Pharmacology
School of Medicine University of Pittsburgh

University of Pittsburgh Physicians

Department of Urology

Part of
UPMC Health System

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412-692-4100
Fax: 412-692-4101

August 30, 2002

RE: [Henry] Shing-Hwa Lu, MD, PhD

To who it may concern,

I certify that Dr. Lu successfully completed neurourology and female urology fellowship from 8/2000 through 8/2002 at the University of Pittsburgh Department of Urology.

Henry has done an excellent job during this time period and beside doing an exceptional job in research participated in inpatient and outpatient patient care and operations.

Henry is fully capable including overall knowledge, technical abilities, and interpersonal skills.

Please let me know if you have any questions.

Warmest regards,

Michael B. Chancellor, MD
Professor Urology, OBGYN, McGowan Institute of Regenerative Medicine

University of Pittsburgh

School of Medicine
Department of Orthopaedic Surgery

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4151 Rangos Research Center
Pittsburgh, PA 15213
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Johnny Huard, Ph.D.
Associate Professor
Department of Orthopaedic Surgery
and Molecular Genetics and
Biochemistry and Bioengineering

Director
Growth & Development Laboratory
Children's Hospital of Pittsburgh

Deputy Director
Cellular Therapeutics Research
McGowan Institute for Regenerative
Medicine

September 5, 2002

To Whom It May Concern:

This letter is written in support of Shing-Hwa Lu, M.D., Ph.D. He worked in our laboratory at the University of Pittsburgh, Department of Orthopaedic Surgery, Growth and Development Laboratory as a Urology post doctoral research fellow from August, 2000 through August, 2002.

Dr. Lu was a very valuable addition to our research team. He did a tremendous job working in our laboratory and in his short time with us he was able to publish one manuscript with two other manuscripts in submission. He also received a poster presentation award from the Society for Urodynamic and Female Urology 2002 in Orlando, Florida during their annual meeting. Dr. Lu also presented four papers at the American Urological Association annual meeting in Orlando, Florida in May, 2002.

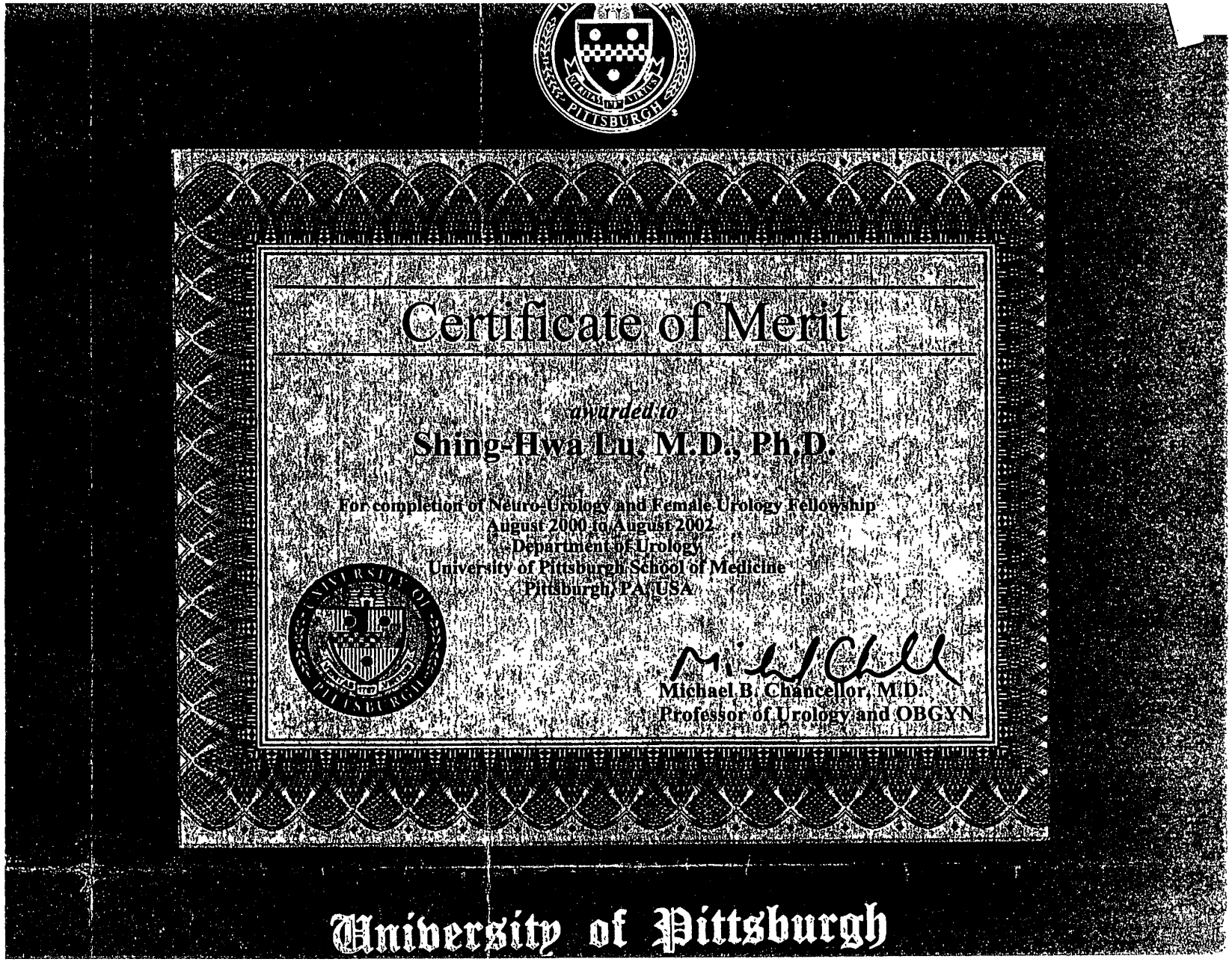
Dr. Lu's experience at the University of Pittsburgh gave him a unique opportunity to collaborate with many other departments in the School of Medicine including: Pharmacology, Urology, and Orthopaedic Surgery as well as in the School of Engineering; Department of Bioengineering.

Without hesitation, I give him the highest recommendation and invite Dr. Lu to return to the United States to work in my laboratory in the future. He will be missed as he returns to his native homeland, Taiwan.

We wish Dr. Lu all of the best as he continues his medical and research career.

Sincerely,

Johnny Huard, Ph.D.
Associate Professor of Medicine
University of Pittsburgh
Department of Orthopaedic Surgery
Director, Growth and Development Laboratory
Children's Hospital of Pittsburgh


Certificate of Merit
awarded to
Shing-Hwa Lu, M.D., Ph.D.
For completion of Neuro-Urology and Female Urology Fellowship
August 2000 to August 2002
Department of Urology
University of Pittsburgh School of Medicine
Pittsburgh, PA, USA
Michael B. Chancellor, M.D.
Professor of Urology and OBGYN
University of Pittsburgh

University of Pittsburgh

Certificate of Merit

awarded to

Shing-Hwa Lu, M.D., Ph.D.

For completion of laboratory work as a Urology Post-Doctoral Fellow

August 2000 – August 2002

Department of Orthopaedic Surgery
Molecular Genetics and Biochemistry and Bioengineering
Growth & Development Lab,
Children's Hospital of Pittsburgh, Pennsylvania USA

Growth & Development Lab

Children's Hospital of Pittsburgh

Johnny Huard, Ph.D.
Associate Professor, Tenured
Director, Growth & Development Laboratory
September 5, 2002

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Brain Research
Volume 946, Issue 1, 9 August 2002, Pages 72-78

DOI: 10.1016/S0006-8993(02)02828-7
PII: S0006-8993(02)02828-7

Research report

Effect of KW-7158, a putative afferent nerve inhibitor, on bladder and vesico-vascular reflexes in rats

Shing-Hwa Lu [a, c], Tsuyoshi Yamagata [b], Kaoru Atsuki [b], Lushen Sun [a], Christopher P. Smith [d], Naoki Yoshimura [d], Michael B. Chancellor [d] and William C. de Groat [a]

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Accepted 14 March 2002. Available online 14 May 2002.

Abstract

The effects of KW-7158, a putative afferent nerve inhibitor, on reflex bladder activity and vesico-vascular reflexes were evaluated in urethane anesthetized SD rats with normal and xylene-irritated bladders. The bladder was filled with saline until the appearance of large amplitude spontaneous bladder contractions (LA-BC). Vesico-vascular reflexes were measured as increases in systolic arterial blood pressure during LA-BC or when the bladder was distended by a range of pressures. In normal rats, KW-7158 (10 and 100 μg/kg, i.v.) did not alter the amplitude or volume threshold for inducing LA-BC but increased the intercontraction interval. After xylene-irritation, which decreased volume threshold and intercontraction interval and induced small amplitude bladder contractions, KW-7158 increased volume threshold (65%) and intercontraction interval (150%) and decreased the number of small amplitude bladder contractions. Vesico-vascular reflexes induced during LA-BC or by bladder distension were suppressed (19.4-100%) by KW-7158. The effect of KW-7158 to depress vesico-vascular reflexes as well as xylene-induced bladder hyperactivity without altering the amplitude of

contractions is consistent with the view that the drug affects reflex bladder activity at least in part by depressing afferent pathways.

Author Keywords: Afferent pathway; Bladder reflex; Inhibition; Rat

Neuroscience classification codes: Endocrine and autonomic regulation, Gastrointestinal and urogenital regulation

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Brain Research
Volume 946, Issue 1, 9 August 2002, Pages 72-78