

編號：CCMP90-CT-45

## 中醫藥研究用動物模式的文獻收集

# Collection of information regarding animal models for research in Chinese traditional medicine

國立成功大學醫學院

鄭 瑞 棠

### 摘要

為了中西醫學整合的推進，使用當代的動物模式來研究中醫藥，必能使所得結果信服國際人仕。因此，本計劃收集了常見疾病的動物模式來供參考。由於時間有限，謹先針對十二種疾病，分別為老年痴呆症(Alzheimer's disease)、中風(stroke)、學習和記憶障礙(learning and memory defect)、高血壓(hypertension)、高血脂(hyperlipidemia)、氣喘(asthma)、心臟衰竭(heart failure)、糖尿病(diabetes mellitus)、痛風(gout)、前列腺肥大(benign prostate hypertrophy)、腎衰竭(renal failure)、和腫瘤(carcinoma)等，來進行收集。依不同疾病，使用不同之關鍵字來檢索，找尋全國博碩士論文摘要檢索系統或英文醫學資料庫(MEDLINE)，取下合適之參考文獻。另外，由國內外圖書(包括日文)尋取可用的資料。然後，配合中醫的理論來加予整理；所得的資訊供國內同好們參考和使用。

關鍵詞：疾病的動物模式、中醫藥研究用、文獻資料。

# Research Center of Chinese Traditional Medicine, College of Medicine, National Cheng Kung University

Juei-Tang Cheng

## Abstract

In an attempt to improve the understanding of Chinese traditional medicine, the present proposal is performed to collect the information regarding the animal model used in the research. Thus, 12 kinds of animal model including Alzheimer's disease, stroke, learning and memory defect, hypertension, hyperlipidemia, asthma, heart failure, diabetes mellitus, gout, benign prostate hypertrophy, renal failure, and tumor or carcinoma were focused. The published paper in English, Japanese or Chinese has been collected. Then, the obtained model will integrate to the view of Chinese traditional medicine. Application of same animal model will help the reliability of results to convince the scientists who majored in modern medicine. Also, the obtained data can be shared with the scientist who is interested in the R & D of herbs and /or Chinese traditional medicine.

Keywords : Animal Model; Reference; Chinese Traditional Medicine

## 壹、前言

不同於講究速效掛帥的西方醫學領域，傳統中藥醫學乃是講究經驗法則，即使是西方醫學判定的同一種疾病，中醫仍會依患者病情的輕重緩急，患者的性別體質，以及發病的歷程及時間，在主要的處方藥劑加減某些藥材來進行最適切之治療，而這些用藥的法則，散見於歷來的典章史籍。儘管中藥醫學的療效及發展潛力無窮，但由於西方科學講求控制組及對照組的處理方式，因此，中醫藥的療效仍受到許多不平等的質疑。近年來，由於許多西方醫學原本束手

無策的疑難雜症在中藥的處理後露出了一線曙光；因此，國際上對中醫藥的相關研究也逐漸重視。由此可知，我國的傳統醫學，包括中醫藥，乃多年的經驗科學。可惜，中西文化的差異，因而造成我國的這項精華被曲解為「不科學」，中藥在歐美國家也只能在唐人街以「食品」來販售。近年，國人的自醒配合國外人仕研究中草藥的熱忱，中西整合醫學的主張日漸受到重視。因此，「中醫藥的現代化」就成為重要的課題！

事實上，傳統醫學要現代化就得設法讓當代醫學的人仕信服；不論國內外的醫藥工作者。因此，使用同樣的模式來評估或研發，恰如有相同的語言一般，所得結果必較易迎得信任。除了目前正在推動的中藥臨床試驗以外，使用國際間常用的疾病動物模式(Animal Model)來評估中藥的藥效或中醫的疾病病因探討，所得成果較易得到國外人仕的認同；對於「中醫藥的現代化」就成為重要的工具。

查詢我們現有的疾病動物模式相關的專業書本，只有吳銘芳和蘇裕家兩人所著「疾病動物模式的介紹」(藝軒圖書公司)及大陸的朱渝與多秀贏所著「實驗動物的疾病模型」(天津科技翻譯出版社)兩本而已。日本方面，田俣順和松本宏所共著的「Handbook of Disease Models in Animal」(醫齒藥出版株式會社)最常被使用。可能由於市場不大，消費者有限。因此，專業書本並不多。當然，參雜在各種疾病的書本，介紹其疾病的動物模式則較常見。

從事研究，往往必須利用有限的人力物力及時間來進行；然而，即使研究者本身已具備豐富的學養及研究經驗，在進行研究之際，相關參考文獻的收集及整理，仍需要耗費可觀的人力及時間來進行。不僅如此，還需再加上一番的整理及研讀，才可以由大量的資訊得到合用的知識；同時，其他進行相同或相似研究的學者，仍會耗費許多時間在進行同樣的文獻的蒐集工作。然而，即使是不同領域的研究者，除了特定的研究目標之外，有許多的基礎資料仍是可以通用的，例如實驗動物模式或實驗方法等。因此，研究人員，若能經由一整合完畢之資料庫找尋主要且基本的文獻，便可集中精力去收集其特定研究目標的文獻，除了可節省多餘的人力時間以進行更多的研究之外，同時，不同的研究內容，也可以具有相同的比較基礎。可惜，這一類的資料庫，目前仍未被建立。

因此，本項計畫就是希望能夠協助這項工作。

## 貳、材料與方法

### 一、資料的檢索

目前最常被使用來檢索參考文獻的資料庫，可分為中文資料庫及西文資料庫兩種。其中與醫藥相關的中文資料庫為全國博碩士論文摘要檢索系統（包含中文博碩士論文論文索引光碟資料庫及中華博碩士論文摘要），該資料庫收錄了台灣、中國大陸、香港、及美加地區各大學研究所中國人博士、碩士畢業論文索引及摘要。西文資料庫則是以利用 OVID 軟體為檢索工具的 MEDLINE (MEDlar on LINE) 醫學資料庫（簡稱 OVID 醫學資料庫），此資料庫目前收錄約 3800 種全世界著名且各學科權威之期刊，其中 75% 為英文文獻；25% 為非英文文獻。主題範圍包括：臨床生命科學、生物科學、解剖學、法醫學、組織、基礎生命科學、心理學、社會醫學、農業、化學與藥物、醫技工業學、醫學資訊學、醫技設備學等學科。由於此二類檢索系統涵蓋廣泛，因此也經常被包含於各種研究資訊網的資料庫提供檢索之用，例如醫藥衛生研究資訊網 (Health-Research Information Network--HINT) 等。本計劃使用合適之關鍵字檢索文獻，並運用布林邏輯運算元(Boolean operators)連繫、交集組合及不同的限制條件尋找適合的文獻。除此之外，再配合 OVID 檢索系統所提供的專題資訊選粹服務 (Selective Dissemination of Information, SDI)，可以隨時取得最新相關的參考文獻。

### 二、檢索方法

#### (一)全國博碩士論文摘要檢索系統(1984 每日更新)：

本系統尚包括中文博碩士論文論文索引光碟資料庫(1956-1997)及中華博碩士論文摘要 (1920-1997)。資料庫內容收集台灣、中國大陸、香港、及美加地區各大學研究所中國人博士、碩士畢業論文索引及摘要，使用飛資得公司開發之中英文全文檢索系統(Fly base)，非一般套裝軟體。FlyBase 針對大量中英文資料的全文檢索，提供友善的使用者介面及迅速的系統回應。以下是 FlyBase

的特點：

1. 模糊檢索 (fuzzy search)：使用者可依需求設定檢索符合率的下限。
2. 多資料庫檢索：使用者可依需求，選擇多個資料庫，同時進行檢索。
3. 欄位可依資料庫特性需求而設計，並可針對各欄位建立權威檔 (thesaurus)。
4. 中文查詢介面，可作欄位群組檢索；有索引檔瀏覽功能，可直接瀏覽索檔。
5. 提供串字功能，並可精確限定鄰近字；具年代、日期、限定檢索功能。
6. 檢索歷史可組合或加上新條件再檢索；可瀏覽任一次檢索結果，並可設定每頁瀏覽筆數；可儲存檢索策略，以後再叫出來執行。
7. 在結果顯示畫面下，使用者查詢之關鍵字會呈現紅色，以方便快速瀏覽，並可進行連結檢索(hyperlink)，直接點選查詢相關資料。
8. 完整的布林邏輯架構：可作欄位與欄位、SET 與 SET 的 and/or/not 邏輯運算。
9. 檢索速度快：FlyBase 將索引檔做最佳化處理，檢索引擎採用壓縮及 cache 技巧，遇全文檢索或多層布林邏輯運算時，系統回應速度仍然很快。
10. 資料輸出格式靈活：可由系統管理者自行設定，於 config 檔中定義輸出格式。
11. 資料庫結構採變長架構：資料不受固定欄位之限制。

## (二) OVID 醫學資料庫

MEDLINE ( MEDlars on LINE ) 自 1964 年美國國家醫學圖館建立全國性醫學文獻網路 MEDLARS，發展至今，已成為目前最重要的生物醫學資料庫，亦是全世界最大的醫學同儕審查資料庫。MEDLINE 每年固定收錄約 3800 種全世界著名且各學科權威之期刊，75%為英文文獻；25%為非英文文獻；49%與 EMBASE 資料庫為不重複收錄；52%文獻 BIOSIS 為不重複收錄者。收錄學科主題範圍涵蓋臨床生命科學、生物科學、解剖學、法醫學、組織、基礎生命科學、心理學、社會醫學、農業、化學與藥物、醫技工業學、醫學資訊學、醫

技設備學等學科。該檢索系統之特色為：

- 1.收錄自 1966 至最新月份的完整 MEDLINE 資料庫。
- 2.MEDLINE 資料庫提供五種方式供使用者選擇：  
complete MEDLINE (1966-present) ;  
MEDfive (the most current five years) ;  
MEDfour (the most current four years) ;  
MEDtwo (the most current two years)
- 3.有特殊 LIMIT (限制指令)。
- 4.有 SAVESEARCH、SORT、MERGE、EXPLODE 等高效率檢索功用。
- 5.有專業人員 COMMAND 檢索方式及讀者的 MENU 檢索方式。
- 6.有超強索引典，幫助使用者快速且精確查尋所要之資料。
- 7.有 SDI 的功能，即時獲取每月所屬專科最新資料資訊。
- 8.有 LOCAL HOLDING 功能，節省讀者查尋期刊目錄的時間。
- 9.有替換索引查尋(PERMUTED INDEX)的功能。可查閱完整、專業的醫學標題或關鍵字。
- 10.有線教學指南(ON-LINE TUTORIALS)及詢問畫面(HELP-SCREENS)。
- 11.有超強 LINK 功能，可與 OVID 全文資料庫相互搭配使用，立即查到全文資料。
- 12.目前擁有 DOS 版、WINDOWS 版及 UNIX 版三種版本。

### 三、大陸文獻檢索方法

由於兩岸的通訊不良，難由網路拿取大陸方面的資料。因此，自中國醫藥學院(台中市)的圖書館檢索現存的資料及其他可用資料。另外，配合主持人現有的大陸出版書籍，加予整理的綜合所成。

### 參、結果

本計劃檢索了常見疾病的動物模式十二類型，分別為老年痴呆症(Alzheimer's disease)、中風(stroke)、學習和記憶障礙(learning and memory defect)。

高血壓(hypertension)、高血脂(hyperlipidemia)、氣喘(asthma)、心臟衰竭(heart failure)、糖尿病(diabetes mellitus)、痛風(gout)、前列腺肥大(benign prostate hypertrophy)、腎衰竭(renal failure) 和腫瘤(carcinoma)等，進行檢索，並經過整理成下列各項的成果，以疾病的英文字母為序，陳述於下，希望成為中醫藥同好或專業人仕合適之參考文獻。

## 一、老年痴呆症(Alzheimer's disease)

### [英文的重要文獻]

- Bodles, A. M., Guthrie, D. J., Greer, B., and Irvine, G. B.: Identification of the region of non-Abeta component (NAC) of Alzheimer's disease amyloid responsible for its aggregation and toxicity. *Journal of Neurochemistry* 2001;78:384-395.
- Alvarez, X. A., Miguel-Hidalgo, J. J., Fernandez-Novoa, L., and Cacabelos, R.: Intrahippocampal injections of the beta-amyloid 1-28 fragment induces behavioral deficits in rats. *Methods & Findings in Experimental & Clinical Pharmacology* 1997; 19:471-479
- Bennett, M. C., Diamond, D. M., Stryker, S. L., Parks, J. K., and Parker, W. D., Jr.: Cytochrome oxidase inhibition: a novel animal model of Alzheimer's disease. *Journal of Geriatric Psychiatry & Neurology* 1992 ; 5:93-101
- Camps, P., El Achab, R., Morral, J., Munoz-Torrero, D., Badia, A., Banos, J. E., Vivas, N. M., Barril, X., Orozco, M., and Luque, F. J.: New tacrine-huperzine A hybrids (huprines): highly potent tight-binding acetylcholinesterase inhibitors of interest for the treatment of Alzheimer's disease. *Journal of Medicinal Chemistry* 2000; 43: 4657-4666.
- DeFeudis, F. V. and Drieu, K.: Ginkgo biloba extract (EGb 761) and CNS functions: basic studies and clinical applications. *Current Drug Targets* 2000; 1:25-58
- Bjugstad, K. B., Flitter, W. D., Garland, W. A., Su, G. C., and Arendash, G. W.: Preventive actions of a synthetic antioxidant in a novel animal model of AIDS dementia. - *Brain Research* 1998; 795(1-2):349-357

- Fernandez-Shaw, C., ina, A., Cazorla, P., Valdivieso, F., and Vazquez, J.: Anti-brain spectrin immunoreactivity in Alzheimer's disease: degradation of spectrin in an animal model of cholinergic degeneration. *Journal of Neuroimmunology* 1997; 77:91-98
- Emre, M. and Qizilbash, N.: Experimental approaches and drugs in development for the treatment of dementia. *Expert Opinion on Investigational Drugs* 2001;10:607-617
- Sugaya, E., Yuyama, N., Kajiwara, K., Tsuda, T., Ohguchi, H., Shimizu-Nishikawa, K., Kimura, M., and Sugaya, A.: Regulation of gene expression by herbal medicines--a new paradigm of gene therapy for multifocal abnormalities of genes. *Research Communications in Molecular Pathology & Pharmacology* 1999;106:171-180
- Hoshino, S., Tamaoka, A., Takahashi, M., Kobayashi, S., Furukawa, T., Oaki, Y., Mori, O., Matsuno, S., Shoji, S., Inomata, M., and Teramoto, A.: Emergence of immunoreactivities for phosphorylated tau and amyloid-beta protein in chronic stage of fluid percussion injury in rat brain. *Neuroreport* 1998 ; 9:1879-1883
- Vaucher, E., Aumont, N., Pearson, D., Rowe, W., Roirier, J., and Kar, S.: Amyloid beta peptide levels and its effects on hippocampal acetylcholine release in aged, cognitively-impaired and -unimpaired rats. *Journal of Chemical Neuroanatomy* 2001 ;21:323-329
- Krugel, U., Bigl, V., Eschrich, K., and Bigl, M.: Deafferentation of the to-hippocampal pathway in rats as a model of the metabolic events in Alzheimer's disease. *International Journal of Developmental Neuroscience* 2001; 19:263-277
- Ksir, C. and Benson, D. M.: Enhanced behavioral response to nicotine in an animal model of Alzheimer's disease. *Psychopharmacology* 1983; 81:272-273

#### [國內研究生的相關論文]

槐花對鵝膏蕈酸誘發大白鼠學習記憶障礙效用研究 (The attenuating effects of Huaihua on IBO induced deficits of learning and memory in rats) 研究生: 錢添發(中國醫藥學院中國醫學研究所; 民 90)

葛根素改善大鼠學習障礙之研究 (The facilitating effects of puerarin on the learning deficit in rats) 研究生: 郭麗萱 (中國醫藥學院中國醫學研究所; 民 89)

六味地黃丸改善大鼠學習障礙之研究 (The facilitating effects of Liu-Wei-Di-Huang-Wan on the learning deficit in rats) 研究生: 鄭頌仁(中國醫藥學院中國醫學研究所; 民 89)

當歸成分( n-butyldenephthalide )改善被動迴避學習障礙之研究 (The attenuating effects of n-butyldenephthalide, a constituent of Angelica Sinensis Radix, on the impairment of passive avoidance response in rats) 研究生: 林穎聰 (中國醫藥學院中國醫學研究所; 民 88)

### [大陸的文獻]

宋前流、宋瑞義、謝湘林: 參歸煎劑對 Quinolinic Acid 損毀海馬所致痴呆大鼠學習評憶的影響。白求恩醫大學報 1995;21:266-268

陳建宗、黃青松、趙學軍: 腦力康對老齡小鼠空間分辦學習和記憶的影響。安徽中醫學院學報 1998;17:63-64

## 二、氣喘(asthma)

### [英文的重要文獻]

Chiba, Y., Arimoto, T., Yoshikawa, T., and Misawa, M.: Elevated nitric oxide synthase activity concurrent with antigen-induced airway hyperresponsiveness in rats. - Experimental Lung Research 2000 ;26:535-549

Elliott, P. J., Pien, C. S., McCormack, T. A., Chapman, I. D., and Adams, J.: Proteasome inhibition: A mechanism to combat asthma. Journal of Allergy & Clinical Immunology 1999;104:294-300

Koh, Y. I., Choi, I. S., Park, S. C., and Kang, K. W.: BCG infection during pre-sensitization or even post-sensitization inhibits airway sensitivity in an animal model of allergic asthma. Journal of Korean Medical Science 2000 ;15:265-272

Mehta, H., Sorkness, R., Kaplan, M. R., Castleman, W. L., and Lemanske, R. F., Jr.: Effects of dexamethasone on acute virus-induced airway dysfunction in adult rats. Pediatric Research 1997 ;41:872-877

Misawa, M. and Chiba, Y.: Repeated antigenic challenge-induced airway hyperresponsiveness and airway inflammation in actively sensitized rats. Japanese Journal of Pharmacology 1993 ;61:41-50

Pauwels, R. A. and Van der Straeten, M. E.: An animal model for adenosine-induced bronchoconstriction. American Review of Respiratory Disease 1987 ;136:374-378

#### [國內研究生的相關論文]

氮氧化物經由脂質過氧化作用導致肺臟毒性效應及其生物效應指標之研究  
(Study on the pulmonary toxic effects and biological effective marker induced by nitrogen oxides via lipid peroxidation) 研究生: 劉鴻斌 (國立成功大學環境醫學研究所; 民 90)

Magnolol 抑制血管平滑肌細胞增生之作用機轉 (Anti-proliferative effect of Magnolol on rat vascular smooth muscle cells) 研究生: 伍怡芬(國防醫學院藥理學研究所; 民 90)

和厚朴酚與厚朴酚對迷你豬氣管平滑肌之反應 (Effects of Honokiol and Magnolol on Tracheal Smooth Muscle in Piglet) 研究生: 柯建新 (慈濟大學醫學研究所;民 90)

利用氣壓描記器評估清醒小老鼠的呼吸道收縮 (Evaluation of airway constriction using barometric plethysmography in conscious, unrestrained mice) 研究生: 李耿中 (國立臺灣大學生理學研究所;民 89)

## [大陸的文獻]

吳清華、米杰：當歸主咳逆上氣例証。山東中醫藥大學學報 1998;22:450-452

王鎮才：當歸精油丸對氣管哮喘止喘作用的臨床觀察。天津中醫 1986;1:4-6

李長福：穴位注射治療支氣管哮喘 20 例。延邊醫學院學報 1991;14:294-297

## 三、前列腺肥大(benign prostate hypertrophy)

### [英文的重要文獻]

Van Coppenolle, F., Slomianny, C., Carpentier, F., Le, Bourhis, X, Ahidouch, A., Croix, D., Legrand, G., Dewailly, E., Fournier, S., Cousse, H., Authie, D., Raynaud, J. P., Beauvillain, J. C., Dupouy, J. P., and Prevarskaya, N.: Effects of hyperprolactinemia on rat prostate growth: evidence of androgeno-dependence. American Journal of Physiology - Endocrinology & Metabolism 2001; 280:E120-9

Engelstein, D., Shmueli, J., Bruhis, S., Servadio, C., and Abramovici, A.: Citral and testosterone interactions in inducing benign and atypical prostatic hyperplasia in rats. Comparative Biochemistry & Physiology 1996;115:169-177

Zhao, G. Q., Holterhus, P. M., Dammshauser, I., Hoffbauer, G., and Aumuller, G.: Estrogen-induced morphological and immunohistochemical changes in stroma and epithelium of rat ventral prostate. Prostate 1992;21:183-99

Netto ior, N. R. and Claro, J. A.: Treatment of benign prostate hypertrophy using Prostatron: a study of the effects of treatment temperature elevation. [French]. Progres en Urologie 1995 ;5:238-243

Matzkin, H., Chayen, R., Goldfarb, H., Gilad, S., and Braf, Z.: Laboratory monitoring of androgenic activity in benign prostate hypertrophy treated with a 5 alpha-reductase inhibitor. Clinical Chemistry 1992 ;38:1304-1306

Servadio, C., Abramovici, A., Sandbank, U., Savion, M., and Rosen, M.: Early stages of the pathogenesis of rat ventral prostate hyperplasia induced by citral. European Urology 1986;12:195-200

Golomb, E., Rosenzweig, N., Eilam, R., and Abramovici, A.: Spontaneous hyperplasia of the ventral lobe of the prostate in aging genetically hypertensive rats. Journal of Andrology 2000;21:58-64

#### [國內研究生的相關論文]

5 alpha-還原酶親和性標籤的合成 (The Synthesis of a Novel 5alpha-Reductase Photoaffinity Label) 研究生: 王耀賢(國立成功大學藥理學研究所; 民 89)  
葛花化學成分與藥理活性之研究 (Phytochemical and Pharmacological Studies) 研究生: 陳怡穎(國防醫學院藥學研究所; 民 89)

#### [大陸的文獻]

Zhang, Y. Y., Li, P. F., Chen, B. L., and Li, D.: Flutamide suppressed prostate hypertrophy in rats and mice. [Chinese] Chung-Kuo Yao Li Hsueh Pao - Acta Pharmacologica Sinica 1999 ;20:537-40

何清湖、陳軍: 中醫藥治療前列腺增生症研究進展。湖南中醫藥導報 1996;1:25-27

何清湖、魏云: 尿癃康對大白鼠前列腺增生的影響。湖南中醫藥導報 1997; 3:61-63

#### 四、腫瘤(carcinoma)

#### [英文的重要文獻]

Archer, S. G. and Gray, B. N.: A new reproducible model of hepatic and peritoneal metastases from colonic carcinoma. European Journal of Cancer & Clinical Oncology 1988 ;24:1623-1632

Bacus, J. W., Bacus, J. V., Stoner, G. D., Moon, R. C., Kelloff, G. J., and Boone, C. W.: Quantitation of preinvasive neoplastic progression in animal models of chemical carcinogenesis. Journal of Cellular Biochemistry - Supplement 1997; 28-29:21-38

Bartoli, R., Fernandez-Banares, F., Navarro, E., Castella, E., Mane, J., Alvarez, M.,

- Pastor, C., Cabre, E., and Gassull, M. A.: Effect of olive oil on early and late events of colon carcinogenesis in rats: modulation of arachidonic acid metabolism and local prostaglandin E(2) synthesis. Gut 2000; 46:191-199
- Bosland, M. C., Prinsen, M. K., and Kroes, R.: Adenocarcinomas of the prostate induced by N-nitroso-N-methylurea in rats pretreated with cyproterone acetate and testosterone. Cancer Letters 1983; 18:69-78
- Carlsson, G., Larsson, P. A., Frosing, R., Hafstrom, L. O., Spears, C. P., Peterson, A., and Gustavsson, B.: 5-Fluorouracil sensitive adenocarcinoma--a new experimental model in the rat. Anticancer Research 1995; 15:433-439
- Deerberg, F., Rehm, S., and Jostmeyer, H. H.: Spontaneous urinary bladder tumors in DA/Han rats: a feasible model of human bladder cancer. Journal of the National Cancer Institute 1985; 75:1113-1121
- Dunnington, D. J., Buscarino, C., Gennaro, D., Greig, R., and Poste, G.: Characterization of an animal model of metastatic colon carcinoma. International Journal of Cancer 1987; 39:248-254
- Garattini, S. and Guaitani, A.: Animal models for the study of cancer-induced anorexia. Cancer Treatment Reports 1981;65 Suppl 5:23-35
- Heatfield, B. M., Lipsky, M. M., and Trump, B. F.: Renal tubular carcinoma; animal model: chemically induced renal tubular carcinoma in rats. American Journal of Pathology 1980; 100:317-320

#### [國內研究生的相關論文]

茶多酚與鞣花酸對化學致癌劑誘發老鼠遺傳損傷的保護作用研究 (The protective effects of (-)-epigallocatechin gallate and ellagic acid on ENU-induced DNA damage and mutations in mice) 研究生: 陳巧倩(中國醫藥學院中國醫學研究所; 民 90)

亞砷酸鈉誘引人類皮膚細胞株 HaCaT 癌轉形之探討 (Study of sodium arsenite-induced neoplastic transformation in human skin HaCaT cells) 研究生:

江明璋 (國立中央大學生命科學研究所; 民 90)

以 EBV NLMP1 基因轉殖老鼠探討 EBV NLMP1 在致癌過程所扮演之角色

(Evaluation of the role of EBV NLMP1 in carcinogenesis using transgenic mice)

研究生: 蘇崧學 (長庚大學基礎醫學研究所; 民 89)

研究人類葡萄糖-6-磷酸去氫酶(G6PD)在癌細胞的表現及抗癌藥物對 G6PD 過

度表現之纖維母細胞的影響 (Study of the expression pattern of human

glucose-6-phosphate dehydrogenase (G6PD) in human cancer cell lines and the

effects of anticancer drugs in G6PD-overexpressing fibroblast cells) 研究生:

林家瑜 (國立臺灣大學動物學研究所; 民 88)

GM-CSF 細胞素腫瘤疫苗用於癌症治療之可行性研究

(GM-CSF-Transduced Tumor Vaccine: Application in an Animal Model of

Cancer Therapy) 研究生: 謝嘉玲 (國立臺灣大學微生物學研究所; 民 88)

中藥靈芝抗老化及抗癌作用之研究 (Studies on the anti-aging and anti-tumor

effects of Ganoderma, a Chinese herbal medicine) 研究生: 蔡勝發 (國立陽明

大學生物藥學研究所; 民 88)

## [大陸的文獻]

邱存平、吳紅: 惡性腫瘤動物模型的建立。醫學與哲學 1999;20:16-18

鄒麗云、吳玉章、賈正才、萬瑛、趙建平: 小鼠肥大細胞瘤 P815 模型的建立與初步應用。免疫學雜誌 2000; 16:339-341

李同度、劉愛國、牛旗、董慧明、宋德勝; 康萊特抗癌症惡病質實驗研究。中國腫瘤臨床 1998; 25:131-133

## 五、糖尿病(diabetes mellitus)

### [英文的重要文獻]

Ahmad, F. and Goldstein, B. J.: Increased abundance of specific skeletal muscle protein-tyrosine phosphatases in a genetic model of insulin-resistant obesity and diabetes mellitus. - Metabolism: Clinical & Experimental 1995; 44:1175-1184

- Albright, A. L., Mahan, J. D., Ward, K. M., Sherman, W. M., Roehrig, K. L., and Kirby, T. E.: Diabetic nephropathy in an aerobically trained rat model of diabetes. *Medicine & Science in Sports & Exercise* 1995; 27:1270-1277
- Altshuler, G. and Ornoy, A.: Thickness of renal glomerular capillary basement membrane in the offspring of diabetic rats fed a regular or high-sucrose diet. *Acta Anatomica* 1986; 126:237-239
- Barbera, A., Fernandez-Alvarez, J., Truc, A., Gomis, R., and Guiart, J. J.: Effects of tungstate in neonatally streptozotocin-induced diabetic rats: mechanism leading to normalization of glycaemia. *Diabetologia* 1997; 40:143-149
- Bone, A. J., Hitchcock, P. R., Gwilliam, D. J., Cunningham, J. M., and Barley, J.: Insulitis and mechanisms of disease resistance: studies in an animal model of insulin dependent diabetes mellitus. *Journal of Molecular Medicine* 1999; 77:57-61
- Carter, W. R., Herrman, J., Stokes, K., and Cox, D. J.: Promotion of diabetes onset by stress in the BB rat. *Diabetologia* 1987; 30:674-675
- Chappel, C. I. and Chappel, W. R.: The discovery and development of the BB rat colony: an animal model of spontaneous diabetes mellitus. *Metabolism: Clinical & Experimental* 1983; 32(7 Suppl 1):8-10
- Chen, S., Yuan, C., Schooley, J. F., Jr., Haddy, F. J., and Pamnani, M. B.: A consistent model of insulin-dependent diabetes mellitus hypertension. *American Journal of Hypertension* 1992; 5:671-680
- Corsetti, J. P., Sparks, J. D., Peterson, R. G., Smith, R. L., and Sparks, C. E.: Effect of dietary fat on the development of non-insulin dependent diabetes mellitus in obese Zucker diabetic fatty male and female rats. *Atherosclerosis* 2000; 148:231-241
- Cosenzi, A., Sacerdote, A., Seculin, P., Odoni, G., Plazzotta, N., Bernobich, E., and Bellini, G.: Lacidipine prevents the hypertension and renal and cardiac changes induced by high-fructose diet in WKY rats. *Journal of Cardiovascular*

Pharmacology 1999; 33:485-491

- Fukuzawa, Y., Watanabe, Y., Inaguma, D., and Hotta, N.: Evaluation of glomerular lesion and abnormal urinary findings in OLETF rats resulting from a long-term diabetic state. Journal of Laboratory & Clinical Medicine 1996; 128:568-578
- Guenifi, A., Abdel-Halim, S. M., Hoog, A., Falkmer, S., and Ostenson, C. G.: Preserved beta-cell density in the endocrine pancreas of young, spontaneously diabetic Goto-Kakizaki (GK) rats. Pancreas 1995; 10:148-153
- Iwase, M., Yamamoto, M., Iino, K., Ichikawa, K., Shinohara, N., Yoshinari, M., and Fujishima, M.: Obesity induced by neonatal monosodium glutamate treatment in spontaneously hypertensive rats: an animal model of multiple risk factors. Hypertension Research 1998; 21:1-6
- Iwase, M., Wakisaka, M., Yoshinari, M., Sato, Y., Yoshizumi, H., Nunoi, K., and Fujishima, M.: Effect of gonadectomy on the development of diabetes mellitus, hypertension, and albuminuria in the rat model. Metabolism: Clinical & Experimental 1996; 45:155-161
- Iwase, M., Kikuchi, M., Nunoi, K., Wakisaka, M., Maki, Y., Sadoshima, S., and Fujishima, M.: A new model of type 2 (non-insulin-dependent) diabetes mellitus in spontaneously hypertensive rats: diabetes induced by neonatal streptozotocin treatment. Diabetologia 1986; 29:808-811
- Jiao, S., Matsuzawa, Y., Matsubara, K., Kubo, M., Tokunaga, K., Odaka, H., Ikeda, H., Matsuo, T., and Tarui, S.: Abnormalities of plasma lipoproteins in a new genetically obese rat with non-insulin-dependent diabetes mellitus (Wistar fatty rat). International Journal of Obesity 1991; 15:487-495
- Kazumi, T., Odaka, H., Hozumi, T., Ishida, Y., Amano, N., and Yoshino, G.: Effects of dietary fructose or glucose on triglyceride production and lipogenic enzyme activities in the liver of Wistar fatty rats, an animal model of NIDDM. Endocrine Journal 1997; 44:239-245
- Koyama, M., Wada, R., Sakuraba, H., Mizukami, H., and Yagihashi, S.: Accelerated

loss of islet beta cells in sucrose-fed Goto-Kakizaki rats, a genetic model of non-insulin-dependent diabetes mellitus. American Journal of Pathology 1998; 153:537-545

Wada, M., Iwase, M., Wakisaka, M., Nunoi, K., Yoshinari, M., and Fujishima, M.: A new model of diabetic pregnancy with genetic hypertension: pregnancy in spontaneously hypertensive rats with neonatal streptozotocin-induced diabetes. American Journal of Obstetrics & Gynecology 1995; 172(2 Pt 1):626-630

Weir, G. C., Clore, E. T., Zmachinski, C. J., and Bonner-Weir, S.: Islet secretion in a new experimental model for non-insulin-dependent diabetes. Diabetes 1981; 30:590-695

Ziegler, M., Ziegler, B., Kohnert, K. D., and Kloting, I.: Genetic control of susceptibility to severe hyperglycaemia evoked by CFA/SZ-induced immune response against beta cells in various rat strains. Biomedica Biochimica Acta 1988;47(4-5):337-342

#### [國內研究生的相關論文]

大蒜精油及其有機含硫成分-二烯丙基硫化物、二烯丙基二硫化物及二烯丙基三硫化物在 streptozotocin 誘發之糖尿病大鼠的抗糖尿病作用 (Antidiabetic effects of garlic oil and its organosulfur compounds-diallyl sulfide, diallyl disulfide and diallyl trisulfide on streptozotocin-induced diabetic rats) 研究生: 王珮琳 (中山醫學院營養科學研究所; 民 90)

椿葉水萃取液在 Alloxan 所誘發的糖尿病鼠中降血糖作用之研究 (The Study of Hypoglycemic Effects of Toona Sinensis Aqueous Leaf Extracts on Alloxan-induced Diabetic Rats) 研究生: 王珮憲 (高雄醫學大學醫學研究所; 民 90)

糙薏仁添加綠豆對 STZ 所誘發之糖尿病大白鼠脂質代謝與醣類代謝的影響 (Effect of Dehulled Adlay Added to Mung Bean on Lipid and Carbohydrate Metabolism in STZ-induced Diabetic Rats) 研究生: 江怡萱(國立海洋大學食

品科學系；民 90)

反轉錄病毒載體表現大白鼠胰島素基因之研究 (The expression of rat insulin gene by retrovirus vector) 研究生：賴敏銓(國立中興大學醫學微生物學研究所；民 89)

由 streptozotocin 引起糖尿病後大白鼠前肢感覺徑路之變化 (The changes in sensory pathway of forelimbs of diabetic rats induced by streptozotocin) 研究生：陳牧君(國立臺灣大學解剖學研究所；民 88)

### [大陸的文獻]

Huang, S., Fu, P., Li, X., and Zhang, X.: Larginine and nitric oxide have effects on glomerulus hyperperfusion of early diabetic rats. [Chinese]. Hua-Hsi i Ko Ta Hsueh Hsueh Pao [Journal of West China University of Medical Sciences] 1997; 28:251-254

洗蘇、黃松、蘇建家、秦映芬、歐超、羅佐杰、長敏怡：STZ 誘導樹鼠糖尿病動物模型研究。廣西醫大學報 2000; 17:945-948

吳希美、謝強敏、唐法暉、王硯、曾玲暉、卡如濂：糖尿病動物模型-大鼠胰腺切除後糖耐量試驗法的探討。中藥藥理與臨床 1999;14:47-48

郭嘯華、劉志紅、李恒、朱加明、黎磊石：實驗性 2 型糖尿病大鼠模型的建立。腎臟病與透析腎移植雜誌 2000; 9:351-353

楊光燃、袁申元、朱良湘、張盛忠、潘素芳、袁明霞：糖尿病大鼠神經形態和山梨醇含量的變化及黃腐酸鈉的作用。基礎醫學與臨床 2000; 20:33-35

袁詠、曲竹秋、周云岩、王作成：六味地黃湯對糖尿病大鼠腎臟抗脂質過氧化損傷的影響。新中醫 1999;31:36-37

### 六、痛風(gout)

#### [英文的重要文獻]

Chou, C. T. and Kuo, S. C.: The anti-inflammatory and anti-hyperuricemic effects of Chinese herbal formula danggui-nian-tong-tang on acute gouty arthritis: a comparative study with indomethacin and allopurinol. American Journal of

Chinese Medicine 1995; 23(3-4):261-271

- Ageel, A. M., Mossa, J. S., al Yahya, M. A., al Said, M. S., and Tariq, M.: Experimental studies on antirheumatic crude drugs used in Saudi traditional medicine. Drugs Under Experimental & Clinical Research 1989; 15:369-372
- Lerman, S., Megaw, J. M., and Gardner, K.: Allopurinol therapy and cataractogenesis in humans. American Journal of Ophthalmology 1982; 94:141-146
- Lussier, A., de Medicis, R., quis, L., and Menard, H.: Inhibition of adjuvant-induced arthritis in the hyperuricemic rat. Agents & Actions 1978; 8:536-542
- Mackin, W. M., Rakich, S. M., and shall, C. L.: Inhibition of rat neutrophil functional responses by azopazone, an anti-gout drug. Biochemical Pharmacology 1986; 35:917-922
- Prakash, S. and Chang, T. M.: In vitro and in vivo uric acid lowering by artificial cells containing microencapsulated genetically engineered E. coli DH5 cells. International Journal of Artificial Organs 2000; 23:429-435
- Terasawa, M., Aratani, H., Iwahisa, Y., Ioshi, T., and uyama, Y.: Effect of pranoprofen on sodium urate crystal-induced inflammation. [Japanese]. Folia Pharmacologica Japonica 1987; 89:129-137

#### [國內研究生的相關論文]

白蛋白與 T-H 蛋白及其糖基在草酸鈣結晶過程中所扮演的角色。研究生: 林和昇 (國立清華大學生命科學系; 民 89)

#### [大陸的文獻]

陳文照、林堅、金策、姜宏、吳士民、顏瑞生：實驗性痛風外周疼痛介質的動態變化。中藥藥理與臨床 2000;16:37-38

金沉銳、鄭軍、劉紹唐：小鼠高尿酸血症模型初探。成都中醫藥大學學報 1999; 22:49-51

#### 七、心臟衰竭(heart failure)

## [英文的重要文獻]

- Bachert, E. L. and Fung, H. L.: Hemodynamic tolerance and pharmacokinetics of nicorandil in experimental heart failure. *Journal of Cardiovascular Pharmacology* 1993; 21:781-785
- Bauer, J. A. and Fung, H. L.: Effects of chronic glyceryl trinitrate on left ventricular haemodynamics in a rat model of congestive heart failure: demonstration of a simple animal model for the study of in vivo nitrate tolerance. *Cardiovascular Research* 1990; 24:198-203
- Howes, L. G., Hodzman, G. P., Maccarrone, C., Kohzuki, M., and Johnston, C. I.: Cardiac 3,4-dihydroxyphenylethylene glycol (DHPG) and catecholamine levels in a rat model of left ventricular failure. *Journal of Cardiovascular Pharmacology* 1989; 13:348-352
- Koyama, S., Kodama, M., Izumi, T., and Shibata, A.: Experimental rat model representing both acute and chronic heart failure related to autoimmune myocarditis. *Cardiovascular Drugs & Therapy* 1995; 9:701-707
- Kumar, D., Kirshenbaum, L. A., Li, T., Danelisen, I., and Singal, P. K.: Apoptosis in adriamycin cardiomyopathy and its modulation by probucol. *Antioxidants & Redox Signaling* 2001; 3:135-145
- Momma, K. and Takao, A.: Right ventricular concentric hypertrophy and left ventricular dilatation by ductal constriction in fetal rats. *Circulation Research* 1989; 64:1137-1146

## [國內研究生的相關論文]

- 細胞凋亡在 Adriamycin 引起老鼠之心肌病變中角色的探討 (The Role of Apoptosis in Adriamycin-Induced Cardiomyopathy in Rats) 研究生: 鄧明生  
(長庚大學基礎醫學研究所 ; 民 87)
- 敗血症大白鼠心臟功能衰竭時蛋白激酶 A、C 和 M 角色之探討(Roles of Protein Kinase A、C and M on the Cardiac Dysfunction in Rat during Sepsis) 研究生:

楊秀蘭(高雄醫學大學醫學研究所; 民 90)

â 1 - 腎上腺素受體基因多形性與早發性冠狀動脈疾病危險因子(Variant of the  $\alpha$ 1-Adrenergic Receptor Gene and Risk Factors of Premature Coronary Atherosclerosis in Taiwanese Subjects) 研究生: 羅文帥(國立臺灣大學藥學研究所; 民 90)

脂多醣體對嚙齒類動物心室肌細胞的抑制作用 (Depressant Effects of Lipopolysaccharide on Rodent Ventricular myocyte and papillary muscle) 研究生: 黃滄佑(國防醫學院藥理學研究所; 民 89)

第一型類胰島素生長因子在心臟重塑作用之角色 (The Role of Insulin-like Growth Factor I in Cardiac Remodeling) 研究生: 李文領(國立陽明大學臨床醫學研究所; 民 89)

類鴉片受體致效劑與拮抗劑對心臟功能影響之研究 (Studies of Opioid Agonists and Antagonists on Cardiac Function) 研究生: 洪啟峰(國立臺灣大學藥理學研究所; 民 88)

### [大陸的文獻]

蔡淑頻、張一卓、曾慶華：內皮素對哺乳動物心肌活動的影響。解剖科學進展 2000; 6: 67 - 69

## 八、高血壓(hypertension)

### [英文的重要文獻]

Aharinejad, S., Schraufnagel, D. E., Bock, P., MacKay, C. A., Larson, E. K., Miksovsky, A., and Marks, S. C.: Spontaneously hypertensive rats develop pulmonary hypertension and hypertrophy of pulmonary venous sphincters. American Journal of Pathology 1996; 148:281-290

Azadzoi, K. M. and Goldstein, I.: Erectile dysfunction due to atherosclerotic vascular disease: the development of an animal model. Journal of Urology 1992; 147:1675-1681

- Belichard, P., Pruneau, D., and Rochette, L.: Influence of spontaneous hypertension and cardiac hypertrophy on the severity of ischemic arrhythmias in the rat. *Basic Research in Cardiology* 1988; 83:560-566
- Bevan, R. D., van Marthens, E., and Bevan, J. A.: Hyperplasia of vascular smooth muscle in experimental hypertension in the rabbit. *Circulation Research* 1976; 38(6 Suppl 2):58-62
- Bomzon, A. and Blendis, L. M.: Vascular reactivity in experimental portal hypertension. *American Journal of Physiology* 1987; 252(2 Pt 1):G158-162
- Burge, D. M., Holbrook, A. G., and Karan, S. J.: Noninvasive assessment of portosystemic shunting in extrahepatic portal hypertension in rats. *Journal of Pediatric Surgery* 1987; 22:211-214
- Burroughs, V., Goldstein, M., and Shenkman, L.: Pheochromocytoma: an animal model. *Hormone Research* 1980; 13:174-179
- Chesney, C. F. and Allen, J. R.: Animal model: pulmonary hypertension, cor pulmonale and endocardial fibroelastosis in monocrotaline-intoxicated nonhuman primates. *American Journal of Pathology* 1973; 70:489-492
- Crandall, D. L., Goldstein, B. M., Lizzo, F. H., Lozito, R. J., and Cervoni, P.: Development of an animal model for investigating disparate myocardial effects of obesity and hypertension. *Journal of Applied Physiology* 1988; 64: 1094-1097
- Haber, S. B. and Friedman, R.: Psychobiology of experimental hypertension: evaluation of the Dahl rat lines. *Behavior Genetics* 1981; 11:505-515
- Herrera, V. L., Makrides, S. C., Xie, H. X., Adari, H., Krauss, R. M., Ryan, U. S., and Ruiz-Opazo, N.: Spontaneous combined hyperlipidemia, coronary heart disease and decreased survival in Dahl salt-sensitive hypertensive rats transgenic for human cholesteryl ester transfer protein. *Nature Medicine* 1999; 5:1383-1389
- Hirano, T., Ebara, T., Furukawa, S., Nagano, S., and Takahashi, T.: Mechanism of hypertriglyceridemia in Dahl salt-sensitive rats, an animal model of spontaneous

- nephrotic syndrome. Metabolism: Clinical & Experimental 1994; 43:248-256
- Hulman, S., Brodsky, N., Miller, J., Donnelly, C., Helms, J., and Falkner, B.: Effect of estrogen withdrawal on blood pressure and insulin resistance in sucrose-fed juvenile rats. American Journal of Hypertension 1996; 9 (12 Pt 1): 1200-1205
- Jannetta, P. J., Segal, R., Wolfson, S. K., Jr., Dujovny, M., Semba, A., and Cook, E. E.: Neurogenic hypertension: etiology and surgical treatment. II. Observations in an experimental nonhuman primate model. Annals of Surgery 1985; 202:253-261
- Kawaguchi, M., Koshimura, K., Murakami, Y., Tsumori, M., Gonda, T., and Kato, Y.: Antihypertensive effect of insulin via nitric oxide production in the Zucker diabetic fatty rat, an animal model for non-insulin-dependent diabetes mellitus. European Journal of Endocrinology 1999; 140: 341-349
- Kentra, D., Susic, D., Machado, E., and Lozzio, B. B.: Animal model of human disease. Hydronephrosis, agenesis of the renal medulla, arterial hypertension. American Journal of Pathology 197; 87:477-480
- King, C. M. and Webb, R. C.: The endothelium partially obscures enhanced microvessel reactivity in DOCA hypertensive rats. Hypertension 1988; 12:420-427
- Kren, V., Pravenec, M., Lu, S., Krenova, D., Wang, J. M., Wang, N., Merriouns, T., Wong, A., St Lezin, E., Lau, D., Szpirer, C., Szpirer, J., and Kurtz, T. W.: Genetic isolation of a region of chromosome 8 that exerts major effects on blood pressure and cardiac mass in the spontaneously hypertensive rat. Journal of Clinical Investigation 1997; 99:577-581

### [國內研究生的相關論文]

合成血管收縮素轉化、抑制劑對自發性高血壓鼠之影響 (Effect of Systhetic Angiotensin-Converting Enzyme Inhibitor on Spontaneously Hypertensive Rats)  
研究生：羅永杰(國立臺灣大學食品科技研究所；民 90)

大鼠高血壓發展中血管內皮細胞的功能性代償反應 (Endothelial Functional Changes during The Development of Hypertension in Spontaneously Hypertensive Rats) 研究生: 柳錦燕(國立成功大學生理學研究所; 民 90)  
川芎素或 captopril 合併血管升壓素衍生物對門脈高壓鼠之血流動力學效應 (Hemodynamic effects of tetramethylpyrazine or captopril combination with terlipressin in portal hypertensive rats) 研究生: 林秉輝(國立陽明大學傳統醫藥學研究所; 民 89)

### [大陸的文獻]

鄭慶珍、白玉山：應激性高血壓動物模型的建立。福建醫學院學報 1994; 28: 424-425

Cai, C., Zou, X., and Xin, D.: Role of pulmonary arterial angiotensin converting enzyme in development of hypoxic pulmonary hypertension. [Chinese]. Chung-Hua Chieh Ho Ho Hu Hsi Tsa Chih Chinese Journal of Tuberculosis & Respiratory Diseases 1997; 20:215-217

周桂梅、邢德富、譚慶霞、周方鈞：針刺對腎動脈狹窄亮血壓大鼠的血壓 SOD、LPO 及五種微量元素的影響。中國中西醫結合雜誌 1994; 14:739-741  
顧勇、孫培吾：野百合鹼肺動脈高壓模型及其血管活性物質的變化。新疆醫學院學報 1997;20:69-71

馬杰、王晉民、胡麗萍、張慧穎：心腦靜片對實驗性腦缺血及高血壓的作用研究。中草藥 2000;31:39-40

### 九、高血脂(hyperlipidemia)

Shimada, K., Yoshida, K., Tadokoro, H., Ueda, M., Shiomi, M., Kitsukawa, S., Takami, A., Komatsu, R., Suzuki, K., Tanada, S., and Masuda, Y.: Adenosine-induced coronary flow reserve in Watanabe heritable hyperlipidemic rabbits. Japanese Circulation Journal 2000 64:971-976

Kashyap, V. S., Santamarina-Fojo, S., Brown, D. R., Parrott, C. L., Applebaum-Bowden, D., Meyn, S., Talley, G., Paigen, B., Maeda, N., and

- Brewer, H. B., Jr. Apolipoprotein E deficiency in mice: gene replacement and prevention of atherosclerosis using adenovirus vectors. - *Journal of Clinical Investigation* 1995;96:1612-1620
- Farese, R. V., Jr., Ruland, S. L., Flynn, L. M., Stokowski, R. P., and Young, S. G.: Knockout of the mouse apolipoprotein B gene results in embryonic lethality in homozygotes and protection against diet-induced hypercholesterolemia in heterozygotes. *Proceedings of the National Academy of Sciences of the United States of America* 1995;92:1774-1778
- Rall, C. J., Hoeg, J. M., Gregg, R. E., Law, S. W., Monge, J. C., Meng, M. S., Zech, L. A., and Brewer, H. B., Jr.: Enhanced apolipoprotein E production with normal hepatic mRNA levels in the Watanabe heritable hyperlipidemic rabbit. *Arteriosclerosis* 1988;8:804-809
- Liu, R., Saku, K., Jimi, S., Ohta, T., Zhang, B., Takebayashi, S., and Arakawa, K.: Mechanism of action of gemfibrozil on HDL metabolism and atherosclerosis in WHHL rabbits. *Cardiovascular Drugs & Therapy* 1997;11:659-668
- Keidar, S., Attias, J., Smith, J., Breslow, J. L., and Hayek, T.: The angiotensin-II receptor antagonist, losartan, inhibits LDL lipid peroxidation and atherosclerosis in apolipoprotein E-deficient mice. *Biochemical & Biophysical Research Communications* 1997;236:622-625
- Palmer, W. K., Emeson, E. E., Johnston, T. P., and Gornik, W.: The poloxamer 407-induced hyperlipidemic atherogenic animal model  
- [Comparative pharmacokinetics of theophylline in hyperlipidemia in animals and humans]. [Polish]. *Medicine & Science in Sports & Exercise* 1997;29:1416-1421
- Simionescu, M., Popov, D., Sima, A., Hasu, M., Costache, G., Faitar, S., Vulpanovici, A., Stancu, C., Stern, D., and Simionescu, N.: Pathobiochemistry of combined diabetes and atherosclerosis studied on a novel animal model. The hyperlipemic-hyperglycemic hamster. *American Journal of Pathology*

1996;148:997-1014

Porter, J. A., Carter, B. L., Johnson, T. P., and Palmer, W. K.: Effects of pravastatin on plasma lipid concentrations in poloxamer 407-induced hyperlipidemic rats. *Pharmacotherapy* 1995;15:92-98

Chinellato, A., Ragazzi, E., Pandolfo, L., Alvano, A. P., Froldi, G., De Biasi, M., Caparrotta, L., Aliev, G., and Fassina, G.: Functional and morphologic characterization of thoracic aorta in heritable hyperlipidemic Yoshida rats of different ages. *Journal of Cardiovascular Pharmacology* 1994;24:216-228

Liu, J., Shen, Z. F., Liu, H. F., Ye, F., and Xie, M. Z.: [An animal model for testing hypoglycemic and hypolipidemic drugs]. [Chinese]. *Yao Hsueh Hsueh Pao - Acta Pharmaceutica Sinica* 1994;29:387-389

Kozarsky, K. F., McKinley, D. R., Austin, L. L., Raper, S. E., Stratford-Perricaudet, L. D., and Wilson, J. M.: In vivo correction of low density lipoprotein receptor deficiency in the Watanabe heritable hyperlipidemic rabbit with recombinant adenoviruses. *Journal of Biological Chemistry* 1994;269:13695-13702

Xiong, W., Zsigmond, E., Gotto, A. M., Reneker, L. W., and Chan, L.: Transgenic mice expressing full-length human apolipoprotein B-100. Full-length human apolipoprotein B mRNA is essentially not edited in mouse intestine or liver. *Journal of Biological Chemistry* 1992;267:21412-2120

### [國內研究生的相關論文]

紅麴粉末對齧齒類動物降血之功能及安全性之研究 (Lipid-lowering effect and safety of Monascus rice powder on rodents) 研究生: 謝孟志(台北醫學院藥學研究所; 民 90)

銀杏萃取物減少餵食高膽固醇兔子經氣球損傷後的新內膜增生及間白素貝它 1 的表現 (Ginkgo Biloba Extract Reduces Neointimal Hyperplasia and Interleukin-1 beta Expression after Balloon Injury in Cholesterol-Fed Rabbits) 研究生: 楊德芳(國立陽明大學傳統醫藥學研究所; 民 88)

## [大陸的文獻]

- 王四旺、謝艷華、朱玲珍：平脂膠囊對鼠血脂和血粘的影響。第四軍醫大學學報 1999; 20: 251- 254
- 閔祥華、顧景范、孫存普、劉佃辛、吳可、何傳民：大豆異黃酮對大鼠血脂和過氧化狀態的影響。營養學報 2000;22:31-33
- 拓步雄、李慧、卓玉英：舒肝脂膠囊對實驗性高血脂症及脂肪肝的影響。中醫藥研究 1998;14:41-44

## 十、學習和記憶障礙(learning and memory defect)

- Strupp, B. J., Himmelstein, S., Bunsey, M., Levitsky, D. A., and Kesler, M.: Cognitive profile of rats exposed to lactational hyperphenylalaninemia: correspondence with human mental retardation. Developmental Psychobiology 1990;23:195-214
- Ashwell, K. W.: Differential target dependence in the developing brain: implications for mental retardation. Medical Hypotheses 1990;32:67-75
- Flint, J.: The genetic basis of cognition. Brain 1999;122:2015-2032
- Muntoni, F., Mateddu, A., and Serra, G.: Passive avoidance behaviour deficit in the mdx mouse. Neuromuscular Disorders 1991;1:121-123

## [國內研究生的相關論文]

- 海馬體及紋狀體於兩種水迷津作業之不同的學習與記憶功能(The Different Roles of Hippocampus and Striatum in Two Water Maze Tasks Learning) 研究生：孫偉倫(高雄醫學大學行為科學研究所;民 90)
- 整合蛋白相關蛋白參與記憶形成之角色及機制探討 (Role and Mechanism of Integrin-associated Protein (IAP) involved in Memory Formation in Rats and Mice) 研究生：張惠萍(國防醫學院生命科學研究所；民 90)
- 槐花對鵝膏蕈酸誘發大白鼠學習記憶障礙效用研究 (The attenuating effects of Huaihua on IBO induced deficits of learning and memory in rats) 研究生：錢添發(中國醫藥學院中國醫學研究所；民 90)

以學習記憶的取向探討安非他命引發地點偏好之神經機制 (Neural Mechanisms Underlying Conditioned Place Preference Induced by Amphetamine) 研究生：林星宏(國立臺灣大學心理學研究所; 民 88)  
檳榔鹼在大白鼠海馬迴之藥理學研究 (Pharmacological studies of arecoline in the rat hippocampus in vitro) 研究生：鄧振銘(國立臺灣大學藥理學研究所; 民 88)

### [大陸的文獻]

趙玲、徐秋萍、司銀楚、王水炎：聽經膠囊對早老齡小鼠腦缺血再灌後學習記憶障礙的影響。北京中醫藥大學學報 2001; 24: 36- 38

楊俊卿、周岐新：亞急性一氧化碳中毒致小鼠遲發性學習記憶障礙機制研究。工業衛生與職業病 2000;26:67-69

趙建新、田元祥、葛建軍、梅寶幸、孫彥輝、吳中秋：電針腎俞、膈俞、百會穴對擬血管性痴呆學習記憶障礙小鼠水迷宮實驗的影響。中國行為醫學科學 2000;9:409-413

### 十一、腎衰竭(renal failure)

Deng, J., St Clair, M., Everett, C., Reitman, M., and Star, R. A.: Buprenorphine given after surgery does not alter renal ischemia/reperfusion injury. Comparative Medicine 2000;50:628-632

Mutti, A., Coccini, T., Alinovi, R., Toubeau, G., Broeckaert, F., Bergamaschi, E., Mozzoni, P., Nonclercq, D., Bernard, A., and Manzo, L.: Exposure to hydrocarbons and renal disease: an experimental animal model. Renal Failure 1999;21:369-385

Thuraisingham, R. C. and Raine, A. E.: Maintenance of normal agonist-induced endothelium-dependent relaxation in uraemic and hypertensive resistance vessels. - Nephrology Dialysis Transplantation 1999;14:70-75

- Barata, K., Yoshida, M., Hokao, R., and Maekawa, A.: Sequential alterations in clinical biochemical indicators of renal function in 5/6 nephrectomized rats--basic study for renal toxicity using 5/6 nephrectomized rats. *Journal of Toxicological Sciences* 1998;23:433-442
- Jouvet, P., Colomer, S., Jugie, M., Meftali, Y., Vassault, A., and Man, N. K.: Continuous venovenous hemodialysis in a neonate model: a two-pump system. *Critical Care Medicine* 1998;26:115-119
- Ohashi, T., Kenmochi, M., Kinoshita, H., Ochi, K., and Kikuchi, H.: [Functional changes in the cochlea of guinea pigs in chronic renal failure--electrocotchleography. Effect of noise exposure]. *Nippon Jibiinkoka Gakkai Kaiho* [Journal of the Oto-Rhino-Laryngological Society of Japan] 1997;100:685-693
- Cheng, Q.: [Effect of cordyceps sinensis on cellular immunity in rats with chronic renal insufficiency]. *Chung-Hua i Hsueh Tsa Chih* [Chinese Medical Journal] 1992;72:27-29, 63
- Abul-Ezz, S. R., Walker, P. D., and Shah, S. V.: Role of glutathione in an animal model of myoglobinuric acute renal failure. *Proceedings of the National Academy of Sciences of the United States of America* 1991;88:9833-9837
- Yokozawa, T., Zheng, P. D., Oura, H., and Koizumi, F.: Animal model of adenine-induced chronic renal failure in rats. *Nephron* 1986;44:230-234
- Robertson, J. A., Felsenfeld, A. J., Haygood, C. C., Wilson, P., Clarke, C., and Llach, F.: Animal model of aluminum-induced osteomalacia: role of chronic renal failure. *Kidney International* 1983;23:327-335

### [國內研究生的相關論文]

大豆蛋白與酪蛋白對慢性腎衰竭大白鼠腎功能的影響 (Effect of Soy Protein and Casein on Renal Function in Partially Nephrectomized Rats) 研究生: 陳淑子  
(台北醫學院保健營養學研究所;民 90)

氧自由基在腎絲球硬化的致病性中所扮演的角色 (Role of Reactive Oxygen Species in the Pathogenesis of Glomerulosclerosis) 研究生: 陳鴻鈞(高雄醫學大學醫學研究所; 民 89)

尿毒症鼠在不同血漿三碘甲狀腺素濃度下腎臟排泄鋅之研究 (Effects of the Alteration of Plasma Triiodothyronine Level on Renal Zinc Excretion in Uremic Rats) 研究生: 邱伯勤(國立陽明大學生理學研究所; 民 88)

冬蟲夏草對 Adriamycin 引起腎絲球傷害之影響 (Effects of Cordyceps sinensis on Adriamycin Induced Glomerular Nephrosis) 研究生: 張權發(國立交通大學生物科技研究所; 民 86)

部份腎臟切除後大白鼠殘存腎臟對抗利尿素的反應 (Response of remnant kidney to arginine vasopressin in partially nephrectomized rats) 研究生: 蔡新茂(國立陽明大學生理學研究所; 民 82)

#### [大陸的文獻]

篤文永：急性腎功能衰竭中醫藥實驗研究進展。中醫研究 1995; 8: 19-20

馬建偉、劉占民、徐麗梅等十一名：健腎沖劑治療慢性腎衰竭大鼠的療效觀察。

空軍總醫院學報 2000;16:107-109

馬建偉、蔡慶、劉占民等八名：滋腎活血解毒方對慢性腎衰竭大鼠腎內皮素基因表達的影響。安徽中醫學院學報 2001; 20:40-43

#### 十二、 中風(stroke)

Beck, H., Acker, T., Wiessner, C., Allegrini, P. R., and Plate, K. H.: Expression of angiopoietin-1, angiopoietin-2, and tie receptors after middle cerebral artery occlusion in the rat. American Journal of Pathology 2000;157:1473-1483

Blezer, E. L., Nicolay, K., Viergever, M. A., Koomans, H. A., and Joles, J. A.: MRI-based quantification of cerebral edema in individual SHRSP rats using averaged criteria determined before the occurrence of edema. Magnetic Resonance Imaging 1999;17:903-907

Borlongan, C. V., Cahill, D. W., and Sanberg, P. R.: Locomotor and passive

avoidance deficits following occlusion of the middle cerebral artery. *Physiology & Behavior* 1995;58:909-917

Clark, W. M., Madden, K. P., Lyden, P. D., and Zivin, J. A.: Cerebral hemorrhagic risk of aspirin or heparin therapy with thrombolytic treatment in rabbits. *Stroke* 1991;22:872-876

Di Fabio, R., Conti, N., De Magistris, E., Feriani, A., Provera, S., Sabbatini, F. M., Reggiani, A., Rovatti, L., and Barnaby, R. J.: Substituted analogues of GV150526 as potent glycine binding site antagonists in animal models of cerebral ischemia. *Journal of Medicinal Chemistry* 1999;42:3486-3493

Futrell, N., Millikan, C., Watson, B. D., Dietrich, W. D., and Ginsberg, M. D.: Embolic stroke from a carotid arterial source in the rat: pathology and clinical implications. *Neurology* 1989;39:1050-1056

Hasser, E. M. and Moffitt, J. A.: Regulation of sympathetic nervous system function after cardiovascular deconditioning. *Annals of the New York Academy of Sciences* 2001;940:454-468

Kato, M., Iwata, H., Okamoto, M., Ishii, T., and Narita, H.: Focal cerebral ischemia-induced escape deficit in rats is ameliorated by a reversible inhibitor of monoamine oxidase-a: implications for a novel animal model of post-stroke depression. *Biological & Pharmaceutical Bulletin* 2000;23:406-410

Khayyam, N., Thavendiranathan, P., Carmichael, F. J., Kus, B., Jay, V., Burnham, W. M., Klein, G. M., Li, H., Sun, P., and Buchan, A. M.: Neuroprotective effects of acetylsalicylic acid in an animal model of focal brain ischemia- Tissue plasminogen activator does not increase neuronal damage in rat models of global and focal ischemia. *Neuroreport* 1999;10:371-374

Mhairi, Macrae, I.: New models of focal cerebral ischaemia. - *British Journal of Clinical Pharmacology* 1992;34:302-308

Nishimura, T., Mizukawa, K., Nakao, K., Yamada, H., Kinoshita, M., and Ochi, J.: Atrial natriuretic polypeptide (ANP)-immunoreactivity and specific atrial

granules in cardiac myocytes of stroke-prone spontaneously hypertensive rat (SHRSP). Archives of Histology & Cytology 1994;57:1-7

Sauer, D., Martin, P., Allegrini, P. R., Bernasconi, R., Amacker, H., and Fagg, G. E.: Differing effects of alpha-difluoromethylornithine and CGP 40116 on polyamine levels and infarct volume in a rat model of focal cerebral ischaemia. Neuroscience Letters 1992;141:131-135

Shi, J., Yang, S. H., Stuble, L., Day, A. L., and Simpkins, J. W.: Hypoperfusion induces overexpression of beta-amyloid precursor protein mRNA in a focal ischemic rodent model. Brain Research 2000;853:1-4

#### [國內研究生的相關論文]

電針對腦中風急性期的動物實驗與臨床研究 (Animal model and Clinical Study in effects of electroacupuncture on Acute Cerebrovascular Accident) 研究生: 高宗桂(中國醫藥學院中國醫學研究所; 民 90)

延胡索對於缺血性-再灌流大鼠腦梗塞效用之研究 (Effect of Rhizoma Corydalis on Cerebral Infarct in Ischemia-Reperfusion Injured Rats) 研究生: 廖恩賜(中國醫藥學院中國醫學研究所; 民 90)

「細胞自戕」在缺糖引發之神經傷害中所扮演之角色 (Role of Apoptosis in Hypoglycemia-induced Cell Death) 研究生: 王瑣瑣(國立中興大學生命科學院碩士在職專班; 民 90)

Carboxyfullerene 對小鼠大腦局部缺氧之調控 (The modulation of murine focal cerebral ischemia by carboxyfullerene) 研究生: 王雅慧(國立成功大學微生物暨免疫學研究所; 民 90)

骨骼型態發生蛋白質在大白鼠初級培養大腦皮質神經細胞的神經保護作用 (Neuroprotective Effects of Bone Morphogenetic Proteins (BMPs) in Primary Cortical Culture) 研究生: 陳素瑜(國防醫學院生理學研究所; 民 90)

十字花科蔬菜衍生物對 Lipopolysaccharide 與 Interferon- $\alpha$  所誘導之一氧化氮的影響 (Suppression of Lipopolysaccharide and Interferon- $\alpha$ -Induced Nitric Oxide

Production by Cruciferous Vegetable Derivatives) 研究生: 戴惠晶(台北醫學院保健營養學研究所; 民 90)

中藥治腦方劑對腦缺氧治療效果之研究 (Therapeutic Effects of Chinese Medicine on Ischemic Stroke-A Study of Cerebral Active Regimens) 研究生: 甘宜弘(台北醫學院醫學研究所; 民 90)

生脈散對於熱中風的療效評估 (Therapeutic evaluation of Sheng Mai San) 研究生: 周呈岳(國立陽明大學生理學研究所; 民 90)

多種藥物對於大白鼠熱中風模式治療評估 (Therapeutic evaluation of several substances in a rat heatstroke model) 研究生: 張丞圭(國立陽明大學生理學研究所; 民 90)

局部腦皮質傷害後迅早基因及神經營養基因表達之改變:著重遠處及延遲性之影響 (The Impact Toward Expressions of Immediate Early Genes And Neurotrophic Genes After Focal Cortical Injury: Emphasis on Delayed Changes in the Distant Brain Areas) 研究生: 劉家壽(高雄醫學大學醫學研究所; 民 89)

腦虛血所引發出血性胃潰瘍之病生理機轉及藥物防治作用之探討 (Pathophysiological Mechanisms of Gastric Mucosal Hemorrhagic Ulceration Induced by Brain-Ischemia: Protection by Several Drugs) 研究生: 林慧茹(國立成功大學藥理學研究所; 民 89)

氫氣自由基在高壓氧氣暴露誘發大腦損傷中所扮演的角色 (The Role of Hydroxyl Radical in Brain Injury Induced by Hyperbaric Oxygen Exposure) 研究生: 林宜興(國防醫學院海底醫學研究所; 民 89)

自由基對神經細胞之致毒作用及其訊息傳遞之研究 (Studies on free radical-induced signal transduction and cytotoxicity on neuronal cells) 研究生: 詹錦豐(國立臺灣大學毒理學研究所; 民 89)

新生動物腦缺氧時麴胺酸鹽接受器與拮抗劑對多巴胺之調節所扮演的角色及其可能之臨床應用 (The role of glutamate receptor and its antagonist in dopamine regulation during neonatal hypoxia and the clinical application) 研究

生：郭夢菲(國立臺灣大學臨床醫學研究所;民 89)

### [大陸的文獻]

宁遜、徐立然、耿新生：活血化瘀治療出血性中風研究進展。河南中醫 1995; 15: 256-259

張春兵、金偉城、沈梅紅：脈絡型對大鼠大腦中動脈阻塞中風 6-酮-PGF<sub>1alpha</sub> 和 TXB<sub>2</sub> 的作用。南京中醫藥大學學報 1998;14:150-152

朱寧、李棟、鄭安、林求鍼、劉楠：中風 II 號干預缺血性中風損傷級聯反應的實驗研究。心血管復健醫學雜誌 2001;10:12-13

## 肆、討論

在短短的三個月不足的期限，主持人受託接下這項幾乎不可能的任務；目的在於幫助建立一項工具，協助中醫藥現代化的推進。當然，由於時間緊逼，所得成果不能十全十美。但是，本著學術的堅持精神，我們自認全力而為了。若有未盡理想之處，敢請 賜諒與指教。

疾病的動物模式(Animal Model)在國外極常使用，因為它是藥物在臨床前的最佳評估工具，也是研究疾病的病因或病狀生理最常用之技術。因此，許多研究人員全力在研發這項技術；由化學物質的傷害到物理或手術方式的介入等。例如：用化學物質的注射來造成動物的肝炎、糖尿病或其他的異常，或是使用血管結紮來造成中風，或用手術來引致異常等。然而，一種疾病常有多種動物模式可供參考使用。對於剛要使用這項技術的中醫藥同好要如何慎選才最恰當呢？否則，使用不妥的話，所得結果可能只能當為「改善這項毒害」而非真正的評估效益了！

慎選恰當的動物模式，要如何來執行呢？首先，可由發表的文獻去尋找「最廣被使用的模式」。以中風為例，文獻列有各種不同的技術可供動物模式，可是，以大腦中動脈阻塞中風(MCA)的技術最被使用。因此，藉由這項技術所得的成果才最易信服當代研究人員。另外，詢問已在從事這項研究工作的專業人員，除了可得到最佳的動物模式之外，更可由其實貴的經驗得到助益的建議。然而，

選擇動物模式最忌「好高騖遠」的心態，例如：中東地區特產的小鼠才會出現的疾病，適合我們使用嗎？因此，身邊容易取得的動物也是需要考慮的因素！

由化學物質引致的動物模式，較易被指責為「毒害」的變化。因此，在生物技術的協助下，基因轉殖動物(Transgenic Animal)就發展成為適用的模式。以第一型糖尿病為例，使用 streptozotocin 來破壞胰島細胞就已日漸被基因改造的 BB/W 大白鼠所取代。高血壓的研究，也都用遺傳型的 SHR 在評估。然而，基因轉殖動物在我國尚屬起步而已，雖然有許多國內學者努力在研發，目前以進口為主。因此，貨源取得較不易。在吳銘芳及蘇裕家共寫的「疾病動物模式的介紹」乙書(藝軒圖書公司)，糖尿病、肥胖、老化、神經病變(癲癇)、高血壓、肝炎或肝癌等基因改變的自發性動物皆有介紹。

到目前為止，動物模式的研發皆全力朝向疾病變化的型式來推展。可是，不幸地，沒有一項動物模式完全與人體的病變相同；可能人體的變化較為複雜所致。因此，所得結果可供為臨床前的「接近人體疾病」之參考，但仍無法成為「絕對性」的效果。然而，在保障病人的權益方面，這項參考成果是極為有益！

在中醫藥研究方面，動物模式的使用日漸廣泛；兩岸的學者皆同。可是，基於中西醫學的思源不同，動物模式在傳統醫學的使用則仍極有限。例如：中風、高血壓或腫瘤等常用動物模式，在傳統醫學的使用並不多見。另外，傳統醫學的「消渴症」最接近當代的「糖尿病」了，可是，中醫將「消渴症」分為「上消」、「中消」和「下消」三種，目前的動物模式只能以接近「下消」來供使用而已。由此可知，中醫適用的動物模式仍需要全力去研發！

## 伍、結論與建議

本項計畫協助收集了十二種疾病的動物模式之文獻，供中醫藥研究之參考。主持人在不到三個月的短暫期間，只能全力以赴，較難達到完美的程度。因此，建議委託的執行期限不宜太短。另外，海峽兩岸的學術通訊管道不佳，為了發揚我國的傳統醫學，這項交流的互通極需打開。

## 陸、參考文獻

1. Abraham, W. M.:The role of leukotrienes in allergeninduced late responses in allergic sheep. Ann N Y Acad Sci 1988;524:26070
2. Advokat, C. and Pellegrin, A. I.:Excitatory amino acids and memory: evidence from Res on Alzheimer's disease and behavioral pharmacol. Neurosci Biobehav Rev 1992;16:1324
3. Ageel, A. M., Mossa, J. S., al Yahya, M. A., al Said, M. S., and Tariq, M.: Exp studies on antirheumatic crude drugs used in Saudi traditional Med Drugs Exp Clini Res 1989; 15:369-372
4. Aharinejad, S., Schraufnagel, D. E., Bock, P., MacKay, C. A., Larson, E. K., Miksovsky, A., and ks, S. C.:Spontaneously hypertensive rats develop pulmonary hypertension and hypertrophy of pulmonary venous sphincters. Am J Pathol 1996; 148:281-290
5. Ahmad, F. and Goldstein, B. J.: Increased abundance of specific skeletal muscle protein-tyrosine phosphatases in a genetic model of insulin-resistant obesity and diabetes mellitus. Metabolism 1995; 44:1175-1184
6. Albright, A. L., Mahan, J. D., Ward, K. M., Sherman, W. M., Roehrig, K. L., and Kirby, T. E.: Diabetic nephropathy in an aerobically trained rat model of diabetes. Med Sci Sports Exer 1995; 27:1270-1277
7. Alder, V. A., Su, E. N., Yu, D. Y., Cringle, S. J., and Yu, P. K.:Diabetic retinopathy: early functional changes. Clin Exp Pharmacol Physiol 1997 ;24:785-758
8. Altshuler, G. and Ornoy, A.: Thickness of renal glomerular capillary basement membrane in the offspring of diabetic rats fed a regular or high-sucrose diet. Acta Anatom 1986; 126:237-239
9. Alvarez, X. A., Miguel-Hidalgo, J. J., Fernandez-oa, L., and Cacabelos, R.: Intrahippocampal injections of the beta-amyloid 1-28 fragment induces behavioral deficits in rats. Methods Findings Exp Clin Pharmacol 1997; 19:471-479

10. Angerio, A. D. and Kot, P. A.: Endothelin1: possible implications in pulmonary vascular disease. *Heart Lung* 1997;26:299-304
11. Archer, S. G. and Gray, B. N.: A new reproducible model of hepatic and peritoneal metastases from colonic carcinoma. *Eur J Cancer Clin Oncol* 1988 ;24:1623-1632
12. Arendt, T.: Alzheimer's disease as a disorder of mechanisms underlying structural brain selforganization. *NeuroSci* 2001;102:723-765
13. Atkinson, J.: Vascular calcium overload. Physiological and pharmacological consequences. *Drugs* 1992;44 Suppl 1:1118
14. Azadzoi, K. M. and Goldstein, I.: Erectile dysfunction due to atherosclerotic vascular disease: the development of an animal model. *J Urol* 1992; 147:1675-1681
15. Bachert, E. L. and Fung, H. L.: Hemodynamic tolerance and pharmacokinetics of nicorandil in Exp heart failure. *J Cardiovasc Pharmacol* 1993; 21:781-785
16. Bacus, J. W., Bacus, J. V., Stoner, G. D., Moon, R. C., Kelloff, G. J., and Boone, C. W.: Quantitation of preinvasive neoplastic progression in animal models of chemical carcinogenesis. *J Cell Biochem - Supplement* 1997; 28-29:21-38
17. Bailleul, B., Brown, K., Ramsden, M., Akhurst, R. J., Fee, F., and Balmain, A.: Chemical induction of oncogene mutations and growth factor activity in mouse skin carcinogenesis. *Environ Health Perspectives* 1989 ;81:237
18. Baliga, R., Ueda, N., Walker, P. D., and Shah, S. V.: Oxidant mechanisms in toxic acute renal failure. *Drug Metabolism Rev* 1999 ;31:971-997
19. Baliga, R., Ueda, N., Walker, P. D., and Shah, S. V.: Oxidant mechanisms in toxic acute renal failure. *Am J Kidney Dis* 1997 ;29:46577
20. Balke, C. W. and Shorofsky, S. R.: Alterations in calcium handling in cardiac hypertrophy and heart failure. *Cardiovasc Res* 1998 ;37:290-299
21. Ball, M. J.: Alzheimer's disease: a challenging enigma. *Archives of Pathol Laboratory Med* 1982 ;106:15762

22. Barbera, A., Fernandez-Alvarez, J., Truc, A., Gomis, R., and Guiart, J. J.: Effects of tungstate in neonatally streptozotocin-induced diabetic rats: mechanism leading to normalization of glycaemia. *Diabetologia* 1997; 40:143-149
23. BarrettConnor, E.: Is insulin-dependent diabetes mellitus caused by coxsackievirus B infection? A review of the epidemiologic evidence. *Rev of Infectious Diseases* 1985 7:20715
24. Bartoli, R., Fernandez-Banares, F., Navarro, E., Castella, E., Mane, J., Alvarez, M., Pastor, C., Cabre, E., and Gassull, M. A.: Effect of olive oil on early and late events of colon carcinogenesis in rats: modulation of arachidonic acid metabolism and local prostaglandin E(2) synthesis. *Gut* 2000; 46:191-199
25. Bauer, J. A. and Fung, H. L.: Effects of chronic glycetyl trinitrate on left ventricular haemodynamics in a rat model of congestive heart failure: demonstration of a simple animal model for the study of in vivo nitrate tolerance. *Cardiovasc Res* 1990; 24:198-203
26. Becker, K. D., Gottshall, K. R., and Chien, K. R.: Strategies for studying Cardiovasc phenotypes in genetically manipulated mice. *Hypertension* 1996;27:495501
27. Belichard, P., Pruneau, D., and Rochette, L.: Influence of spontaneous hypertension and cardiac hypertrophy on the severity of ischemic arrhythmias in the rat. *Basic Res Cardiol* 1988; 83:560-566
28. Bennett, M. C., Diamond, D. M., Stryker, S. L., Parks, J. K., and Parker, W. D., Jr.: Cytochrome oxidase inhibition: a rodent animal model of Alzheimer's disease. *J Geriatr Psychiatry Neurol* 1992 ; 5:93-101
29. Berdanier, C. D.: The BHE rat: an animal model for the study of noninsulin-independent diabetes mellitus. *FASEB J* 1991 ;5:213944
30. Bevan, R. D., van Thens, E., and Bevan, J. A.: Hyperplasia of vascular smooth muscle in Exp hypertension in the rabbit. *Cir Res* 1976; 38:58-62
31. Bianchi, G. and Ferrari, P.: A genetic approach to the pathogenesis of priy

hypertension and to its treatment. Clin Exp Pharmacol Physiol 1995;22:S399405

32. Bianchi, G., Cusi, D., Ferrari, P., Barlassina, C., Pati, P., Salardi, S., Torielli, L., Ferrandi, M., Salvati, P., and Vezzoli, G.:Renal abnormalities at the prehypertensive stage of essential hypertension. J Cardiovasc Pharmacol 1988;12 Suppl 3:S438
33. Bianchi, G., Ferrari, P., Cusi, D., Salardi, S., Guidi, E., Niutta, E., and Tripodi, G.:Genetic and Exp hypertension in the animal modelsimilarities and dissimilarities to the development of human hypertension. J Cardiovasc Pharmacol 1986;8 Suppl 5:S6470
34. Bjugstad, K. B., Flitter, W. D., Garland, W. A., Su, G. C., and Arendash, G. W.: Preventive actions of a synthetic antioxidant in a el animal model of AIDS dementia. - Brain Res 1998; 795:349-357
35. Blitzer, A.:Regional behavioral variations of epidermoid carcinoma of the head and neck: a study in an animal model.. Laryngoscope 1982;92:121938
36. Bodles, A. M., Guthrie, D. J., Greer, B., and Irvine, G. B.: Identification of the region of non-Abeta component (NAC) of Alzheimer's disease amyloid responsible for its aggregation and toxicity. J Neurochem 2001;78:384-395.
37. Boel, E., Selmer, J., Flodgaard, H. J., and Jensen, T.:Diabetic late complications: will aldose reductase inhibitors or inhibitors of advanced glycosylation endproduct formation hold promise?. J Diabetes Complications 1995;9:10429
38. Bomzon, A. and Blendis, L. M.: Vascular reactivity in Exp portal hypertension. Am J Physiol 1987; 252:G158-162
39. Bone, A. J., Hitchcock, P. R., Gwilliam, D. J., Cunningham, J. M., and Barley, J.: Insulitis and mechanisms of disease resistance: studies in an animal model of insulin dependent diabetes mellitus. J Mol Med 1999; 77:57-61
40. Bosland, M. C., Prinsen, M. K., and Kroes, R.: Adenocarcinomas of the prostate induced by N-nitroso-N-methylurea in rats pretreated with cyproterone acetate

and testosterone. *Cancer Let* 1983; 18:69-78

41. Bowman, M. A., Leiter, E. H., and Atkinson, M. A.:Prevention of diabetes in the NOD mouse: implications for therapeutic intervention in human disease. *Immunol Today* 1994;15:11520
42. Brindley, D. N. and Russell, J. C.:Metabolic abnormalities linked to obesity: effects of dexfenfluramine in the corpulent rat. *Metabolism* 1995 ;44:237
43. Burge, D. M., Holbrook, A. G., and Karran, S. J.: Noninvasive assessment of portosystemic shunting in extrahepatic portal hypertension in rats. *J Pediatric Surgery* 1987; 22:211-214
44. Burroughs, V., Goldstein, M., and Shenkman, L.: Pheochromocytoma: an animal model. *Horm Res* 1980; 13:174-179
45. Cai, C., Zou, X., and Xin, D.: Role of pulmonary arterial angiotensin converting enzyme in development of hypoxic pulmonary hypertension.. *Chung-Hua Chieh Ho Ho Hu Hsi Tsa Chih Chinese J Tuber Resp Dis* 1997; 20:215-217
- 46.Califf, R. M., Fortin, D. F., Frid, D. J., Harlan, W. R., III, Ohman, E. M., Bengtson, J. R., Nelson, C. L., Tcheng, J. E., k, D. B., and Stack, R. S.:Restenosis after coronary angioplasty: an overview. *J Am Coll Cardiol* 1991;17:2B13B
47. Camps, P., El Achab, R., Morral, J., Munoz-Torrero, D., Badia, A., Banos, J. E., Vivas, N. M., Barril, X., Orozco, M., and Luque, F. J.: New tacrine-huperzine A hybrids (huprines): highly potent tight-binding acetylcholinesterase inhibitors of interest for the treatment of Alzheimer's disease. *J Med Chem* 2000; 43: 4657-4666.
48. Carlsen, R. C., Gray, S. D., and Pickar, J. G.:Na+, K(+)-pump activity and skeletal muscle contractile deficits in the spontaneously hypertensive rat. *Acta PhysiolScandina* 1996 ;156:23745
49. Carlsson, G., Larsson, P. A., Frosing, R., Hafstrom, L. O., Spears, C. P., Peterson, A., and Gustavsson, B.: 5-Fluorouracil sensitive adenocarcinoma—a new Exp model in the rat. *Anticancer Res* 1995; 15:433-439

50. Carter, W. R., Herman, J., Stokes, K., and Cox, D. J.: Promotion of diabetes onset by stress in the BB rat. *Diabetologia* 1987; 30:674-675
51. Cattabeni, F., Gardoni, F., and Di Luca, M.: Pathophysiological implications of the structural organization of the excitatory synapse. *Eur J Pharmacol* 1999;375:339-347
52. Chang, T. W.: The pharmacological basis of antiIgE therapy. *Nat Biotechnol* 2000 ;18:157-162
53. Chappel, C. I. and Chappel, W. R.: The discovery and development of the BB rat colony: an animal model of spontaneous diabetes mellitus. *Metabolism* 1983; 32:8-10
54. Chen, S., Yuan, C., Schooley, J. F., Jr., Haddy, F. J., and Pamnani, M. B.: A consistent model of insulin-dependent diabetes mellitus hypertension. *Am J Hypertens* 1992; 5:671-680
55. Chesney, C. F. and Allen, J. R.: Animal model: pulmonary hypertension, cor pulmonale and endocardial fibroelastosis in monocrotaline-intoxicated nonhuman primates. *Am J Pathol* 1973; 70:489-492
56. Chiba, Y., Arimoto, T., Yoshikawa, T., and Misawa, M.: Elevated nitric oxide synthase activity concurr with antigen-induced airway hyperresponsiveness in rats. - *Exp Lung Res* 2000 ;26:535-549
57. Chou, C. T. and Kuo, S. C.: The anti-inflammatory and anti-hyperuricemic effects of Chinese herbal formula danggui-nian-tong-tang on acute gouty arthritis: a comparative study with indomethacin and allopurinol. *Am J Chinese Med* 1995; 23):261-271
58. Christman, J. W., Sadikot, R. T., and Blackwell, T. S.: The role of nuclear factor kappa B in pulmonary diseases. *Chest* 2000;117:1482-1487
59. Clark, T. A. and Pierce, G. N.: Cardiovasc complications of noninsulindependent diabetes: the JCR:LAcp rat. *J Pharmacol Toxicolo Methods* 2000; 43:1-10
59. Colaco, C. A., Ledesma, M. D., Harrington, C. R., and Avila, J.: The role of the

- Maillard reaction in other pathologies: Alzheimer's disease. *Nephrol Dialysis Transplantation* 1996;11 Suppl 5:712
60. Cole, R. K. and Austic, R. E.:Hereditary uricemia and articular gout in chickens. *Poultry Sci* 1980 ;59:95175
  61. Constantinescu, C. S., Freitag, P., and Kappos, L.:Increase in serum levels of uric acid, an endogenous antioxidant, under treatment with glatiramer acetate for multiple sclerosis. *Multiple Sclerosis* 2000;6:378-381
  62. Corsetti, J. P., Sparks, J. D., Peterson, R. G., Smith, R. L., and Sparks, C. E.: Effect of dietary fat on the development of non-insulin dependent diabetes mellitus in obese Zucker diabetic fatty male and female rats. *Atherosclerosis* 2000; 148:231-241
  63. Cosenzi, A., Sacerdote, A., Seculin, P., Odoni, G., Plazzotta, N., Bernobich, E., and Bellini, G.: Lacidipine prevents the hypertension and renal and cardiac changes induced by high-fructose diet in WKY rats. *J Cardiovasc Pharmacol* 1999; 33:485-491
  64. Coyle, J. T., OsterGranite, M. L., and Gearhart, J. D.:The neurobiologic consequences of Down syndrome. *Brain Res Bulletin* 1986 16:77387
  65. Crandall, D. L., Goldstein, B. M., Lizzo, F. H., Lozito, R. J., and Cervoni, P.: Development of an animal model for investigating disparate myocardial effects of obesity and hypertension. *J Applied Physiol* 1988; 64: 1094-1097
  66. Crowther, R. A.:Steps towards a mouse model of Alzheimer's disease. . *Bioessays* 1995;17:5935
  67. Culetto, E. and Sattelle, D. B.:A role for *Caenorhabditis elegans* in understanding the function and interactions of human disease genes. *Human Molecular Genetics* 2000 ;9:869-877
  68. Cvetkovic, B. and Sigmund, C. D.:Understanding hypertension through genetic manipulation in mice. *Kidney Int* 2000 ;57:863-874
  69. Dakshinamurti, K., Lal, K. J., and Ganguly, P. K.:Hypertension, calcium channel

- and pyridoxine (vitamin B6). *Mol Cell Biochem* 1998;188:137-148
70. Das, A. K., Horan, P., Leggett, R. E., and Levin, R. M.:Use of abdominal fascia to create partial outlet obstruction in rabbits. *Neurourol Urodynamics* 1998;17:2319
71. De Jong, G. I., De Vos, R. A., Steur, E. N., and Luiten, P. G.:Cerebrovascular hypoperfusion: a risk factor for Alzheimer's disease? Animal model and postmortem human studies. *Ann N Y Acad Sci* 1997;826:56-74
72. De Sanctis, G. T., Daheshia, M., and Daser, A.:Genetics of airway hyperresponsiveness. *J Allergy Clin Immunol* 2001; 108:11-20
73. Deerberg, F., Rehm, S., and Jostmeyer, H. H.: Spontaneous urinary bladder tumors in DA/Han rats: a feasible model of human bladder cancer. *J Nat Cancer Institute* 1985; 75:1113-1121
74. DeFeudis, F. V. and Drieu, K.: Ginkgo biloba extract (EGb 761) and CNS functions: basic studies and Clin applications. *Curr Drug Targets* 2000; 1:25-58
75. Dellperger, K. C., Clothier, J. L., Koyanagi, S., Inou, T., and cus, M. L.:Effects of coronary artery occlusion in animals with hypertension and left ventricular hypertrophy. *J Cardiovasc Pharmacol* 1991;17 Suppl 2:S405
76. Doetschman, T., Shull, M., Kier, A., and Coffin, J. D.:Embryonic stem cell model systems for vascular morphogenesis and cardiac disorders. *Hypertension* 1993 ;22:61829
77. Dunnington, D. J., Buscarino, C., Gennaro, D., Greig, R., and Poste, G.: Characterization of an animal model of metastatic colon carcinoma. *Int J Cancer* 1987; 39:248-254
78. Elble, R. J.:Animal models of action tremor. *Movement Disorders* 1998;13:35-39
79. Elliott, P. J., Pien, C. S., McCormack, T. A., Chapman, I. D., and Adams, J.: Proteasome inhibition: A mechanism to combat asthma. *J Aller Clin Immunol* 1999;104:294-300
80. Emre, M. and Qizilbash, N.: Exp approaches and drugs in development for the treatment of dementia. *Expert Opin Invest Drugs* 2001;10:607-617

81. Engelstein, D., Shmueli, J., Bruhis, S., Servadio, C., and Abramovici, A.: Citral and testosterone interactions in inducing benign and atypical prostatic hyperplasia in rats. *Compara Biochem Physiol* 1996;115:169-177
82. Farine, J. C.:Animal models in autoimmune disease in immunotoxicity assessment. *Toxicol* 1997 11;119:2935
83. Farooqui, A. A., Litsky, M. L., Farooqui, T., and Horrocks, L. A.:Inhibitors of intracellular phospholipase A2 activity: their neurochemical effects and therapeutical importance for neurological disorders. *Brain Res Bulletin* 1999 ;49:139-153
84. Fernandez-Shaw, C., ina, A., Cazorla, P., Valdivieso, F., and Vazquez, J.: Anti-brain spectrin immunoreactivity in Alzheimer's disease: degradation of spectrin in an animal model of cholinergic degeneration. *J Neuroimmunol* 1997; 77:91-98
85. Fisher, W. R., Zech, L. A., and Stacpoole, P. W.:ApoB metabolism in familial hypercholesterolemia. Inconsistencies with the LDL receptor paradigm. *Arteriosclerosis Thrombosis* 1994 ;14:50110
86. Flint, J. and Corley, R.:Do animal models have a place in the genetic analysis of quantitative human behavioural traits?. *J Molecular Med* 1996 ;74:51521
87. Flint, J.:The genetic basis of cognition. *Brain* 1999 ;122 :2015-2032
88. Forno, L. S.:Neuropathologic features of Parkinson's, Huntington's, and Alzheimer's diseases.. *Ann N Y Acad Sci* 1992 11;648:616
89. Fukuzawa, Y., Watanabe, Y., Inaguma, D., and Hotta, N.: Evaluation of glomerular lesion and abnormal urinary findings in OLETF rats resulting from a long-term diabetic state. *J Lab Clin Med* 1996; 128:568-578
90. GablerHalle, D., Halle, J. W., and Chung, Y. B.:The effects of aerobic exercise on psychological and behavioral variables of individuals with Dev disabilities: a critical review. *Res Dev Disabilities* 1993 ;14:35986
91. Gagliardino, J. J.:An overview of Argentine contributions to diabetes Res in the

- ade of the 1990s. *Diabetes/Metab Res Rev* 2000;16:43-60
92. Garattini, S. and Guaitani, A.: Animal models for the study of cancer-induced anorexia. *Cancer Treat Reports* 1981;65 Suppl 5:23-35
93. Gardner, D. G.:Some Curr concepts on the Pathol of ameloblastomas. *Oral Surgery, Oral Med, Oral Pathol, Oral Radiol, Endodontics* 1996 ;82:6609
94. Geenen, V., tens, H., Brilot, F., Renard, C., Franchimont, D., and Kecha, O.:Thymic neuroendocrine selfantigens. Role in Tcell development and central Tcell selftolerance. *Ann of the New York Acad Sci* 2000; 917:710-723
95. Gibson, G. E., Park, L. C., Zhang, H., Sorbi, S., and Calingasan, N. Y.:Oxidative stress and a key metabolic enzyme in Alzheimer brains, cultured cells, and an animal model of chronic oxidative deficits. *Ann N Y Acad Sci* 1999;893:79-94
96. Golomb, E., Rosenzweig, N., Eilam, R., and Abramovici, A.: Spontaneous hyperplasia of the ventral lobe of the prostate in aging genetically hypertensive rats. *J Androl* 2000;21:58-64
97. Gonatas, N. K., Gonatas, J. O., and Stieber, A.:The involvement of the Golgi apparatus in the pathogenesis of amyotrophic lateral sclerosis, Alzheimer's disease, and ricin intoxication. *Histochemistry Cell Biol* 1998 ;109:591-600
98. Gordon, T. P., Reid, C., Rozenbilds, M. A., and Ahern, M.:Crystal shedding in tic arthritis: case reports and in vivo evidence in an animal model. *Australian New Zealand J Med* 1986 ;16:33640
99. Green, L. R.:Programming of endocrine mechanisms of Cardiovasc control and growth . *J Society Gynecol Invest* 2001; 8:57-68
100. Groopman, J. D. and Kensler, T. W.:The use of monoclonal antibody affinity columns for assessing DNA damage and repair following exposure to aflatoxin B1. *Pharmacol Therapeutics* 1987;34:32134
101. Guenifi, A., Abdel-Halim, S. M., Hoog, A., Falkmer, S., and Ostenson, C. G.: Preserved beta-cell density in the endocrine pancreas of young, spontaneously diabetic Goto-Kakizaki (GK) rats. *Pancreas* 1995; 10:148-153

102. Haas, M., Kerjaschki, D., and er, G.:Lipidlowering therapy in membranous nephropathy. *Kidney Int Supplement* 1999 1;71:S110-112
103. Haber, S. B. and Friedman, R.: Psychobiol of Exp hypertension: evaluation of the Dahl rat lines. *Behavior Genetics* 1981; 11:505-515
104. Hales, C. N.:Noninsulindependent diabetes mellitus. *British Medical Bulletin* 1997 ;53:10922
105. Hammerer, P., Graefen, M., Steuber, T., and Huland, H.:[Chemoprevention of prostatic carcinoma]. *Urologe Ausgabe A* 2000 ;39:304-308
106. Hanafusa, T., Miyagawa, J., Nakajima, H., Tomita, K., Kuwajima, M., Matsuzawa, Y., and Tarui, S.:The NOD mouse. *Diabetes Res Clin Practice* 1994 ;24 Suppl:S30711
107. Hasenfuss, G.:Animal models of human Cardiovasc disease, heart failure and hypertrophy. *Cardiovasc Res* 1998 ;39:60-76
108. Hasser, E. M. and Moffitt, J. A.:Regulation of sympathetic nervous system function after Cardiovasc conditioning. *Ann N Y Acad Sci* 2001; 940: 454-468
109. Havel, R. J., Yamada, N., and Shames, D. M.:Watanabe heritable hyperlipidemic rabbit. Animal model for familial hypercholesterolemia. *Arteriosclerosis* 1989 ;9:I338
110. Head, R. J.:Hypennoradrenergic innervation: its relationship to functional and hyperplastic changes in the vasculature of the spontaneously hypertensive rat. *Blood Vessels* 1989;26:120
111. Heatfield, B. M., Lipsky, M. M., and Trump, B. F.: Renal tubular carcinoma; animal model: chemically induced renal tubular carcinoma in rats. *Am J Pathol* 1980; 100:317-320
112. Heckman, C. J.:Alterations in synaptic input to motoneurons during partial spinal cord injury. *Med Sci Sports Exerc* 1994 ;26:148090
113. Hegele, R. G., Hayashi, S., Hogg, J. C., and Pare, P. D.:Mechanisms of airway narrowing and hyperresponsiveness in viral respiratory tract infections. *Am J*

Resp Crit Care Med 1995 ;151:165964; discussion 16645

114. Hellerstrom, C., Swenne, I., and Eriksson, U. J.:Is there an animal model for gestational diabetes?. Diabetes 1985 ;34 Suppl 2:2831
115. Henderson, C. J., McLaren, A. W., Moffat, G. J., Bacon, E. J., and Wolf, C. R.:Piclass glutathione Stransferase: regulation and function. ChemicoBiological Interactions 1998 ;111-112:69-82
- 116.Herrera, V. L., Makrides, S. C., Xie, H. X., Adari, H., Krauss, R. M., Ryan, U. S., and Ruiz-Opazo, N.: Spontaneous combined hyperlipidemia, coronary heart disease and reased survival in Dahl salt-sensitive hypertensive rats transgenic for human cholesteryl ester transfer protein. Nat Med 1999; 5:1383-1389
117. Hirai, A. and Kumagai, A.:[Animal model for gout]. Jikken Dobutsu
118. Hirano, T., Ebara, T., Furukawa, S., Nagano, S., and Takahashi, T.: Mechanism of hypertriglyceridemia in Dahl salt-sensitive rats, an animal model of spontaneous nephrotic syndrome. Metabolism 1994; 43:248-256
119. Hokfelt, T., Broberger, C., Diez, M., Xu, Z. Q., Shi, T., Kopp, J., Zhang, X., Holmberg, K., Landry, M., and Koistinaho, J.:Galanin and NPY, two peptides with multiple putative roles in the nervous system. Horm Metab Res 1999 ;31:330-334
120. Hoshino, S., Tamaoka, A., Takahashi, M., Kobayashi, S., Furukawa, T., Oaki, Y., Mori, O., Matsuno, S., Shoji, S., Inomata, M., and Teramoto, A.: Emergence of immunoreactivities for phosphorylated tau and amyloid-beta protein in chronic stage of fluid percussion injury in rat brain. Neuroreport 1998 ; 9:1879-1883
121. Howes, L. G., Hodzman, G. P., Maccarrone, C., Kohzuki, M., and Johnston, C. I.: Cardiac 3,4-dihydroxyphenylethylene glycol (DHPG) and catecholamine levels in a rat model of left ventricular failure. J Cardiovasc Pharmacol 1989; 13:348-352
122. Huang, S., Fu, P., Li, X., and Zhang, X.: L-arginine and nitric oxide have effects

- on glomerulus hyperperfusion of early diabetic rats.. Hua-Hsi i Ko Ta Hsueh Hsueh Pao [J West China University of Medical Sci] 1997; 28:251-254
123. Hulman, S., Brodsky, N., Miller, J., Donnelly, C., Helms, J., and Falkner, B.: Effect of estrogen withdrawal on blood pressure and insulin resistance in sucrose-fed juvenile rats. Am J Hypertens 1996; 9: 1200-1205
124. Hyman, B. T. and Tanzi, R. E.:Amyloid, dementia and Alzheimer's disease. Curr Opin Neurol Neurosurg 1992 ;5:8893
125. Iannini, J. P. and Spinale, F. G.:The identification of contributory mechanisms for the development and progression of congestive heart failure in animal models. J Heart Lung Transplant 1996 ;15:113850
126. Irvin, C. G.:Sinusitis and asthma: an animal model. J Allerg Clin Immunol 1992 ;90:52133
127. Iwase, M., Kikuchi, M., Nunoi, K., Wakisaka, M., Maki, Y., Sadoshima, S., and Fujishima, M.: A new model of type 2 (non-insulin-dependent) diabetes mellitus in spontaneously hypertensive rats: diabetes induced by neonatal streptozotocin treatment. Diabetologia 1986; 29:808-811
128. Iwase, M., Wakisaka, M., Yoshinari, M., Sato, Y., Yoshizumi, H., Nunoi, K., and Fujishima, M.: Effect of gonectomy on the development of diabetes mellitus, hypertension, and albuminuria in the rat model. Metabolism 1996; 45:155-161
129. Iwase, M., Yamamoto, M., Iino, K., Ichikawa, K., Shinohara, N., Yoshinari, M., and Fujishima, M.: Obesity induced by neonatal monosodium glutamate treatment in spontaneously hypertensive rats: an animal model of multiple risk factors. Hypertens Res 1998; 21:1-6
130. netta, P. J., Segal, R., Wolfson, S. K., Jr., Dujovny, M., Semba, A., and Cook, E. E.: Neurogenic hypertension: etiol and surgical treatment. II. Observations in an Exp nonhuman primate model. Ann Surg 1985; 202:253-261
131. y, B. and Basbaum, C. B.:Mucin in disease. Modification of mucin gene expression in airway disease. Am Rev Resp Dis 1991 ;144:S3841

132. Jiao, S., Matsuzawa, Y., Matsubara, K., Kubo, M., Tokunaga, K., Odaka, H., Ikeda, H., Matsuo, T., and Tarui, S.: Abnormalities of plasma lipoproteins in a new genetically obese rat with non-insulin-dependent diabetes mellitus (Wistar fatty rat). *Int J Obes* 1991; 15:487-495
133. Joffe, B. and Zimmet, P.: The thrifty genotype in type 2 diabetes: an unfinished symphony moving to its finale? *Endocrine* 1998 ;9:139-141
134. Johnston, M. V. and Harum, K. H.: Recent progress in the neurology of learning: memory molecules in the developing brain. *J Dev Behav Pediatr* 1999 ;20:50-56
135. Kawaguchi, M., Koshimura, K., Murakami, Y., Tsumori, M., Gonda, T., and Kato, Y.: Antihypertensive effect of insulin via nitric oxide production in the Zucker diabetic fatty rat, an animal model for non-insulin-dependent diabetes mellitus. *Eur J Endocrinol* 1999; 140: 341-349
136. Kazumi, T., Odaka, H., Hozumi, T., Ishida, Y., Amano, N., and Yoshino, G.: Effects of dietary fructose or glucose on triglyceride production and lipogenic enzyme activities in the liver of Wistar fatty rats, an animal model of NIDDM. *Endocr J* 1997; 44:239-245
137. Kentera, D., Susic, D., Machado, E., and Lozzio, B. B.: Animal model of human disease. Hydronephrosis, agenesis of the renal medulla, arterial hypertension. *Am J Pathol* 197; 87:477-480
138. Kett, M. M., Anderson, W. P., Bertram, J. F., and Alcorn, D.: Structural changes in the renal vasculature in the spontaneously hypertensive rat: no effect of angiotensin II blockade. *Clin Exp Pharmacol Physiol Suppl* 1996;3:S1325
139. King, C. M. and Webb, R. C.: The endothelium partially obscures enhanced microvessel reactivity in DOCA hypertensive rats. *Hypertension* 1988; 12:420-427
140. Kirby, R. F. and Johnson, A. K.: Regulation of sodium and body fluid homeostasis during development: implications for the pathogenesis of hypertension.. *Experientia* 1992 15;48:34551

141. Kirchengast, M.:PreClin considerations and results with the combination of verapamil and trandolil: blood pressure reduction and beyond. *J Hypertens Suppl* 1997 ;15:S2733
142. Knuepfer, M. M. and Mueller, P. J.:Review of evidence for a el model of cocaineinduced Cardiovasc toxicity. *Pharmacol, Biochem Behavior* 1999 ;63:489-500
143. Koh, Y. I., Choi, I. S., Park, S. C., and Kang, K. W.: BCG infection during pre-sensitization or even post-sensitization inhibits airway sensitivity in an animal model of allergic asthma. *J Korean Medical Sci* 2000 ;15:265-272
144. Kola, I. and Hertzog, P. J.:Animal models in the study of the biological function of genes on human chromosome 21 and their role in the pathophysiol of Down syndrome. *Human Mol Genetics* 1997; 6:1713-1727
145. Koyama, M., Wada, R., Sakuraba, H., Mizukami, H., and Yagihashi, S.: Accelerated loss of islet beta cells in sucrose-fed Goto-Kakizaki rats, a genetic model of non-insulin-dependent diabetes mellitus. *Am J Pathol* 1998; 153:537-545
146. Koyama, S., Kodama, M., Izumi, T., and Shibata, A.: Exp rat model representing both acute and chronic heart failure related to autoimmune myocarditis. *Cardiovasc Drugs Ther* 1995; 9:701-707
147. Kraft, M.:The role of bacterial infections in asthma. *Clinics in Chest Medicine* 2000;21:301-313
148. Krakoff, L. R., Eliovich, F., and Barry, C.:The role of vasopressin in Exp and Clin hypertension. *Am J Kidney Dis* 1985 ;5:A407
149. Kren, V., Pravenec, M., Lu, S., Krea, D., Wang, J. M., Wang, N., Merriouns, T., Wong, A., St Lezin, E., Lau, D., Szpirer, C., Szpirer, J., and Kurtz, T. W.: Genetic isolation of a region of chromosome 8 that exerts major effects on blood pressure and cardiac mass in the spontaneously hypertensive rat. *J Clin Invest* 1997; 99:577-581

150. Krugel, U., Bigl, V., Eschrich, K., and Bigl, M.: Deafferentation of the to-hippocampal pathway in rats as a model of the metabolic events in Alzheimer's disease. *Int J Dev NeuroSci* 2001; 19:263-277
151. Ksir, C. and Benson, D. M.: Enhanced behavioral response to nicotine in an animal model of Alzheimer's disease. *Psychopharmacol* 1983; 81:272-273
152. Ku, D., Kirshenbaum, L. A., Li, T., Danelisen, I., and Singal, P. K.: Apoptosis in adriamycin cardiomyopathy and its modulation by probucol. *Antioxidants Redox Signal* 2001; 3:135-145
153. Kwan, C. Y.:Dysfunction of calcium handling by smooth muscle in hypertension. *Can J Physiol Pharmacol* 1985 ;63:36674
154. Lamm, D. L.:Optimal BCG treatment of superficial bladder cancer as defined by Am trials. *Eur Urol* 1992;21 Suppl 2:126
155. Lancaster, W. D. and Jenson, A. B.:Natural history of human papillomavirus infection of the anogenital tract. *Cancer Metastasis Rev* 1987;6:65364
156. Lee, M. A., Bohm, M., Paul, M., Bader, M., Ganten, U., and Ganten, D.:Physiological characterization of the hypertensive transgenic rat TGR(mREN2)27. *Am J Physiol* 1996 ;270:E91929
157. LeiningerMuller, B. and Siest, G.:The rat, a useful animal model for pharmacological studies on apolipoprotein E. *Life Sci* 1996;58:45567
158. Lemiere, C., Malo, J. L., and Gautrin, D.:Nonsensitizing causes of occupational asthma. *Medical Clinics of North America* 1996 ;80:74974
159. Lerman, S., Megaw, J. M., and Gardner, K.: Allopurinol therapy and cataractogenesis in humans. *Am J Ophthalmol* 1982; 94:141-146
160. Louis, W. J. and Howes, L. G.:Genealogy of the spontaneously hypertensive rat and WistarKyoto rat strains: implications for studies of inherited hypertension.. *J Cardiovasc Pharmacol* 1990;16 Suppl 7:S15
161. Ludolph, A. C., Meyer, T., and Riepe, M. W.:The role of excitotoxicity in ALSwhat is the evidence? *J Neurol* 2000 ;247 :I7-16

162. Lussier, A., de Medicis, R., quis, L., and Menard, H.: Inhibition of adjuvant-induced arthritis in the hyperuricemic rat. Agents Actions 1978; 8:536-542
163. Mackin, W. M., Rakich, S. M., and shall, C. L.: Inhibition of rat neutrophil functional responses by azopazone, an anti-gout drug. Biochem Pharmacol 1986; 35:917-922
164. iotti, A., Doan, M. P., and Mawhinney, M.:Collagen and cellular proliferation in spontaneous canine benign prostatic hypertrophy. J Urol 1982 ;127:7957
165. Matalon, R., Michals, K., and Kaul, R.:Canavan disease: from spongy degeneration to molecular analysis. J Pediatr 1995 ;127:5117
166. Matsumori, A. and Sasayama, S.:Immunomodulating agents for the management of heart failure with myocarditis and cardiomyopathylessons from animal experiments. Eur Heart J 1995 ;16 Suppl O:1403
167. Matzkin, H., Chayen, R., Goldfarb, H., Gilad, S., and Braf, Z.: Laboratory monitoring of androgenic activity in benign prostate hypertrophy treated with a 5 alpha-reductase inhibitor. Clin Chem 1992 ;38:1304-1306
168. McBean, D. E. and Kelly, P. A.:Rodent models of global cerebral ischemia: a comparison of twovessel occlusion and fourvessel occlusion. General Pharmacol 1998 ;30:4314
169. McGonigle, K. F. and Berek, J. S.:Earlystage squamous cell and adenocarcinoma of the cervix. Curr Opin Obstetr Gynecol 1992 ;4:10919
170. Mehta, H., Sorkness, R., Kaplan, M. R., Castleman, W. L., and Lemanske, R. F., Jr.: Effects of dexamethasone on acute virus-induced airway dysfunction in adult rats. Pediatr Res 1997 ;41:872-877
171. Meyer, U. A., Schuurmans, M. M., and Lindberg, R. L.:Acute porphyrias: pathogenesis of neurological manifestations. Seminars Liver Dis 1998;18:43-52
172. Mhairi, Macrae, I:New models of focal cerebral ischaemia. British J Clin Pharmacol 1992 ;34:3028

173. Michaelson, M.:Crush injury and crush syndrome. World J Surgery 1992 ;16:899903
174. Michel, M. C., Philipp, T., and Brodde, O. E.:Alpha and betaadrenoceptors in hypertension: molecular biol and pharmacological studies. Pharmacol Toxicol 1992 ;70:S110
175. Miller, C. C. and Anderton, B. H.:Alzheimer's disease: transgenic models to test new chemicals and pharmaceuticals. Curr Opin Biotechnol 1992 ;3:6836
176. Misawa, M. and Chiba, Y.: Repeated antigenic challenge-induced airway hyperresponsiveness and airway inflammation in actively sensitized rats. Japanese J Pharmacol 1993 ;61:41-50
177. Momma, K. and Takao, A.: Right ventricular concentric hypertrophy and left ventricular dilatation by ductal constriction in fetal rats. Circulation Res 1989; 64:1137-1146
178. Montinaro, V., Gesualdo, L., and Schena, F. P.:Priy IgA nephropathy: the relevance of Exp models in the understanding of human disease. Nephron 1992;62:37381
179. Muir, J. L., Page, K. J., Sirinathsinghji, D. J., Robbins, T. W., and Everitt, B. J.:Excitotoxic lesions of basal forebrain cholinergic neurons: effects on learning, memory and attention. Behavioural Brain Res 1993 30;57:12331
180. Muir, J. L.:Acetylcholine, aging, and Alzheimer's disease. Pharmacol, Biochemistry Behavior 1997 ;56:68796
181. Netto ior, N. R. and Claro, J. A.: Treatment of benign prostate hypertrophy using Prostatron: a study of the effects of treatment temperature elevation. Progres Urol 1995 ;5:238-243
182. Oh, D. H., Eulau, D., Tokugawa, D. A., McGuire, J. S., and Kohler, S.:Five cases of calciphylaxis and a review of the literature. [see comments]. J the Am Acad of Dermatol 1999 ;40:979-987
183. Overstreet, D. H.:Organophosphate pesticides, cholinergic function and

- cognitive performance in advanced age. Neurotoxicol 2000; 21:75-81
184. Owen, R. W.:Faecal steroids and colorectal carcinogenesis. Scandinavian J Gastroenterol Supplement 1997;222:7682
185. Ozanne, S. E. and Hales, C. N.:The longterm consequences of intrauterine protein malnutrition for glucose metabolism. Proceedings of the Nutrition Society 1999;58:615-619
186. Parkinson, J. F., Mitrovic, B., and Merrill, J. E.:The role of nitric oxide in multiple sclerosis. J Molecular Med 1997;75:174-186
187. Pauletto, P., Scannapieco, G., Vescovo, G., Angelini, A., Dalla, Libera L., and Dal Palu, C.:Catecholamineinduced Cardiovasc disease in the spontaneously hypertensive and atherosclerotic turkey. Methods Findings in Exp Clin Pharmacol 1988 ;10:35762
188. Pauluhn, J.:Predictive testing for respiratory sensitisation. Toxicol Let 1996 ;86:17785
189. Pauwels, R. A. and Van der Straeten, M. E.: An animal model for adenosine-induced bronchoconstriction Am Review of Respiratory Disease 1987 ;136:374-378
190. Penney, D. G. and Howley, J. W.:Is there a connection between carbon monoxide exposure and hypertension?. Environmental Health Perspectives 1991 ;95:1918
191. Phillips, K. A., Andrulis, I. L., and Goodwin, P. J.:Breast carcinomas arising in carriers of mutations in BRCA1 or BRCA2: are they prognostically different? J Clin Oncol 1999;17:3653-3663
192. Pickering, T. G.:Reascular hypertension: etiol and pathophysiol. Seminars in Nuclear Med 1989 ;19:7988
193. Piepkorn, B., Kann, P., Forst, T., Andreas, J., Pfutzner, A., and Beyer, J.:Bone mineral density and bone metabolism in diabetes mellitus. Hormone Metabolic Res 1997;29:584-591

194. Polonsky, K. S.:Lilly Lecture 1994. The betacell in diabetes: from molecular genetics to Clin Res. Diabetes 1995 ;44:70517
195. Pope, J. C., Brock, J. W., III, Adams, M. C., Stephens, F. D., and Ichikawa, I.:How they begin and how they end: classic and new theories for the development and deterioration of congenital anomalies of the kidney and urinary tract, CAKUT. J the Am Society of Nephrol 1999 ;10:2018-2028
196. Porter, G. A.:Exp contrastassociated nephropathy and its Clin implications. Am J Cardiol 1990 26;66:18F22F
197. Prakash, S. and Chang, T. M.: In vitro and in vivo uric acid lowering by artificial cells containing microencapsulated genetically engineered E. coli DH5 cells. Int J Artificial Organs 2000; 23:429-435
198. Price, D. L., tin, L. J., Sisodia, S. S., Wagster, M. V., Koo, E. H., Walker, L. C., Koliatsos, V. E., and Cork, L. C.:Aged nonhuman primates: an animal model of ageassociated neurodegenerative disease. Brain Pathol 1991 ;1:28796
199. Rabiitch, A.:An update on cytokines in the pathogenesis of insulinindependent diabetes mellitus. DiabetesMetabolism Rev 1998 ;14:129-151
200. Rapp, J. P.:Genetic analysis of inherited hypertension in the rat. Physiological Rev 2000 ;80:135-172
201. Rashba, E. J., Reich, E. P., eway, C. A., and Sherwin, R. S.:Type 1 diabetes mellitus: an imbalance between effector and regulatory T cells?. Acta Diabetologica 1993;30:619
202. Roggendorf, M. and Tolle, T. K.:The woodchuck: an animal model for hepatitis B virus infection in man. Intervirol 1995;3810012
203. Sakata, T., Yoshimatsu, H., and Kurokawa, M.:Hypothalamic neuronal histamine: implications of its homeostatic control of energy metabolism. Nutrition 1997 ;13:403-411
204. Sanders, B. J. and Lawler, J. E.:The borderline hypertensive rat (BHR) as a model for environmentallyinduced hypertension: a review and update. NeuroSci

Biobehavioral Rev 1992;16:20717

205. Schlom, J., Kantor, J., Abrams, S., Tsang, K. Y., Panicali, D., and Hamilton, J. M.:Strategies for the development of recombinant vaccines for the immunotherapy of breast cancer. Breast Cancer Res Treatment 1996;38:2739
206. Schoene, R. B. and Goldberg, S.:The quest for an animal model of high altitude pulmonary edema. Int J Sports Med 1992 ;13 Suppl 1:S5961
207. Sen, S.:Regression of cardiac hypertrophy. Exp animal model. Am J Med 1983 26;75:8793
208. Servadio, C., Abramovici, A., Sandbank, U., Savion, M., and Rosen, M.: Early stages of the pathogenesis of rat ventral prostate hyperplasia induced by citral. Eur Urol 1986;12:195-200
209. Shapiro, E., Tsitlik, J. E., and Lepor, H.:Alpha 2 adrenergic receptors in canine prostate: biochemical and functional correlations. J Urol 1987 ;137:56570
210. Shechter, Y., Meyerovitch, J., and Amir, S.:The use of postbinding agents in studying insulin action and its relation to Exp diabetes. Biochemical Pharmacol 1988 15;37:18916
211. Shiosaka, S.:Attempts to make models for Alzheimer's disease. NeuroSci Res 1992 ;13:23755
212. Sica, A. L., Greenberg, H. E., Ruggiero, D. A., and Scharf, S. M.:Chronicintermittent hypoxia: a model of sympathetic activation in the rat]. Respiration Physiol 2000 ;121:173-184
213. Siegel, R. M., Katsumata, M., Komori, S., Wadsworth, S., GillMorse, L., JerroldJones, S., Bhandoola, A., Greene, M. I., and Yui, K.:Mechanisms of autoimmunity in the context of Tcell tolerance: insights from natural and transgenic animal model systems.]. Immunological Rev 1990 ;118:16592
214. Siegler, R. L.:The hemolytic uremic syndrome. Pediatric Clinics of North America 1995 ;42:150529

215. Simpkins, J. W., Green, P. S., Gridley, K. E., Singh, M., de Fiebre, N. C., and Rajaku, G.:Role of estrogen replacement therapy in memory enhancement and the prevention of neuronal loss associated with Alzheimer's disease. Am J Med 1997;103:19S-25S
216. Steers, W. D.:Rat: overview and innervation. Neurourol Urodynamics 1994;13:97118
217. Steinberg, D.:Is there a potential therapeutic role for vitamin E or other antioxidants in atherosclerosis? Curr Opin Lipidol 2000; 11:603-607
218. Strange, K. S., Kerr, L. R., Andrews, H. N., Emerman, J. T., and Weinberg, J.:Psychosocial stressors and mamry tumor growth: an animal model. Neurotoxicol Teratol 2000;22:89-102
219. Sugaya, E., Yuyama, N., Kajiwara, K., Tsuda, T., Ohguchi, H., Shimizu-Nishikawa, K., Kimura, M., and Sugaya, A.: Regulation of gene expression by herbal Meds--a new paradigm of gene therapy for multifocal abnormalities of genes. Res Comm Mol Pathol Pharmacol 1999;106:171-180
220. Surwit, R. S. and Williams, P. G.:Animal models provide insight into psychosomatic factors in diabetes.. Psychosomatic Med 1996 ;58:5829
221. Takamori, M., uta, T., and Komai, K.:LambertEaton myasthenic syndrome as an autoimmune calciumchannelopathy. NeuroSci Res 2000;36:183-191
222. Tallal, P.:Hormonal influences in Dev learning disabilities. Psychoneuroendocrinol 1991;16:20311
223. Tariot, P. N., Sunderland, T., Murphy, D. L., Cohen, M. R., Welkowitz, J. A., Weingartner, H., Newhouse, P. A., and Cohen, R. M.:Design and interpretation of opiate antagonist trials in dementia. Progress in NeuroPsychopharmacol Biol Psychiatry 1986;10:61126
224. Tateyama, M.:[Mechanism of suppression of colchicine in Exp allergic encephalomyelitis]. Hokkaido Igaku Zasshi Hokkaido J Medical Sci 1988 ;63:729

225. Terasawa, M., Aratani, H., Iwahisa, Y., Ioshi, T., and Uyama, Y.: Effect of pranoprofen on sodium urate crystal-induced inflammation. *Folia Pharmacologica Japonica* 1987; 89:129-137
226. Triggle, C. R. and Laher, I.:A review of changes in vascular smooth muscle functions in hypertension: isolated tissue versus in vivo studies. *Can J Physiol Pharmacol* 1985 ;63:35565
227. Van Coppenolle, F., Slomianny, C., Carpentier, F., Le, Bourhis, X, Ahidouch, A., Croix, D., Legrand, G., Dewailly, E., Fournier, S., Cousse, H., Authie, D., Raynaud, J. P., Beauvillain, J. C., Dupouy, J. P., and Prevarskaya, N.: Effects of hyperprolactinemia on rat prostate growth: evidence of androgeno-dependence. *Am J Physiol Endocrinol Metab* 2001; 280:E120-9
228. Vargaftig, B. B.:What can we learn from murine models of asthma? *Clin Exp Allergy* 1999 ;29 1:9-13
229. Vaucher, E., Aumont, N., Pearson, D., Rowe, W., Poirier, J., and Kar, S.: Amyloid beta peptide levels and its effects on hippocampal acetylcholine release in aged, cognitively-impaired and -unimpaired rats. *J Chem Neuroanat* 2001 ;21:323-329
230. Velasquez, M. T., Kimmel, P. L., and Michaelis, O. E.:Animal models of spontaneous diabetic kidney disease. *FASEB J* 1990 ;4:28509
231. Velasquez, M. T., Kimmel, P. L., and Michaelis, O. E.:Animal models of spontaneous diabetic kidney disease. *FASEB J* 1990 ;4:2850-2859
232. Victery, W.:Evidence for effects of chronic lead exposure on blood pressure in Exp animals: an overview. *Envir Health Perspect* 1988 ;78:716
233. Wada, M., Iwase, M., Wakisaka, M., Nunoi, K., Yoshinari, M., and Fujishima, M.: A new model of diabetic pregnancy with genetic hypertension: pregnancy in spontaneously hypertensive rats with neonatal streptozotocin-induced diabetes. *Am J Obstetr Gynecol* 1995; 172:626-630
234. Wang, Z., Ikeda, K., Wada, Y., Foster, H. E., Weiss, R. M., and Latifpour,

- J.:Expression and localization of basic fibroblast growth factor in diabetic rat prostate. *Bju Int* 2000 ;85:945-952
235. Wardrop, R. M., III and Whitacre, C. C.:Oral tolerance in the treatment of inflammatory autoimmune diseases. *Inflam Res* 1999 ;48:106-119
236. Wasantwisut, E.:Nutrition and development: other micronutrients' effect on growth and cognition. *Southeast Asian J Tropical Med Public Health* 1997;28 :78-82
237. Watson, R. R., Huls, A., Araghinikuam, M., and Chung, S.:Dehydroepiandrosterone and diseases of aging. *Drugs Aging* 1996 ;9:27491
238. Weber, M.:Emerging treatments for hypertension: potential role for vasopeptidase inhibition. *Am J Hypertens* 1999 ;12:139S-147S
239. Weinstein, D. B. and Heider, J. G.:Protective action of calcium channel antagonists in atherogenesis and Exp vascular injury. *Am J Hypertension* 1989 ;2:20512
240. Weir, G. C., Clore, E. T., Zmachinski, C. J., and Bonner-Weir, S.: Islet secretion in a new Exp model for non-insulin-dependent diabetes. *Diabetes* 1981; 30:590-695
241. Welsch, C. W.:Host factors affecting the growth of carcinogeninduced rat mammary carcinomas: a review and tribute to Charles Brenton Huggins. *Cancer Res* 1985 ;45:341543
242. Wong, F. S., Dittel, B. N., and eway, C. A., Jr.:Transgenes and knockout mutations in animal models of type 1 diabetes and multiple sclerosis. *Immunol Rev* 1999 ;169: 93-104
243. WoodruffPak, D. S. and Troowski, J. Q.:The older rabbit as an animal model: implications for Alzheimer's disease. *Neurobiol Aging* 1996 ;17:28390
244. Yamada, K., Ren, X., and Nabeshima, T.:Perspectives of pharmacotherapy in Alzheimer's disease. *Japan J Pharmacol* 1999;80:9-14

245. Zhang, Y. Y., Li, P. F., Chen, B. L., and Li, D.: Flutamide suppressed prostate hypertrophy in rats and mice. [Chinese] Chung-Kuo Yao Li Hsueh Pao - Acta Pharmacol Sinica 1999 ;20:537-40
246. Zhao, G. Q., Holterhus, P. M., Dammshauser, I., Hoffbauer, G., and Aumuller, G.: Estrogen-induced morphological and immunohistochemical changes in stroma and epithelium of rat ventral prostate. Prostate 1992;21:183-99
247. Zhao, Y. J. and Lu, F. N.: [Clin and Exp study of benign prostatic hyperplasia with intraglandular injection of chuan shen tong]. ChungKuo Chung Hsi i Chieh Ho Tsa Chih 1994 ;14:213, 4
248. Ziegler, M., Ziegler, B., Kohnert, K. D., and Kloting, I.: Genetic control of susceptibility to severe hyperglycaemia evoked by CFA/SZ-induced immune response against beta cells in various rat strains. Biome Biochim Acta 1988;47:337-342