欢迎辞

在中国共产党第十八次代表大会成功召开的欢庆时刻，由中国科学院昆明动物研究所主办，昆明医科大学、昆明理工大学、香港中文大学和云南省基础研究发展促进会联合协办的“第一届灵长类动物模型学术论坛”在美丽的春城昆明顺利召开了，我谨向大会表示热烈的祝贺！向与会的各位领导和嘉宾表示亲切的问候和良好的祝愿！

人类疾病动物模型是是疾病机理研究和疫苗新药研发的重要基础。长期以来，生物医学基础研究主要依赖于啮齿类动物模型。由于啮齿类动物与人类之间存在巨大的种属差异，使得基础研究成果不能有效地转化为临床应用。灵长类动物与人类的亲缘关系最为密切，生理特征也最接近人类，因此灵长类动物研究成果可望直接转化为临床应用，也能更有效地预测新疫苗、新药、新诊断试剂等在临床应用中的有效性。目前，人类疾病的灵长类动物模型十分缺乏，成为制约人口健康领域发展的瓶颈。突破转化医学困境的有效途径是重点发展和使用灵长类动物创建人类疾病的动物模型。

我国西南地区尤其是云南省灵长类动物资源极其丰富。中国科学院昆明动物研究所早在上一世纪 60 年代就开展了大规模灵长类动物饲养繁殖工作，是中科院灵长类饲养繁殖中心和树鼩饲养繁殖基地，长期以来为国内外企事业科研院校提供遗传背景清楚、生理指标稳定的灵长类实验动物，近二十年来依托灵长类动物资源优势，开展了多种疾病模型创建工作，形成了较为广泛的国际和国内影响。中国科学院和相关国家部委高度重视灵长类实验动物及动物模型的发展，前瞻性地在昆明动物研究所布局了“中国科学院昆明灵长类研究中心”、“国家昆明高等级生物安全灵长类动物实验中心”和“昆明国家生物产业基地实验动物中心”，并部署了一批集群项目和基础前沿专项，用于重点支持该领域的发展。

我相信来自全国各地的专家围绕灵长类动物模型相关问题展开积极的交流和讨论，将深化合作、携手共进，进一步推动灵长类动物模型及其相关研究向纵深发展。

预祝“第一届灵长类动物模型学术论坛”取得圆满成功！

张亚平（签字）：

中国科学院副院长，中国科学院院士

会议组织

一、会议举办单位

主办单位：中国科学院昆明动物研究所

协办单位（排名不分先后）

昆明医科大学

昆明理工大学

香港中文大学

云南省基础研究发展促进会

二、会议组织机构

名誉主席：张亚平 院士

主　　席：姚永刚 研究员

秘 书 长：梁　斌 研究员

组织委员会：徐　林、张　云、郑永唐、梁　斌、陈勇彬、赵旭东、陈策实、夏雪山、张荣平、陈伟仪

三、赞助单位

昆明纳瑞科技有限公司

纽恩（上海）生物科技有限公司

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青岛海尔特种电器有限公司

昆明友宁科技有限公司

总目录

参会注意事项

一、注册报到

1. 报到时间：2012 年 11 月 30 日 8:00-24:00
2. 报到地点：云安会都.清华池
3. 报到现场会务组备有电脑，请报告者提前将 PPT 拷至会务组电脑上。

二、会场

1. 会议嘉宾请佩戴嘉宾证进入会场、参加会议以及参加各项活动；
2. 为保证会议按时召开，请与会嘉宾提前 5 分钟入场就坐；
3. 为表示对会议发言者的尊重，会议期间请关闭手机或调至震动状态。

三、住宿

1. 愿意合住的参会嘉宾，会务组统一安排合住，费用问题请协商解决；若安排不开需要单住，请谅解。
2. 房间可免费上网，凭房卡可享受宾馆提供的免费温泉游泳，请自备泳衣。
3. 退房时间：12 点之前，12:00-18:00 加收半天房费，超过 18:00 加收一天房费。

四、用餐

1. 早餐凭当日餐券在宾馆指定餐厅用餐；中餐和晚餐凭会议餐券就餐。
2. 自助餐可选择聚贤堂或回味堂(回族餐厅)；中餐时间 11:30-13:30，晚餐时间 17:30-19:30，报到当日的自助晚餐可延长至 20:30，20:30 以后自行解决。

五、交通

大会不安排接送，请各位代表自行到**云安会都 . 清华池**报到（联系电话：0871-8171666），交通路线如下：

（1）昆明长水机场：直接乘出租车至云安会都；乘坐空港一号线至西驿酒店，然后换乘 100 路公交车至云安会都站下车；乘坐空港二号线至泰丽酒店，然后在民航路口换乘 51 路公交汽车至云安会都站下车。

（2）昆明火车站，直接乘出租车至云安会都。

六、其它

大会备有常见应急药品，如有需要，请直接与会务组联系。

会议日程

时　间		内　容	备　注
11 月 30 日	8:00-24:00	**报到注册**	清华池
	17:30-20:30	**晚　餐**	聚贤堂自助餐厅
12 月 1 日	7:00-8:30	**早　餐**	聚贤堂自助餐厅
	10:00-10:50	**开幕式、集体合影**	云安会堂 4 楼 1 号会议室
	10:50-11:50	**学术报告**	
	12:00	**午　餐**	聚贤堂自助餐厅
	14:00-18:00	**学术报告**	云安会堂 4 楼 1 号会议室
	18:00	**欢迎晚宴**	聚贤堂玉兰厅
12 月 2 日	7:00-8:30	**早　餐**	聚贤堂自助餐厅
	8:30-12:00	**学术报告**	云安会堂 4 楼 1 号会议室
	12:00	**午　餐**	聚贤堂自助餐厅
	14:00-17:20	**学术报告**	云安会堂 4 楼 1 号会议室
	17:20-17:50	**闭 幕 式**	
	18:00	**晚　餐**	聚贤堂自助餐厅

学术报告安排

12 月 1 日 上午

主持人：姚永刚

10:00-10:50 开幕式、集体合影

10:50-11:30 姚永刚（中科院昆明动物所）：树鼩模式化和基础数据收集

11:30-11:50 曾 林（军事医学科学院）：我国实验灵长类动物工作的发展状况

12 月 1 日下午

主持人： 徐林

14:00-14:20 徐 林（中科院昆明动物所）：社会竞争失败病因学的抑郁症树鼩模型

14:20-14:40 张鸣沙（中科院神经科学研究所）：Parietal cortical neuronal activity is selective for express saccades

14:40-14:55 张惠云（山东中医药大学）：Premenstrual dysphoric disorder and luteal phase stress in the dominant social status female monkeys

14:55-15:15 胡新天（中科院昆明动物所）：社会应激，基因背景与抑郁症—基于猕猴模型的研究

15:15-15:35 王庆国（北京中医药大学）：树鼩抑郁症病证结合动物模型评价指标的建立

15:35-15:55 马原野（中科院昆明动物所）：药物成瘾的猕猴模型及其学习记忆机制的研究

15:55-16:15 茶 歇

主持人：郑永唐

16:15-16:35 吴玉章（第三军医大学）：树鼩 HBV 感染模型的建立及初步应用

16:35-16:55 郑永唐（中科院昆明动物所）：艾滋病灵长类动物模型的建立和研究

16:55-17:15 黄 韧（广东省实验动物检测所）：猴感染禽流感病毒模型

17:15-17:35 杨贵波（中国疾病预防控制中心）：粘膜免疫与艾滋病预防控制

17:35-17:55 李 瑗（广西壮族自治区肿瘤防治研究所）：新生期树鼩接种 HBV 后可形成类似人慢性乙肝的组织学改变

12 月 2 日上午

主持人： 张云

8:30-8:50 王京昆（云南省药物研究所）：灵长类动物在药物非临床安全性评价中的应用

8:50-9:05 徐 娟（中国医学科学院医学生物学研究所）：树鼩呼肠孤病毒的分离鉴定

9:05-9:20 梁 斌（中科院昆明动物所）：非酒精性脂肪肝树鼩模型

9:20-9:40 谭兆祥（香港中文大学）：报告题目待定

9:40-10:00 陈伟仪（香港中文大学）：报告题目待定

10:00-10:20 茶 歇

主持人：霍文哲

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11:00-11:20 李树清（昆明医科大学）：树鼩局部脑缺血与缺血后适应的脑保护信号转导机制的研究

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11:40-12:00 李文辉（北京生命科学研究所）：Identification of NTCP as a functional receptor for HBV and HDV

12 月 2 日下午

主持人： 秦川

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14:20-14:40 高 翔（南京大学）：IMPC: understanding the gene function in vivo

14:40-15:00 陈 彪（首都医科大学）：灵长类动物疾病模型在转化医学中的作用：机遇与挑战

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15:35-15:55 唐惠儒（中科院武汉物理与数学研究所）：Metabotyping is an important aspect of molecular phenotyping

15:55-16:15　茶 歇

主持人：张荣平

16:15-16:30　隋　南（中科院心理研究所）：新型抑郁症树鼩模型：抑郁症树鼩模型行为表象一致性研究进展报告

16:30-16:45　杨世华（昆明理工大学）：中缅树鼩精子生物学研究

16:45-17:00　黄晓燕（中国医学科学院医学生物学研究所）：树鼩 IL-2 基因序列的克隆及分子特征分析

17:00-17:20　陈策实（中科院昆明动物所）：灵长类动物癌症模型的探索

17:20-17:50　闭幕式（主持人：徐林）

摘要目录

（按姓氏汉语拼音排序）

会议摘要集

LPS-induced immune activation and SIV replication in Chinese Rhesus Macaques

Rong Bao[1, #], Li Ye [1, #], Ming Guo [1], Jing Zhang [1], Ming Dai[1], Yan Rao [1], Yong Wang [1], Qiao-Yang Xian [1], Zhi-Xiang Huang [1], Zhi-Jiao Tang [1], Jie-Liang Li[2], Yuri Persidsky[2], Wen-Zhe Ho[1, 2, *]

1. The Center for Animal Experiment/Animal Biosafety Level III Laboratory, Wuhan University School of Medicine, Wuhan, Hubei 430071, P.R. China; 2. Department of Pathology and Laboratory Medicine, Temple University School of Medicine, Philadelphia, Pennsylvania 19140, USA

Abstract: Chronic immune activation is a hallmark of progressive HIV infection and the major factor of disease progression. Bacterial lipopolysaccharide (LPS) in the circulation has been implicated as a key factor in HIV-related systemic immune activation. We thus investigated the impact of LPS on systemic immune activation in simian immunodeficiency virus (SIV) infection of Chinese rhesus macaques (CRMs). The animals inoculated with either SIVmac239 or SIVmac251 became infected as evidenced by the increased plasma SIV RNA and decreased CD4/CD8 ratio. The plasma viral loads reached to the peak level at week 2 post-infection and then declined to a stable level, although fluctuated during the course of infection. The CD4/CD8 ratios had a ~ 50% drop at the early stage of infection (20 days post-infection) and subsequently recovered to the stable levels that were still lower than those prior to infection. Intravenous administration of LPS induced a transient immune activation as evidenced by elevated expression of IL-6, IL-8, IFN-α, TNF-α, and TLR4 in PBMC from LPS-treated animals. LPS treatment also resulted in a transient and significant increase of viral load in both plasma and CSF. SIV-infected animals had relatively higher levels of creative kinase (CK) in the CSF, a biomarker of brain injury, than uninfected animals. LPS administration increased the plasma levels of CK in SIV-infected animals. In contrast, LPS had little effect on the CSF levels of CK. These data demonstrated that LPS induced immune activation and SIV replication in CRMs that are a suitable non-human primate model for investigating the immunopathogenesis of HIV disease.

Key words: Lipopolysaccharide (LPS); Chinese rhesus macaque; SIV; Immune activation

# Rong Bao and Li Ye contributed equally to this work.

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大学医学院儿科系，1986-1989 年在美国费城儿童医院免疫传染科作临床研究员，1990-1993 在美国宾夕法尼亚大学 Wistar 研究所作分子病毒学博士后，师从美国著名病毒疫苗学家 Stanley A. Plotkin 教授。历任美国宾夕法尼亚大学医学院助理教授、副教授、正教授及费城儿童医院传染与免疫科病毒室主任等职，并获宾夕法尼亚大学公共卫生系 MPH 学位，2009 年任美国天普大学医学院病理系及细胞生物系终身正教授，现任《Virology: Research and Treatment》杂志主编，《PlosOne》、《J. Neuroimmune Pharmacology》、《J. NeuroVirology》3 种美国科研杂志编委，《中华儿科杂志》国际编委。具有二十余年从事临床病毒免疫研究工作的经验，尤其是对艾滋病毒及丙型肝炎病毒病毒复制与天然免疫的研究有扎实的理论基础和丰富的科研经验，已发表 SCI 收录论文 130 篇（其中以第一作者和通讯作者发表的论文 112 篇），包括：J Clin Invest (IF:16.915)，Blood (IF：10.432)，Hepatology (IF：11.355)， PNAS USA (IF：9.380)；共被引用 3000 多次，参编美国教科书及专著 8 部；获美国专利局专利 1 项。

Microbe biodiversity in the wild tree shrew

Fu-Kai Bao[1, 3*], Ai-Hua Liu [2]

1.Department of Microbiology and Immunology, Kunming Medical University, Kunming，Yunnan 650500, China; 2. Department of Biochemistry and Molecular Biology, Kunming Medical University, Kunming, Yunnan 650500, China; 3. The Institute for Tropical Medicine, Kunming Medical University, Kunming, Yunnan 650500, China

Abstract: To investigate bacterial carriage of tree shrew. Bacteria were isolated from hair samples, tracheal secretions and ileo-colonic contents of tree shrews, and identified by morphology, staining, serial biochemical tests, serology, and ribotyping. *Staphyloccus aureus*, *Staphyloccus epidermis*, *Pseudomonas*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Proteus*, and *Serratia* were isolated from tree shrews, but no α-hemolytic streptococcus, β-hemolytic streptococcus, γ-streptococcus, Salmonella, Shigella, Klebsiella and Enterobacter were isolated. Tree shrews carry several kinds of pathogenic bacteria. During the translational process of tree shrews from wildlife to experimental animals, tree shrew-bore pathogens should be carefully monitored and controlled.We investigated the taxonomic identities and phylogenetic relationships of fungal species isolated from tree shrew hair samples, using a combination of morphological and molecular approaches. Morphological differences among the seventy-one fungal isolates indicate that diverse distinct morphotypes might be present on the hosts. Seven representative isolate taxa were selected for further molecular phylogenetic analysis using nuclear ribosomal internal transcribed spacer (ITS1 and ITS2) DNA sequencing. The 71 isolates were identified to the species level based on fungal sequences with known identities in GenBank. Our results suggest that 7 fungal genera are the dominant fungal parasites on the tree hairs.

Key words: tree shrew; pathogenic bacteria; fungus; microbial identification

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南微生物学会理事。担任国内 6 个核心期刊编委、长期审稿人和 25 个国际英文同行评议杂志（包括 10 份 SCI 杂志）的共同主编、副主编、编委或长期审稿人。长期从事医学微生物学、免疫学教学和科研工作。主要研究方向为热带虫媒传染病、结核分枝杆菌与结核病。主持或参加过国家自然科学基金项目、美国 NIH 项目、云南省自然基金项目等共计 15 个项目的研究。在莱姆病研究中有多项重要发现；长期致力于结核病免疫与致病机理研究；近年也从事树鼩实验动物标准化研究及动物模型（结核病、莱姆病等）研究。建立了海量生物医学数据库，主要包括英文专著、百科全书等 40 万部，热带医学文献 20 余万篇（部）。至今发表研究论文及综述 120 多篇，其中国际权威杂志《Nature》1 篇（4），《Cell》1 篇（7），《J Exp Med》1 篇（1），《J Infect Dis》1 篇；SCI 收录 14 篇，影响因子累计达 89.8；申请发明专利 3 项，主编、副主编或参编本科专著、教材 6 部。

Parietal cortical neuronal activity is selective for express saccades

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Abstract: Saccadic eye movements are central to primate behavior and serve to move the eyes to visual objects of interest. Express saccades, unlike regular saccades, occur with very short reaction times, a behavior necessary for speeded reactions in goal-directed behavior. Previous studies have shown that introduction of a blank interval (gap) between the fixation point offset and the saccadic target onset leads to an increase in the number of express saccades and that the superior colliculus (SC) plays a crucial role in the generation of express saccades. A longstanding hypothesis asserted that express saccades are mediated largely by a subcortical circuit, circumventing extrastriate visual cortex. An alternative “posterior pathway” hypothesis proposed the involvement of posterior parietal cortex. In the present study, using a gap saccade task, we investigated the role of non-human primate’s lateral intraparietal cortex (LIP) in generation of express saccades. We show that roughly half of recorded LIP neurons were modulated during the gap interval. Moreover, a group of neurons with persistent activity in a memory-guided saccade task enhanced their activity during express saccades relative to that during regular saccades. After reducing the target’s certainty by increasing the potential target locations, neuronal activity remained in the similar level during express saccades but markedly reduced during regular saccades that correlated with the increase of saccadic reaction time (SRT) in the regular saccade. Our results suggest that area LIP is directly involved in generating saccades in express mode.

Key words: Non-human primates; Electrophysiology; Single neuron recording; Lateral intraparietal cortex (LIP); Express saccades

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Alternative splicing of rhesus macaque MHC IA allele and its regulatory mechanisms in immune system

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Abstract: Major histocompatibility complex (MHC) class I molecules play a pivotal role in the regulation of immune responses by presenting antigenic peptides to cytotoxic T lymphocytes (CTL) and by regulating cytolytic activities of natural killer cells (NK). In the human, mouse and nonhuman primate system, MHC I molecules, which are constitutively expressed on the surface of almost all nucleated cells, are made of a highly polymorphic glycosylated transmembrane heavy chain (HC), associated with non-MHC encoded β2-microglobulin (β2m), a nonpolymorphic light chain, and an 8-9 residue peptide. Peptide binds within a groove formed by the α1 and α2 domains of the protein, supported by the α3 domain and β2m. Before MHC class I HC/β2m/peptide complexes are secreted to the cell surface expression, peptides are loaded onto MHC I via an assembly complex in the ER of the cell, where many proteins participate in the correct assembly and folding of MHC I molecule.

As with other immunological relevant genes, MHC I transcripts have been reported to undergo alternative splicing by numerous investigators. Numerous studies have demonstrated that the alternative splicing of MHC I transcript takes place to a small extent in virtually all cells and may be a common phenomenon in different species. However, little is known as to how the MHC I splice variants regulate and influence the full-length MHC I molecules.

Here, we show that MHC IA in rhesus macaque can be alternatively spliced, generating a novel MHC IA isoform (termed MHC IA-sv1) devoid of α3 domain. Despite the absence of β2-microglobulin (β2m), MHC IA-sv1 proteins reached the cell surface of K562-transfected cells, as endoglycosidase H-sensitive glycoproteins which could form disulphide-bonded homodimers. Cycloheximide-based protein chase experiments showed that MHC IA-sv1 proteins were more stable than full-length MHC IA in transiently or stably transfected cell lines. Of particular interest, our studies demonstrated that the MHC IA-sv1 could form β2m-free heterodimers with its full-length protein in HEK293-MHC IA-sv1/MHC IA transfectants. The formation of heterodimer was accompanied by a reduction in full-length MHC IA ubiquitination and consequent stabilization of the protein. Taken together, these results demonstrate MHC Ⅰ A-sv1 and MHC IA can form a novel heterodimeric complex as a result of the displacement of β2m and also illustrate the relevance of regulated MHC IA protein degradation in the β2m-free heterodimerization-dependent control, which may have some implications for the MHC IA

splice variant in the fine tuning of classical MHC IA/TCR and MHC IA/KIR interactions.

Key words: Rhesus macaque; MHC; Alternative spling; Splice variant; Heterodimer; Ubiquitin; Degradation

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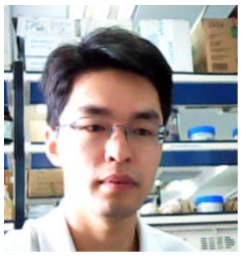

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Comparative study on acute toxicity of are coline to tree shrews and mice

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Abstract: Acute toxicity tests are the principal experiments for drug evaluation. Mostly, acute toxicity tests were carried out on mice and rats. However, the effects of drugs detected in rodents or other non-primate species may differs from that induced in humans. Here we used tree shrew, a non-human primate animal more economical than monkey, in acute toxicity study. In order to determine whether the acute toxicity reaction in tree shrew differs from mice, a comparative study on acute toxicity of arecoline in tree shrews and mice was carried out. Arecoline, the major alkaloid of betel nut, is known to be a partial agonist of muscarinic acetylcholine receptors. It is the primary active ingredient responsible for the central nervous system effects of the areca nut. Arecoline has been noted for its potential cognition-enhancing effects in patients with Alzheimer's disease and it has been proved to have a bioavailability of the 85% when compared with bioavailability following intramuscular administration. But areca nut use is associated with oral and pharyngeal cancers. According to report, the median lethal dose (LD50) of arecoline in mice is 190 mg/kg. It can cause systemic tremor reaction in mice and inhibition of the movement of mice in the dose 10 mg/kg. We repeated the experiments on mice at the dose 190 mg/kg and got a consistent result with the report. Then three male tree shrews were intraperitoneal (i.p.) administrated with 190 mg/kg arecoline saline, all of them died within twenty minutes. In consideration of that we made a half dose for another three male tree shrews i.p. administration, all tree shrews survived this time. After that, we set up three groups based on three different doses: 120, 145 and 170 mg/kg, ten tree shrews per group, male and female half-and-half. Through the experiments and statistics the LD50 interval of arecoline to tree shrews was 120 to 130mg/kg. Furthermore, we set up experiments to test the No Observed Adverse Effect Level (NOAEL) of arecoline to tree shrew, which was also lower than that in mice. Therefore, we conclude that tree shrew is more sensitive to arecoline than mice.

Key words: Arecoline; Acute toxicity reaction; Tree shrew; Mice; LD50

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几种实验动物和人类组织表达肿瘤相关抗原的比较研究

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摘要：实验动物小鼠、大鼠、比格犬（*Beagle Dogs*）、猕猴（*Macaca fascicularis*），已被广泛用于抗肿瘤药物的药效学、安全性、体内分布、体内代谢等研究，其也属多国官方药物临床试验批准机构指定的临床前研究用实验动物。系统比较小鼠、大鼠、比格犬、猕猴和人类组织肿瘤相关抗原的表达和分布，将为更好地应用这些实验动物进行相关药物研究和开发提供基础。本研究在这四种实验动物和人类的 11 种正常组织（脑、心、肺、肾、肝、胃、胸腺、脾、前列腺、卵巢、骨骼肌），比较肿瘤相关抗原 CD176（Thomsen-Friedenreich antigen，Galβ1-3GalNcα1-R）的表达和分布情况。其结果表明，CD176 在小鼠、大鼠、比格犬、猕猴、人类的正常组织中基本不表达。但在部分上皮细胞的腔面，如肾远曲小管和集合管上皮细胞，前列腺上皮细胞，有轻到中度表达。这些免疫屏障部位表达 CD176，不会与血液中自然的 CD176 抗体和治疗的 CD176 抗体结合。我们的研究表明，小鼠、大鼠、比格犬、猕猴均可用于肿瘤相关抗原 CD176 抗癌疫苗和抗体药物的研究和开发。在本研究中我们还发现，在这 4 种哺乳类动物中，其肿瘤相关抗原在正常组织中的表达与分布，与人类正常组织不完全相同。即使在进化较高的非人灵长类动物如猕猴，其肿瘤相关抗原的表达与分布，也与人类有一定差异。这些发现提示，在应用实验动物进行抗肿瘤药物的研究和开发中，系统观察药物靶点分子在实验动物正常组织中的表达与分布是需要的。

关键词：小鼠；大鼠；比格犬；猕猴；正常组织；肿瘤相关抗原；CD176

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天麻素对老年痴呆树鼩海马老年斑的影响及 BDNF 的表达

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摘要：探讨天麻素对老年痴呆树鼩脑内老年斑的作用及可能的机制。用 β-淀粉样蛋白（Aβ）侧脑室注射建立树鼩老年痴呆模型。从模型制作后第 2 天开始，治疗组树鼩连续 30 天灌胃给予天麻素。通过免疫组化检测海马内老年斑，RT-PCR 检测脑源性神经营养因子（BDNF）mRNA 的表达。结果显示，天麻素治疗组树鼩海马老年斑的面积百分比和数量均低于模型对照组（$P<0.05$），海马 BDNF mRNA 在治疗组的表达高于模型组（$P<0.05$）。天麻素能在一定程度上减少痴呆树鼩海马老年斑，这种作用可能与上调 BDNF 的表达有关。

关键词：树鼩；老年痴呆；天麻素；BDNF 表达

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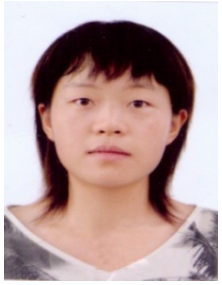

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SIV/TB Coinfection of Chinese Rhesus Monkey

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Abstract: Tuberculosis (TB) is the most common opportunistic infection, and the leading cause of the death for HIV-infected patients. Similarly, HIV infection is associated with an increased risk of latent TB infection progressing to active TB disease. Thus, to establish an animal model for both TB and HIV infections is critical to the understanding of the pathological interactions between these two pathogens. In this study, we first inoculated Chinese Rhesus monkeys with SIV mac239 strain. The animals became infected as evidenced by increased plasma levels of SIV RNA and protein. In addition, there was a significant decrease in the CD4+/CD8+ T cell ratio, which was negatively associated with plasma SIV RNA levels. At 6th week postinfection with SIV, the animals were intra-bronchially inoculated with Mycobacterium tuberculosis (M.tb) H37Rv strain. Comparing with SIV mono-infected monkeys, SIV/TB co-infected animals had little differences in SIV viral load, CD4+ /CD8+ T cell ratio. In contrast, SIV/M.tb co-infected animals had lower levels of IFN-gamma and IL-22 than M.tb mono-infected animals. The chest X-ray showed that the monkeys coinfected with SIV/TB had disseminated lesions in both left and right lungs, while the lung lesions in TB mono-infected monkeys were localized in right lung. All three animals coinfected with SIV and M.tb died at week 16, 18, 19 post-M.tb infection, respectively, while the animals infected with M.tb only had longer survival time. All three SIV mono-infected animals are still alive. The necropsy demonstrated that the co-infected animals had more severed M.tb infection not only in the lungs but also in other organs including spleen, pancreas, liver, kidneys and heart than M.tb-mono-infected animals. These data demonstrated that although M.tb infection had little effect on SIV infection, SIV infection compromised the host specific immunity against M.tb, resulting in the M.tb dissemination. Our ongoing studies will further investigate the mechanisms involved in the impact of SIV and M.tb interactions on disease progression in Chinese rhesus monkeys.

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可能用于灵长类脑网络示踪技术

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摘要：人脑中约有一千亿个神经元，通过约十万亿个突触交织形成无数的不同范围的神经元网络，作为大脑行使一切功能的结构基础；同时，神经网络的异常是各类神经精神疾病的结构基础。但长期以来，因缺乏合适的技术方法，在回路水平上的介观研究几乎无法开展，成为神经生物学和神经科学在宏观和微观研究之间的一大鸿沟。基于部分种类嗜神经病毒的神经元感染和沿突触传播的能力所发展起来的标记系统，为相关研究打开了一个全新的视窗。我将把神经回路标记的现状略作介绍，并以我们几年来在相关研究中的一些结果展示这类工具的应用，将就实验室正在发展的新方法及其用途，与会者研究中的需求和合作进行探讨。

High-fat diet induced dyslipidemia and potential atherosclerosis

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Abstract: Atherosclerosis is a common chronic cardiovascular disease resulted from accumulated fatty matters such as cholesterol that is usually found in various dietary sources. Although non-human primate model of high-fat diet induced by elevation of cholesterol and low-density lipoprotein (LDL) has shown great pathological values for better understanding the pathogenesis of dyslipidemia and prognosis of potential atherosclerosis, many questions still remains to be answered. To further expose the value of this model, ten cynomolgus monkeys were used to investigate if the model is suitable for investigation of dyslipidemia and can be used for predicting atherosclerosis. Animals were divided into 2 groups fed with 2 types of fat-content diet. During 6-month study, animal's blood lipid levels were closely monitored and intima-media thickness and vessel diameter were measured by MRI. The result demonstrated that both diets showed limited ability to elevate triglycerides and high-density lipoproteins (HDL). However, the high fat diets had greater effects to accumulate cholesterol and LDL. In addition, 6 months after high fat diet, increased intima-media thickness, narrowed vessel diameter and soft fatty plague were found in all tested monkeys. The results support the notion that non-human primate can be used as a model for dyslipidemia and used for testing new drugs for preventive or curative treatments of atherosclerosis.

树鼩 IL-2 基因序列的克隆及分子特征分析

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摘要：树鼩作为人类疾病良好模型已受到广泛关注，但对其白细胞介素-2 方面的研究尚属空白。本实验以培养的树鼩淋巴细胞总 RNA 为材料，通过 RT-PCR 技术克隆出长度约为 465bp 的树鼩 IL-2 完整开放阅读框（ORF），并通过 Clustal W 等软件对其序列和分子特征进行了分析,发现树鼩 IL-2 cDNA 编码一个由 154 个氨基酸组成的蛋白质，采用 MEGA5.0 构建进化树发现，树鼩与人、恒河猴亲缘关系较近。本研究为今后树鼩 IL-2 单克隆抗体的制备及功能研究奠定了基础。

Key words: Tree shrews; Interleukin 2; Cloning; Structure; Function

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A defensin antimicrobial peptide from the tree shrew, *Tupaia belangeri*

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Abstract: A novel beta-defensin antimicrobial peptide was purified and characterized from the serum of the tree shrew of *Tupaia belangeri.* This peptide was named β-defensin 1TB. Its amino acid sequence was determined by Edman degradation, mass spectrometry analysis, and cDNA cloning. Matureβ-defensin 1TB contains 36 amino acid residues in length. β-defensin 1TB showed maximal similarity to the β-defensin 1 identified from cotton-top tamarin, Saguinus Oedipus by evolution analysis. This antimicrobial peptide exerted potential antimicrobial activities against wide spectrum of microorganisms including Gram-negative and -positive bacteria and fungi. It exerted little hemolitic activity to human or rabbit red cells. To the best of our knowledge, this is the first report of antimicrobial peptide from Tupaiidae.

Animal model of Parkinson's disease: future expectation

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Abstract: Parkinson's disease (PD) is one of the most prevalent neurodegenerative diseases characterized by the dopamine (DA) neuron degeneration in substantia nigra (SN) and manifested by the rest tremor, bradykinesia, rigidity, postural and gait disturbance, and other non-motor symptoms. With the help of animal models remarkable achievements have been made in recent years for better understanding the disease and developing appropriate therapies. Animal models ranging from C. elegans, drosophila, zebra fish, rodents to non-human primates have been employed for such purposes. Among them rodents are mostly used animals to model PD by injuring the nigro-striatal pathway through the application of neurotoxins, inflammation agents, ubiquitin proteasome inhibitors, and genetic manipulations. All of the currently used animal models, however, have not fully met the core requirement to recapitulate the clinical, pathological, and biochemical phenotypes of PD. The advances in biotechnology and genetics in recent years may enable us to generate more representative animal models of the disease.

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HIV/AIDS infection in pigtailed macaques -- an overview

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Abstract: Nonhuman primate animal models play an important role in studying HIV-1 pathogenesis and in testing drugs and vaccines. Due to the lack of animals that can be directly infected with HIV-1, SIV/SHIV-infected macaques are widely used in AIDS research. Although these models are somewhat similar to human AIDS, they have many limitations resulting from the genetic distance between SIV/SHIV and HIV-1. Developing a suitable nonhuman primate animal model is still the focus in HIV/AIDS research. Pigtailed macaques are the only macaques in Old World monkeys that can infect HIV-1 and offer many benefits in HIV-1 intravenous and sexual transmission models. Here, we review the characteristics of the pigtailed macaque model infected by SIV, HIV, SHIV and HSIV via intravenous and mucosal routes. Relevant molecular mechanisms are introduced briefly, and also the limitations and prospects of the pigtailed macaques model for AIDS research are discussed.

Keywords: Pigtailed macaques; HIV/AIDS; Animal models

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G6PD mRNA 在树鼩组织中的表达

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摘要：作为磷酸戊糖途径的限速酶的葡萄糖-6-磷酸脱氢酶（G6PD, EC1.1.1.49）是看家酶，广泛存在于生物体各组织细胞中。已有研究表明 G6PD 与人类溶血性疾病、糖尿病、肿瘤、病毒感染等相关，而树鼩 G6PD 的组织分布尚未见报道。本文应用荧光定量 PCR(Real-time PCR)技术，采用两步法 RT-PCR 反应体系对树鼩全血、心、肝、脾、肺、肾、肌肉、胰腺、胸腺、肾上腺、脑、海马、嗅球、皮肤、睾丸、精囊腺、子宫、卵巢等组织中 G6PD 相对含量的表达水平进行分析。结果上述组织中相对表达量最高的是肾上腺（1.3883±0.6217），其它组织表达由高到低依次是全血（0.8850±0.9470）、肺（0.5809±0.4167）、睾丸（0.4867±0.0896）、脾（0.4467±0.2190）、胸腺（0.3617±0.2092）、皮肤（0.2550±0.1754）、子宫（0.1897±0.1282）、卵巢（0.1623±0.0849）、嗅球（0.1330±0.0592）、精囊腺（0.1300±0.0693）、海马（0.0922±0.0445）、小脑（0.0690±0.0426）、大脑（0.0591±0.0247）、胰腺（0.0158±0.0204）、肾（0.0109±0.0146）、肝（0.0051±0.0040）、肌肉（0.0048±0.0035）、心（0.0047±0.0028）。G6PD mRNA 在树鼩组织中的表达分布可为树鼩疾病动物模型研究提供参考。

关键词：树鼩；葡萄糖-6-磷酸脱氢酶；荧光定量 PCR；mRNA

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树鼩解剖数据的测定分析

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摘要：解剖数据是实验动物主要的生物学特性指标之一，对实验动物种属标准化鉴定有一定意义。树鼩由于其特殊的分类学地位及生物学特性，已被广泛于应用于生命科学的各个领域。本文对实验室驯养树鼩（7～9 月龄）的体尺、骨骼及乳头、脏器重量及系数、肠道等解剖学数据进行了测定与分析。体尺等 31 项解剖数据测量结果：体高、右耳宽、回肠、结肠雌雄间差异显著（P＜O.O5），体斜长、胸深、躯干长、左、右前肢长、右后肢长、左、右耳长、左耳宽、龙骨长、左、右胫长、十二指肠、空肠等 14 项指标雌雄间差异极显著（P＜O.O1）。以动物体长为因变量，以尾长、躯干长、左前肢长、右前肢长、左后肢长、右后肢长为自变量，作逐步回归分析，回归方程为：体长=13.900 + 尾长*0.163；37 项脏器及系数测定结果：体重、肺、右肾、膀胱、小肠、左、右海马、左、右颌下腺、左肾上腺、左、右甲状腺脏器重量及系数雌雄间有显著性差异（P＜O.O5）。脾、左肾脏器重量雌雄间有显著性差异（P＜O.O5），胃、脑、右肾上腺脏器系数雌雄间有显著性差异（P＜O.O5）。以动物体重为因变量，以主要脏器指标：心、肺、肝、脾、左肾、右肾、脑为自变量，作逐步回归分析，回归方程为：体重=62.726+左肾*79.213+心*24.090。实验室驯养树鼩不同性别对体尺、脏器及系数、肠道等解剖数据有一定影响，该数据为树鼩实验动物化及疾病动物模型研究提供基础数据。

关键词： 树鼩；解剖数据；脏器重量；脏器系数

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Measurement and analysis of the hematology physiological indicators in *Tupaia belangeri chinensis*

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Abstract: By automatic blood cell analyzer determinating hematology physiological index value of *Tupaia belangeri chinensis*，and using SPSS statistics software to analysis data of determination, Then between determination value of *Tupaia belangeri chinensis* in hematology physiological index value and the human with hematology physiological index reference value is compared .Finally, The result is that *Tupaia belangeri chinensis* in female and male hematology physiology index value has significant differences(P<0.05), such as red blood cell count, hemoglobin, hematocrit, hemoglobin concentration, red cell distribution width coefficient of variation, and the rest of the index shows no significant differences(P>0.05). *Tupaia belangeri chinensis* merge, female and male hematology physiology index value and the human hematology physiological index reference values are compared, which concluded that the white blood cell, neutrophil, eosinophil percentage percentage, absolute value of neutrophilic granulocyte, monocyte, absolute value of mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, erythrocyte hemoglobin distribution width are lower than the reference value. And the percentage of lymphocytes, red blood cell count, hemoglobin, hematocrit, red cell distribution width coefficient of variation, platelet counts are higher than the reference value., And mononuclear cell percentage, basophil percentage, absolute value of lymphocytes, basophils absolute values in the human reference value range.

Key words: *Tupaia belangeri chinensis*; Hematology physiological indicators; Measurement; Analysis

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The interferon system in tree shrews (*Tupaia belangeri*): genomic sequence retrieval, molecular identification and characteristic predication

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Abstract: The interferon (IFN) system constitutes the first line of host-defense against infections and other danger signals. As shown to be susceptible to several human viruses, tree shrews (*Tupaia belangeri*) are potentially useful models for analyzing viral infection but the family members and their receptors of tree shrew IFNs have not been systemically studied previously. We used the whole genome sequence data of tree shrews generated by the Broad Institute to retrieve contigs for all the possible IFN coding sequences and their cognate receptors. GenScan, BLASTN and BLASTZ revealed that tree shrew IFN system includes: type I IFN: α (with five specific subtypes: α1, α2, α4, α9, α22), β, ω, κ, ε, δ; type II IFN: γ and type III IFN: IFN-λ3. Retrieved and cloned coding sequences showed that tree shrew IFNs are indeed, as expected, more closely related to their human counterparts than mice, rats and other mammals. Further detailed bioinformatics analysis and 3-D molecular modeling (Discovery Studio and PyMoL) predicted that tree shrew IFNs and receptors retained all the possible functional domains as in other mammals. However, differences in the numbers and positions of cysteines and potential N-glycosylation sites were readily identifiable in tree shrew IFNs against other species and more splicing variants of receptors were cloned. Constitutional tissue distribution of its receptor subunits and rapid induction kinetics of IFN-λ expression confirmed the importance of IFN system for the innate defense in tree shrews. This initial study lays the foundations for further analysis of the IFN system and their functions in infection models in tree shrews. (Part of the results has been published in Zoological Research [33(1):67-74; 2010] and the remaining findings submitted to the PLoS ONE [PONE-S-12-43117].)

Key words: Tree shrew; Interferon; Interferon reporters; Genomic analysis; Bioinformatics

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Tree shrew, a potential experimental animal for sepsis model

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Abstract: Sepsis is a systemic inflammatory response syndrome following bacterial infection with 30-70% of mortality and limited therapeutic options. Experimental sepsis models in rodent could not well mimic the sepsis in human, which limit the investigation of novel therapeutic strategies. Emerging evidences demonstrate that tree shrew is a small non-human primate, and is suitable to replicate several human diseases without disadvantages existing in other non-human primates. In our previous study, two bacterial infection models have been established in tree shrew burned skin, suggesting tree shrew is susceptible to human bacterial pathogens. In the present study, we aim to investigate whether tree shrew (*Tupaia belangeri chinensis*) is a promising experimental animal to replicate sepsis similar to that of human. To mimic the clinical condition of bacterial infection, sepsis in tree shrew was induced by a severe thermal burn following P. aeruginosa intra-subcutaneous inoculation. The bacterial load in skin, blood, and lung in blood were determined at different time interval after bacterial inoculation. Increased bacterial burden were observed in skin, blood and lung 24 h after a high dose of P. aeruginosa inoculation. Lipopolysaccharide (LPS) molecules are the main components of the outer membrane of Gram-negative bacteria and lead to cytokine storm and organ failure during sepsis. After LPS stimulation, NO concentration in tree shrew serum was increased at 8 hours, reached up to the highest at 45 h and maintained to 72 h, after then backed to normal level at 140 h. In contrast, NO concentration in ICR mice serum after LPS stimulation was increased quickly at 1 h, and fell to the normal level at 5 h. Consistent with the dynamics of NO production in vivo, death of tree shrew occurred beyond 7 days after LPS challenge, in contrast, mice usually died within 48 h. The human sepsis in clinical usually take days to weeks resulting in obvious organ failure and even death. NO usually up-regulate in sepsis patients for days and act as indicator for prognosis of sepsis. The results presented in this study indicate that the course of experimental sepsis in tree shrew may similar to that of human sepsis, similar dynamics of NO production between tree shrew and human sepsis inspires us to further investigate the potential of tree shrew as small non-human primate for replicating human sepsis.

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树鼩局部脑缺血与缺血后适应的脑保护信号转导机制的研究

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摘要：脑血管病为人类致死致残的常见多发病，我国脑血管病发病率高达 250/10 万，其中缺血性脑血管病占 70%以上，已成为严重制约我国经济发展和社会进步的重大问题。因此，建立相应的实验模型并揭示其发病机制具有重要意义。本室长期以来一直致力于树鼩脑血管疾病模型的创建，主要包括①光化学诱导树鼩脑血栓形成模型；②树鼩大脑中动脉闭塞（MCAO）模型；③树鼩糖尿病合并脑缺血模型；④树鼩缺血后适应（postconditioning,PC）模型及低温 PC 模型。本文重点介绍树鼩血栓性局部脑缺血模型及缺血 PC 脑保护信号转导机制的研究。健康成年树鼩 80 只（雌雄不拘）随机分为假手术组、脑缺血组和缺血 PC 组。采用本室研制的《SQ-Ⅲ型脑血栓形成装置》，将动物置于实验装置下，用中心波长（λ）560nm，带宽（Δλ）60nm 的特殊光束照射树鼩颅骨表面 10min 诱导树鼩血栓性脑缺血（光强度 1.0w/cm2，温度控制在 36.0 ± 0.5℃），照后缝合皮肤、保温待动物清醒后放回饲养笼内观察。并于脑缺血 4 h、24 h 及 72 h 动态监测光镜、电镜、TUNEL、局部脑血流（rCBF）、细胞色素 C(Cyt C)、AKT[pT308]/ AKT [pS473]以及海马微血管紧密连接蛋白（Occludin 和 ZO-1）等指标的改变；选择缺血 4 h 为后适应干预的“时间窗”。结果证实树鼩脑缺血后梗死体积的改变随 rCBF 的降低而增大（P＜0.01）；发现海马神经密度减少与胞质内 Cyt C 表达增强以及内质网应激相平行，且 CA1 区 TUNEL 阳性细胞明显增多（P＜0.01）；脑缺血时海马 Occludin 和 ZO-1 表达降低而 AKT[pT308]和 Akt [pS473]活化水平升高（P＜0.05）。首次证明缺血 PC 在增加海马 rCBF（P＜0.01），促进紧密连接蛋白表达的同时，可抑制海马神经元 Cyt C 的释放并使 AKT[pT308]/Akt[pS473]明显下调（P＜0.05）。用 FC 抑制星形胶质细胞（AS）代谢则可显著降低 PC 的脑保护效应，甚至具有加重脑损伤的趋势。显然，缺血 PC 的抗凋亡及脑保护效应与 AS 功能的正常密切相关；PC 脑保护的机制可能与调节紧密连接蛋白表达与 AKT 信号通路有关，其增加海马 rCBF 可能是 PC 脑保护的关键所在。

关键词：光化学；脑血栓形成；海马超微结构；局部脑血流；缺血后适应；信号转导；树鼩

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新生期树鼩接种人乙型肝炎病毒后可以形成体内慢性感染状态并发生类似人类慢性乙肝的肝组织学改变

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摘要：迄今国内外尚无实验动物慢性感染乙型肝炎病毒（HBV）成功的报道；树鼩能否在体内形成慢性 HBV 感染一直存在争议。本研究用本实验室人工繁育的新生树鼩，于 1、3 日龄分别两次接种取自乙肝病人或已知持续感染 HBV 的树鼩血清，300~500μl/只/次。从接种后第 4~6 周开始，定期对树鼩采集静脉血和肝活检组织，每 4~12 周 1 次。所有血清标本全部通过 ELISA 方法定性检测乙肝血清免疫学标志“两对半”，其中 HBsAg 阳性标本加用 TRFIA 方法进行 HBsAg 定量检测；全部血清和肝组织标本标本以荧光定量 PCR（FQ-PCR）检测 HBV DNA；部分初检阳性的血清和肝组织标本作巢式 PCR（nPCR）、Southern blot、Dot blot 检测 HBV DNA 和 HBV cccDNA，用免疫组化染色检测 HBsAg、HBcAg，用电镜观察 HBV 颗粒，同时进行常规病理组织学观察。结果显示，46 只新生期接种的树鼩中，6 只确定为持续感染（接种后 48 周以上）、4 只疑为持续感染（接种后 48 周以上间断显示血清 HBsAg、血清或肝组织 HBV DNA 弱阳性）；其中，1 只确定持续感染的动物（121-1）和 2 只疑似持续感染的动物（117 和 121–2）的接种物为已确定感染 HBV 的树鼩（90-1）的血清，提示树鼩间传代感染成功；感染时间最长的一只动物（90-1）于接种后 6 年余处死检查肝组织，可见显著的肝细胞增生和变性、肝组织纤维化和炎细胞浸润等类似人类 HBV 感染后慢性肝病的组织学改变。同期观察的 49 只非新生期接种 HBV 的树鼩无一显示明确感染。本研究还对多种可能影响树鼩体内慢性 HBV 感染的因素进行了探讨，筛选出一些可能提高感染率的优化因素。总之，本研究结果表明树鼩于新生期接种 HBV 后可以在体内形成慢性感染状态并发生肝组织学改变。本模型有可能用于研究人类慢性 HBV 感染相关的疾病过程、机体清除 HBV 的免疫学机制以及个体对 HBV 易感的因素。

关键词：树鼩；乙型肝炎病毒（HBV）；动物模型

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链脲佐菌素诱导树鼩 2 型糖尿病初探

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摘要：2 型糖尿病（Type 2 diabetes mellitus,T2DM）是由多病因引起的复杂代谢性疾病，主要特征是胰岛素抵抗和胰岛素相对缺乏从而产生高血糖。我国已成为世界第一糖尿病大国（Yang et al., 2010）,推进与糖尿病相关的研究迫在眉睫。糖尿病疾病动物模型是阐明糖尿病发病机理、早期诊断和预防、药物筛选和评价的必要手段。树鼩（*Tupaia belangeri chinenisis*）被认为是灵长类的近亲，相对于啮齿类在进化上更接近于人类。与其它非人灵长类动物相比，树鼩体型小、繁殖快，成本低廉，已被用于生命医学研究近 30 多年。然而，目前还没有 2 型糖尿病树鼩模型成功建立的报道。链脲佐菌素（Streptozotocin, STZ）是一种链球菌产生的天然化合物，对哺乳动物的胰岛 B 细胞有特异毒性，广泛用于诱导 1 型和 2 型糖尿病。因此，本研究探索利用 STZ 诱导树鼩 2 型糖尿病。24 只树鼩分对照组（6 只）、不同 STZ 浓度实验组（6 只/组）。实验组动物腹腔注射 STZ（剂量 40–120mg/kg ），对照组腹腔注射生理盐水。STZ 诱导后，实验组树鼩出现明显“三多一少”糖尿病症状；口服糖耐量受损；其空腹血糖（FBG）、糖化血红蛋白（Hb1Ac）、尿素氮及胰岛素显著上升，但酮体未变；病理剖检及病理切片显示，肾脏出现病变，胰岛 B 细胞部分损伤。我们目前的研究结果表明：高剂量 STZ 导致树鼩血糖过高致死，低剂量 STZ 可以诱导树鼩 2 型糖尿病病症，STZ 的剂量决定成模率及糖尿病类型。

关键词：2 型糖尿病（T2DM）；树鼩（*Tupaia belangeri chinenisis*）；链脲佐菌素（Streptozotocin, STZ）

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Phylogenetic patterns of *APP*, *ADAM10*, *PSEN-1* and *BACE-1* genes in Chinese tree shrew *(Tupaia belangeri chinensis*)

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Abstract: The APP, ADAM10, PSEN-1 and BACE-1 genes are actively involved in the APP amyloidogenic and non-amyloidogenic signaling pathways, which are greatly important for pathological progression of Alzheimer's disease (AD). Here, we compared the phylogenetic patterns of these AD-related genes in Chinese Tree Shrew (*Tupaia belangeri chinensis*) and other related species. The amino acid sequences of tree shrew APP, ADAM10, PSEN-1 and BACE-1 share a high similarity with human, with a sequence identity of 97.52%, 98.48%, 96.96% and 97.60%, respectively. In particular, the amino acid sequence of Aβ1-42 in tree shrew is identical to human. Phylogenetic trees reconstructed using the neighbor-joining (NJ) method and the maximum-likelihood (ML) method on the basis of combined amino acid sequence of these genes show that tree shrew and primates are grouped together. Furthermore, no selection pressure is detected for these genes. These results suggest that genes involved in the AD-associated amyloidogenic and non-amyloidogenic pathways are highly conserved between human and Chinese tree shrew. Therefore, Chinese tree shrew may be a promising experimental animal for creating AD model.

Key words: Tree shrew; Alzheimer's disease (AD); APP; ADAM10; PSEN-1; BACE-1; Neighbor-joining (NJ) method; Maximum-likelihood (ML) method; Selection pressure

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自发性肥胖、高血糖猕猴筛选

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摘要：猕猴因进化和生理等与人类非常接近，广受生物医药研究的重视，被用于肥胖、糖尿病、心脑血管疾病等代谢性疾病的研究。为了研究探索猕猴群体中自发肥胖和高血糖状况，我们对昆明动物所饲养繁殖的 1357 只猕猴（雄性：583，雌性：774，年龄 1-25 岁）进行肥胖和高血糖症的筛选。1357 只猕猴按年龄分为幼年组(0-3 岁)、青年组(4-6 岁)、中壮年组(7-9 岁) 、中老年组 (10-12 岁) 和老年组(13 岁以上)。结果表明：幼年组平均体重为 2.94±0.84Kg，平均血糖 4.20±1.0mmol/L；青年组平均体重为 5.97±2.2Kg，平均血糖 4.12±1.3mmol/L；中壮年组平均体重为 7.46±2.35Kg，平均血糖 4.41±1.72 mmol/L；中老年组平均体重为 7.14±2.37Kg，平均血糖 4.67±1.49 mmol/L；老年组平均体重为 7.43±2.29Kg，平均血糖 4.85±1.86mmol/L。随着年龄的增长，肥胖和高血糖发生的机率上升。依据 BMI≥38，腰围/臀围≥0.78 作为成年猕猴肥胖的标准，筛选到 84 只肥胖的猕猴，其中有 10 只呈现重度肥胖，他们的 BMI≥44，腰围/臀围≥0.94，而且年龄在 10 岁以上。132 只成年猕（雌性：103，雄性： 29）空腹血糖浓度≥5.60 mmol/L，其中 104 只猕猴的空腹血糖为 5.60-7 mmol/L，28 只猕猴的空腹血糖＞7 mmol/L，且多数年龄在 10 岁以上，可能存在糖尿病的风险。结合肥胖和血糖指标，发现 22 只猕猴（雄性：10，雌性：12）不仅肥胖，且空腹血糖≥5.60 mmol/L，占总体 1.62%，其中 14 只年龄在 10 岁以上。这些结果表明，这个猕猴群体中，存在自发性肥胖和高血糖猕猴，而且多发生于中老年猕猴。目前，我们正在对这些肥胖，高血糖猕猴开展相应的研究工作。

关键词：猕猴； 肥胖；BMI；空腹血糖；糖尿病

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Characterization of 12 polymorphic microsatellite markers in Chinese tree shrew (*Tupaia belangeri chinensis*)

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Abstract: Chinese tree shrew (*Tupaia belangeri chinensis)* is a small experimental animal with a close affinity to primate. It has long been proposed to be an alternative experimental animal to primates in biomedical research. Despite of decades of study, there is no pure breed for this animal and the overall genetic diversity of wild population remains largely unknown. Here we developed 12 polymorphic microsatellite markers from genomic DNA sequence of tree shrew and genotyped a wild population of 117 Chinese tree shrews from Kunming, China. Our results showed that the 12 polymorphic microsatellite markers exhibited a high heterozygosity (0.616) in wild population. Other parameters (used for forensic purpose) calculated on the basis of these 12 microsatellites showed that these markers had sufficient power for individual identification and parentage testing. These microsatellite markers will be of usage in evaluating genetic diversity and lineage tracing for tree shrew.

Key words: Chinese tree shrew; Microsatellite; Heterozygosity; Individual identification; Parentage testing

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树鼩习得性无助动物模型的初步探索

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摘要：树鼩是一种类灵长类动物，与啮齿类实验动物相比具有与人类亲缘关系更近的优势，又保持了小型动物易于饲养和操作的特点。树鼩的应激系统与人类更接近，是抑郁症及相关药物研究的更理想模式动物。本研究拟采用树鼩构建习得性无助的抑郁症模型。习得性无助是指动物在经历不可逃避电击后对可逃避电击的逃避失败，是一种经典的抑郁症动物模型。此模型表面效度和预测效度较好，被广泛用于抑郁相关、尤其是抗抑郁药物的筛选研究。实验首先采用梯度强度电击探索树鼩电击敏感性（0.1-0.7mA 7 个电流强度；每个电流强度 15 次电击），再以足部电击为应激方式、采用穿梭箱单侧和双侧两种不可逃避电击训练，并检测训练后树鼩对可控电击的逃避状况以检验模型效度及筛选抑郁样个体，而后进行慢性口服给药的药效检测。为改进传统习得性无助模型不检测抑郁症核心症状的缺憾，本实验还在开始电击前和给药结束后对树鼩进行糖水偏爱和糖水操作性觅食行为的测试，以探测动物快感和动机水平的变化。现有数据显示，在 13 只处理组树鼩中，0.2mA 电流可产生警觉-喷鼻及运动加快，0.3mA 电击可使部分树鼩在电击间隙出现僵直行为， 0.7mA 电击则产生间隙期完全僵直行为。单侧不可逃避电击（60 次，0.7mA，每次持续 15s，电击间隔 30-90s 随机）后，树鼩仍然逃避可逃避电击（30 次，5 次 FR1，25 次 FR2，0.3mA，每次持续 30s，电击间隔 30-90s 随机）；而双侧不可控电击后，树鼩逃跑潜伏期明显增长（p=0.017），同时主动逃避行为减少（p=0.02）。综上所述，树鼩对电击敏感性较高，且双侧不可控电击适合构建具有较好表面效度的树鼩习得性无助模型。这些数据为建立和掌握人类抑郁症的树鼩模型提供了丰富的信息。

关键词：树鼩；习得性无助模型；电击敏感性；表面效度

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新型树鼩社会挫败模型的建立

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摘要：背景 树鼩介于食虫目和灵长目之间，其应激系统与人类相似性远高于大鼠与人类的相似性。同时，树鼩是一种独居动物，具有较强的领地意识。因此，利用社会挫败模型在树鼩中创建抑郁症动物模型可能比大鼠的抑郁症模型具有更高的效度。

研究目的 已有的树鼩社会挫败模型只模拟了活动量减少、标记行为消失等少数抑郁症状，而未反应快感缺失、动机缺乏等抑郁症的核心症状，因此，本实验旨在建立一个能够反应快感缺失、动机缺乏、兴趣减退、活性降低等抑郁症核心症状的树鼩社会挫败模型。

方法 22 只雄性树鼩在适应一周后，检测糖水操作性条件反射（反应动机水平）、糖水偏爱（反应快感水平）、自发活动性等行为的基值。分对打斗阶段，每天让动物自由打斗 1 小时，打斗结束后用网格板分开动物，使之不能直接接触但可以看见对方、听到对方的声音、闻到对方的气味。所有动物在打斗开始后每周进行一次糖水操作行为测试及糖水偏爱测试，并于最后一次检测时增加新颖物体寻求和偏爱食物取食潜伏期检测，以探查社交挫败模型中树鼩的动机、快感、兴趣及活性水平等抑郁相关指标的变化和发展过程。

结果 经历一周社会挫败应激之后，实验组动物相比于对照组糖水偏爱分数未见显著变化，而动物的糖水操作行为的断点水平则显著低于对照组。这些数据提示，社会挫败应激的确适合在树鼩中建立抑郁症模型，且这种抑郁症模型造成各种抑郁样行为可能具有时间特异性。这些数据为建立和掌握人类抑郁症的树鼩模型提供了丰富的信息。

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Premenstrual dysphoric disorder and luteal phase stress in the dominant social status female monkeys

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Abstract: The goal of the present study was to extend our previous work, to develop nonhuman primate models to prospectively study exact mechanism underlying different types of premenstrual syndrom (PMS). Previously, we have established premenstrual depression syndrome rhesus monkey (*Macaca mulatta*) model by isolation with physical restraint low social status young female monkeys during their luteal phase. But different behavioral responese to this stress could be observed in the dominant social status female rhesus monkeys. This study was performed in the young high status female monkeys (*Macaca mulatta*) treated by the same way. Since the eighteenth day to the twenty-second day of their menstrual cycle, monkeys had being singly imprisoned in the isolating-cages specially designed. The moveable doors of these cages were readjusted until monkeys could not move freely. During the five days, monkeys had being in this immovable state for 7 hours per day. At the end of the stress period, the animal was returned to its regular housing. These monkeys had being treated as above way for two consecutive menstrual cycles. For the whole experimental period, the behavior and expression of monkeys have been photographing by automatic vidicon; the changes in serum content of progesterone, estradiol were checked by radioimmunoassay, and serum levels of 5-hydroxytryptamine (5-HT), noradrenalin (NA) and dopamine (DA) were detected by High Performance Liquid Chromatography. After suffered from above stress, 70% monkeys presented premenstrual dysphoric symptoms during three poststress consecutive menstrual cycles. Compared with that in normal monkeys, serum levels of estradiol and progesterone decreased evidently. Moreover, and the secretive peak values in their follicular phase and late luteal phase did not come into being. Serum contents of 5-HT and DA in the dysphoric monkeys were significantly lower, but NA serum level was obvious higher. These data are approximately in line with clinical observations of PMDD patients. Our findings indicated that it is feasible to make PMDD monkey models mimicking the severe subtypes of PMS by specially treating dominant social status monkeys.

Key words: Premenstrual dysphoric disorder; Macaque model; Estradiol; Progesterone; Prolactin; 5-hydroxytryp- tamine; Dopamine; Noradrenalin

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非人灵长类动物模型在重大疾病研究中的应用

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摘要：非人灵长类动物因其特有的近人遗传特性和表型特征而被广范应用于医学和生命科学研究，特别是在一些人类重大疾病，如艾滋病、结核、神经退行性疾病研究中显得尤为重要，概括如下：

非人灵长类动物艾滋病模型较其他动物模型而言，目前依然是最理想的疾病参比模型。为了针对性建立模型，灵长类艾滋病模型平台提供 SIV/SAIDS、SHIV/SAIDS、RT-SHIV/SAIDS 等不同用途动物模型，建立了包括 13 种毒株的规范化病毒库，开展不同靶标病毒构建，不同策略攻毒模式研究，同时进行了发病机制、艾滋病脑病等研究。

非人灵长类动物结核模型在肺结核研究中凸显优势，能够弥补小鼠、豚鼠等动物模型缺乏肺部结核病变的不足，更能实现拟人肺结核发病机制、药物筛选、疫苗评价的需要，同时可充分利用临床病理学、行为学、影像学等技术进行比较医学研究。

非人灵长类 SARS、流感模型动物在研究病原中和抗体产生、疫苗评价、抗病保护等方面显示了良好作用。非人灵长类动物平台为我国 SARS、禽流感、甲流等突发、再发传染病应急研究以及三聚菁胺等重大公共卫生事件毒性评价方面提供了有力的科技支撑作用。

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社会压力，基因和 HPA 轴——基于猕猴的研究

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摘要：五羟色胺(5-HT)是体内重要的神经递质，在调节情绪方面起着不可替代的作用。在所有单胺类神经递质中，5-HT 被用来调节其他神经递质系统和内分泌系统，其功能降低会导致这些系统处于失调状态。5-HT 虽有多种突触前后受体亚型，但只能被五羟色胺转运体(5-HTT)这种单一蛋白转运入突触前神经元用于再循环。因此，5-HTT 转运体基因成为研究情绪调节和应激反应性的重要候选基因。猕猴 5-HTT 基因在其转录起始位点上游大约 1kb 处有一个多态性重复序列(rh-5HTTLPR)，S 型等位基因表现低转录活性，携带 S 型等位基因的个体，其 5-HT 回吸收能力低，而 L 型等位基因则表现出高转录活性，快速重吸收 5-HT，提高 5-HT 的循环效率。在本研究中，我们第一次发现携带 SS 基因型的低地位猕猴在经历应激事件时，其下丘脑-垂体-肾上腺轴(HPA 轴)表现出比其它基因型(LL 和 LS)猕猴更高水平的激活状态，分泌更高浓度的可的松。HPA 轴的持续激活可以诱发抑郁症的发生，这可以解释为何抑郁行为更多地存在于低地位组猕猴中。

社会压力，基因和抑郁——基于猕猴的研究

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摘要：非人灵长类由于与人类在遗传学、解剖结构和生理功能上的相似性，成为研究抑郁症的理想模型。该研究通过将社会地位作为一种慢性应激，成功建立第一个成年雌性猕猴抑郁模型。将所有猕猴表现蜷缩行为的持续时间由小到大排列并分成四等份，我们将蜷缩时间大于第三四分位数的猕猴定义为抑郁组猕猴。与低地位和高地位正常组猕猴相比，抑郁组猕猴表现出更高频率和更长时间的蜷缩行为，更低频率和更短时间的自主活动行为，以及更短时间的对刺激反应的活动行为。这种抑郁行为更多地表现于低地位组猕猴中，社会地位和猕猴蜷缩行为的发起频率和持续时间存在明显的负相关，与对刺激反应的活动行为的发起频率和持续时间则存在明显的正相关。除此之外，抑郁组猕猴还表现出比低地位正常组猕猴和高地位正常组猕猴更高浓度的毛发可的松，以及全脑局部脑血流的降低。

五羟色胺(5-HT)是体内重要的神经递质，在调节情绪方面起着不可替代的作用。猕猴 5-HTT 基因在其转录起始位点上游大约 1kb 处有一个多态性重复序列(rh-5HTTLPR)，S 型等位基因表现低转录活性，携带 S 型等位基因的个体，其 5-HT 回吸收能力低，而 L 型等位基因则表现出高转录活性，快速重吸收 5-HT，提高 5-HT 的循环效率。我们第一次发现 S 等位基因携带者与抑郁症的发生有较强的正相关，尤其是在携带者暴露更多的应激事件时。我们通过研究猕猴 rh-5HTTLPR 和环境对其蜷缩行为的交互影响，第一次发现携带 SS 基因型的猕猴在经历更多应激事件时（包括受到的攻击和表现的屈服）表现出比其它基因型(LL 和 LS)猕猴更长持续时间的蜷缩行为。

Metabotyping: an essential aspect of molecular phenotyping

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Abstract: Metabolism represents all (bio)chemical changes in biological processes and is the basic feature of living systems. Analysis of the metabolite composition (metabonome) is thus an essential aspects of molecular phenotyping. In fact metabolic analysis has been an important way to understand the molecular aspects of biological activities ever since metabolites were recognized. As a branch of science concerned with the metabolite compliment of biological systems and its dynamic responses to the changes of both endogenous and exogenous factors, metabonomics has shown rapid development in methodologies and found widespread applications in fundamental biological, environmental and biomedical sciences. Metabonomics involves comprehensive analysis of metabolite composition in biofluids, tissues and whole organisms with metabonomic complexity on one hand and demands for acquisition of quantitative information in situ on the other. It is thus obvious that the development and optimization of novel methods remain to be the essential requirements for further progress of metabonomics. The combined NMR-MS analysis and the integration of metabonome and other biological information (such as proteome, transcriptome and microbiome) have become the most effective ways to achieve holistic understandings of the molecular mechanistic aspects of biological systems and pathophysiology. In this report, we will report some of recent progresses in the combined LC-MS/NMR metabonomic analytical methods and integrated metabonome-transcriptome metobotypic alterations induced by various exposomic stresses. We will discuss the future development in metabotyping with the usefulness and effectiveness of integrated metabonomic analysis particularly reflected in this presentation.

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A panel of monoclonal antibodies for tree shrew regulatory T cells

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Abstract: Regulatory T (Treg) cells are now generally recognized to play a pivotal role in immune functions and diseases. However, no antibodies are available for studies in tree shrews. We have first cloned the full-length coding genes for the surface markers and functional molecules of tree shrew Tregs [CD3 (ε chain), CD4, CD25, CD127, CTLA-4 and PD-1] and then successfully generated a full panel of monoclonal antibodies against them. Optimal clones showed high binding affinity specific to their perspective molecules and performed well for analysis by flow cytometry (FACS) on un-stimulated and stimulated peripheral blood mononuclear cells (PBMCs) of tree shrews. Monoclonal antibodies for intracellular staining of β-actin and Foxp3 were also identified. This panel of monoclonal antibodies, in conjunction with other marker genes and functional molecules we have cloned for B, NK and NKT cells, provides invaluable basic tools for studies of immune cells in tree shrews and their roles in disease models.

Key words: Tree shrew; Regulatory T cells; Monoclonal antibodies

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Basic physiological indexes in domesticated tree shrews

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Abstract: Tree shrew model affords an important mean of investigating the etiology and pathology mechanism of human disease. However, the basic physiological indexes of tree shrew have not been systematically detected before. Here we measured some basic physiological indexes including basic metabolism, circadian rhythm and stress related hormone level in domesticated male tree shrews (*Tupaia belangeri chinensis*). In the basic metabolism measurement, body weight, 24 hour diet and daily urinary volume were tested once per day. The result showed that daily urinary volume is dependent on the food moisture content. Blood glucose and oral glucose tolerance (OGTT) were measured. Animals were fasted with free access to water for 12 hours before experiment. Then the fasting blood glucose (FBG) and 1 hour postprandial blood glucose (PBG) after feeding were tested from tail pointed blood of tree shrews. Furthermore, the tree shrews or Sprague-Dawley rats were given glucose/saline by intragastric administration (i.g.) after 0 point test in OGTT. The blood glucose was tested at 30min, 60 min, 90 min, 120 min and 360 min after i.g. Compared with rats, tree shrews were more sensitive to sucrose. It would be a good model animal to investigate etiology and pathophysiology of diabetes in future. Moreover, the result of sugar preference test showed that tree shrew liked the 5% sugar concentration best. We also measured the systolic and diastolic pressure, heart rate and core body temperature by telemetric monitoring in freely moving tree shrews. In the circadian rhythm measurement, we videotaped and analyzed locomotors from 8:00 to 20:00 by Noldus EthoVision XT Version 8.0 video tracking system. The result indicated that the activity peak period in tree shrews that fed in the lab was only from 17:30 to 19:30 to adapt the laboratory environment. The stress related hormones were also tested. 12 hours urine samples at every hour from 08:00 to 20:00 were collected and kept at -20℃ to test the urine cortisol rhythm. It was measured with an Iodine [125I] cortisol radioimmunoassay kit and γ radio-immunity counter. The result showed that there were two peaks at 8:00 and 17:00 respectively, which was matched with activity peak in the wild. It demonstrated that the behavior of domesticated tree shrews changed with environment but not endocrine. Serum testosterone (T), estradiol (E2), cortisol, norepinephrine (NE), adrenocorticotrophic hormone (ACTH) and corticotrophin releasing hormone (CRH) were detected by Enzyme-Linked Immuno Sorbent Assay (ELISA). Compared with rat and macaque, the stress related hormone of tree shrew and macaque are cortisol but corticosterone in rat. Circadian rhythm habit of tree shrew and macaque are diurnal, but rat is nocturnal animal. These results demonstrate that tree shrew is more closed to non-human primate, and the animal model of tree shrew is better than rodents' especially stress related model animal.

Key words: Domestication tree shrew; Physiological indexes; Basic metabolism; Circadian rhythm; Stress

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Fine motor model of tree shrew: a new animal model to evaluate movement disorder

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Abstract: The aetiology and precise biological mechanisms that underlie movement disorders are still poorly understood. Rodents and non-human primates are the main animal models of these diseases such as Huntington's, Parkinson's and Amyotrophic Lateral Sclerosis. However, walking task on rodents is not exact enough to be a prophase testing means of movement disorders. Although primates are most close to humans, higher cost and ever-increasing restrictions to the use of these animals for research limit the application of the non-human primate model. Evolutionary genetic studies have provided strong evidence supporting that tree shrew is one of a sister to primate. Agile movement and grasp things with manus are the characteristics of tree shrews, which make we turn our attention to the tree shrew to develop a non-primate animal model of movement disorders. In this study, we use these features to establish a fine motor model on tree shrews. 40 pieces of candy (0.2 g, red and green) were put in a 16×5 centrifuge tube shelf at regular intervals as the detector of digital exercise of tree shrews. There were two phases in the paradigm. Training phase (16:00-17:30), tree shrews were practiced to pick small sweets up from holes which limited only to use forepaw. Test phase (9:30-11:00 next day), tree shrews were tested the ability of grasp small sweets by fasted overnight to enhance feeding motivation. The successful rate (eaten number/caught number) was recorded. The results showed that tree shrew could learn to grasp small sweets from holes with manus in one day, and prefer green to red sweets. It suggests that tree shrews have color discrimination ability and strong learning ability. The fine motor model of tree shrew will be an ideal animal model to evaluate and investigate the pathogenesis of movement disorders.

Key words: Fine motor; Movement disorders; Tree shrew; Animal model

树鼩模型在中医药研究中的应用

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摘要：中医理论以整体观和辨证论治为核心，病证结合动物模型最大程度上符合了中医药理论对疾病和证候的认识，但目前利用啮齿类动物获得与临床模拟度较高的病证结合动物模型十分困难。2007 年始，本团队探索将与人类有更高相似度的非人灵长类动物树鼩引入中医药病证结合动物模型中，探索出适宜树鼩居住的环境温度、湿度、光照时间、噪音及通风等条件，制定了规范化的卫生管理标准，自制了诱捕、固定树鼩的固定筒及树鼩开口器，确定了注射操作角度、深度及针感，灌胃管型号、操作角度等注意事项，建立了北方地区长期人工培育树鼩的饲养管理方法和实验操作技术；通过对树鼩表皮扫描的结果，计算出树鼩 Meeh-Rubner 氏公式 K 值为 7.0，树鼩与人的等效剂量换算系数为 5.1，以及树鼩与各常用实验动物的等效剂量换算系数；通过自制“回”形迷宫对树鼩进行训练，探索评价了树鼩认知能力的训练时间、达标次数等指标的基准值；通过检测体温下降、睁眼不能、运动不能，并观察宏观体征，采集树鼩的抑郁症状，初步建立了树鼩抑郁症模型宏观体征评分量表，评分结果体现出分数梯度；体温改变和宏观体征评分是可用于评价该模型的指标。

关键词：树鼩；病证结合动物模型；等效剂量换算系数；抑郁症；评价指标

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Anti-parkinsonian effects of LK001 in 1-methyl-4-phenyl-1, 2, 3, 6 tetrahydropyridine-treated monkeys

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Abstract: To investigate the neuroprotective effects of LK001 in a nonhuman primate model of Parkinson's disease induced by 1-Methyl-4-phenyl-1,2,3,6 tetrahydropyridine (MPTP), 16 female cynomolgus monkeys (middle age) were randomly divided into 4 groups: Control, LK001 only (40mg/kg), Model (MPTP only), MPTP+LK001 (40mg/kg). The MPTP only monkeys were administrated with 0.2mg/kg MPTP (i.v., once per day) until parkinsonian clinical score of the animals reached the certain level. After given LK001 for 12 weeks, behavioral test (parkinsonian clinical score and viewpoint analysis), tyrosine hydroxylase (TH) immunohistochemistry staining and HPLC for dopamine (DA) and its metabolites were used for analysis the efficacy of the testing article. The result from the present study indicated that oral administration of LK001 significantly improved the parkinsonian clinical score in MPTP-treated monkeys ($P<0.01$). Comparing with MPTP only group, there were more TH-positive neurons in the substantia nigra ($P<0.01$) in the LK001 treatment group. In addition, MPTP treatment remarkably reduced levels of DA and its metabolites in striatum in MPTP only group ($P<0.001$). However, there was no significance between LK001 treatment and MPTP only group due to the sample size. Since all animals showed well tolerated this drug, LK001 could be considered as a potential candidate agent for treatment of Parkinson's disease.

Key words: LK001; Neuroprotective effect; MPTP; Cynomolgus monkey; Substantia nigra

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树鼩 BMSC 和 HSC 联合移植促进脊髓损伤树鼩后肢运动功能恢复

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摘要：树鼩脊髓损伤模型建立及干细胞移植研究可为人类干细胞移植治疗脊髓损伤提供前期资料，具有重要的科学意义和现实价值。本室在建立树鼩神经干细胞（NSC）、骨髓基质干细胞（BMSC）、嗅髓鞘细胞（OEC）、造血干细胞（HSC）培养方法的基础上，应用这些干细胞及其组合方案移植治疗树鼩脊髓损伤。先将树鼩进行 T7 和 T10 脊髓左、右横断，再分别将 NSC、HSC、BMSC、OEC 及 BMSC+HSC 移植入损伤脊髓。每组 5 只动物，术后不同时间点（1、3、5、7、9、11、14d）用 BBB 评分评价树鼩后肢运动功能改进情况；显微镜下观察移植细胞在脊髓存活、迁移及分化。结果　不同时间点 BBB 评分显示，各单细胞移植组在观察时间点均没有明显增加 BBB 分值，即单纯干细胞移植未明显改善脊髓损伤树鼩后肢运动功能。比较之，BMSC+HSC 联合移植组 BBB 评分自第 11 天起与单纯脊髓损伤组比较明显增加，差异有统计学意义（$P<0.05$），说明联合移植有效。显微镜观察发现各种移植干细胞能在脊髓存活、迁移并有少量细胞分化为神经元及胶质细胞（GFAP+）。结论 BMSC 和 HSC 联合移植明显促进树鼩脊髓损伤大鼠后肢运动功能恢复。结果证明低等灵长类干细胞移植应用脊髓损伤治疗有一定可行性。

关键词：树鼩；干细胞；联合移植；脊髓损伤

Attempts to establish a persistent HBV infection model in adult tree shrews (*Tupaia belangeri*) by adopting strategies using immunosuppressive drugs and their cocktails

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Abstract: Background Tree shrews are squirrel-like mammals which are close to primates in evolution. Compelling evidence suggests that they are susceptible to HBV infection but currently the lack of a persistent infection model for practical and routine use in HBV research demands major technical breakthroughs.

Methods We have chosen several immunosuppressive drugs in clinical use for organ transplantations and administrated to dozens of adult tree shrews. Dexamethasone was injected im and AZA (azathioprine) and FK506 (tacrlimus) were fed orally, each alone or in combination for two weeks. Then HBV-producing cells (HepG2.2.15) were inoculated ip and the drug treatment was continued for two more weeks. Treated tree shrews were examined every day for ascites. Serum was sampled once a week for HBV viral load detection by real-time PCR. Other serological markers of HBV infection were monitored by enzyme-linked immunosorbent assays simultaneously.

Results Severe intestinal tympanites and urinary retention were observed after dexamethasone treatment but no signs for ascites production as indication of Hep2.2.15 survival and growth. Weak positive of HBV viral load were detected in the first week after inoculation of virus-producing cells. However, viral loads diminished to undetectable level in following weeks accompanied with strongly positive of antibodies against HBsAg (anti-HBs), HBcAg (anti-HBc) and HBeAg (anti-HBe).

Conclusions Tree shrews were transiently infected by HBV in the current settings but the virus was cleared rapidly by the immune system. Further optimization of the choice of drugs and their dosage is needed. Novel strategies are also being tested for the possibility and effectiveness of using alternative agents to induce immunosuppressive regulatory T and B cells and immunotolerogenic dendritic cells in adult tree shrews in vivo.

Key words Tree shrew; immunosuppressive; drug cocktail; persistent HBV infection

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Relationships between body weight, fasting blood glucose, sex, and age in tree shrews (*Tupaia belangeri chinensis*)

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Abstract: The tree shrew (*Tupaia belangeri chinensis*) is a squirrel-like lower primate or a relative of primate commonly used as an animal model in biomedical research. Despite more than three decades of usage in research, the clear relationships between body weight, fasting blood glucose, sex, and age among tree shrews remains unclear. Based on an investigation of 992 tree shrews (454 males and 538 females) aged between 4 mons and 4 yrs old,, we found that male tree shrews have significantly higher body weight and fasting blood glucose than female tree shrews (P<0.001). The concentration of fasting blood glucose slightly increases with body weight in males (r=0.152, P<0.001). Meanwhile, in female, the body weight, concentration of fasting blood glucose, and waist circumstance positively increase with age (P<0.001). Additionally, 17 tree shrews with Lee index above 290 had significantly higher body weight, waist circumstance, and HbA1c than non-obese tree shrews with a Lee index score below 290 (P<0.001). Interesting, 6 out of 992 tree shrews (3 males and 3 females, 2 to 4 yrs old) displayed impaired plasma triglycerides (TG), glycated hemoglobin HbA1c, low-density lipoprotein (LDL), and oral glucose tolerance test (OGTT), suggestive of the early symptoms of metabolic syndrome. This study provides the first clear relationships between body weight, fasting blood glucose, sex, and age in tree shrews, furthering improving our understanding of this relationship in metabolic syndrome (MetS), which given their similarity to humans and non-human primates, makes them a potential model.in the research of MetS.

Key words: Tree shrew (*Tupaia belangeri chinensis*); body weight; fasting blood glucose; sex; age, relationship

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Cloning and characteristics of Stearoyl-CoA desaturase genes in tree shrew *(Tupaia belangeri chinensis*)

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Abstract: Stearoyl-CoA desaturase (SCD) is an integral membrane protein of the endoplasmic reticulum (ER) that catalyzes the formation of monounsaturated fatty acids from saturated fatty acids at the delta-9 position. These monounsaturated fatty acids are the key components of triglycerides and membrane phospholipids, cholesterol and wax esters. On the other hand, Imbalance of the ratio of unsaturated fatty acids to saturated fatty acids is often associated with diseases like diabetes, cardiovascular diseases, fatty liver and cancers etc. Multiple SCD isoforms are well characterized in rodents, especially in mice with four characterized isoforms. In humans and other primates, two SCD isoforms have been described: scd1 and scd5. Tree shrew (*Tupaia belangeri chinensis*) is a new type of animal model to study human diseases, however, the number of SCD isoforms, their expression patterns and biological functions in tree shrews are still unknown. In this study, we cloned the SCD genes in tree shrew, and determined their tissue specific expression and biological functions. Our results revealed that there are two SCD isoforms in tree shrew: scd1 and scd5. scd1 expressed ubiquitous and highly expressed in muscle, liver and kidney, whereas scd5 mainly expressed in brain. The cDNA sequences of scd1 and scd5 in tree shrew were in lengths of 1080 bp and 990bp. The sequence alignment revealed that the sequence homology of SCD genes in tree shrew with humans were up to 86.7% in scd1 and 99.3% in scd5. The three histidine motifs and four transmembrane hydrophobic domains detected in other mammals were also found in SCD genes of tree shrews. The phylogenetic analysis based on SCD genes suggested that a gene duplication event occurred in SCD genes in early vertebrate evolution, and revealed that tree shrew has a close relationship with primates. Additionally, transformation of both tree shrew isoforms to yeast ole1 mutant revealed both SCD genes had similar delta-9 desaturase activity.

Key words: Stearoyl-CoA desaturase; Tree shrew; Cloning; Characteristics

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Characterization of spontaneous and medroxyprogesterone acetate-accelerated 7, 12-dimethylbenz(a)anthracene-induced mammary tumors in tree shrews (*Tupaia belangeri chinenesis*)

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Abstract: A suitable animal model is essential for discovering novel preventive and therapeutic approaches to curing the breast cancer. Tree shrews (*Tupaia Belangeri Chinensis*) have a closer evolutionary relation with human being compared to rodents and have been successful used to establish animal models for hepatocellular carcinomas and pulmonary adenocarcinomas. Despite the first spontaneous breast cancer was observed as early as 1966, there is no following reports about the tree shrew breast cancer. A high frequency of spontaneous breast tumors of tree shrews were observed in tree threw populations, indicating that tree shrews may be suitable for establishing breast cancer models. We analyzed four spontaneous breast tumors by the H&E and immunohistochemistry staining (IHC). Three spontaneous tumors are intraductal papillary carcinomas and one is invasive duct carcinoma with lung metastasis. We further established the experimental breast cancer model of tree shrews using carcinogenes. 7, 12-dimethylbenz(a)anthracene (DMBA), a chemical carcinogen selectively induced mammary tumor in rodents, was chosen to induce mammary tumor in tree shrews. Medroxyprogesterone acetate (MPA), a derivation of progestin, was shown to accelerate the development of DMBA-induced mammary tumors.

Forty virgin tree shrews were chosen and divided into three groups. Group 1 and group 2, with fifteen tree shrews respectively, were intragastric administration with a dose of 20 mg per animal of DMBA in peanut oil. The residual ten tree shrews in group 3 received only peanut oil as the control. DMBA treatment was repeated for three times every 3 weeks. After that, tree shrews in group 1 were anesthetized and implanted s.c. in the dorsal area with 90 day-release MPA. MPA was replaced for twice at an interval of three months. The observation of tumor incidence lasted for 45 weeks. The first appearance of the palpable tumor was observed in tree shrew #11 at 25-week after the first DMBA treatment. Then three other tumors were identified in tree shrews #7, 12, and 30. Administration of MPA elevated the tumor incidence (20%) compared with the DMBA alone (6.7%). No tumors were identified in the control group. Three tumors (#11, 12, and 30) were identified as intraductal papillary carcinomas and one (#7) was invasive duct carcinoma. IHC showed that all tumors are PR positive but HER-2 negative. The Ki-67 was highly expressed in all tumors. These findings suggest that DMBA can induce breast tumor at a low frequency in tree shrews and MPA can accelerate the tumor incidence initiated by DMBA.

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目前的癌症动物模型绝大部分是用小鼠和大鼠模型。少数用狗等大动物自发肿瘤模型。癌症的灵长类动物模型还没有建立。由于灵长类动物与人高度类似，我们将探索建立灵长类树鼩以及猕猴肿瘤模型。我们将采用慢病毒表达癌基因以及抑制肿瘤抑制基因的方法建立可靠的灵长类肿瘤模型，并进一步开发和评价肿瘤预防和治疗新方法。

Neurodegeneration study: from molecules to big animal models

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Abstract: Appropriate connections or interactions among different neural cell types are essential for the correct and efficient functioning of the nervous system during development and regeneration after trauma or degeneration. The aim of my research is to understand the molecular events that mediate communication among neural cells, in the nervous system during development, myelination, learning and memory, degeneration, and regeneration. These studies have yielded insights into the therapeutic potential of cell signalling molecules to ameliorate or even ablate the detrimental consequences of nervous system injury and neurodegenerative diseases, including stroke, traumatic brain injury, spinal cord injury, Alzheimer Disease (AD), and Multiple Sclerosis (MS).

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树鼩呼肠孤病毒的分离鉴定

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摘要：致病性病毒严重危害树鼩的生存和健康，有关树鼩自然感染病毒情况鲜见报道。采集6份因腹泻死亡的野生树鼩粪便，用Vero细胞进行病毒分离，72h后细胞发生病变，特征为颗粒增多，破碎，变圆固缩，拉网，脱落；电镜观察显示该病毒为球形，双层衣壳，完整直径75nm左右；纯化的病毒经核酸PAGE电泳，呈现出10个核酸节段，并为典型的3:3:4排列；经哺乳动物呼肠孤病毒（Mammalian Orthoreovirus，MRV ）L1基因保守区RT-PCR检测、序列分析、进化树构建，结果表明，该病毒株属于 MRV, 且与蝙蝠，猪和人的呼肠孤病毒同源性较高。MRV是人兽共传染病毒，我们首次从树鼩体内成功分离到的MRV，为实验树鼩微生物学检测，及有效预防该病毒在树鼩与人类之间传播提供了实验依据。

关键词：树鼩；呼肠孤病毒；分离；鉴定

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STING, a surrogate of MAVS, positively regulates MDA5 mediated antiviral response in Chinese tree shrews

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Abstract: Tree shrew (*Tupaia belangeri*) is currently placed in Order Scandentia and has a wide distribution in Southeast Asia and Southwest China. Due to its unique characteristics, such as small body size, high brain-to-body mass ratio, short reproductive cycle and life span, and low-cost of maintenance, tree shrew has been proposed to be an alternative experimental animal to primates in biomedical research. Tree shrews have been used in creating animal models for hepatitis B virus and hepatitis C virus infection, but it is difficult to form persistent infection of tree shrews. Recognition of pathogens is mainly mediated by the pattern recognition receptors (PRRs), including Toll-like receptors (TLRs), RIG-I-like receptors (RLRs) and NOD-like receptors (NLRs), which trigger signal cascades to production of type I interferon (IFN) that is thought to be crucial for antiviral infection. Here we characterized key genes of the MAVS signal pathway in Chinese tree shrews. We found that: i) LGP2 is a positive regulator of MAVS signal pathway. ii) Virus infection induces IFN-β activation in an unknown pathway that is associated with STING instead of MAVS pathway. These results implied a novel antiviral pathway exists in tree shrews.

Key words: Chinese tree shrews, RLR, MAVS, STING, LGP2

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颈内动脉注射 MPTP 诱导偏侧恒河猴帕金森病模型及其在体评价

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摘要：目的 对手术临时夹闭颈外动脉经颈总动脉穿刺注射 MPTP 制备的偏侧猴帕金森病(Parkinson's disease , PD) 模型的稳定性进行评估,并探讨其评价体系。

方法 健康恒河猴 4 只行夹闭颈外动脉经右侧颈总动脉注射 MPTP,术后应用 Noldus 软件定期行为学观察和评估,包括运动障碍评分、阿扑吗啡诱发旋转实验；术后 6 个月进行 PET、SPECT 影像学检查；免疫组织化学染色观察黑质酪氨酸氢化酶(tyrosine hydroxylase , TH)阳性神经元。

结果 夹闭颈外动脉颈总动脉注药法均一次建模成功。行为学观察可见猴的自主运动明显减少，阿扑吗啡(apomorphine, APO) 试验可诱发出向健侧旋转行为。MPTP 注射侧多巴胺转运蛋白密度及葡萄糖代谢率低于对侧。病理检查可见损毁侧黑质内 TH 阳性细胞较对侧明显减少。结论　颈外动脉夹闭颈总动脉注药法能够建立满意的偏侧猴 PD 模型。应用 Noldus 软件进行运动障碍定量分析、SPECT 在体检测多巴胺转运蛋白，以及黑质多巴胺能神经元病理变化是评定灵长类帕金森病动物模型的重要量化指标。

关键词： 帕金森病；恒河猴；MPTP；多巴胺转运蛋白；颈内动脉注射

The development of laboratory primates in China

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Abstract: The kinship of nonhuman primates and human is closest. As a extremely valuable experimental animal. Primate resources worldwide and presents a unbalanced distribution, and therefore for the need of scientific research and technological strategic resource reserves, the developed countries to establish a research and production of many experimental primate breeding center. The Primate of China is one of minority richest countries in the world, more than 200 species of primates in the world and china existing distribution 4 families, 7 genera and 23 species of 39 subspecies. Currently, China has become largest primate research resources supplying countries in the world, China has long been the world's primate laboratory animals industries has been playing the role of the "inexpensive raw material suppliers, Artificial domestication and breeding of primates resources is single, less types of artificial domestication and breeding of primates, some commonly used primate resources research even still blank, with the rapid development of the field of biomedicine, nonhuman primates as a strategic resource paid more and more attention in the United States, Japan, Europe and other developed countries,. In order to protect our own resources to meet the needs of the national level of the primate, it is necessary to attach importance to the building of primate resources, integrate our existing common primate resources, to achieve the level of germplasm resource of resource preservation. and introduce alien species of foreign commonly used but domestic shortage, to accomplish the experimental primates resources strategic reserve, Relying on domestic Primate Resource Center has been established, and the establishment of several around the state science and technology strategic planning and regional characteristics of the National Primate Research Center, and accelerate the primate research and technical back-up personnel training with the reserves. Break through the bottleneck of the development of the industry, to improve competitiveness and to better serve the technology, and the benefit of mankind

Key words: primates; resources; development; strategy

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委员会委员。中国实验动物学报第二届编辑委员会编委，实验动物与比较医学第四届编辑委员会编委国家自然科学基金委员会第十四届生命科学部动物学评审专家。主持国家科技基础平台建设项目 1 项、重大传染病分题 8 项、国家自然基金面上项目 1 项、国家自然科学基金重点项目 1 项，军队新药创制重大课题 1 项，国际合作课题 1 项。近两年发表学术论文 31 篇，其中 SCI 收录 7 篇，通讯作者 9 篇，编写专著 8 部。先后获科技奖 6 项，其中全军科技进步三等奖 3 项（排名第 1，2，3 各 1 项），四等奖 1 项（排名第 1）。培养硕士研究生 5 名，博士研究生 2 名。

Evidence of bimodality of plasma glucose distributions in Cynomolgus Macaque

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Abstract: Type 2 diabetes mellitus (T2D) animal models are of importance in understanding the pathogenesis and in developing potential therapeutic agents for this disease. Old World nonhuman primates (NHPs), especially cynomolgus macaques, can be a valuable animal model of T2D because they have the biological and genetic similarities to humans and the disease is also common in older, obese populations. However the criteria for diagnosis of T2D in NHPs still remain obscure. In this study, we present the fasting plasma glucose (FPG) distribution study of 190 cynomolgus macaques, age 9~18 year old, utilizing the statistic method of bimodality for providing some insights in developing diagnostic criteria for cynomolgus macaques. The results of this study demonstrate that the distribution of plasma glucose level of c. macaques is very comparable to the early findings in humans in the studies by others. The bimodality found in the FPG distributions also provides a reference value that can be used to separate individual c. macaques into normal or abnormal glycemia in diagnosis criteria of T2D models.

中国猕猴与人类表达上皮细胞连接分子和粘蛋白的比较研究

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摘要：上皮细胞连接分子和粘蛋白构成了胃肠粘膜屏障的重要成分，粘膜屏障的破坏和多种疾病如胃炎、胃溃疡、胃癌等有密切关系。关于人体组织细胞连接和粘蛋白的研究很多，而对于这些分子在非人灵长类动物的表达研究尚属罕见。在本研究中，我们应用免疫组化方法检测了上皮连接分子（紧密连接分子 Symplekin 和 ZO-1；附着连接分子 α-catenin、β-catenin、γ-catenin； 桥粒连接分子，DSG2）和粘蛋白（MUC1 和 MUC2）在猕猴胃肠组织的表达，并与人体组织进行比较。Symplekin 在猕猴胃肠上皮的细胞核与淋巴细胞染色，ZO-1、α-catenin、β-catenin、γ-catenin 和 DSG2 在表面上皮和腺上皮的细胞膜染色。经过高碘酸盐氧化作用后，MUC1 可在上皮细胞胞膜检测到。MUC2 定位于上皮细胞的胞膜和胞浆。本研究证实猕猴胃肠组织表达这些上皮连接分子和粘蛋白，与人体组织相似。这表明对于研究人类粘膜屏障和相关疾病，猕猴是合适的实验动物模型。

关键词：猕猴；细胞连接；粘蛋白；胃肠上皮

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The establishment of tree shrew model of non-alcoholic fatty liver disease

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Abstract: Non-alcoholic fatty liver disease (NAFLD), a severe liver disease that ranges from simple hepatic steatosis to hepatocellular carcinoma, is now worldwide threatening people health mainly resulted from excessive intake of high fat diet as well as decreased exercise in work and life. Animal models are necessary to explore the pathogenesis and therapies of human NAFLD. Tree shrew (*Tupaia belangeri chinensis*), a relative of primates or a lower primate, has been used in biomedical research for more than three decades. However, it is unknown whether tree shrew could be used as a new animal model of human NAFLD. In this study, high fat diet was used to induce NAFLD in tree shrew. We found that the levels of aspartate aminotransferase (AST) and alanine aminotransferase (ALT), two indexes related to liver injury, were significantly increased in high fat diet (HFD) fed animals than in normal diet (Control) fed animals after 10 weeks induction.. In addition, the levels of plasma triacylglycerols and cholesterol were also significantly increased in HFD animals. The liver tissue sections indicated by Hematein & Eosin staining showed severe steatosis with a large amount of fat accumulation in HFD animals Furthermore, we are investigating the pathogenesis of tree shrew NAFLD compared with human NAFLD. In conclusion, we successfully established the tree shrew model of NAFLD via high fat diet induction. This work demonstrated that tree shrew is a new animal model for research of NAFLD.

Key words: Non-alcoholic fatty liver disease NAFLD; tree shrew (*Tupaia belangeri chinensis*); animal model

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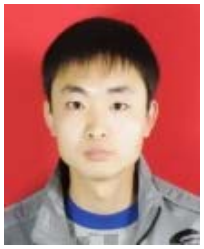

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Molecular characterization, balancing selection, and genomic organization of the tree shrew (*Tupaia belangeri*) MHC class I gene

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Abstract: The major histocompatibility complex (MHC) class I genes play a pivotal role in the adaptive immune response among vertebrates. Accordingly, in numerous mammals the genomic structure and molecular characterization of MHC class I genes have been thoroughly investigated. To date, however, little is known about these genes in tree shrews, an increasingly popular animal model. To address this issue, we analyzed the structure and characteristic of the tree shrew MHC class I genes (Tube-MHC I) and performed a comparative gene analysis of the tree shrew and other species. We found the full-length cDNA sequence of the tree shrew MHC class I was 1074bp in length. The deduced peptide is composed of 357 amino acids containing a leader peptide, an α1 and α2 domain, an α3 domain, a transmembrane domain and a cytoplasmic domain, with the percentage of identity between the tree shrew and other mammalian species ranging from 57% to 79%, and 77.5% with humans. Among these peptides, the cysteines, CD8+ interaction and N-glycosylation sites are all well conserved. Furthermore, the genomic sequence of the tree shrew MHC class I gene was identified to be 3,180 bp in length, containing 8 exons and 7 introns. In 21 MHC class I sequences, we conducted an extensive study of nucleotide substitutions. The results indicated that in the peptide binding region (PBR) the rate of non-synonymous substitutions (dN) to synonymous substitutions (dS) was great than 1, suggesting balancing selection at the PBR. These findings provide valuable contributions in furthering our understanding of the structure, molecular polymorphism, and function of the MHC class I genes in tree shrews.

Key words: *Tupaia belangeri*; Tree shrew; Allele; Splice variant; Haplotype

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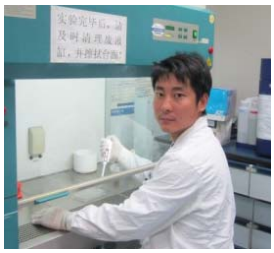

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Transcriptome-wide analysis of disease pathways and the immune gene repertoire of the Chinese tree shrew (*Tupaia belangeri chinensis*)

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Abstract: Chinese tree shrew (*Tupaia belangeri chinensis*) embraces many distinctive features for a good experimental animal model. It's genome has been sequenced and will be in public soon. But, the genomic information is insufficient for further study. We generated a large and comprehensive transcriptome with 61,583 coding protein transcripts, including 38,094 sequences annotated with KEGG pathways. 4.16% of the transcripts were identified in human disease pathways and 6.07% of the transcripts are involved in cancer and cancer pathways. Moreover, 5.25% of the transcripts are closely annotated in virus and bacteria infection pathways, in which 624 transcripts are related to HTLV-I infection. In addition, 190 prostate cancer related transcripts were identified, and specific mutations were found in related oncogenes and tumor suppressors. The analysis of immune related transcripts revealed a complex repertoire of innate immune system and adaptive immune system, including 1,784 recognition receptors and downstream members. We identified 115 interleukins/interleukin receptors, in which interleukin-16 and interleukin-17 receptors are most prominent. Only 9 out of 20 NLRs with 22 transcripts were identified in the transcriptome, indicating 11 other NLRs were lowly expressed. This data are useful in comprehensive disease pathway-focused association analysis and experimental disease model construction.

Key words: Tree shrew; transcriptome; disease pathway; innate immune system; adaptive immune system

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树鼩抑郁症病证结合动物模型评价指标的建立

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摘要：中医理论以整体观和辨证论治为核心，病证结合动物模型最大程度上符合了中医药理论对疾病和证候的认识，但目前利用啮齿类动物获得与临床模拟度较高的病证结合动物模型十分困难。本团队探索将与人类有更高相似度的非人灵长类动物树鼩引入中医药病证结合动物模型中，探索出适宜树鼩居住的环境温度、湿度、光照时间、噪音及通风等条件，制定了规范化的卫生管理标准，自制了诱捕、固定树鼩的固定筒及树鼩开口器，确定了注射操作角度、深度及针感，灌胃管型号、操作角度等注意事项，建立了北方地区长期人工培育树鼩的饲养管理方法和实验操作技术；通过对树鼩表皮扫描的结果，计算出树鼩 Meeh-Rubner 氏公式 K 值为 7.0，树鼩与人的等效剂量换算系数为 5.1，以及树鼩与各常用实验动物的等效剂量换算系数；通过自制“回”形迷宫对树鼩进行训练，探索评价了树鼩认知能力的训练时间、达标次数等指标的基准值；通过检测体温下降、睁眼不能、运动不能，并观察宏观体征，采集树鼩的抑郁症状，初步建立了树鼩抑郁症模型宏观体征评分量表，评分结果体现出分数梯度；体温改变和宏观体征评分是可用于评价该模型的指标。

关键词：树鼩；病证结合动物模型；等效剂量换算系数；抑郁症；评价指标

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Effects of neural stem cell transplantation in tree shrew with spinal cord injury

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Abstract: Spinal cord injury is one of the world's medical problems, while stem cell therapy could improve neurological behavior after spinal cord injury(SCI) in rats. However，the usage of stem cells derived from three threw for the treatment of the SCI awaits to be established. In this study, both left (T7) and right (T10)hemisected spinal cord injury of tree shrews were established. Neural stem cells from hippocampus of three shrews were prepared in vitro. This was followed by a intravenous transplantation into injured spinal cord of tree shrew at chronic phase (7-10 days). The cell transplantation effect indicated by BBB scores was observed on day 1, 3, 5, 7, 9, 11,14 and 28. Fate of stem cells' survival and differentiation as well as changes of spinal morphology in the spinal cord was also tested. All data were processed statistical analysis. Results: After thoracic spinal cord injury, hind limb motor function disappeared within 3 days. Subsequently, locmotor function improvement indicated by BBB score was found with the time going in SCT group. Comparatively, stem cell transplantation showed no any significant function improvement besides tissues spared in the NSC engrafted group increased than in tree threw with SCT. The present findings suggested that neural stem cell transplantation has not been effective in promoting recovery of hind limb locomotor function in tree shrews with spinal cord injury, but increases the tissues sparing. Conclusion: Transplanted neural stem cells can improve spinal cord morphology. However its effect on hind limb motor function recovery is not significant.

Key words: Neural stem cells; Transplantation; Spinal cord injury; Tree shrew

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Study on the biological characteristics in Vitro of Neural Stem Cells From Hippocampus of Tree Shrew

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Abstract: Tree shrews as lower primates between rats and monkeys has been paid attention gradually in recent years. Establishment of culture method of neural stem cells from hippocampus of tree shrew has become the foundation of biology characteristic research of neural stem cell. In this experiment, 5 pregnant tree shrews (30 days) were used; embryos were removed by cesarean section after anesthesia, and flushed under sterile conditions with PBS. The embryos' brains were taken out after craniotomy was opened, then meninges were removed so that hippocampus was exposed. The hippocampus was then incubated in 0.125% trypsin at 37 ℃ for 30 minutes. Then the digest reaction was terminated with DMEM medium with 5% serum. This was followed a centrifuge, then cells were collected then inoculated into a culture plate with 24 holes （5×105 个/mL）. The growth character of stem cells was observed on 0 hour, day 3 and 7. Part of stem cells of 7th day was fixed by smearing slice and identified by Nestin staining. The rest cultured stem cells were cultured in serum containing medium to promote their differentiation. Subsequently, the immunohistochemical SP staining with NeuN, GFAP and BMP antibody was used to observe their differentiation. Result: Under microscope, neural stem cells from hippocampus of tree shrew were round and bright, and some floating balls containing dozens of cells were visible after culturing 3 days. Then the volume and the quantity increased further. Cell spheres which displayed nestin positive by immunohistochemical staining were proved to be neural stem cells. At the same time, a small amount of neural stem cells of tree shrew could differentiate into NeuN positive cells under the cases of the serum inducing. More cells presenting GFAP and BMP positive staining proved its ability of differentiation. Conclusion: This study successfully established culture method of the neural stem cells of tree shrew, and showed hippocampal neural stem cells of tree shrew had the ability of proliferation and differentiation into neural and glial cells.

Key words: Tree shrew; Hippocampus; Neural stem cells; In vitro culture; Immunohistochemistry

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The establishment of lateral hemisection of thoracic spinal cord injury model in tree shrew and neurological behavior evaluation

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Abstract: It is increasing attractive attention for the usage of Neurological disease animal model of tree shrews into translational medicine research. While the spinal cord injury model of tree shrew awaits to be established and the method for assessment of locomotor function in hind limb need to determined. In this study, based on indication of BBB scores in rat spinal cord injury, we performed tree shrews spinal cord injury, and established the method of Neurological behavior in tree shrew. 10 adult tree shrews were divided in 2 groups, among which five were conducted T10 spinal left hemisection, and the other five conducted sham controls. BBB score of the hind limb motor behavior was observed on day 1, 3, 5, 7, 9, 11, 14, 16 postoperatively. Statistical analysis was processed. The results showed that BBB scored 0 after 1 day in the hemisection side. This was followed by a gradual increase on 3 days postoperation. Importantly, BBB scores showed an obvious increase on day 11 than seen on 3 days (the difference was statistically significant). These suggested motor functions were impaired after spinal cord injury in tree shrews, but over time there was a certain recovery, indicating the spinal cord had neural plasticity after injury. The present experiment indicated that hemisection of spinal cord injury model in tree shrew has been established successfully, and Spontaneous partial recovery of the ipsilateral hindlimb function occurred in the tree shrew with time on, which indicated the functional plasticity in the spinal cord after hemisection injury.

Key words: Spinal cord injury; Animal model; Tree shrew; Neurological behavior evaluation

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艾滋病灵长类动物模型的建立和研究

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摘要：我们发现旧大陆猴北平顶猴与鹰猴一样存在着 TRIM5α/CypA 融合基因现象，但基因融合模式和表达剪切与鹰猴不同；研究证明该融合基因不限制 HIV-1 复制是北平顶猴对 HIV-1 易感的重要分子机制。同时发现，北平顶猴 PBMC 对 HIV-1 易感，不限制 HIV-1 在 PBMC 内的复制；但可有效地限制 HIV-2 的复制，对 SIV 则只有十分微弱的限制活性；北平顶猴 npmTRIMCyp 可能识别逆转录病毒衣壳蛋白的区域存在较高的多态性。这些研究结果在细胞和分子水平上支持了北平顶猴是较理想的艾滋病模型动物，为建立基于北平顶猴的艾滋病灵长类动物模型提供了科学依据。发现熊猴也存在类似平顶猴模式的 TRIM5-CypA 基因融合现象,提示熊猴极有希望成为一种新的艾滋病模型灵长类动物。

建立了 SIV 和 SHIV 感染中国猕猴的艾滋病动物模型。研究了 DC 和 Treg 细胞在 SIVmac239 感染中国恒河猴艾滋病模型中的作用及机制。发现 pDC 分泌 IFN-α 的能力在急性感染期会显著提高，提示 SIVmac239 感染的中国恒河猴在急性感染期提高了免疫活化，从而可能加速了疾病进程。病毒感染早期 pDC 由于高表达 CD4 和 CCR5，可能成为 SIV 感染的主要靶细胞之一，其凋亡比例显著提高，而 mDC 的凋亡却没有显著变化，表明 SIV 很可能选择性地剔除 pDC。同时，pDC 的 CD4 表达随时间显著降低并与病毒载量呈负相关，pDC 的 CCR5 表达却随时间而显著升高，并与病毒载量呈正相关。在急性感染期，mDC 和 pDC 的 CD80 和 CD86 表达均与病毒载量呈正相关，显示出 DC 亚群受病毒影响而处于活化状态，从而提升了整个机体的免疫活化，可能影响艾滋病的疾病进程。发现 SIVmac239 感染恒河猴后，分布于外周血 PBMC 中的 Treg 在绝对数量和相对数量上均有上调 Treg 可以被 SIV 感染。应用建立的中国猕猴艾滋病动物模型，进行了治疗性疫苗、杀微生物剂及药物的效果评价研究。

关键词：艾滋病；灵长类动物；动物模型；SIV；SHIV；HIV

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22 项，国际专利授权 1 项。获省部级科技奖 6 项，其中 2004 年获云南省自然科学奖二等奖(排名第 1)和 2009 年获云南省科技进步奖一等奖(排名第 1)。目前正在主持和承担包括国家科技重大专项、973、863 等科研项目 20 多项。主要从事艾滋病动物模型、艾滋病免疫学和抗 HIV 药物研究。

第一届灵长类动物模型学术论坛

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