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10:20-10:40 SIV and M.tb infection of Chinese Rhesus macaques

10:40-11:00 HCV

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14:20-14:40 IMPC: understanding the gene function in vivo

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15:15-15:35 Neurodegeneration Study: From molecules to big animal models

15:35-15:55 Metabotyping is an important aspect of molecular phenotyping

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LPS-induced immune activat ion 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, *]

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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- Ď TNF- Ď 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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Microbe biodiversity in the wild tree shrew

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

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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 .-hemolytic streptococcus, -hemolytic streptococcus, -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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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

Zheng-Xi Dai[1, 2], Gao-Hong Zhang[1], Xi-He Zhang[1, 2], Hou-Jun Xia[1, 2], Shao-You Li[1, 2], Yong-Tang Zheng[1, *]

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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 2-microglobulin (2m), a nonpolymorphic light chain, and an 8-9 residue peptide. Peptide binds within a groove formed by the .1 and .2 domains of the protein, supported by the .3 domain and 2m. Before MHC class I HC/ 2m/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 .3 domain. Despite the absence of 2-microglobulin (2m), 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 2m-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 A-sv1 and MHC IA can form a novel heterodimeric complex as a result of the displacement of 2m and also illustrate the relevance of regulated MHC IA protein degradation in the 2m-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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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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SIV/TB Coinfection of Chinese Rhesus Monkey

Wen-zhe Ho

The Center for Animal Experiment and ABSL-3 Laboratory, Wuhan University, Wuhan, China

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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High-fat diet induced dyslipidemia and potential atherosclerosis

Fengai-Selena Huang, Guo-Dong Zhang, De-qiao Yi, Feng-Francis Yue, Piu Chan

Wincon Theracells Biotechnologies Co., Ltd.

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.

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

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A defensin antimicrobial pe ptide from the tree shrew, Tupaia belangeri

Ren Lai

Key Laboratory of Animal Models and Human Disease Mechanisms, Kunming Institute of Zoology, Chinese Academy of Sciences, Kunming, Yunnan 650223, China

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 -defensin 1TB. Its amino acid sequence was determined by Edman degradation, mass spectrometry analysis, and cDNA cloning. Mature -defensin 1TB contains 36 amino acid residues in length. -defensin 1TB showed maximal similarity to the -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

Wei-Dong Le

Institute of Health Sciences, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences

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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Nature Genetics Proc. Natl. Acad. Sci. USA Journal of Neuroscience Progress in Neurobiology Brain JAMA Cancer Research

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Plos One, Journal of Alzheimer's disease Autophagy Neurodegenerative Disease Drug Design Bioscience

HIV/AIDS infection in pigtailed macaques -- an overview

Ai-Hua Lei[1, 2], Wei Pang[1], Gao-Hong Zhang[1], Yong-Tang Zheng[1,*]

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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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1988 1 2006~2010 2010 HIV/AIDS

G6PD mRNA

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G6PD
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0.4867±0.0896 0.4467±0.2190 0.3617±0.2092 0.2550±0.1754
0.1897±0.1282 0.1623±0.0849 0.1330±0.0592
0.1300±0.0693 0.0922±0.0445 0.0690±0.0426 0.0591±0.0247
0.0158±0.0204 0.0109±0.0146 0.0051±0.0040 0.0048±0.0035
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* E-mail: jiaojianlin66@163.com

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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

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Tupaia belangeri chinenisis

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2 T2DM *Tupaia belangeri chinenisis*

Streptozotocin, STZ

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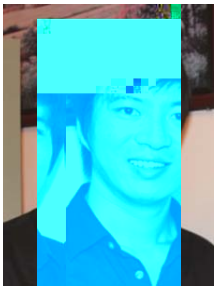

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Phylogenetic patterns of *APP*, *ADAM10*, *PSEN-1* and *BACE-1* genes in Chinese tree shrew *(Tupaia belangeri chinensis*)

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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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Yunlong Li and Yu Fan contribute equally to this work.

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International Journal of Cancer Molecular Imaging and Biology International Journal of Hematology 3 SCI

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4.12±1.3mmol/L 7.46±2.35Kg 4.41±1.72 mmol/L
7.14±2.37Kg 4.67±1.49 mmol/L
7.43±2.29Kg 4.85±1.86mmol/L
BMI≥38 / ≥0.78 84
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≥5.60 mmol/L 1.62% 14 10

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

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30-90s p=0.017
p=0.02

* Email suin@psych.ac.cn

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

Ming-Qi Qiao [1, 2, *], Qi-Tao Zhao [1, 2], Sheng Wei [1, 2], Ling Xue [2], Hui-Yun Zhang [2]

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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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Metabotyping: an essential aspect of molecular phenotyping

Hui-Ru Tang, Yu-Lan Wang

Biospectrocopy and Metabonomics Research Centre, State Key Lab Magn Reson Atom Mol Phys, Wuhan Inst Phys Math, Chinese Academy of Sciences, Wuhan 430071, PR China.

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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“Preparation and characterization of polyclonal antibody against severe acute respiratory syndrome-associated coronavirus spike protein”

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

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 ve

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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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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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Cell Metabolism PLoS ONE J. Neurosci 20

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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*)

Hou-Jun Xia[1]

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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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Born in Shanghai, China, Xiao Zhi-Cheng holds a Doctor of Natural Science Degree from Swiss Federal Institute of Technology, Zurich. He was also trained in Harbin Medical University, University of Science and Technology of China, and Beijing Medical University as a medical student and a MSc and PhD candidate. He was a postdoctoral fellow of University of California, Irvine, University of Southern California, University of Rochester in USA, McGill University in Canada, and University Hamburg in Germany. He was a Principal Investigator, Singapore General Hospital in the fall of 2000. In 2004, hw became cross-appointed, at the rank of Associate Professor, to the Institute of Molecular and Cellular Biology. In 2009, he was appointed as a Director, Dept. of Innovative Research, GlaxoSmithKline after a short stay in the University of Hong Kong as an Associate Professor. From Oct. 2010 to now, he worked as a full Professor in Monash University.

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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

# These authors contributed equally to this work

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SPECT (tyrosine hydroxylase , TH)

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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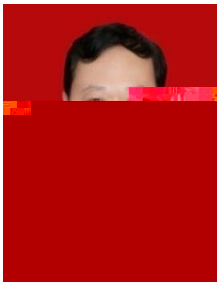

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Evidence of bimodality of plasma glucose distributions in Cynomolgus Macaque

Guo-Dong Zhang, De-Qiao Yi, Chun-Llin Zhou, Charles X Zhu, Piu Chan

Wincon Theracells Biotechnologies Co., Ltd.

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.

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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*

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

Xi-He Zhang[1, 2], Zheng-Xi Dai[1], Gao-Hong Zhang[1], Jian-Bao Han[1], Yong-Tang Zheng[1, *]

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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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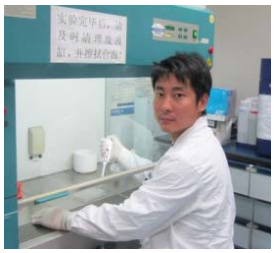

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Transcriptome-wide analysis of disease pathways and the immune gene repertoire of the Chinese tree shrew (*Tupaia belangeri chinensis*)

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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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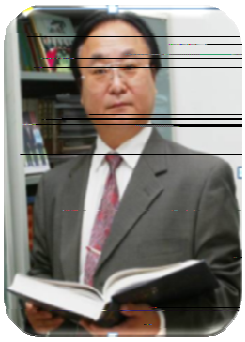

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Effects of neural stem cell transplantation in tree shrew with spinal cord injury

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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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SCI Neurobiology of Disease, Brain Research Neuroscience Letter, Acta pharmacology Sinica Neurochemical Research,

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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 /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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TRIM5α/CypA

HIV-1

HIV-1 PBMC HIV-1 HIV-1

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npmTRIMCyp

TRIM5-CypA

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SIV SHIV DC Treg SIVmac239

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SIVmac239

pDC CD4 CCR5 SIV

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CCR5 mDC pDC

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