

Twitter Thread by Anna

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@2020Gladiator



Chuan Qin, a party member of CCP, Director of the Institute of Laboratory Animal Sciences, CAMS; 1st person on finding and establishing the 1st animal model of SARS infection & also awarded the Advanced Individual Award of the United Front Work System due to the finding in 2003

The screenshot shows the official website of the Institute of Laboratory Animal Sciences (ILAS), Chinese Academy of Medical Sciences. The header features the ILAS logo and navigation links: About, Introduction, and Department. A search bar is also present. The main content area displays the profile of Qin Chuan, dated February 4, 2020, with the source cited as Pathology and pathophysiology. The profile text describes her as a female MD and researcher, Director of ILAS, and expert of special allowance by the State Council. It highlights her work in experimental pathology, development of neurodegenerative disease models, and establishment of animal models of human diseases. The text also mentions her research on disease mechanisms, drug development models, and the discipline of medical comparative medicine. A sidebar on the left lists various categories: About, Director Speech, Current Directors (selected), Organization, Academic Commi..., IACUC, Development Hist..., 30th Anniversary..., Park Style, and Position.

Qin Chuan

2020年02月04日 Source: Pathology and pathophysiology

Qin Chuan, a female MD and researcher, is the Director of the Institute of Laboratory Animal Sciences, Chinese Academy of Medical Sciences, expert of Medical Sciences and expert of special allowance by State Council. She received her doctorate in pathology and pathophysiology in 2006. She is mainly engaged in experimental pathology development, and has established a series of neurodegenerative disease models, China's largest resource bank of animal models of human diseases, Comparative Medical Technology Platform and National Platform for Animal Model of Infectious Diseases. In addition, she has been worked on the development of animal models of human diseases, the research of disease mechanism and the application of drug development models for a long time, and created the discipline of medical comparative medicine. The relevant representative research results were published in the journals of Nature Medicine, Nature Microbial, and Nature Communication, respectively. She published 283 papers as the first or corresponding author, 110 SCI papers of Nature Microbiol, Nature Med, and the like included, which were cited for 1595 times. She has obtained 10 authorized invention patents, and she was the editor-in-chief of 17 monographs and 5 textbooks, 3 industry training materials, training 81 graduate students and postdoctoral. She also led establishment of 152 standards and won 18 awards of science and technology (including the First National Innovation Top Prize, the third prize of National Prize for Progress in Science and Technology), achieving the honors of the National "March 8th" Red Banner, National Excellent Science and Technology Workers, etc.

In addition, she and her team applied a patent regarding to the animal model fo SARS infection.

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[54] 发明名称 一种 SARS 相关冠状病毒的灵长类
动物模型及其构建方法和用途

[57] 摘要

本发明涉及一种 SARS 相关冠状病毒的灵长类
动物模型，尤其是恒河猴及食蟹猴动物模型，其构
建方法以及用途。

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From the beginning of the SARS-CoV-2 pandemic, Chuan Qin published papers in journals on the application of humanized mouse model experiments in SARS-CoV-2. <https://t.co/h2tnuFfys8>
<https://t.co/7VE46nGYf2>

Something more, she invented a recombinant vaccine-SARS vaccine and shared the patent with Alan Diamond AIDS Research Center of Columbia University.

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Patent

2020年02月24日 Source:

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Number	Name of Invention	Patent Type	First Inventor	Other Inventors	Patent Number	Patentee
1	A recombinant vaccine-SARS vaccine and a preparation method	patent for invention	Qin Chuan	Wei Qiang, Gao Hong, Tu Xinming, Chen Zhiwei, Zhang linqi, Hedayi	ZL 2006 1 0003011.0	Institute of Laboratory Animal Sciences, Chinese Academy of Medical Sciences <u>Alan Diamond AIDS Research Center</u>
2	Application of Ginsenoside Rb1 used to prepare drugs for the treatment of dilated cardiomyopathy	patent for invention	Zhang Lianfeng	Zhao Haiping, Qin Chuan, Li Wan	ZL 2008 1 0116202.7	Institute of Laboratory Animal Sciences, CAMS
3	A subunit hybrid vaccine for human enterovirus 71	patent for	Qin Chuan	Zhang Lianfeng, Liu	ZL 2010 1 0105060.1	Institute of Laboratory Animal Sciences, CAMS

Not surprisingly, she engaged in the CCP's 11th Five-Year Plan, the MCF's long-term strategic plan, in 2008, and worked on the study of Laboratory Animal Technology Platform, a subset of Prevention and Control of Major Infectious Diseases such as AIDS and Viral Hepatitis Project

Due to her passion on developing #UnrestrictedBioweapon for CCP, she received RMB 15.15 million of research funding and applied for 18 domestic and international patents from the State Council and the PLA.

科研成果

近5年来，承担省部级课题60多项，国际合作课题10多项，其中在十一五期间承担"艾滋病和病毒性肝炎等重大传染病防治"科技重大专项"实验动物技术平台"课题，获得科研经费1515万元，申请国内外专利18项。

FOLLOW THE MONEY■■■■(1)

A suspected contractor of Chuan QIN team - Cyagen, a biotechnological CRO founded in Guangzhou and established several branches globally, including Santa Clara, California. Cyagen is the world's largest provider of custom-engineered mouse and rat models

A research team led by Chuan Qin at the Institute of Laboratory Animal Sciences, Chinese Academy of Medical Sciences, was the first in the world to report the establishment of a new coronavirus-infected hACE2 mouse model, which was obtained by in situ injection using an expression vector constructed from the mouse mAce2 promoter and the hACE2 gene. hACE2 transgenic mice were infected with SARS-CoV-2 virus. The hACE2 transgenic mice were infected with SARS-CoV-2 virus, which resulted in weight loss, high levels of viral load detected in the lungs, and moderate interstitial pneumonia with a large number of lymphocytes and monocytes infiltrating the alveolar interstitium and macrophage accumulation in the alveolar cavity.

三、小鼠模型在新冠病毒（SARS-CoV-2）研究中的应用进展

无论是核酸还是氨基酸序列比较分析都证实，SARS-CoV-2与SARS-CoV的相似性非常高（分别约为80%和76%），而且SARS-CoV-2也是通过细胞表面的ACE2受体与宿主发生相互作用，引起与SARS-CoV感染相似（虽然不是完全相同）的严重急性呼吸道困难综合征等临床表现。因此，上面介绍的针对SARS-CoV感染的相关小鼠模型构建策略与方法，也适合于SARS-CoV-2感染小鼠模型的建立。目前小鼠模型在新冠病毒感染研究中的最新应用研究都是由中国科学家们完成。

转基因人源化ACE2小鼠模型

中国医学科学院医学实验动物研究所秦川主导的研究团队全球首先报道建立新冠病毒感染hACE2小鼠模型，该转基因hACE2小鼠模型是应用小鼠mAce2启动子和hACE2基因构建的表达载体，通过原核注射方法获得转基因hACE2小鼠模型。hACE2转基因小鼠受到SARS-CoV-2病毒感染后，小鼠会出现了体重下降，小鼠肺部可检测到高水平的病毒载量，且病毒感染小鼠出现中度间质性肺炎，肺泡间质中大量淋巴细胞和单核细胞浸润，肺泡腔内巨噬细胞聚集等病理学特征。

另外，研究者们还首次应用该hACE2转基因小鼠对新冠病毒灭活疫苗的安全性及有效性进行了评价。实验结果表明，不同剂量和不同时间的灭活疫苗免疫hACE2小鼠，未观察到小鼠出现炎症和不良反应。检测分析灭活疫苗的免疫原性显示，小鼠体内可被诱导产生针对SARS-CoV-2的S蛋白和RBD特异性的IgG，且针对RBD特异性的IgG占S蛋白抗体反应高达50%，提示RBD是新冠病毒灭活疫苗的主要免疫原。

定点插入人源化hACE2小鼠模型

中检院实验动物资源研究所主导的研究团队首次报道成功构建定点插入hACE2-K1/NIFDC小鼠模型。该人源化小鼠构建策略是将hACE2基因定点插入小鼠mAce2基因启动子之下，并将tdTomato基因插入到hACE2基因的下游，使该人源化小鼠在内源性mAce2基因的调控下，共表达hACE2和tdTomato基因。SARS-CoV-2病毒经鼻感染青年和老年hACE2小鼠感染后，小鼠的肺、气管和脑中均出现较高的病毒载量，而在小鼠脾、肾、肝、肠和血清中没有发现病毒RNA。青年和老年hACE2小鼠均发生了间质性肺炎，表现为炎症细胞浸润、肺泡间隔增厚和明显的血管系统损伤。但未见感染小鼠死亡。分析SARS-CoV-2感染小鼠的主要靶细胞表明，Clara细胞分泌蛋白（CC10）阳性Clara细胞是SARS-CoV-2在气道中的主要靶细胞。

FOLLOW THE MONEY■■■■(2)

Not easy to find evidence on Qin's involvement in the serial passage experiments. But quite easy to find sth from their contractor. Obviously this company contracts their program of humanised rats regarding to #SARS_CoV_2 and passage experiments on rats

二、应用小鼠模型研究

SARS-CoV感染致病性有哪些策略与方法？

There are currently three types of mouse models of SARS-CoV infection depending on the strategy and method of mouse construction:

1. direct infection of inbred mice with human SARS-CoV virus;

2. application of gene editing mouse technology to knock out mouse-related genes or transfer human host cell virus-binding receptors (e.g. ACE2) into mice;

3. transfer of wild-type SARS-CoV virus in mice to undergo an iterative adaptive evolutionary process to obtain a more pathogenic mouse-adapted virus, thereby establishing a mouse model of viral infection capable of causing a distinct clinical phenotype.

根据小鼠构建策略与方法不同，目前SARS-CoV感染小鼠模型分为三种：1. 应用人SARS-CoV病毒直接感染近交系小鼠；2. 应用基因编辑小鼠技术，敲除小鼠相关基因，或将人宿主细胞病毒结合受体（比如ACE2）转入小鼠体内；3. 将野生型SARS-CoV病毒在小鼠体内进行反复适应进化过程，获得致病性更强的小鼠适应病毒，从而建立能引起明显临床表型的病毒感染小鼠模型。关于SARS-CoV感染疾病小鼠模型，主要的研究进展集中于以下几个方面：

1. 直接应用近交系小鼠模型研究病毒致病性

最早开展SARS-CoV感染小鼠模型的研究，是直接在近交系BALB/c小鼠上进行的。在年轻BALB/c小鼠（4-6周）鼻腔里感染SARS-CoV临床株(Urbani)的实验发现，小鼠上/下呼吸道出现病毒复制现象，第3天达高峰，到第7天被清除。但小鼠体重持续增加，没有出现任何相关的临床症状。幼鼠被注射免疫血清后，其呼吸道出现明显抵抗病毒复制的作用，提示人SARS-CoV可以诱导小鼠产生有效的体液免疫反应。另外，也有应用年轻C57BL/6小鼠（5-6周）进行类似的实验，结果如同BALB/c小鼠一样，伴随体重缓慢增加的同时，也有小鼠的上/下呼吸道以及大脑的病毒复制现象，而在SARS-CoV感染患者中，还未见该病毒在大脑中有复制现象。所以，这种只有病毒复制，但缺乏致病作用的所谓感染小鼠模型，很难有效准确用于评估干预治疗效果等方面的研究。

由于SARS-CoV感染人群造成病死率的增加，与年纪较大的患者（大于60岁）发生严重急性呼吸道困难综合征（ARDS）的增加有关，为了探讨能模拟老年人感染SARS-CoV更适合的小鼠模型，有研究分别应用12-14月大的BALB/c、C57BL/6和129S6近交系野生小鼠进行实验，结果发现，此三种老年小鼠经SARS-CoV感染后，都有短暂（平均约7天左右）的临床症状表现，比如体重减少、乱的毛发、弓背和脱水等，更为重要的是，在组织病理学方面，表现有血管周围和细支气管周围炎性细胞渗入，细支气管细胞坏死，以及间质性肺炎发生等现象。而且，BALB/c小鼠的广泛肺泡破坏可持续到第9天，非常接近人SARS-CoV感染的临床病理症状。该研究也是第一次阐明了不同宿主遗传及年龄特征，可以显著影响SARS-CoV感染致病性强弱，同时也再次表明，病毒感染性疾病的发生，不仅与病毒本身特性有关，宿主自身相关因素也发挥极为重要的作用。

2. 应用基因编辑技术建立病毒感染疾病小鼠模型

-- The End --

Believe/not, developments of #UnrestrictedBioweapon have become a mature manufacturing chain since 2000s/earlier. MCF, 5-Year plans...these facts shows #CCP always has plans. This is not an accident or some individual's misbehaviour. Qin isn't the only 1
#LimengYan