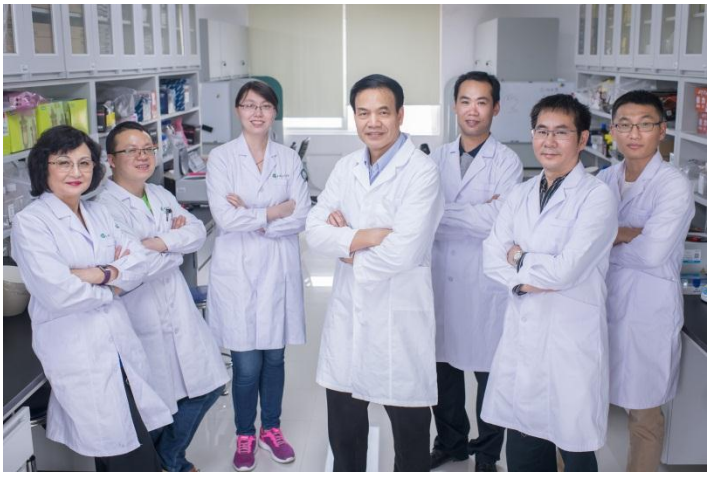
中国科学家 Cell 报道首例亨廷顿舞蹈病基因敲入猪

Chinese Scientists Have Reported A Huntingtin Knockin Pig Model for the First Time in Cell

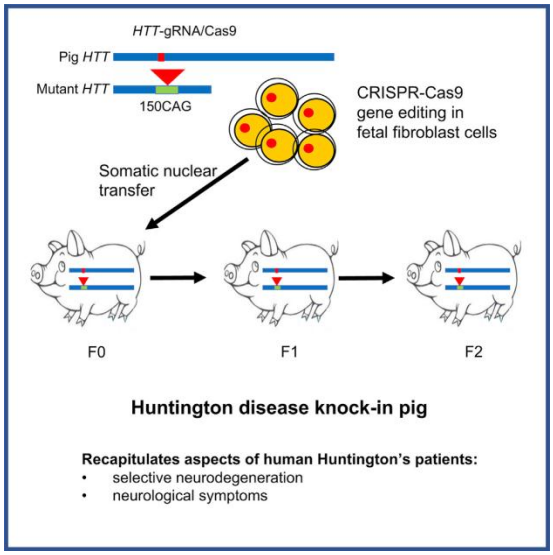


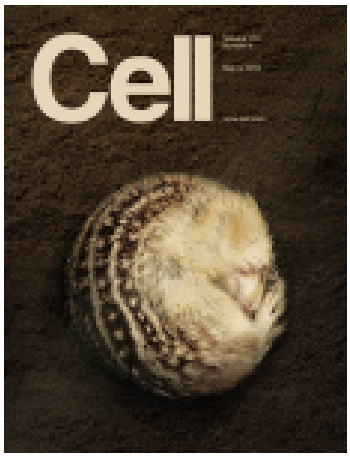
团队成员

【Cell 系列】2018 年 5 月 3 日，发表在 Cell 杂志上题为“A Huntingtin Knockin Pig Model Recapitulates Features of Selective Neurodegeneration in Huntington’s Disease”的论文中，由中国科学院广州生物医药与健康研究院、暨南大学等院校科研人员组成的国际研究团队经过四年努力，首次利用基因编辑技术（CRISPR/Cas9）和体细胞核移植技术，成功培育出世界首例亨廷顿舞蹈病基因敲入猪，精准地模拟出人类神经退行性疾病。

亨廷顿舞蹈症、阿尔茨海默病、帕金森病、肌萎缩侧索硬化症等是当今社会严重威胁人类健康的神经退行性疾病。这些疾病伴随年龄渐长而产生、可遗传、呈渐进性发展，由于缺乏合适的动物模型进行药物筛选，目前尚无有效的治疗方法。亨廷顿舞蹈病是由单基因突变导致的神经退性疾病，是一个理想的疾病模式，可用于研究蛋白质错误折叠如何引起选择性的神经退性病变，是以后研究多基因突变病症的基础。

这一新成果的发表为开发治疗亨廷顿舞蹈病的新手段提供了稳定、可靠的动物模型，也为培育其他神经退行性疾病大动物模型提供了技术范本和理论依据。研究将推动我国发展出大动物疾病模型的医药研发产业链，也可用于干细胞治疗等手段的临床前评价，最终造福于人类。





A Huntingtin Knockin Pig Model Recapitulates Features of Selective Neurodegeneration in Huntington's Disease

一种 Huntingtin 敲入猪模型能够概括亨廷顿舞蹈病中选择性神经退化的特征

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Huntington's disease (HD) is characterized by preferential loss of the medium spiny neurons in the striatum. Using CRISPR/Cas9 and somatic nuclear transfer technology, we established a knockin (KI) pig model of HD that endogenously expresses full-length mutant huntingtin (HTT). By breeding this HD pig model, we have successfully obtained F1 and F2 generation KI pigs. Characterization of founder and F1 KI pigs shows consistent movement, behavioral abnormalities, and early death, which are germline transmittable. More importantly, brains of HD KI pig display striking and selective degeneration of striatal medium spiny neurons. Thus, using a large animal model of HD, we demonstrate for the first time that overt and selective neurodegeneration seen in HD patients can be recapitulated by endogenously expressed mutant proteins in large mammals, a finding that also underscores the importance of using large mammals to investigate the pathogenesis of neurodegenerative diseases and their therapeutics.