proceed for longer subgenomic or even genomic RNAs.

However, the mechanism underlying this determination is poorly understood.

In October 2014, Professor Yeh and Dr. Wu published a study in Cell Host & Microbe on the mechanisms underlying the transition from discontinuous to continuous transcription in coronaviruses.

The research team first implicated the glycogen synthase kinase-3 (GSK-3) in host cells as responsible for viral nucleocapsid phosphorylation. GSK-3 inhibition selectively reduces the generation of genomic RNA and longer subgenomic RNAs, but less effect on shorter subgenomic RNAs. Thus, these authors proposed that the phosphorylated nucleocapsid protein plays an important role in regulating the transition from discontinuous to continuous transcription.

In addition, these authors also reported that phosphorylated nucleocapsid recruits the cellular RNA helicase, DDX1, for binding with the viral genome, facilitating the read-through of templates and enabling the synthesis of longer subgenomic RNAs.

This study sheds light on the key mechanisms underlying the continuous and discontinuous RNA synthesis in coronaviruses. Because this mechanism is conserved among most coronavirus species, including SARS-CoV and MERS-CoV, it has become a potential target for novel antiviral drug development.

Reference

Chia-Hsin Wu, Pei-Jer Chen, and Shiou-Hwei Yeh. Nucleocapsid phosphorylation and RNA helicase DDX1 recruitment enables coronavirus transition from discontinuous to continuous transcription. Cell Host Microbe, 16 (2014), pp. 462–472. DOI: 10.1016/j.chom.2014.09.009.

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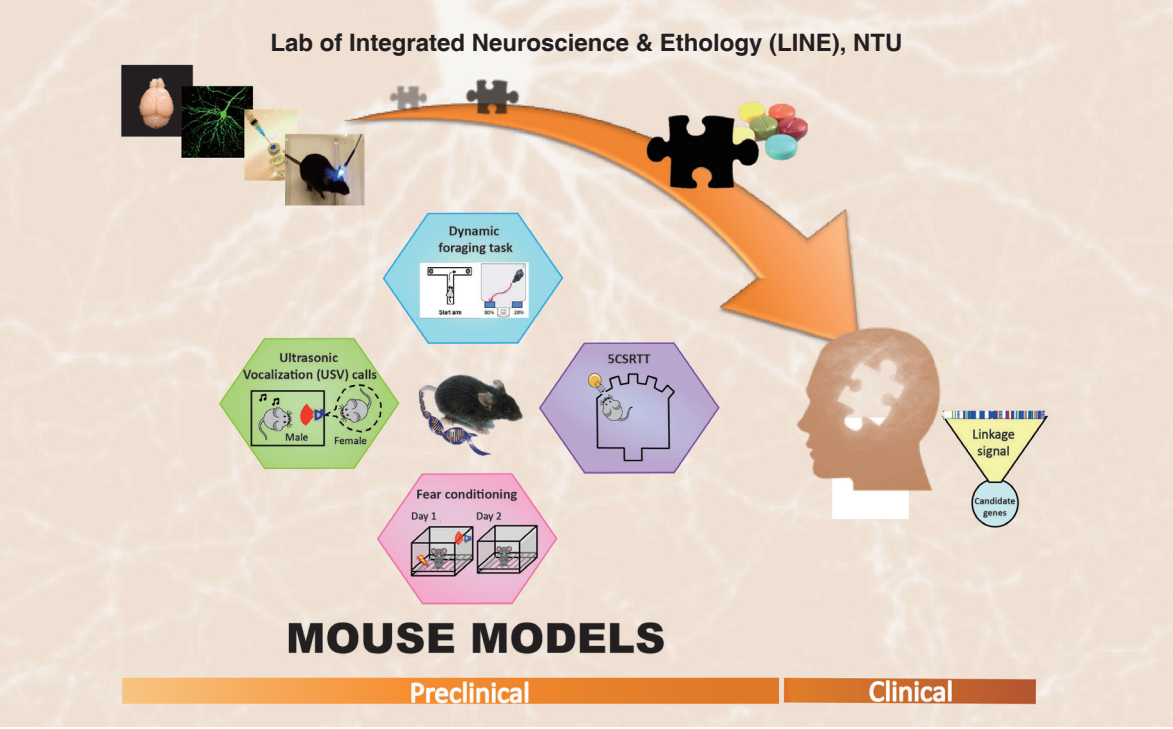
Assessing schizophrenia-relevant deficits and treatments in mice

Mouse models of neuropsychiatric disorders have been an indispensable tool for studying pathological mechanisms and for the in vivo testing of novel therapeutic agents

As noted by Nobel Laureate Dr. Eric Kandel in 2009, "Understanding the biology of mental illness would be a paradigm shift in our thinking about mind... it would also tell us more about who we are and how we function." Schizophrenia is a severe mental disorder, with tremendous cost to our society. The extended timeline and high attrition rate make drug development for schizophrenia (and other psychiatric disorders) an expensive and risky business. The negative and cognitive symptoms of schizophrenia represent an unmet medical need for antipsychotic development. Schizophrenia and other psychiatric disorders are generally diagnosed based upon a collection of symptoms that are defined by the combination of an individual's feelings, perceptions, and behaviors. The exact causes of schizophrenia remain elusive, although both genetic predisposition and environmental risk factors play crucial roles in its development, especially before young adulthood.

As a complement to human studies, animal models not only provide a practical approach to elucidating causal relationships between genes and related symptoms but also play an indispensable role in the discovery and verification of potential drugs and treatments. Although



An illustration of the basic ideas and concepts for assessing schizophrenia-relevant phenotypes and treatments in mice in the Laboratory of Integrated Neuroscience and Ethology (LINE) at National Taiwan University (Image credit: Wei-Li Hung).

it is nearly impossible to capture the full phenotypic spectrum of schizophrenia in mice, the major role of behavioral tests in mice has been to provide insights into the underlying neurobiological mechanisms and the development of new therapeutics for schizophrenia. Given that the recovery of cognitive and social abilities significantly benefits functional outcomes, there has been increasing interest in characterizing cognitive and social functions in normal mice as well as genetically engineered mice.

The Laboratory of Integrated Neuroscience and Ethology (LINE, http://www.psy.ntu.edu.tw/LINE/), led by Dr. Wen-Sung Lai in the Department of Psychology at the National Taiwan University, has established a comprehensive behavioral test battery and the required equipment (including over 500 individually ventilated cages for animal housing) to conduct functional assays and drug screening in mice. This laboratory also provides technical support for preclinical drug screening, generates data for patent applications, and delivers services for the pharmaceutical industry in Taiwan. In this review article, a selection of conventional behavioral tasks and specific mouse behavioral tasks are described and introduced. The researchers also highlight how the choice of specific behavioral tasks during the experiment-planning phase should take into consideration a variety of factors, including their validity, reliability, sensitivity, utility, and specificity. Based upon the hypothesized hypofunction of the N-methyl-D-aspartate receptor (NMDAR)-mediated signaling pathways underlying common cognitive and social impairments in schizophrenia, three NMDAR-related compounds/drugs, D-serine, sarcosine, and D-cycloserine, are discussed in this article as examples for drug testing.

Reference

Ching-Hsun Huang, Ju-Chun Pei, Da-Zhong Luo, Ching Chen, Yi-Wen Chen and Wen-Sung Lai. Assessing schizophrenia-relevant cognitive and social deficits in mice: a selection of mouse behavioral tasks and potential therapeutic compounds. Current Pharmaceutical Design, 20(32), 5139-5150, 2014 (doi: 10.2174/1381612819666140110122750).

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