【演者】

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【演題】

Leveraging genetic rat models of intellectual and developmental disabilities for basic science and translational research

【講演要旨】

Genetic mouse models of intellectual and developmental disabilities (IDD) have been instrumental in our understanding of the consequences associated with disease-causing human mutations. Neurobehavioral deficits are prominent in IDD, and the use of tools such as the laboratory mouse is one approach to identify potential therapies that may improve these impairments. However, given the concerns that findings from mouse models may not necessarily reflect changes that are relevant to the human condition, and the possibility that such models may be sub-optimal for translational studies, we set out to determine the extent to which genetic manipulation in a second mammalian rodent species, the laboratory rat, results in similar and/or different neurobehavioral and molecular deficits. The laboratory rat displays unique advantages for studying behavioral phenotypes including social and cognitive assessments. Using both conventional neurobehavioral assays and assays that are uniquely suited for studies in the rat, we found that several genetic rat models of IDD-related genes display phenotypes that are not completely consistent with reported findings in the mouse including abnormalities in social behavior, one primary endophenotype that is typically studied in rodent models given its significance to IDD. However, other neurobehavioral phenotypes and molecular alterations in rat models are indeed concordant with historical mouse model findings. Taken together, these studies underscore the value of genetic rat models as complementary tools to the existing repertoire of IDD animal models, and highlight the benefit of cross-species analyses in identifying preclinical outcome measures with potentially greater disease-relevance.