EDITORIAL

Genetics of neurological and psychiatric disorders

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Advances in molecular genetics and genomics over the past 30 years have revealed the causative genes and pathophysiology of many neurological and psychiatric disorders for which we had no clue, and have rewritten the textbooks. Neurological and psychiatric diseases include those caused by single gene abnormalities, such as Huntington's disease, spinocerebellar degeneration, and muscular dystrophy, and multifactorial diseases with mostly sporadic but some Mendelian inheritance, such as Alzheimer's disease, schizophrenia, Parkinson's disease, and amyotrophic lateral sclerosis (ALS). The discovery of abnormalities in some mendelian genes in sporadic diseases has led to the elucidation of molecular pathogenesis and therapeutic strategies. And clinical trials based on molecular mechanisms have been conducted and some of them are now on the market. Susceptibility genes for multifactorial neurological diseases have been identified by genome-wide association analysis, and rare variants, which are rare but have a significant effect on pathogenesis, are also important. In the future, personal genome analysis will be applied to medical research.

For example, in the case of intractable neurological diseases, recent therapeutic developments that have been revealed by analyzing the molecular pathogenesis of causative agents include amyloid tetramer stabilizer and first siRNA therapy for amyloid polyneuropathy; hormonal agents for spinal and bulbar muscular atrophy; antisense nucleic acids, AAV gene therapies, and splice corrective small molecule drugs for spinal muscular atrophy; amino acid drugs for MELAS; antisense nucleic acids for Duchenne muscular dystrophy; thalidomide for POEMS; and various new therapies for multiple sclerosis and neuromyelitis optica were launched. Also, there are many more in clinical trials, including CoQ10 for multiple system atrophy, neurotrophic factor for ALS, sialic acid for distal myopathy, Aβ antibody therapy for Alzheimer's disease, and antisense nucleic acids for familial ALS, Huntington's disease, and Fukuyama muscular dystrophy.

In addition, the Japanese Society of Neurology, the Japanese Society for Neurotherapy, and other related societies jointly submitted the revised Proposal 2022 for the Promotion of Research to Conquer Neurological Diseases. Currently, the topics for the treatment of intractable neurological diseases include technological innovation and clinical application of nucleic acid medicine, development of therapies using mouse/iPS cells, biomarkers for disease detection, and models that reflect early-stage pathological conditions. Here, several authors review recent advances in genetics and molecular targeted therapy for neurological and psychiatric diseases.

Tatsushi Toda [1]✉

[1]*Department of Neurology, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan.* ✉*email: toda@m.u-tokyo.ac.jp*

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