Accurate modeling of neurodevelopmental disorders using patients'-derived iPS cells

Takanobu Nakazawa[1,2], Ryota Hashimoto[3,4], Kazuhiro Takuma[1,5], Hitoshi Hashimoto[2,5,6,7,8]

[1]Dept Pharmacol, Grad Sch Dentistry, Osaka Univ., [2]Lab Mol Neuropharmacol, Grad Sch Pharmaceut Sci, Osaka Univ., [3]Dept Pathol Mental Dis, Natl Inst Mental Health, Natl Ctr Neurol Psychiatry, [4]Osaka Univ., [5]Mol Res Ctr Children's Mental Dev, United Grad Sch Child Dev, Osaka Univ., [6]Inst Datability Sci, Osaka Univ., [7]Inst Open Transdiscip Res Initiatives, Osaka Univ., [8]Dept Mol Pharmaceut Sci, Grad Sch Med, Osaka Univ.

Previous studies have suggested the abnormal central nervous development as the causes of psychiatric disorders, however, much remains unknown about the molecular and cellular etiology of these disorders. In addition to the potential cumulative effect of a large number of common genetic variants with small individual effects, psychiatric disorders are strongly associated with rare variants with high penetrance. Recent studies have suggested that *de novo* mutations, genomic spontaneous mutations identified in an affected child, but not unaffected parents, contribute to the risk of psychiatric disorders. Recently, we and other groups have identified that *POGZ* is one of the most recurrently *de novo* mutated genes in patients with autism spectrum disorders (ASD), suggesting that *de novo POGZ* mutations can be associated with ASD pathogenesis. Using iPSC technology, we have identified the role of POGZ in central nervous system development. In addition to *de novo* point mutations, we have been focusing on copy number variants, which represent large genomic duplications or deletions, and found that 3q29 deletion impaired central nervous system development in patient's-derived neural stem cells. These findings provide important insights into the cellular basis of ASD.