Comprehensive integrative analyses identify *GLT8D1* and *CSNK2B* as schizophrenia risk genes

With the support by the National Natural Science Foundation of China and the Chinese Academy of Sciences, the research team led by Professors Chen YongBin (陈勇彬) and Luo XiongJian (罗雄剑) at the Key Laboratory of Animal Models and Human Disease Mechanisms of the Chinese Academy of Sciences & Yunnan Province, Kunming Institute of Zoology, Chinese Academy of Sciences, used comprehensive integrative analyses to identify *GLT8D1* and *CSNK2B* as schizophrenia risk genes, which was published in *Nature Communications* (2018, 9(1): 838).

Schizophrenia (SCZ) is a severe mental disorder with a lifetime prevalence of ~ 0.5%—1% across all human populations. This disease is characterized by positive symptoms (i. e., delusions and hallucinations), negative symptoms (i. e., apathy, impaired motivation, and social withdrawal), and cognitive impairment (i. e., disorganized thoughts, impaired working memory, and executive function). As one of the most common mental diseases, SCZ has the highest heritability among neuropsychiatric disorders. Recent genome-wide association studies (GWAS) have identified multiple risk loci that show strong associations with schizophrenia. However, pinpointing the potential causal genes at the reported loci remains a major challenge. Here, they identify candidate causal genes for schizophrenia using an integrative genomic approach. Sherlock integrative analysis shows that *GLT8D1* and *CSNK2B* are SCZ risk genes, which are validated using independent brain expression quantitative trait loci (eQTL) data and integrative analysis method (SMR). Consistently, gene expression analysis in schizophrenia cases and controls further supports the potential role of these genes in the pathogenesis of SCZ. Finally, they show that *GLT8D1* and *CSNK2B* knockdown promote the proliferation and inhibit the differentiation abilities of neural stem cells, and alter morphology and synaptic transmission of neurons. Based on the functional roles of *GLT8D1* and *CSNK2B* in neural stem cells, they are also characterizing the potential roles of these genes in human glioma stem/initiating cells. This study links some of the risk variants from the largest GWAS of SCZ to specific genes, which not only provides a framework to investigate how genetic variants contribute to SCZ risk through modulating gene expression, but also provides a starting point to dissect the possible role of the identified genes in the pathophysiology of central nervous system.

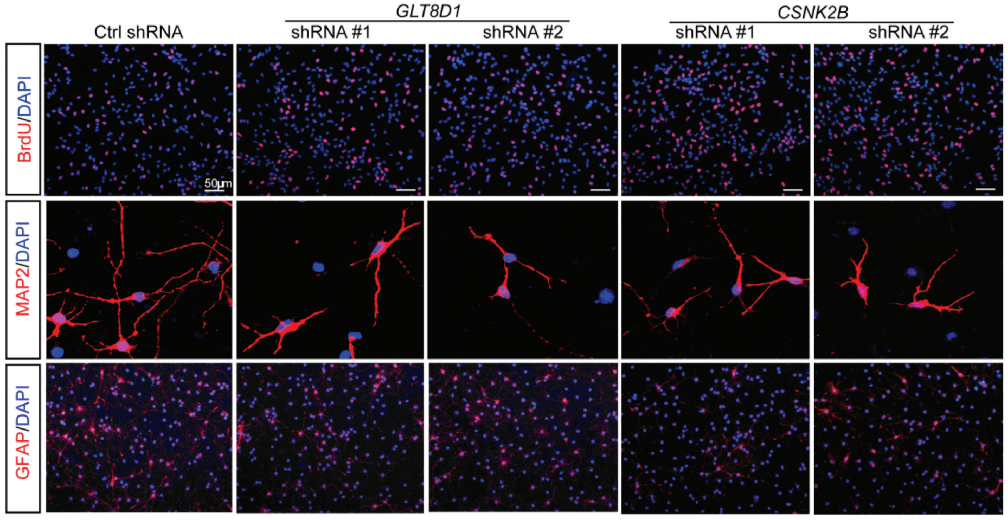

Figure Knockdown of *GLT8D1* and *CSNK2B* promote proliferation and inhibit the differentiation abilities of NSCs.