DGCR2 Important Functioning in Anxiety within the Context of the Hippocampus

Heath Robinson, Zhibing Tan, Bin Luo, Wenbing Chen, Lin Mei

Department of Neurosciences, Case Western Reserve University, School of Medicine, Cleveland, OH 44106, USA

Schizophrenia impacts 1% of the population and is a severely debilitating mental disorder. An older hypothesis of Schizophrenia points to impairments in brain regions connectivity that has been supported by more recent studies showing impairments between the prefrontal cortex and hippocampus. Chromosome 22q11.2 microdeletion is a microdeletion syndrome containing a 30 megabase region with 46 genes, whose subjects displays symptoms of cranial-facial abnormalities, immune system deficits and gastrointestinal problems, as well as exhibits a broad array of cognitive impairments. These two diseases, however, possess a large amount of comorbidity. For instance, 1% of Schizophrenia patients are due to Chromosome 22q11.2 microdeletion syndrome, whereas up to 25% of Chromosome 22q11.2 syndrome patients display symptoms diagnosable of Schizophrenia. In patients suffering from Chromosome 22q11.2 or Schizophrenia, a large contingent also posses' anxiety disorders, especially Chromosome 22q11.2 patients of whom 40-70% possess anxiety disorders. Therefore, the 46 genes contained within Chromosome 22q11.2 are not only important to the pathophysiology Chromosome 22q11.2 microdeletion syndrome, but likely for the pathology of Schizophrenia and Anxiety Disorders.

DGCR2 is one such gene within the Chromosome 22q11.2 region that shares importance with Chromosome 22q11.2 microdeletion syndrome, as well as Schizophrenia, due to the DGCR2 gene possessing single nucleotide polymorphisms (SNP's) and low expression levels in diagnosed Schizophrenic patients. DGCR2 is expressed broadly in the brain shown by quantitative-PCR (qtPCR), beta-galactosidase (beta-gal) staining and western blot analysis shown here. Furthermore, in DGCR2 knock down mice generated here, DGCR2 lacz/lacz mice showed a pronounced increase in anxiety in behavioral testing. The medial prefrontal cortex (mPFC) and ventral hippocampus (vHPC) are involved in the circuitry of anxiety, yet by exactly what mechanisms remains unknown. Preliminary evidence in this abstract shows DGCR2 is expressed in the cortex, prefrontal cortex and hippocampus. Furthermore, data provided here shows that DGCR2 lacz/lacz mice, a mouse with reduced DGCR2 expression, exhibit hippocampal power spectrum density decrease and excitatory presynaptic transmission deficits. In conclusion, DGCR2 is expressed broadly in the brain and when deficient leads to pre-synaptic excitatory transmission issues that impact hippocampal functioning.