Towards understanding the neuronal circuits of psychosis in 22q11.2 deletion syndrome

Stanislav S. Zakharenko, M.D., Ph.D.

Department of Developmental Neurobiology, St. Jude Children's Research Hospital, Memphis TN, USA

The 22q11.2 deletion syndrome (22q11DS) is associated with a high risk of developing schizophrenia symptoms, including psychosis in the form of auditory hallucinations. Such symptoms typically arise during adolescence or early adulthood, and in most patients, they are alleviated by antipsychotics. In my talk, I will discuss recent advances in our understanding of the neuronal circuits that underlie psychotic symptoms. I will describe the disruption of synaptic transmission within a neuronal circuit in mouse models of 22q11DS. This disruption is age-dependent, specific to the auditory cortex, and is rescued by antipsychotics, which makes it a candidate for a cellular mechanism underlying psychotic symptoms. I will discuss the causative gene(s) and molecular mechanisms that underlie the disruption of the auditory neuronal circuit. I will also hypothesize why this disruption occurs later in life and touch upon ongoing research that aims to elucidate the activity patterns in the auditory cortex of behaving mouse models of 22q11DS at the level of individual neurons. Together, the results of this research provide an initial step toward understanding the pathogenic neuronal mechanisms of psychotic symptoms.