

Brain Anomalies in Del22q11 Syndrome

Abstract

Some *del22q11* patients exhibit neurobehavioral defects, the pathogenesis of which is unknown. This investigation attempts to elucidate the genetic and developmental causes of the neurobehavioral defects in *del22q11*. High resolution SNP analysis verified the homogeneity of the *del22q11* patients' 1.5 or 3 Mb deletions. Re-sequencing candidate genes on the remaining copy of the 22q11 region in the cohort of patients with del22q11 syndrome and polymicroglia, I identified a 21-bp duplication in Claudin 5 in one patient and a missense mutation in ARVCF in another. I verified that neither mutation is a reported polymorphism, and began functional analysis of the mutations. Preliminary histological analysis of the brains of mice carrying the deletion orthologous to the 22q11 region indicates that the brains appear to be structurally normal. Though del22q11 patients with severe neurobehavioral features are more difficult to identify and recruit into a study, genetic analysis of human patients seems more promising than histological studies of the LgDel mouse model as a future source of insight into the pathogenesis of complex neurobehavioral features such as those associated with del22q11 syndrome.