GATAD2B-associated neurodevelopmental disorder (GAND) GATAD2B syndro

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GATAD2B (GATA zinc finger domain containing 2B) variants are associated with the neurodevelopmental syndrome GAND, characterized by intellectual disability (ID), infantile hypotonia, apraxia of speech, epilepsy, macrocephaly and distinct facial features. GATAD2B encodes for a subunit of the Nucleosome Remodeling and Histone Deacetylase (NuRD) complex. NuRD controls transcriptional programs critical for proper neurodevelopment by coupling histone deacetylase with ATP-dependent chromatin remodeling activity. To study mechanisms of pathogenesis for GAND, we characterized a mouse model harboring an inactivating mutation in Gatad2b. Homozygous Gatad2b mutants die perinatally, while haploinsufficient Gatad2b mice exhibit behavioral abnormalities resembling the clinical features of GAND patients. We also observed abnormal cortical patterning, and cellular proportions and cell-specific alterations in the developmental transcriptome in these mice. scRNAseq of embryonic cortex indicated misexpression of genes key for corticogenesis and associated with neurodevelopmental syndromes such as Bcl11b, Nfia and H3f3b and Sox5. These data suggest a crucial role for Gatad2b in brain development.