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Identifying Downstream Targets of HCFC1: A Gene Linked to Severe Neurological Disease

Derivatives of cobalamin (Vitamin B-12) are important to the function of enzymes required for metabolism. Failure to convert cobalamin into its derivative forms leads to build up of methylmalonic acid and/or homocysteine in blood and urine. One of the genes responsible for the metabolism of cobalamin is MMACHC. Combined methylmalonic acidemia and hyperhomocysteinemia type cblX is characterized by missense mutations in HCFC1, a global transcriptional regulator that is associated with severe neurological disease. Individuals affected by cblX have craniofacial symptoms that are more severe than other cobalamin disorders, most likely caused by the dysregulation of other downstream genes of HCFC1. Analyzing RNA sequencing data from a cblX-affected-individual, 4 candidate genes were identified and their expression was tested in various zebrafish knockouts of hcfc1a, a zebrafish paralog of the human gene HCFC1, with qPCR (quantitative Polymerase Chain Reaction). Preliminary experimental results show that hcfc1a regulates the gene grin2aa, which is a neurotransmitter shown to be associated with epilepsy, autism, and intellectual impairment.