MYT1L syndrome (MYT1L variants and 2p25.3 deletions)

https://pubmed.ncbi.nlm.nih.gov/32065501/

Both point mutations and deletions of the MYT1L gene as well as microdeletions of chromosome band 2p25.3 including MYT1L are associated with intellectual disability, obesity, and behavioral problems. Thus, MYT1L is assumed to be the-at least mainly-causative gene in the 2p25.3 deletion syndrome. Here, we present comprehensive descriptions of nine novel individuals bearing MYT1L mutations; most of them single nucleotide variants (SNVs). This increases the number of known individuals with causative deletions or SNVs of MYT1L to 51. Since eight of the nine novel patients bear mutations affecting MYT1L only, the total number of such individuals now nearly equals the number of individuals with larger microdeletions affecting additional genes, allowing for a comprehensive phenotypic comparison of these two patient groups. For example, 55% of the individuals with mutations affecting MYT1L only were overweight or obese as compared to 86% of the individuals with larger microdeletions. A similar trend was observed regarding short stature with 5 versus 35%, respectively. However, these differences were nominally significant only after correction for multiple testing, further supporting the hypothesis that MYT1L haploinsufficiency is central to the 2p25.3 deletion phenotype. Most importantly, the large number of individuals with MYT1L mutations presented and reviewed here allowed for the delineation of a more comprehensive clinical picture. Seizures, postnatal short stature, macrocephaly, and microcephaly could be shown to be over-represented among individuals with MYT1L mutations.