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GPSM2 and Chudley-McCullough syndrome: a Dutch founder variant brought to North America.

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Abstract: Chudley-McCullough syndrome (CMS) is characterized by profound sensorineural hearing loss and brain anomalies. Variants in GPSM2 have recently been reported as a cause of CMS by Doherty et al. In this study we have performed exome sequencing of three CMS patients from two unrelated families from the same Dutch village. We identified one homozygous frameshift GPSM2 variants c.1473delG in all patients. We show that this variant arises from a shared, rare haplotype. Since the c.1473delG variant was found in Mennonite settlers, it likely originated in Europe. To support DNA diagnostics, we established an LOVD database for GPSM2 containing all variants thus far described.