Title: Case report with biallelic variants in *GCNT2* implicates exon 1B in congenital cataracts

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Introduction: *GCNT2*-related congenital cataract (with or without the adult i blood phenotype) is caused by biallelic variants in *GCNT2*, which has 3 major isoforms, differentiated by alternative splicing of the first exon (known as exon 1A, B, and C). While the transcript that includes exon 1C is thought to be key for the adult i blood phenotype, it is not clear which transcript(s) are clinically relevant for the congenital cataract disease phenotype.

Methods: Using trio-based exome sequencing with follow-up chromosomal microarray, we investigated the cause of disease in a proband with congenital cataracts and other ophthalmologic manifestations, endocrine abnormalities, allergic reactions, reproductive malformations, and neurologic manifestations.

Results: The congenital cataracts phenotype was explained by two *GCNT2* variants found *in trans*: a ~75 kb deletion (approximate breakpoints hg19 chr6:10,500,208-10,575,042del) encompassing exons 1B and 1C, and a truncating variant in exon 1B (NM_001491.3:c.760dup p.H254Pfs*2). A genetic cause for the additional features was not identified.

Conclusions: This report strongly suggests that NM_001491.3, which includes exon 1B, is a clinically relevant transcript for *GCNT2*-related cataracts and adds to the variant spectrum for this understudied gene-disease relationship. This finding has implications for genotype-phenotype correlations of *GCNT2* related congenital cataracts and variant classification, particularly for truncations in exon 1B, which should likely receive strong pro-pathogenic weight based on this being a clinically relevant exon.