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The genetic determinants of symptoms in a rare chromosomal deletion disorder

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Individuals with 2p15p16.1 microdeletion syndrome present with intellectual disability, microcephaly, delayed growth, dysmorphic craniofacial features, and digital abnormalities. The precise genetic region responsible for this syndrome has been challenging to identify. However, recent reports indicate that 4 genes (*XPO1*, *USP34*, *BCL11A*, and *REL*) are commonly deleted in this syndrome.

A study in the current issue of *JCI Insight* describes 8 new subjects with microdeletions in chromosomal region 2p15p16.1 and provides evidence that loss of *XPO1*, *REL*, and *BCL11A* underlie this syndrome. Mark O'Driscoll, Cheryl Gregory-Evans, Evica Rajcan-Separovic, and colleagues at University of Sussex and the University of British Columbia reviewed all published cases of 2p15p16.1 microdeletion syndrome and characterized the microdeletions present in 8 newly identified patients.

Cells from patients had reduced expression of *XPO1*, *USP34*, *BCL11A*, and *REL*. Moreover, knock down of 3 of these homologous genes in zebrafish resulted in abnormalities consistent with patient phenotypes.

Together, the results of this study provide strong evidence that the combined loss of *XPO1*, *BCL11A*, and *REL* is responsible for 2p15p16.1 microdeletion syndrome.

More information: Hani Bagheri et al. Identifying candidate genes for 2p15p16.1 microdeletion syndrome using clinical, genomic, and

functional analysis, *JCI Insight* (2016). DOI: 10.1172/jci.insight.85461