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Functional consequences of genomic abnormalities

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Copy number changes (CNV) cause an abnormal phenotype in 15% of cases with developmental delay. Typically, genomic changes are correlated with abnormalities at the "whole body" level, however, the functional consequences of CNVs at the cellular level, are rarely investigated. We are interested to determine if genes integral to CNVs show abnormal function in patient cells by testing their expression at the RNA and protein level and their known cellular functions. We identified abnormal cellular function of genes from CNVs from 1q21.1, 2p13.2 and Xq21.1. In case of the 1q21.1 CNV, the copy number change of its integral genes *CHD1L* and *PRKAB2* resulted in perturbed chromatin remodeling and AMPK function, while in subjects with recurrent 2p13.2 CNV dysfunction of retinoic and notch signaling pathway implicated two genes from this CNV: *CYP26B1* and *EXOC6B*, respectively. Finally, the CNV from Xq21.1 disrupted the *MAGT1* gene, which has a role in Mg homeostasis, and resulted in reduced Mg influx in patient cells. Studying functional defects of CNVs is important as it identifies cellular pathways that are defective and offers treatment strategies to minimize their functional defects (e.g. restricted vitamin A diet in case of an abnormal retinoic acid metabolism in patients with 2p13.2 CNV or reducing the skin defects by adding Mg to the diet or as ointment in patients with *MAGT1 CNV*). Our work allows the establishment of a closer link between the genomic abnormality and its cellular and clinical consequences, and offers opportunities for treatment for some of the phenotypic defects.

Biography

Evica Rajcan-Separovic is an Associate Professor at the University of British Columbia and a Career Scholar funded by the Michael Smith Foundation of Health Research and the Canadian Institutes of Health Research (CIHR). She has a broad interest in the field of genomic abnormalities and their role in abnormal prenatal and postnatal human development. She has served on the review panels for agencies including Welcome Trust, MRC England and CIHR.

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