Institute of Molecular Genetics
of the Czech Academy of Sciences

Regular Wednesday IMG seminar

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"BRAT1 links Integrator and defective RNA processing with neurodegeneration"

Mutations in BRAT1, encoding BRCA1-associated ATM activator-1, have been associated with neurological disorders characterized by heterogeneous phenotypes with varying levels of clinical severity. However, the exact mechanism/s by which mutations in BRAT1 gene trigger neurological disorders are largely unknown. Recently, we have identified a homozygous missense (c.185T>A) variant in BRAT1 that significantly reduced BRAT1 protein levels in patients with non-progressive cerebellar ataxia. Despite the molecular role currently proposed for BRAT1 in ATM regulation, our data indicate that this decreased BRAT1 level does not interfere with ATM kinase activation or DNA damage response. Surprisingly, we show that the BRAT1 protein interacts with and modulates the function of the core endonuclease subunits INTS9/INTS11 of the Integrator complex. This complex is involved in the 3'end processing of a number of non-coding RNAs and is able to regulate the expression of specific protein-coding mRNAs. Importantly, defects in Integrator functions are also evident in patient-derived cells from BRAT1 related neurological disease. Based on the pathology of the BRAT1 patients, our data link defects in the Integrator endonuclease complex with hereditary neurodegenerative diseases.

The seminar will be held

on Wednesday 4th May 2022 at 15:00

in the Milan Hašek Auditorium at IMG

(Institute of Molecular Genetics of the Czech Academy of Sciences, Vídeňská 1083, Prague 4)