Sadaf Mohtashami et al., J Neurol Neurophysiol 2017, 8:3 (Suppl)
http://dx.doi.org/10.4172/2155-9562-C1-049

Expression and proteomic analyses of KIF1A/25B in hereditary sensory and autonomic neuropathies type II

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Hereditary sensory and autonomic neuropathies form a group of genetic disorders characterized by variable sensory and autonomic dysfunctions. HSAN type II (HSANII) is a debilitating subtype manifesting in early childhood with distal numbness and loss of pain, temperature and touch. The first cluster of HSANII cases was reported in eastern Canada, with half the patients of French-Canadian descent. Our laboratory has reported truncating mutations in a nervous-tissue-specific exon (*HSN2*) of the *WNK1* gene. The *WNK1* isoform containing the alternatively spliced exon (*HSN2*) is referred to as the *WNK1/HSN2* isoform. Interestingly the protein region encoded by the alternatively spliced exon was found to interact with a particular isoform of another HSANII causative gene, *KIF1A*. The HSANII-causing *KIF1A* isoform is referred to as *KIF1A/25B* since disease-causing mutations were exclusively found in the alternative exon *"25B"*. *KIF1A* belongs to a superfamily of microtubule-dependent proteins that mediate specific and diverse motile processes within the cell.

Materials & Methods: The expression profile of *KIF1A/25B* across the nervous system is determined by performing WB immunodetection using tissues from wild-type mice and a rabbit antiserum. The function of the protein encoded by exon 25B is assessed through a profiling of its interacting partners by performing co-immunoprecipitation for full-length *KIF1A/25B* protein, full-length *KIF1A/25B* minus exon *25B*, the protein that correspond to exon *25B* and *EGFP* protein as a negative control. Positive interactions are confirmed using liquid chromatography–mass spectrometry.

Results: *KIF1A/25B* is the transit system through which *WNK1/HSN2* traffics within the cells and offers the two proteins an opportunity to interact with other cellular elements relevant to the sensory and nociceptive aspects of HSANII.

Conclusions: This study answers fundamental questions regarding the molecular pathophysiology of HSANII, though our findings have an impact on the understanding of other neuropathies and of normal neuronal processing.

Biography

Sadaf Mohtashami is a Master's student in the Division of Experimental Medicine in the Faculty of Medicine at McGill University. She is pursuing her research under the supervision of Dr. Guy Rouleau who has contributed to the identification of over 20 disease-causing genes and new mutational mechanisms. The laboratory team of Dr. Rouleau is focused on identifying genes involved in neurological and psychiatric diseases and on understanding the biological function of those genes.

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