IMPACT OF MYOSIN5A MUTATION IN NEURODEGENERATION: A RAT ANIMAL MODEL

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Myosin5a (Myo5a) is an actin-dependent motor protein that is highly expressed in the brain, and involved in vesicular/organelles transport and its absence leads to movement disorders in humans and animal species (Griscelli and Elejalde syndromes in humans), rodents (dilute lethal phenotype in mice, and dilute-opisthotonus of Wistar rats), and Arabian horses Lavender Foal Syndrome.

A spontaneous autosomal recessive rat model for neurodegeneration caused by a mutation in the Myo5a gene was developed in our laboratory. The pleiotropic effects of this mutation affect the coat color, central nervous and neuroendocrine systems.

Preliminary data from our model of Myo5a mutant Berlin-Druckrey (BD-IV) “shaker” rats demonstrated marked alterative changes involving the alpha-synuclein (a-syn) overexpression, decrease dopamine (DA) levels, alteration of DA metabolism, and overexpression of tau protein in specific anatomical area of brain in shaker rats compared with non-affected siblings. The mechanisms responsible for neurological phenotypes in the deficient Myo5a affected animals are less understood and suggest pleiotropic origins.

These neurological degenerative changes are common in human neurodegenerative diseases such as Alzheimer, Parkinson’s, and Lewis Body dementia, which make this animal model ideal for mechanistically investigating human diseases with potential development of novel therapy, which can lead to translational studies. The main challenge for the future will be to investigate the molecular mechanisms of Myo5a and interaction with other proteins underlying its functions.