Movement disorder and neurodegeneration in a rat model with myosin 5a mutation

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Myosin 5a (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 alteration changes involving the alpha-synuclein (α-syn) overexpression, decrease dopamine (DA) levels, alteration of DA metabolism, and overexpression of tau protein in specific anatomical areas of brain in shaker rats compared with non-affected siblings. The movement disorder and alteration biochemical changes increased in severity after 15 days postnatal. The mechanisms responsible for neurological phenotypes in the deficient Myo5a affected animals are less understood and deserve further investigation. Possible role of diverse myosins in synaptic transmission or plasticity has not been investigated. Similar 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 neurodegeneration and its interaction with other proteins underlying its functions.

Biography
George Stoica is a DVM, MSc and a PhD degree holder. He is a Professor in the Department of Veterinary Pathobiology at Texas A & M University, USA. He received his Master’s degree in Veterinary Pathology from Ohio State University and PhD in Experimental Pathobiology from Michigan State University. He has been with Texas A&M University since 1984 and was advanced to Full Professor in 1996. His area of expertise is in experimental neuropathology and his area of research span from chemical carcinogenesis, viral carcinogenesis, comparative neuro-oncology and neurodegenerative disorders in animal models. He published over 100 scientific articles in peer reviewed journals and wrote several chapters in various books.

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