

Drosophila spichthyin inhibits BMP signaling and regulates synaptic growth and axonal microtubules Xinnan Wang, W Robert Shaw, Hilda T H Tsang, Evan Reid & Cahir J O'Kane

To understand the functions of NIPA1, mutated in the neurodegenerative disease hereditary spastic paraplegia, and of ichthyin, mutated in autosomal recessive congenital ichthyosis, we have studied their *Drosophila melanogaster* ortholog, spichthyin (Spict). Spict is found on early endosomes. Loss of Spict leads to upregulation of bone morphogenetic protein (BMP) signaling and expansion of the neuromuscular junction. BMP signaling is also necessary for a normal microtubule cytoskeleton and axonal transport; analysis of loss- and gain-of-function phenotypes indicate that Spict may antagonize this function of BMP signaling. Spict interacts with BMP receptors and promotes their internalization from the plasma membrane, implying that it inhibits BMP signaling by regulating BMP receptor traffic. This is the first demonstration of a role for a hereditary spastic paraplegia protein or ichthyin family member in a specific signaling pathway, and implies disease mechanisms for hereditary spastic paraplegia that involve dependence of the microtubule cytoskeleton on BMP signaling.