NIPA1-HSP: is abnormal BMP signalling the key?

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The hereditary spastic paraplegias (HSPs) are genetic conditions showing prominent distal axonopathy. A group of 5 HSP genes encode proteins (named spastin, spartin, NIPA1, maspardin and protrudin) that localise to endosomes. Cahir O'Kane (Department of Genetics) has shown that spicthyin, the *Drosophila* homologue of NIPA1, is an endosomal protein that acts as an inhibitor of bone morphogenic protein (BMP) signalling. My talk will focus on the role of NIPA1 in mammalian cells. I will discuss data showing that mammalian NIPA1 localises to the plasma membrane and to endosomes. I will show that mammalian NIPA1 is an inhibitor of BMP signalling and that the mechanism of this inhibition involves down-regulation of BMP receptors by promoting their endocytosis and degradation in lysosomes. I will speculate on the mechanism by which such a dysregulation of BMP signalling could lead to pathology in NIPA1-HSP.