

Evan Reid

“Roles of spastin in membrane traffic”

Mutations in the gene encoding the microtubule severing protein spastin are the most common cause of hereditary spastic paraplegia, in which axons of the corticospinal tracts degenerate. Spastin has two main isoforms, a 68kD full-length and a 60kD short form. I discuss data that shows that these two isoforms preferentially function in different membrane traffic pathways. 68kD spastin is principally located at the early secretory pathway, where it regulates ER-to-Golgi traffic. 60kD spastin is located on endosomes and the cytokinetic midbody and its recruitment to these sites requires its ESCRT-III-interacting MIT domain. Loss of midbody microtubules accompanies the abscission stage of cytokinesis, although the machinery responsible is unknown. I show that spastin is required for the microtubule disruption event that accompanies abscission and suggest that this event represents spastin-mediated microtubule severing. These results support a model in which spastin's microtubule severing activity is functionally coupled to membrane traffic. Since spastin also has a role in axonal processes where there is co-ordinated microtubule regulation and membrane traffic, I propose that this model is relevant in the axon.