Elucidating the molecular function of ZFYVE27 (Protrudin)

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ZFYVE27 is a member of the FYVE-finger family of proteins. The FYVE-finger domain is suggested to be responsible for endosomal localization of these proteins and the majority of the FYVE-finger proteins serve as regulators of endocytic membrane trafficking. ZFYVE27 was identified as a spastin interacting protein and previously, we characterized its interaction with spastin in mammalian cells. More importantly, we identified a German family in which mutation in ZFYVE27 causes autosomal dominant form of hereditary spastic paraplegia (HSP). A comprehensive expression analysis of ZFYVE27 in mouse revealed a high level of expression primarily in the HSP affected tissues such as brain, cerebellum and spinal cord. Immunohistochemical analysis of tissue sections from various subdivisions of brain and spinal cord showed expression in both cell soma and axons of the motor-neurons. To gain further insight into the molecular function of ZFYVE27, we used the yeast two-hybrid approach to identify novel ZFYVE27 interacting proteins. Using ZFYVE27 as bait, we identified reticulon 1 (RTN1) and ZFYVE27 itself as potential interacting proteins.

To elucidate the molecular function of ZFYVE27 *in vivo*, we are generating a loss of function mouse model by knockout strategy.Conceivably the phenotype of these mouse models might mimic the pathological features of HSP, therefore will provide us with a valuable model system to study the underlying cause for HSP etiology.