Hereditary spastic paraplegia development associated with changes in endoplasmic reticulum

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Hereditary spastic paraplegias (HSP) are a group of hereditary diseases that result in progressive loss of motor function in the lower limbs, and mutations in many different genes have been implicated in disease progression. One common feature of HSP is the progressive degradation of the axons of cortical motor neurons; however, it is not fully understood how mutations in is so many different genes result in axonal degradation.

In this issue of the *Journal of Clinical Investigation*, Christian Hübner and colleagues at Jena University develop a mouse model of HSP by introducing a human-associated mutation into the gene encoding receptor accessory protein 1 (REEP1). Mice with this *Reep1* mutation exhibited age-dependent loss of motor function and axonal degradation in the spinal cord.

The authors revealed a role for REEP1 in maintaining the shape of the endoplasmic reticulum (ER) and changes in ER structure associated with *Reep1* mutations might impair ER function.

In the companion commentary, Ariel Deutch and colleagues at Vanderbilt University discuss how this new mouse model will be useful for understanding the how changes in ER morphology result in HSP-associated axon loss.

More information: A spastic paraplegia mouse model reveals REEP1-dependent ER shaping, J Clin Invest. 2013;123(10):4273–4282. DOI: 10.1172/JCI65665

REEPing the benefits of an animal model of hereditary spastic paraplegia, J Clin Invest. 2013;123(10):4134–4136. DOI: 10.1172/JCI72324