

Impaired myelination in calnexin-deficient mice

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Calnexin is a ubiquitously expressed, type I integral membrane ER protein involved in protein folding and quality control in the secretory pathway. The protein binds monoglucosylated carbohydrate on newly synthesized glycoproteins to function as molecular chaperone. Calnexin-deficient mice develop apparent neurological defects including lower limb motor disorder, gait disturbance and ataxia. We examined both neuronal growth and the ability to evoke fictive locomotion in the spinal cord and found that loss of calnexin has no effect on neuronal growth or function. Cell biological analysis revealed striking myelination problems in the spine, brain stem and sciatic nerve of calnexin-deficient animals. Peripheral neuropathies are common human diseases characterized by progressive deterioration of the peripheral nerves. The myelin sheaths display a unique structure that depends on precisely regulated protein synthesis and trafficking. Biochemical analysis indicates that calnexin is critical for folding of key myelin proteins PMP22 and P0. These studies indicate that calnexin, a ubiquitously expressed endoplasmic reticulum molecular chaperone, is pivotal in the correct folding and targeting of myelin proteins, and the subsequent formation and maintenance of myelin. The protein may play important role in the pathology of myelin diseases.

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