Deficiency of the zinc finger protein ZFP106 causes motor and sensory neurodegeneration.

Zinc finger motifs are distributed amongst many eukaryotic protein families, directing nucleic acid-protein and protein-protein interactions. Zinc finger protein 106 (ZFP106) has previously been associated with roles in immune response, muscle differentiation, testes development and DNA damage, although little is known about its specific function. To further investigate the function of ZFP106, we performed an in-depth characterization of Zfp106 deficient mice (Zfp106(-/-)), and we report a novel role for ZFP106 in motor and sensory neuronal maintenance and survival. Zfp106(-/-) mice develop severe motor abnormalities, major deficits in muscle strength and histopathological changes in muscle. Intriguingly, despite being highly expressed throughout the central nervous system, Zfp106(-/-) mice undergo selective motor and sensory neuronal and axonal
degeneration specific to the spinal cord and peripheral nervous system. Neurodegeneration
does not occur during development of Zfp106(-/-) mice, suggesting that ZFP106 is likely
required for the maintenance of mature peripheral motor and sensory neurons. Analysis of
embryonic Zfp106(-/-) motor neurons revealed deficits in mitochondrial function, with an
inhibition of Complex I within the mitochondrial electron transport chain. Our results highlight a
vital role for ZFP106 in sensory and motor neuron maintenance and reveal a novel player in
mitochondrial dysfunction and neurodegeneration.