Study: Mea6 deficiency in oligodendrocytes affects white matter formation in the brain

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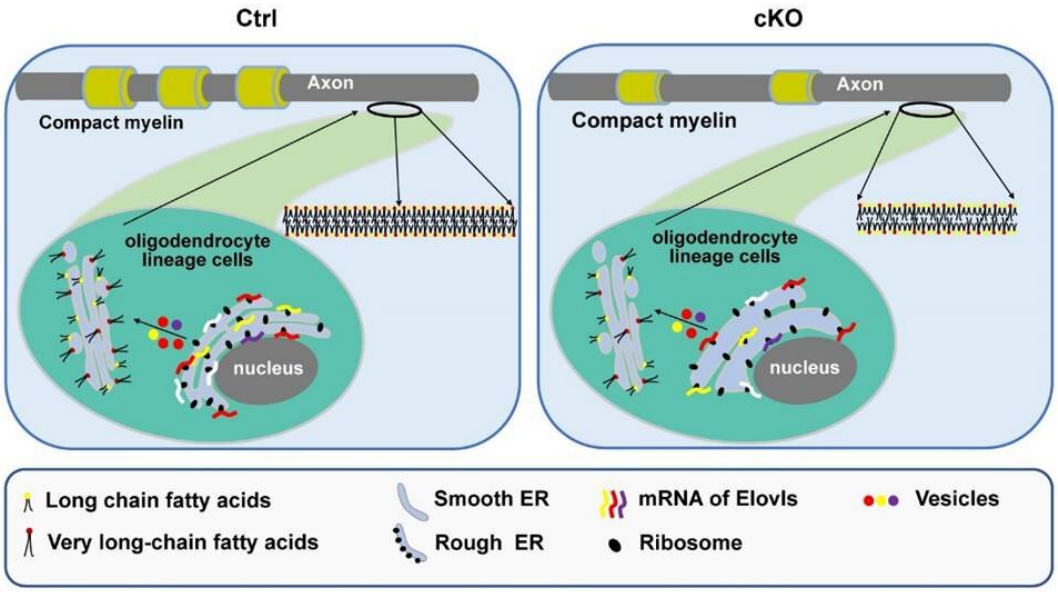

Model for the function of Mea6 in oligodendrocyte. Mea6 is involved in the transport of different lipids from the ER to the Golgi apparatus, and plays an essential role in the formation and/or maintenance of white matter. cKO of Mea6 affects the composition of major myelin lipid, especially different VLCFAs, leading to the hypomyelination of axons. . Credit: Tiantian Ma, Wei Mao, Shaohua Zhang, Yaqing Wang, Tao Wang, Jinghua Liu, Lei Shi, Rong Xue, Guanghou Shui, Zhiheng Xu

About half of adult human brain volume is made up of white matter. Lipid-rich myelin is a special structure formed by oligodendrocytes wrapping neuronal axons to form the major components of white matter. Abnormal myelin sheath is associated with many neurological diseases. Mea6/ cTAGE5C is essential for vesicle trafficking from ER to Golgi. However, its biological function in oligodendrocyte and white matter development remains unclear.

Scientists from Institute of Genetics and Developmental Biology of Chinese Academy of Sciences generated mice with conditional knockout (cKO) of Mea6 in oligodendrocytes. Using different models of diffusion magnetic resonance imaging, they detected the dramatically affected gross structure and microstructure of white matter, as well as its lipid and water diffusion capacity, in Mea6-cKO brains.

A significant decrease in whole-brain cholesterol and triglycerides was detected in cKOs. In addition, they performed the first lipidomic analysis of purified myelin sheath and found that Mea6 elimination significantly altered the proportion of lipid components in myelin lipidome, especially very long-chain fatty acids (VLCFAs).

In particular, the levels of most VLCFA-containing phosphatidylcholines were significantly lower in cKOs. The reduction of VLCFAs is likely due to the reduced expression of ELOVLs (elongation of very long chain fatty acids proteins). This study is published on March 23, 2023 online in *Life Metabolism*.

This study of an animal model with white matter malformation and the comprehensive lipid profiling could provide clues for future studies of myelin lipids and new insight into the pathogenesis of white matter diseases.

More information: Tiantian Ma et al, Ablation of Mea6/cTAGE5 in

oligodendrocytes significantly impairs white matter structure and lipid content, *Life Metabolism* (2023). DOI: 10.1093/lifemeta/load010