MedicalXpress

New advances in the study of megalencephalic leukoencephalopathy

March 26 2014

Several forms of leukodystrophies, genetic degenerative disorders that affect the myelin, are associated with vacuolization of myelin sheaths that enwrap axons of central neurons. Megalencephalic leukoencephalopathy (MLC), caused by mutations in MLC1 and GlialCAM, is a rare disease that entails this type of vacuoles. To date, there is not any treatment for patients.

A new international study published in the journal *Nature Communications* establishes that chloride channel dysfunction CLC-2 entails myelin vacuolization. The study is led by researchers Raúl Estévez, lecturer of the Department of Physiological Sciences II at the University of Barcelona (UB), and member of the Centre for Biomedical Network Research on Rare Diseases (CIBERER); Thomas J. Jentsch, from the Leibniz-Institute for *Molecular Pharmacology* (FMP-MDC, Berlin), and Virginia Nunes, lecturer of Genetics at UB, researcher at the Bellvitge Biomedical Research Institute (IDIBELL) and member of CIBERER.

The new study is based on the development of mouse models manifesting the disease that causes megalencephaly, spasticity and ataxia in humans. The study of these models shows that proteins MCL1 and GlialCAM play a crucial role in localization and regulation of chloride channel CLC-2 in the glia, and proves that the channel is involved in the disease.

The relationship between the ionic channel CLC-2 and the protein MLC

was described in a previous study, led by the group of Raúl Estévez, together with the scientific teams of CIBERER and FMP-MDC (Neuron, 2012). The study of these new mouse models means an advance in the knowledge of disease's development mechanisms and an opportunity to implement new therapeutic strategies for patients.

More information: Maja B. Hoegg-Beiler, Sònia Sirisi, Ian J. Orozco, Isidre Ferrer, Svea Hohensee, Muriel Auberson, Kathrin Gödde, Clara Vilches, Miguel López de Heredia, Virginia Nunes, Raúl Estévez y Thomas J. Jentsch. "Disrupting MLC1 and GlialCAM and ClC-2 interactions in leukodystrophy entails glial chloride channel dysfunction." *Nature Communications*, 5, marzo de 2014. DOI: 10.1038/ncomms4475.