Incurable Leigh Syndrome: Scientists create first human model for rare disease

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The group of Prof. Alessandro Prigione at the Department of General Pediatrics at the University Hospital Duesseldorf, Germany, in collaboration with the groups of Prof. Markus Schuelke at the Department of Neuropediatrics, Charite Universitaetsmedizin Berlin, and Prof. Nikolaus Rajewsky at the Berlin Institute for Medical Systems Biology (BIMSB), Max Delbrueck Center for Molecular Medicine (MDC), have now developed the first human model of Leigh syndrome caused by SURF1 mutations.

In brain organoids from Leigh syndrome patients, neurons do not mature properly. This is due to an impaired activation of mitochondrial metabolism in cells that generate neurons which are called neural precursors. The authors demonstrate that helping the activation of mitochondrial metabolism in neural precursors can revert the defects. They achieved this using two strategies that may be applicable in the clinics: 1) gene correction with CRISPR/Cas9 or viral-based delivery of the healthy gene, 2) increasing the expression of the metabolic regulator PGC1-alpha using the FDA-approved drug Bezafibrate. Credit: Dr. Agnieszka Rybak-Wolf

Leigh syndrome is the most severe mitochondrial disease in children. It causes severe muscle weakness, movement defects, and intellectual disabilities. It usually leads to death within the first years of life. No causative treatment is currently available. One of the genes frequently mutated in patients is SURF1, which encodes for a protein involved in the process of energy generation in the cells. Animal models did not recapitulate the defects seen in the patients carrying mutations in SURF1. Therefore, the scientists did not have the tool to start understanding the disease mechanisms and to identify possible targets for treatment. They report about the first human model for this rare disease in Nature Communications, published on March 26th.
disease Leigh syndrome, which is an orphan disease with high medical needs.


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