New study of gene mutations causing Leigh syndrome shows effects on embryonic development

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Embryonic stem cells (ESCs) prove to be an excellent model system for determining at what stage the mutations in the Complex I gene, known to cause Leigh syndrome, begin to affect embryonic development. The mutations leading to Complex I deficiency disrupt the energy-producing processes in cells, and in mouse ESC models have a negative effect on neuronal development and the initiation of a heartbeat in embryoid bodies, according to a new study published in *Stem Cells and Development*.

Jacqueline Johnson and coauthors from Monash University (Clayton), Royal Children's Hospital and University of Melbourne (Melbourne), and The Australian National University (Canberra), Australia report on the generation of mouse ESC lines that have no mutations in the Complex I NDUFS4 gene, mutations in one copy of the gene, or mutations in both copies of the gene. In the article "Deletion of the Complex I Subunit NDUFS4 Adversely Modulates Cellular Differentiation ", the researchers show that loss of NDUFS4 function did not affect the expression of other genes in the mitochrondria, which houses the energy-producing machinery of cells. Loss of NDUFS4 function did, however, lead to significant differences in early patterns of cellular gene expression.

"This highly experienced team has provided an elegant demonstration that the deletion of NDUFS4 in mouse embryonic stem cells and their

subsequent neural differentiation shows a phenotype caused by the deletion itself rather than chromosomal or mitochondrial sequelae," says Editor-in-Chief Graham C. Parker, PhD, The Carman and Ann Adams Department of Pediatrics, Wayne State University School of Medicine, Detroit, MI.

More information: Jacqueline Johnson et al. Deletion of the Complex I Subunit NDUFS4 Adversely Modulates Cellular Differentiation, *Stem Cells and Development* (2016). DOI: 10.1089/scd.2015.0211