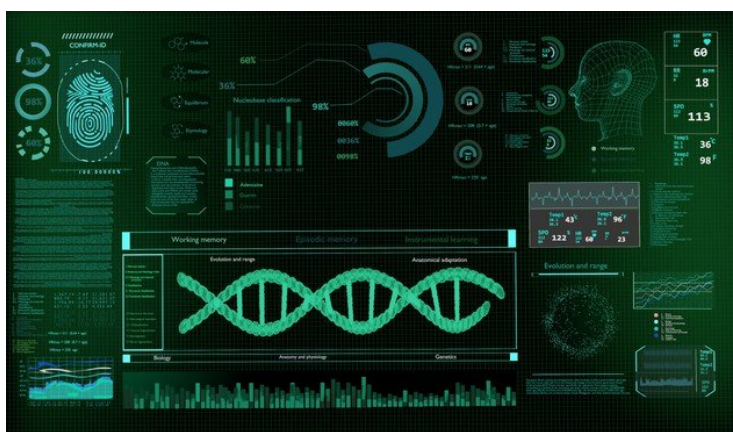


Japanese–European research team discovers novel genetic mitochondrial disorder

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Team of Japanese and European scientists identify a novel genetic mitochondrial disorder by analyzing DNA samples from three distinct families



Japanese-European team of scientists, including researchers from Fujita Health University, describe mutations in the *LIG3* gene, which plays a crucial role in mitochondrial DNA replication. These mutations cause a previously unknown syndrome characterized by gut dysmotility, leukoencephalopathy, and neuromuscular abnormalities.

In [an article recently published in the peer-reviewed journal *Brain*](#), a team of European and Japanese scientists, led by Dr. Mariko Taniguchi-Ikeda from Fujita Health University Hospital, describes a set of seven patients with a novel mitochondrial disorder caused by biallelic variants in the gene that encodes the *LIG3* protein, called the “*LIG3*” gene. Their report provides a description of the patients’ symptoms and a mechanistic exploration of the mutations’ effects.

Having detected a novel genetic mitochondrial disorder, Dr. Taniguchi-Ikeda wished to conduct further research by identifying other patients with pathogenic *LIG3* variants. Patients experienced a complex syndrome involving severe gut dysmotility and neurologic abnormalities as the most consistently observed clinical signs. The neurologic abnormalities included leukoencephalopathy, epilepsy, migraine, stroke-like episodes, and neurogenic bladder. Muscle pathology assessments revealed decreased staining intensities for cytochrome C oxidase.

To better characterize how the patients’ *LIG3* mutations could lead to such phenotypes. The *in vitro* experiments with patient-derived fibroblasts showed that the mutations resulted in reduced *LIG3* protein levels and diminished ligase activity. The consequent deficits in mitochondrial DNA maintenance would do much to explain the patients’ presentations. Experiments with zebrafish showed that disrupting the *lig3* gene produced brain alterations and gut transit impairments analogous to those observed in the patients.

The study brings to light a novel disorder resulting from disruption of a gene that plays a critical role in the maintenance of mitochondrial DNA. Study may facilitate efforts to diagnose patients with mitochondrial diseases.