Intellectual disability

Intellectual disability (ID) is one of neurodevelopmental disorders characterized by serious defects in both intelligence and adaptive behavior. Although it has been suggested that genetic aberrations associated with the process of cell division underlie ID, the cytological evidence for mitotic defects in actual patient's cells is rarely reported.

An informed consent can be said to have been given based upon a clear appreciation and understanding of the facts, implications, and consequences of an action. To give informed consent, the individual concerned must have adequate reasoning faculties and be in possession of all relevant facts. Impairments to reasoning and judgment that may prevent informed consent include basic intellectual or emotional immaturity, high levels of stress such as PTSD or a severe intellectual disability, severe mental illness, intoxication, severe sleep deprivation, Alzheimer disease, or being in a coma.

Okamoto et al. report a novel mutation in the STARD9 (also known as KIF16A) gene found in a patient with severe ID, characteristic features, epilepsy, acquired microcephaly, and blindness. Using whole-exome sequence analysis, we sequenced potential candidate genes in the patient. We identified a homozygous single-nucleotide deletion creating a premature stop codon in the STARD9 gene. STARD9 encodes a 4,700 amino acid protein belonging to the kinesin superfamily. Depletion of STARD9 or overexpression of C-terminally truncated STARD9 mutants were known to induce spindle assembly defects in human culture cells. To determine cytological features in the patient cells, we isolated lymphoblast cells from the patient, and performed immunofluorescence analysis. Remarkably, mitotic defects, including multipolar spindle formation, fragmentation of pericentriolar materials and centrosome amplification, were observed in the cells. Taken together, our findings raise the possibility that controlled expression of full-length STARD9 is necessary for proper spindle assembly in cell division during human development. We propose that mutations in STARD9 result in abnormal spindle morphology and cause a novel genetic syndrome with ID [1)].

1)
Okamoto N, Tsuchiya Y, Miya F, Tsunoda T, Yamashita K, Boroevich KA, Kato M, Saitoh S, Yamasaki M, Kanemura Y, Kosaki K, Kitagawa D. A novel genetic syndrome with STARD9 mutation and abnormal spindle morphology. Am J Med Genet A. 2017 Aug 4. doi: 10.1002/ajmg.a.38391. [Epub ahead of print] PubMed PMID: 28777490.