Murakami et al. described ten unrelated families with biallelic mutations in PIGB, a gene that encodes phosphatidylinositol glycan class B, which transfers the third mannose to the glycosylphosphatidylinositol (GPI). Ten different PIGB variants were found in these individuals. Flow cytometric analysis of blood cells and fibroblasts from the affected individuals showed decreased cell surface presence of GPI-anchored proteins. Most of the affected individuals have global developmental and/or intellectual delay, all had seizures, two had polymicrogyria, and four had peripheral neuropathy. Eight children passed away before four years old. Two of them had a clinical diagnosis of DOORS syndrome (deafness, onychodystrophy, osteodystrophy, mental retardation, and seizures), a condition that includes sensorineural deafness, shortened terminal phalanges with small finger and toenails, intellectual disability, and seizures; this condition overlaps with the severe phenotypes associated with inherited GPI deficiency. Most individuals tested showed elevated alkaline phosphatase, which is a characteristic of the inherited GPI deficiency but not DOORS syndrome. It is notable that two severely affected individuals showed 2-oxoglutaric aciduria, which can be seen in DOORS syndrome, suggesting that severe cases of inherited GPI deficiency and DOORS syndrome might share some molecular pathway disruptions [1)].

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