POMT1 Gene

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Contributor: Lily Guo

protein O-mannosyltransferase 1

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1. Introduction

The *POMT1* gene provides instructions for making one piece of the protein O-mannosyltransferase (POMT) enzyme complex. The other piece is produced from the *POMT2* gene. This enzyme complex is present in many different tissues in the body but is particularly abundant in the muscles used for movement (skeletal muscles), fetal brain, and testes.

The POMT complex helps modify a protein called alpha (α)-dystroglycan. Specifically, this complex adds a sugar molecule called mannose to α-dystroglycan through a process called glycosylation. Glycosylation is critical for the normal function of α-dystroglycan.

The α-dystroglycan protein helps anchor the structural framework inside each cell (cytoskeleton) to the lattice of proteins and other molecules outside the cell (extracellular matrix). In skeletal muscles, glycosylated α-dystroglycan helps stabilize and protect muscle fibers. In the brain, it helps direct the movement (migration) of nerve cells (neurons) during early development.

2. Health Conditions Related to Genetic Changes

2.1. Walker-Warburg syndrome

At least 24 mutations in the *POMT1* gene have been found to cause Walker-Warburg syndrome, the most severe form of a group of disorders known as congenital muscular dystrophies. Individuals with Walker-Warburg syndrome have skeletal muscle weakness and abnormalities of the brain and eyes. Because of the severity of the problems caused by this condition, affected individuals usually do not survive past early childhood.

POMT1 gene mutations that cause Walker-Warburg syndrome lead to the formation of nonfunctional POMT enzyme complexes that cannot transfer mannose to α-dystroglycan, preventing its normal glycosylation. As a result, α-dystroglycan can no longer effectively anchor cells to the proteins and other molecules that surround them. Without functional α-dystroglycan to stabilize the muscle fibers, they become damaged as they repeatedly contract and relax with use. The damaged fibers weaken and die over time, which affects the development, structure, and function of skeletal muscles in people with Walker-Warburg syndrome.

Defective α-dystroglycan also affects the migration of neurons during the early development of the brain. Instead of stopping when they reach their intended destinations, some neurons migrate past the surface of the brain into the fluid-filled space that surrounds it. Researchers believe that this problem with neuronal migration causes a brain abnormality called cobblestone lissencephaly, in which the surface of the brain lacks the normal folds and grooves and instead appears bumpy and irregular. Less is known about the effects of *POMT1* gene mutations in other parts of the body.

2.2. Other disorders

Mutations in the *POMT1* gene are also involved in less severe forms of muscular dystrophy, including muscle-eye-brain disease and *POMT1*-related congenital muscular dystrophy (also known as MDDGB1). Muscle-eye-brain disease is similar to Walker-Warburg syndrome (described above), although affected individuals usually survive into childhood or adolescence. *POMT1*-related congenital muscular dystrophy causes muscle weakness, brain abnormalities, and intellectual disability, but usually does not affect the eyes.

POMT1 gene mutations that cause these conditions result in POMT enzyme complexes with reduced function. As a result, glycosylation of α-dystroglycan is impaired. The severity of the resulting condition appears to be related to the level of α-dystroglycan glycosylation; the less glycosylation, the more severe the condition.

3. Other Names for This Gene

- dolichyl-phosphate-mannose--protein mannosyltransferase 1
- dolichyl-phosphate-mannose-protein mannosyltransferase
- LGMD2K
- MDDGA1
- MDDGB1
- MDDGC1
- POMT1_HUMAN
- protein O-mannosyl-transferase 1
- protein-O-mannosyltransferase 1
- RT

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