COG4 Gene

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component of oligomeric golgi complex 4

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1. Normal Function

The *COG4* gene provides instructions for making a protein called component of oligomeric Golgi complex 4 (COG4). As its name suggests, COG4 is one piece of a group of proteins known as the conserved oligomeric Golgi (COG) complex. This complex is important for maintaining normal functions in the Golgi apparatus, which is a cell structure in which newly produced proteins are modified so they can carry out their functions. An example of a protein modification process that occurs in the Golgi apparatus is glycosylation, by which sugar molecules (oligosaccharides) are attached to proteins and fats. Glycosylation modifies proteins so they can perform a wider variety of functions.

The COG complex plays an important role in a process called retrograde transport, through which proteins are moved from the Golgi apparatus to another cellular structure called the endoplasmic reticulum. Among its many functions, the endoplasmic reticulum folds and modifies newly formed proteins so they have the correct 3-dimensional shape. This transport pathway is called retrograde because it is in reverse order of the usual process for newly produced proteins. New proteins undergo initial processing in the endoplasmic reticulum then move to the Golgi apparatus for further modification before being released from the cell (secreted). Retrograde transport is important for sending unneeded proteins to the endoplasmic reticulum to get recycled and for relocating misplaced proteins within the cell.

For retrograde transport, proteins first must be incorporated into sac-like structures called vesicles that get attached to the Golgi apparatus membrane. The COG complex controls the attachment (tethering) of the vesicles to the Golgi membrane in preparation for transport. Once the proteins are incorporated, the vesicles detach and carry the proteins to the endoplasmic reticulum.

2. Health Conditions Related to Genetic Changes

2.1. Saul-Wilson Syndrome

At least two mutations in the *COG4* gene have been found to cause Saul-Wilson syndrome, a condition characterized by short stature (dwarfism) and other skeletal abnormalities. The mutations change single DNA building blocks (nucleotides) in the *COG4* gene. These two nucleotide changes result in the same alteration in the COG4 protein. The protein building block (amino acid) glycine is switched to the amino acid arginine at position 516 in the protein (written as Gly516Arg or G516R).

The amino acid change in the COG4 protein alters its structure, but the abnormal protein is still able to be a part of the COG complex. When the abnormal COG4 protein is incorporated into the COG complex, retrograde transport of proteins between the Golgi apparatus and the endoplasmic reticulum is increased. Because the *COG4* gene mutations enhance the COG complex's function, they are described as "gain-of-function." It is unclear how increased retrograde transport impairs bone growth and leads to the signs and symptoms of Saul-Wilson syndrome.

2.2. Other Disorders

Mutations in the *COG4* gene have also been found to cause a condition called *COG4*-congenital disorder of glycosylation (*COG4*-CDG). This condition often leads to developmental delay, intellectual disability, seizures, and an unusually small head size (microcephaly). Mutations in the *COG4* gene that cause *COG4*-CDG reduce the amount of COG4 protein or

eliminate it completely, which likely impairs COG complex formation and its role in maintaining the normal function of the Golgi apparatus. A dysfunctional Golgi apparatus results in abnormal protein glycosylation, which can affect multiple body systems, leading to the signs and symptoms of *COG4*-CDG.

3. Other Names for This Gene

- COD1
- COD1, S. CEREVISIAE, HOMOLOG OF
- COG4 gene

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