

CHMP2B Gene

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charged multivesicular body protein 2B

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1. Normal Function

The *CHMP2B* gene provides instructions for making a protein called charged multivesicular body protein 2B. This protein is active in the brain, where it appears to be essential for the survival of nerve cells (neurons).

Charged multivesicular body protein 2B forms one part (subunit) of a group of proteins known as the ESCRT-III complex. This complex helps transport other proteins from the cell membrane to the interior of the cell, a process known as endocytosis. In particular, the ESCRT-III complex is involved in the endocytosis of proteins that need to be broken down (degraded) by the cell. The complex helps sort these proteins into structures called multivesicular bodies (MVBs), which deliver them to lysosomes. Lysosomes are compartments within cells that digest and recycle many different types of molecules.

Charged multivesicular body protein 2B is regulated by a segment at one end of the protein known as the C-terminal domain. This domain usually keeps the protein turned off (inactive). The inactive protein is unable to interact with other subunits of the ESCRT-III complex, which prevents the complex from forming when it is not needed. The C-terminal domain also plays an important role in disassembling the ESCRT-III complex through its interaction with a protein called vacuolar protein sorting 4 (Vps4).

2. Health Conditions Related to Genetic Changes

2.1. CHMP2B-Related Frontotemporal Dementia

Several changes in the *CHMP2B* gene have been identified in people with frontotemporal dementia. At least two of these genetic changes are thought to be mutations that cause the disease. It is unclear whether the other genetic changes also cause disease; they may be rare variations that are unrelated to the development of frontotemporal dementia.

Most people with *CHMP2B*-related frontotemporal dementia are members of a single, large Danish family. Affected individuals in this family have a particular mutation, written as 532-1G>C, that changes a single DNA building block (base pair) in the *CHMP2B* gene. This mutation leads to the production of two abnormal versions of charged multivesicular body protein 2B, both of which are missing the C-terminal domain.

Without the C-terminal domain, charged multivesicular body protein 2B is constantly turned on (active) as part of the ESCRT-III complex. It cannot interact with Vps4, so the complex cannot be disassembled when it is no longer needed. As a result, the ESCRT-III complex builds up within cells and disrupts the transport and degradation of other proteins. These abnormalities ultimately lead to the death of neurons in the brain.

A gradual loss of neurons throughout the brain is characteristic of *CHMP2B*-related frontotemporal dementia. Many of the features of this disease result from neuronal death in regions near the front of the brain called the frontal and temporal lobes. The frontal lobes are involved in reasoning, planning, judgment, and problem-solving, while the temporal lobes help process hearing, speech, memory, and emotion. It is unclear why the signs and symptoms of this disease are related primarily to the frontal and temporal lobes.

2.2. Amyotrophic Lateral Sclerosis

Amyotrophic lateral sclerosis

3. Other Names for This Gene

- CHM2B_HUMAN
- CHMP family, member 2B
- CHMP2.5
- chromatin modifying protein 2B
- DMT1
- hVps2-2
- vacuolar protein sorting-associated protein 2-2
- VPS2 homolog B
- VPS2-2
- VPS2B

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