DYNC1H1 Gene

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Dynein Cytoplasmic 1 Heavy Chain 1

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1. Normal Function

The *DYNC1H1* gene provides instructions for making a protein that is part of a group (complex) of proteins called dynein. This complex is found in the fluid inside cells (cytoplasm). Dynein is turned on (activated) by attaching (binding) to another complex called dynactin. This dynein-dynactin complex binds to various materials within cells. Using energy provided by molecules called ATP, the dynein-dynactin complex moves material along a track-like system of small tubes called microtubules, similar to a conveyer belt. The dynein-dynactin complex is necessary for protein transport, positioning of cell compartments, movement of structures within the cell, and many other cell processes. Dynein helps neighboring nerve cells (neurons) communicate by transporting sac-like structures called synaptic vesicles that contain chemical messengers. When synaptic vesicles are passed from one neuron to another, the dynein-dynactin complex transports the vesicle from the edge of the cell to the nucleus, where the chemical message is received.

The parts (subunits) of a dynein complex are classified by weight as heavy, intermediate, light intermediate, or light chains. Two heavy chain proteins bind together to form the core of the dynein complex. Combinations of intermediate, light intermediate, and light chains make up the rest of the complex. The protein produced from the *DYNC1H1* gene is a heavy chain. Other subunits are produced from different genes.

2. Health Conditions Related to Genetic Changes

2.1 Charcot-Marie-Tooth Disease

2.2 Spinal Muscular Atrophy with Lower Extremity Predominance

At least eight mutations in the *DYNC1H1* gene have been found to cause a condition called spinal muscular atrophy with lower extremity predominance (SMA-LED). This condition is characterized by muscle weakness and wasting (atrophy) in the lower limbs that often begins in infancy or childhood. The *DYNC1H1* gene mutations that cause SMA-LED replace single protein building blocks (amino acids) in the heavy chain subunit of the dynein complex. These changes alter the core of the dynein complex and impair its function. As a result, the movement of proteins, synaptic vesicles, and other materials within cells is reduced. Decreased synaptic vesicle transport in neurons that control muscle movement (motor neurons), leading to impaired neuronal growth, is thought to contribute to the muscle weakness and atrophy experienced by people with SMA-LED. It is unclear why this condition primarily affects the lower limbs.

2.3 Other Disorders

DYNC1H1 gene mutations have been identified in some people who have intellectual disability. These affected individuals often have a brain malformation called polymicrogyria. Normally, the surface of the brain has many ridges or folds, called gyri. In people with polymicrogyria, the brain develops too many folds, and the folds are unusually small. In addition to intellectual disability, some affected individuals develop seizures and movement problems.

The *DYNC1H1* gene mutations that cause intellectual disability are typically in a different region of the gene than those that cause SMA-LED (described above). It is unclear whether the site of the mutation is associated with the location in the body most affected by the disease, with SMA-LED-associated mutations primarily affecting motor neurons and intellectual disability-associated mutations primarily affecting neurons in the brain.

3. Other Names for This Gene

- cytoplasmic dynein 1 heavy chain 1
- cytoplasmic dynein heavy chain 1
- DHC1
- DHC1a
- DNCH1
- Dnchc1
- DNCL
- DNECL
- DYHC
- DYHC1_HUMAN
- dynein heavy chain, cytosolic
- dynein, cytoplasmic 1, heavy chain 1
- dynein, cytoplasmic, heavy polypeptide 1
- HL-3
- p22

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