# STAC3 Gene

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SH3 and cysteine rich domain 3: The STAC3 gene provides instructions for making a protein whose function is not completely understood.

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## 1. Normal Function

The *STAC3* gene provides instructions for making a protein whose function is not completely understood. It plays a role in muscles used for movement (skeletal muscles). For the body to move normally, skeletal muscles must tense (contract) and relax in a coordinated way. Muscle contractions are triggered by changes in the concentration of certain charged atoms (ions) in muscle cells. The STAC3 protein aids in the process that triggers the release of calcium ions within muscle cells to start (initiate) muscle contraction.

The STAC3 protein interacts with two structures in muscle cells that are critical for calcium ion flow, dihydropyridine receptor (DHPR) and ryanodine receptor 1 (RYR1). However, STAC3's role in this formation is unknown. RYR1 forms a channel (the RYR1 channel) through which calcium ions can flow. In response to certain signals, DHPR turns on (activates) the RYR1 channel, and the activated RYR1 channel releases calcium ions stored in structures inside muscle cells. The resulting increase in the calcium ion concentration within muscle cells stimulates muscles to contract, allowing the body to move. The process by which certain chemical signals trigger muscle contraction is called excitation-contraction (E-C) coupling.

## 2. Health Conditions Related to Genetic Changes

### 2.1. STAC3 disorder

At least five mutations in the *STAC3* gene have been found to cause STAC3 disorder (formerly known as Native American myopathy). This condition is a muscle disorder characterized by weakness, droopy eyelids (ptosis) and other distinctive facial features, joint deformities (contractures), and increased risk of a condition known as malignant hyperthermia, which is a severe reaction to particular anesthetic drugs that are often used during surgery and other invasive procedures.

Mutations in the *STAC3* gene reduce the amount or impair the function of the STAC3 protein. Although the mechanism is unclear, studies show that a shortage of working STAC3 protein affects the function of DHPR and prevents the release of calcium ions by RYR1 channels, resulting in a buildup of calcium in storage. A disruption in calcium ion release prevents muscles from contracting normally, leading to the muscle weakness characteristic of STAC3 disorder.

It is unclear how these *STAC3* gene mutations lead to malignant hyperthermia in susceptible individuals. Mutations in other genes related to malignant hyperthermia activate the RYR1 channel improperly in response to certain drugs. As a result, large amounts of calcium ions are released from storage within muscle cells. An overabundance of available calcium ions causes skeletal muscles to contract abnormally, which leads to muscle rigidity. An increase in calcium ion concentration also activates processes that generate heat (leading to increased body temperature) and produce excess acid (leading to acidosis). It is unknown if *STAC3* gene mutations have a similar effect on RYR1 channel activity.

## 3. Other Names for This Gene

- SH3 AND CYSTEINE-RICH DOMAINS 3
- STAC3 gene

## References


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