# TCIRG1 Gene

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TCIRG1 Gene: T cell immune regulator 1, ATPase H+ transporting V0 subunit a3. The TCIRG1 gene provides instructions for making one part, the a3 subunit, of a large protein complex known as a vacuolar H+-ATPase (V-ATPase).

Keywords: genes

## 1. Normal Function

The *TCIRG1* gene provides instructions for making one part, the a3 subunit, of a large protein complex known as a vacuolar H+-ATPase (V-ATPase). V-ATPases are a group of similar complexes that act as pumps to move positively charged hydrogen atoms (protons) across membranes. This movement of protons helps regulate the relative acidity (pH) of cells and their surrounding environment. Tight control of pH is necessary for most biological reactions to proceed properly.

The V-ATPases containing the a3 subunit play an essential role in specialized cells called osteoclasts. These cells break down bone tissue as part of the normal process of bone remodeling, in which old bone is removed and new bone is created to replace it. Bones are constantly being remodeled, and the process is carefully controlled to ensure that bones stay strong and healthy.

On the surface of osteoclasts, V-ATPases are embedded in a specialized, highly folded membrane called the ruffled border. The ruffled border faces the surface of bone, where it helps form a tightly sealed compartment between the osteoclast and the bone surface. V-ATPases pump protons into the compartment, making it very acidic. This acidic environment is necessary to break down bone.

## 2. Health Conditions Related to Genetic Changes

### 2.1. Osteopetrosis

More than 60 mutations in the *TCIRG1* gene have been identified in people with osteopetrosis. These mutations cause the most severe form of the disorder, autosomal recessive osteopetrosis (ARO).

Many *TCIRG1* gene mutations change how the gene's instructions are used to make the a3 subunit of V-ATPase. Other mutations change single protein building blocks (amino acids) in the a3 subunit or lead to the production of an abnormally short version of the subunit. Studies suggest that most of the *TCIRG1* gene mutations responsible for osteopetrosis eliminate the function of the a3 subunit.

Without the a3 subunit, V-ATPases cannot pump protons out of osteoclasts. As a result, the compartment between the ruffled border and the bone surface is not acidified, and bone cannot be broken down. When old bone is not broken down as new bone is formed, bones throughout the skeleton become unusually dense. The bones are also structurally abnormal, making them prone to fracture. These problems with bone remodeling underlie the major features of autosomal recessive osteopetrosis.

### Severe congenital neutropenia

## 3. Other Names for This Gene

- Atp6i
- ATP6N1C
- ATP6V0A3
- ATPase, H+ transporting, 116kD

- OC-116
- OC-116 kDa
- OC-116kDa
- OC116
- OPTB1
- osteoclastic proton pump 116 kDa subunit
- specific 116-kDa vacuolar proton pump subunit
- Stv1
- T cell immune response cDNA7 protein
- T-cell immune regulator 1
- T-cell immune regulator 1, ATPase H+ transporting V0 subunit a3
- T-cell immune response cDNA 7
- T-cell immune response cDNA7 protein
- T-cell, immune regulator 1, ATPase, H+ transporting, lysosomal V0 protein a
- T-cell, immune regulator 1, ATPase, H+ transporting, lysosomal V0 protein A3
- T-cell, immune regulator 1, ATPase, H+ transporting, lysosomal V0 subunit A3
- TIRC7
- V-ATPase 116 kDa
- V-ATPase 116-kDa
- V-type proton ATPase 116 kDa subunit a
- V-type proton ATPase 116 kDa subunit a isoform 3
- vacuolar proton translocating ATPase 116 kDa subunit A
- Vph1
- VPP3_HUMAN

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