ACP5 Gene

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1. Normal Function

The *ACP5* gene provides instructions for making an enzyme called tartrate-resistant acid phosphatase type 5 (TRAP). The TRAP enzyme primarily regulates the activity of a protein called osteopontin, which is produced in bone cells called osteoclasts and in immune cells. Osteopontin performs a variety of functions in these cells. Two versions (isoforms) of the TRAP enzyme are produced: TRAP5a is found primarily in immune cells and TRAP5b is found primarily in bone cells called osteoclasts.

Osteoclasts are specialized cells that break down and remove (resorb) bone tissue that is no longer needed. These cells are involved in bone remodeling, which is a normal process that replaces old bone tissue with new bone. During bone remodeling, osteopontin is turned on (activated), allowing osteoclasts to attach (bind) to bones. When the breakdown of bone is complete, TRAP5b turns off (inactivates) osteopontin, causing the osteoclasts to release themselves from bone.

In the immune system, osteopontin is found primarily in cells called macrophages and dendritic cells. The protein helps fight infection by promoting inflammation, regulating immune cell activity, and turning on various immune system cells that are necessary to fight off foreign invaders such as bacteria and viruses. Like TRAP5b in bone cells, the TRAP5a enzyme inactivates osteopontin in macrophages and dendritic cells when it is no longer needed.

2. Health Conditions Related to Genetic Changes

2.1 Spondyloenchondrodysplasia with immune dysregulation

At least 10 mutations in the *ACP5* gene have been found to cause spondyloenchondrodysplasia with immune dysregulation (SPENCDI). This condition is characterized by abnormalities in bone growth and immune system function. The *ACP5* gene mutations that cause SPENCDI typically change single protein building blocks (amino acids) in the TRAP enzyme or result in the production of an abnormally short enzyme. These mutations affect both TRAP isoforms and impair or eliminate TRAP's ability to inactivate osteopontin. As a result, osteopontin is abnormally active, prolonging bone breakdown by osteoclasts and triggering abnormal inflammation and immune responses by immune cells.

In people with SPENCDI, increased bone breakdown contributes to the skeletal abnormalities, including irregularly shaped bones and short stature. An overactive immune system leads to increased susceptibility to autoimmune disorders, which occur when the immune system malfunctions and attacks the body's own tissues and organs. Immune system abnormalities also impair the body's normal response to harmful invaders, resulting in frequent infections. SPENCDI has several additional features, including movement disorders and intellectual disability, but it is unknown how changes in TRAP enzyme function lead to these other signs and symptoms.

3. Other Names for This Gene

- PPA5_HUMAN
- tartrate-resistant acid ATPase
- tartrate-resistant acid phosphatase type 5
- TRAP
- TrATPase

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