PRPS1 Gene

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phosphoribosyl pyrophosphate synthetase 1

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1. Normal Function

The *PRPS1* gene provides instructions for making an enzyme called phosphoribosyl pyrophosphate synthetase 1, or PRPP synthetase 1. This enzyme helps produce a molecule called phosphoribosyl pyrophosphate (PRPP). PRPP is involved in making purine and pyrimidine nucleotides. These nucleotides are building blocks of DNA, its chemical cousin RNA, and molecules such as ATP and GTP that serve as energy sources in the cell.

Purines and pyrimidines may be manufactured from smaller molecules, or they can be recycled from the breakdown of DNA and RNA in a series of reactions called the salvage pathway. Manufacturing purines and pyrimidines uses much more energy and takes more time than recycling them, which makes recycling these molecules more efficient. The salvage pathway ensures that cells have a plentiful supply of purines and pyrimidines.

PRPP synthetase 1 and PRPP are involved in the manufacture of new purines and pyrimidines, and are also essential for the purine salvage pathway.

2. Health Conditions Related to Genetic Changes

2.1. Arts syndrome

At least three *PRPS1* gene mutations have been identified in people with Arts syndrome, a disorder that causes serious neurological problems in males. Females can also be affected by this condition, but they typically have much milder symptoms.

The *PRPS1* gene mutations that cause Arts syndrome change single protein building blocks (amino acids) in the PRPP synthetase 1 enzyme. The mutations are believed to result in the production of an unstable enzyme with little or no activity. The lack of functional PRPP synthetase 1 enzyme disrupts both the manufacture and recycling of purines. The manufacture of pyrimidines is also affected, but not the pyrimidine salvage pathway. The disruption of purine production, and to a lesser extent pyrimidine production, may impair energy storage and transport in cells. Impairment of these processes may have a particularly severe effect on tissues that require a large amount of energy, such as the nervous system, resulting in the neurological problems characteristic of Arts syndrome.

2.2. Phosphoribosylpyrophosphate synthetase superactivity

At least seven mutations in the *PRPS1* gene that cause a severe form of phosphoribosylpyrophosphate synthetase superactivity (PRS superactivity) have been identified. These mutations change single amino acids in the PRPP synthetase 1 enzyme, resulting in a poorly regulated, overactive enzyme. In a milder form of PRS superactivity, the *PRPS1* gene is overactive for reasons that are not well understood. *PRPS1* gene overactivity increases the production of normal PRPP synthetase 1 enzyme, which increases the availability of PRPP. In both forms of the disorder, excessive amounts of purines are generated.

Under these conditions, uric acid, a waste product of purine breakdown, accumulates in the body. A buildup of uric acid can cause gout, which is a form of arthritis resulting from uric acid crystals in the joints. Affected individuals may also develop kidney or bladder stones formed from uric acid crystals.

People with the severe form of PRS superactivity have additional symptoms including loss of hearing caused by changes in the inner ear (sensorineural hearing loss), weak muscle tone (hypotonia), impaired muscle coordination (ataxia), and developmental delay. It is unclear how the *PRPS1* gene mutations that cause the severe form of PRS superactivity are related to these neurological problems.

3. Other Names for This Gene

- ARTS
- CMTX5
- dJ1070B1.2 (phosphoribosyl pyrophosphate synthetase 1)
- KIAA0967
- PPRibP
- PRPS1_HUMAN
- PRSI

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