# SLC22A12 Gene

Subjects: Genetics & Heredity
Contributor: Karina Chen

solute carrier family 22 member 12

Keywords: genes

## 1. Normal Function

The *SLC22A12* gene provides instructions for making a protein called urate transporter 1 (URAT1). This protein is found in the kidneys, specifically in structures called proximal tubules. These structures help to reabsorb needed nutrients, water, and other materials into the blood and excrete unneeded substances into the urine. Within the proximal tubules, the URAT1 protein helps transport molecules by exchanging negatively charged atoms (anions) for a substance called urate. Urate is a byproduct of certain normal chemical reactions in the body. In the bloodstream it acts as an antioxidant, protecting cells from the damaging effects of unstable molecules called free radicals. The URAT1 protein helps reabsorb urate into the bloodstream or release it into the urine, depending on the body's needs. Most urate that is filtered through the kidneys is reabsorbed into the bloodstream; about 10 percent is released into urine.

## 2. Health Conditions Related to Genetic Changes

### 2.1. Renal hypouricemia

More than 30 mutations in the *SLC22A12* gene have been found to cause renal hypouricemia. This condition results in a reduced amount of urate in the blood. Renal hypouricemia often does not cause any health problems but can lead to pain and nausea after exercise, kidney stones, or blood in the urine (hematuria). Most of the mutations that cause renal hypouricemia replace single protein building blocks (amino acids) in the URAT1 protein and reduce the protein's ability to reabsorb urate into the bloodstream. The most common mutation in affected Japanese and South Korean individuals replaces the amino acid tryptophan at position 258 with a premature stop signal (Trp258Ter or W258X), resulting in an abnormally short protein. A reduction in URAT1's ability to reabsorb urate results in a shortage of urate in the blood and an excessive amount lost through the urine. While it is not clear how these changes in urate levels lead to the signs and symptoms of renal hypouricemia, it is likely that the loss of urate's antioxidant properties in combination with the increase in urate passing through the kidneys to be released in urine contribute to the characteristic features of this condition.

### 2.2. Other disorders

Some studies have found variations in the *SLC22A12* gene to be associated with a condition called gout, which is a form of arthritis resulting from urate crystals in the joints. These variants likely impair the URAT1 protein's ability to release urate into the urine. As a result, too much urate is reabsorbed into the bloodstream, causing a buildup of urate in the body. This excess urate often accumulates in the body's joints in the form of crystals, leading to painful arthritis. Other studies, however, have not found an association between *SLC22A12* gene variants and gout. While the role of the *SLC22A12* gene in gout may be unclear, it is known that a combination of lifestyle, genetic, and environmental factors play a part in determining the risk of this complex disorder.

## 3. Other Names for This Gene

- OAT4L
- organic anion transporter 4-like protein
- renal-specific transporter
- RST
- solute carrier family 22 (organic anion/cation transporter), member 12
- solute carrier family 22 (organic anion/urate transporter), member 12

- URAT1
- urate anion exchanger 1
- urate transporter 1

## References


1. Kaito H, Ishimori S, Nozu K, Shima Y, Nakanishi K, Yoshikawa N, Iijima K.Molecular background of urate transporter genes in patients with exercise-inducedacute kidney injury. Am J Nephrol. 2013;38(4):316-20. doi: 10.1159/000355430.
2. Stiburkova B, Sebesta I, Ichida K, Nakamura M, Hulkova H, Krylov V, KryspinovaL, Jahnova H. Novel allelic variants and evidence for a prevalent mutation inURAT1 causing renal hypouricemia: biochemical, genetics and functional analysis. Eur J Hum Genet. 2013 Oct;21(10):1067-73. doi: 10.1038/ejhg.2013.3.
3. Tasic V, Hynes AM, Kitamura K, Cheong HI, Lozanovski VJ, Gucev Z, Jutabha P,Anzai N, Sayer JA. Clinical and functional characterization of URAT1 variants.PLoS One. 2011;6(12):e28641. doi: 10.1371/journal.pone.0028641.
4. Vázquez-Mellado J, Jiménez-Vaca AL, Cuevas-Covarrubias S, Alvarado-Romano V,Pozo-Molina G, Burgos-Vargas R. Molecular analysis of the SLC22A12 (URAT1) genein patients with primary gout. Rheumatology (Oxford). 2007 Feb;46(2):215-9.