

SLC2A9 gene

solute carrier family 2 member 9

Normal Function

The *SLC2A9* gene provides instructions for making a protein called glucose transporter 9 (GLUT9). This protein is found mainly 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 GLUT9 protein helps reabsorb or excrete a substance called urate.

Urate is a byproduct of certain normal biochemical reactions in the body. In the bloodstream it acts as an antioxidant, protecting cells from the damaging effects of unstable molecules called free radicals. When more urate is needed in the body, the GLUT9 protein helps reabsorb it into the bloodstream. Most urate that is filtered through the kidneys is reabsorbed into the bloodstream; about 10 percent is released into urine.

The GLUT9 protein also plays a role in reabsorbing and excreting the simple sugar glucose.

Health Conditions Related to Genetic Changes

Renal hypouricemia

At least 17 mutations in the *SLC2A9* 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 kidney stones, blood in the urine (hematuria), or pain and nausea after exercise. Most of the mutations that cause renal hypouricemia replace single protein building blocks (amino acids) in the GLUT9 protein and severely reduce or eliminate the protein's ability to reabsorb urate into the bloodstream. As a result, an excessive amount of urate is 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 the urine contribute to the characteristic features of this condition.

Gout

Genetic changes in the *SLC2A9* gene are associated with a condition called gout, which is a form of arthritis. Gout develops when elevated urate levels in the blood (

hyperuricemia) lead to the formation of urate crystals in joints, triggering an inflammatory response from the immune system.

SLC2A9 gene changes associated with gout likely increase the production of a form of the GLUT9 protein that is 28 amino acids shorter than the full-length version. This shorter version of GLUT9 reabsorbs urate into the bloodstream more readily than the full length version. An increase in the short GLUT9 protein raises the levels of urate in the blood and reduces its release into the urine. As a result, urate can accumulate in the body's joints in the form of crystals, leading to painful arthritis.

While changes in the *SLC2A9* gene can alter urate levels in the body, they are likely not enough to cause gout by themselves. A combination of dietary, genetic, and other environmental factors play a part in determining the risk of developing this complex disorder.

Other Names for This Gene

- glucose transporter type 9
- GLUT-9
- GLUT9
- GLUTX
- human glucose transporter-like protein-9
- solute carrier family 2 (facilitated glucose transporter), member 9
- solute carrier family 2, facilitated glucose transporter member 9
- UAQTL2
- urate voltage-driven efflux transporter 1
- URATv1

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of SLC2A9 ([https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=56606\[geneid\]](https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=56606[geneid]))

Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28%28SLC2A9%5BTIAB%5D%29+OR+%28GLUT9%5BTIAB%5D%29+OR+%28glucose+transporter+type+9%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D%29%29>)

Catalog of Genes and Diseases from OMIM

- SOLUTE CARRIER FAMILY 2 (FACILITATED GLUCOSE TRANSPORTER), MEMBER 9; SLC2A9 (<https://omim.org/entry/606142>)

Gene and Variant Databases

- NCBI Gene (<https://www.ncbi.nlm.nih.gov/gene/56606>)
- ClinVar ([https://www.ncbi.nlm.nih.gov/clinvar?term=SLC2A9\[gene\]](https://www.ncbi.nlm.nih.gov/clinvar?term=SLC2A9[gene]))

References

- Kaito H, Ishimori S, Nozu K, Shima Y, Nakanishi K, Yoshikawa N, Iijima K. Molecular background of urate transporter genes in patients with exercise-induced acute kidney injury. *Am J Nephrol.* 2013;38(4):316-20. doi: 10.1159/000355430. Epub 2013 Oct 4. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/24107611>)
- Kawamura Y, Matsuo H, Chiba T, Nagamori S, Nakayama A, Inoue H, Utsumi Y, Oda T, Nishiyama J, Kanai Y, Shinomiya N. Pathogenic GLUT9 mutations causing renal hypouricemia type 2 (RHUC2). *Nucleosides Nucleotides Nucleic Acids.* 2011 Dec;30(12):1105-11. doi: 10.1080/15257770.2011.623685. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/22132964>)
- Kottgen A, Albrecht E, Teumer A, Vitart V, Krumsiek J, Hundertmark C, Pistis G, Ruggiero D, O'Seaghdha CM, Haller T, Yang Q, Tanaka T, Johnson AD, Kutalik Z, Smith AV, Shi J, Struchalin M, Middelberg RP, Brown MJ, Gaffo AL, Pirastu N, Li G, Hayward C, Zemunik T, Huffman J, Yengo L, Zhao JH, Demirkan A, Feitosa MF, Liu X, Malerba G, Lopez LM, van der Harst P, Li X, Kleber ME, Hicks AA, Nolte IM, Johansson A, Murgia F, Wild SH, Bakker SJ, Peden JF, Dehghan A, Steri M, Tenesa A, Lagou V, Salo P, Mangino M, Rose LM, Lehtimäki T, Woodward OM, Okada Y, Tin A, Müller C, Oldmeadow C, Putku M, Czumara D, Kraft P, Frogger L, Thun GA, Grotevendt A, Gislason GK, Harris TB, Launer LJ, McArdle P, Shuldiner AR, Boerwinkle E, Coresh J, Schmidt H, Schallert M, Martin NG, Montgomery GW, Kubo M, Nakamura Y, Tanaka T, Munroe PB, Samani NJ, Jacobs DR Jr, Liu K, D'Adamo P, Ulivi S, Rotter JI, Psaty BM, Vollenweider P, Waeber G, Campbell S, Devuyst O, Navarro P, Kolcic I, Hastie N, Balkau B, Froguel P, Esko T, Salumets A, Khaw KT, Langenberg C, Wareham NJ, Isaacs A, Kraja A, Zhang Q, Wild PS, Scott RJ, Holliday EG, Org E, Viigimäe M, Bandinelli S, Metter JE, Lupo A, Trabetti E, Sorice R, Döring A, Lattka E, Strauch K, Theis F, Waldenberger M, Wichmann HE, Davies G, Gow AJ, Bruinenberg M; LifeLines Cohort Study; Stolk RP, Kooner JS, Zhang W, Winkelmann BR, Boehm BO, Lucae S, Penninx BW, Smit JH, Curhan G, Mudgal P, Plenge RM, Portas L, Persico I, Kirin M, Wilson JF, Mateo Leach I, van Gilst WH, Goel A, Ongen H, Hofman A, Rivadeneira F, Uitterlinden AG, Imboden M, von Eckardstein A, Cucca F, Nagaraja R, Piras MG, Nauck M, Schurmann C, Budde K, Ernst F, Farrington SM, Theodoratou E, Prokopenko I, Stumvoll M, Jula A, Perola M, Salomaa V, Shin SY, Spector TD, Sala C, Ridker PM, Kahonen M, Viikari J, Hengstenberg C, Nelson CP; CARDIoGRAM Consortium; DIAGRAM Consortium;

ICBP Consortium; MAGIC Consortium; Meschia JF, Nalls MA, Sharma P, Singleton AB, Kamatani N, Zeller T, Burnier M, Attia J, Laan M, Klopp N, Hillege HL, Kloiber S, Choi H, Pirastu M, Tore S, Probst-Hensch NM, Volzke H, Gudnason V, Parsa A, Schmidt R, Whitfield JB, Fornage M, Gasparini P, Siscovick DS, Polasek O, Campbell H, Rudan I, Bouatia-Naji N, Metspalu A, Loos RJ, van Duijn CM, Borecki IB, Ferrucci L, Gambero G, Deary IJ, Wolfenbuttel BH, Chambers JC, Marz W, Pramstaller PP, Snieder H, Gyllenstein U, Wright AF, Navis G, Watkins H, Witteman JC, Sanna S, Schipf S, Dunlop MG, Tonjes A, Ripatti S, Soranzo N, Toniolo D, Chasman DI, Raitakari O, Kao WH, Ciullo M, Fox CS, Caulfield M, Bochud M, Gieger C. Genome-wide association analyses identify 18 new loci associated with serum urate concentrations. *Nat Genet.* 2013 Feb;45(2):145-54. doi: 10.1038/ng.2500. Epub 2012 Dec 23. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/23263486>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3663712/>)

- Merriman T. Genomic Influences on Hyperuricemia and Gout. *Rheum Dis Clin North Am.* 2017 Aug;43(3):389-399. doi: 10.1016/j.rdc.2017.04.004. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/28711141>)
- Wei WH, Guo Y, Kindt AS, Merriman TR, Semple CA, Wang K, Haley CS. Abundant local interactions in the 4p16.1 region suggest functional mechanisms underlying SLC2A9 associations with human serum uric acid. *Hum Mol Genet.* 2014 Oct 1;23(19):5061-8. doi: 10.1093/hmg/ddu227. Epub 2014 May 12. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/24821702>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4159153/>)

Genomic Location

The *SLC2A9* gene is found on chromosome 4 (<https://medlineplus.gov/genetics/chromosome/4/>).

Last updated August 1, 2018