

Grange Syndrome

Subjects: **Genetics & Heredity**

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Grange syndrome is a rare condition that primarily affects the blood vessels. It is characterized by narrowing (stenosis) or blockage (occlusion) of arteries that supply blood to various organs and tissues, including the kidneys, brain, and heart.

genetic conditions

1. Introduction

Stenosis or occlusion of the arteries that supply blood to the kidneys (renal arteries) can result in chronic high blood pressure (hypertension). Blockage of the arteries that carry blood to the brain (cerebral arteries) can cause a stroke.

Additional features of Grange syndrome can include short fingers and toes (brachydactyly), fusion of some of the fingers or toes (syndactyly), fragile bones that are prone to breakage, and learning disabilities. Most people with this disorder also have heart defects that are present from birth.

2. Frequency

Grange syndrome has been reported to affect at least six individuals from three families.

3. Causes

Grange syndrome results from mutations in the *YY1AP1* gene. The protein produced from this gene is part of a group of proteins (a complex) that helps regulate several critical functions within cells. These include gene activity (expression), repair of damaged DNA, cell specialization (differentiation), and cell growth and division (proliferation). Researchers believe that this protein complex plays a particularly important role in smooth muscle cells, which line the walls of blood vessels.

Mutations in the *YY1AP1* gene likely disrupt the function of the complex, which leads to reduced proliferation and differentiation of smooth muscle cells. However, it is unclear how these changes lead to narrowing and blockage of arteries. It is also unknown how *YY1AP1* gene mutations are related to other features of Grange syndrome, such as bone abnormalities and learning disabilities.

3.1. The gene associated with Grange syndrome

- YY1AP1

4. Inheritance

This condition is thought to be inherited in an autosomal recessive pattern, which means both copies of the *YY1AP1* gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

5. Other Names for This Condition

- arterial occlusive disease, progressive, with hypertension, heart defects, bone fragility, and brachysyndactyly
- Grange occlusive arterial syndrome
- GRNG

References

1. Grange DK, Balfour IC, Chen SC, Wood EG. Familial syndrome of progressive arterial occlusive disease consistent with fibromuscular dysplasia, hypertension, congenital cardiac defects, bone fragility, brachysyndactyly, and learning disabilities. *Am J Med Genet.* 1998 Feb 17;75(5):469-80.
2. Guo DC, Duan XY, Regalado ES, Mellor-Crummey L, Kwartler CS, Kim D, Lieberman K, de Vries BBA, Pfundt R, Schinzel A, Kotzot D, Shen X, Yang ML; University of Washington Center for Mendelian Genomics, Bamshad MJ, Nickerson DA, Gornik HL, Ganesh SK, Braverman AC, Grange DK, Milewicz DM. Loss-of-Function Mutations in *YY1AP1* Lead to Grange Syndrome and a Fibromuscular Dysplasia-Like Vascular Disease. *Am J Hum Genet.* 2017 Jan 5;100(1):21-30. doi:10.1016/j.ajhg.2016.11.008.
3. Volonghi I, Frigerio M, Mardighian D, Gasparotti R, Del Zotto E, Giossi A, Costa P, Poli L, Jeannin G, Gregorini GA, Padovani A, Pezzini A. Grange syndrome: an identifiable cause of stroke in young adults. *Am J Med Genet A.* 2012 Nov;158A(11):2894-8. doi: 10.1002/ajmg.a.35593.
4. Wallerstein R, Augustyn AM, Wallerstein D, Elton L, Tejeiro B, Johnson V, Lieberman K. A new case of Grange syndrome without cardiac findings. *Am J Med Genet A.* 2006 Jun 15;140(12):1316-20.
5. Weymann S, Yonekawa Y, Khan N, Martin E, Heppner FL, Schinzel A, Kotzot D. Severe arterial occlusive disorder and brachysyndactyly in a boy: a further case of Grange syndrome? *Am J Med*

Genet. 2001 Mar 15;99(3):190-5.

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