# Legius Syndrome

Subjects: Genetics & Heredity
Contributor: Camila Xu

Legius syndrome is a condition characterized by changes in skin coloring (pigmentation).

Keywords: genetic conditions

## 1. Introduction

Almost all affected individuals have multiple café-au-lait spots, which are flat patches on the skin that are darker than the surrounding area. Another pigmentation change, freckles in the armpits and groin, may occur in some affected individuals.

Other signs and symptoms of Legius syndrome may include an abnormally large head (macrocephaly) and unusual facial characteristics. Although most people with Legius syndrome have normal intelligence, some affected individuals have been diagnosed with learning disabilities, attention-deficit disorder (ADD), or attention-deficit/hyperactivity disorder (ADHD).

Many of the signs and symptoms of Legius syndrome also occur in a similar disorder called neurofibromatosis type 1. It can be difficult to tell the two disorders apart in early childhood. However, the features of the two disorders differ later in life.

## 2. Frequency

The prevalence of Legius syndrome is unknown. Many individuals with this disorder are likely misdiagnosed because the signs and symptoms of Legius syndrome are similar to those of neurofibromatosis type 1.

## 3. Causes

Mutations in the *SPRED1* gene cause Legius syndrome. The *SPRED1* gene provides instructions for making the Spred-1 protein. This protein controls (regulates) an important cell signaling pathway that is involved in the growth and division of cells (proliferation), the process by which cells mature to carry out specific functions (differentiation), cell movement, and the self-destruction of cells (apoptosis). Mutations in the *SPRED1* gene lead to a nonfunctional protein that can no longer regulate the pathway, resulting in overactive signaling. It is unclear how mutations in the *SPRED1* gene cause the signs and symptoms of Legius syndrome.

### 3.1. The gene associated with Legius syndrome

- SPRED1

## 4. Inheritance

This condition is inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder.

## 5. Other Names for This Condition

- neurofibromatosis type 1-like syndrome
- NFLS

## References


1. Brems H, Chmara M, Sahbatou M, Denayer E, Taniguchi K, Kato R, Somers R,Messiaen L, De Schepper S, Fryns JP, Cools J, Marynen P, Thomas G, Yoshimura A,Legius E. Germline loss-of-function mutations in SPRED1 cause a neurofibromatosis1-like phenotype. Nat Genet. 2007 Sep;39(9):1120-6.
2. Denayer E, Chmara M, Brems H, Kievit AM, van Bever Y, Van den Ouweland AM, VanMinkelen R, de Goede-Bolder A, Oostenbrink R, Lakeman P, Beert E, Ishizaki T,Mori T, Keymolen K, Van den Ende J, Mangold E, Peltonen S, Brice G, Rankin J, VanSpaendonck-Zwarts KY, Yoshimura A, Legius E. Legius syndrome in fourteenfamilies. Hum Mutat. 2011 Jan;32(1):E1985-98. doi: 10.1002/humu.21404.
3. Legius E, Stevenson D. Legius Syndrome. 2010 Oct 14 [updated 2020 Aug 6]. In: Adam MP, Ardinger HH, Pagon RA, Wallace SE, Bean LJH, Stephens K, Amemiya A,editors. GeneReviews® [Internet]. Seattle (WA): University of Washington,Seattle; 1993-2020. Available from http://www.ncbi.nlm.nih.gov/books/NBK47312/
4. Messiaen L, Yao S, Brems H, Callens T, Sathienkijkanchai A, Denayer E, SpencerE, Arn P, Babovic-Vuksanovic D, Bay C, Bobele G, Cohen BH, Escobar L, Eunpu D,Grebe T, Greenstein R, Hachen R, Irons M, Kronn D, Lemire E, Leppig K, Lim C,McDonald M, Narayanan V, Pearn A, Pedersen R, Powell B, Shapiro LR, Skidmore D,Tegay D, Thiese H, Zackai EH, Vijzelaar R, Taniguchi K, Ayada T, Okamoto F,Yoshimura A, Parret A, Korf B, Legius E. Clinical and mutational spectrum ofneurofibromatosis type 1-like syndrome. JAMA. 2009 Nov 18;302(19):2111-8. doi:10.1001/jama.2009.1663. Erratum in: JAMA. 2010 Jun 23;303(24):2477.
5. Pasmant E, Sabbagh A, Hanna N, Masliah-Planchon J, Jolly E, Goussard P,Ballerini P, Cartault F, Barbarot S, Landman-Parker J, Soufir N, Parfait B,Vidaud M, Wolkenstein P, Vidaud D, France RN. SPRED1 germline mutations caused a neurofibromatosis type 1 overlapping phenotype. J Med Genet. 2009Jul;46(7):425-30. doi: 10.1136/jmg.2008.065243.
6. Spurlock G, Bennett E, Chuzhanova N, Thomas N, Jim HP, Side L, Davies S, Haan E, Kerr B, Huson SM, Upadhyaya M. SPRED1 mutations (Legius syndrome): anotherclinically useful genotype for dissecting the neurofibromatosis type 1 phenotype.J Med Genet. 2009 Jul;46(7):431-7. doi: 10.1136/jmg.2008.065474.


---