SMARCA2 Gene

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1. Normal Function

The *SMARCA2* gene provides instructions for making one piece (subunit) of a group of similar protein complexes known as SWI/SNF complexes. These complexes regulate gene activity (expression) by a process known as chromatin remodeling. Chromatin is the network of DNA and proteins that packages DNA into chromosomes. The structure of chromatin can be changed (remodeled) to alter how tightly DNA is packaged. Chromatin remodeling is one way gene expression is regulated during development; when DNA is tightly packed, gene expression is lower than when DNA is loosely packed. SWI/SNF complexes help with chromatin remodeling by moving parts of chromatin called nucleosomes, which makes DNA more accessible for gene expression. To provide energy for chromatin remodeling, the SMARCA2 protein uses a molecule called ATP.

SWI/SNF complexes regulate genes that are involved in many processes, including repairing damaged DNA; copying (replicating) DNA; and controlling the growth, division, and maturation (differentiation) of cells. The SMARCA2 protein and other SWI/SNF subunits are thought to act as tumor suppressors, which keep cells from growing and dividing too rapidly or in an uncontrolled way.

2. Health Conditions Related to Genetic Changes

2.1. Nicolaides-Baraitser syndrome

At least 50 mutations in the *SMARCA2* gene have been found to cause Nicolaides-Baraitser syndrome. This condition is characterized by multiple abnormalities, primarily sparse scalp hair, small head size (microcephaly), distinctive facial features, short stature, abnormal fingers, recurrent seizures (epilepsy), and moderate to severe intellectual disability with impaired language development. Almost all *SMARCA2* gene mutations that cause Nicolaides-Baraitser syndrome change single protein building blocks (amino acids) in the protein. These mutations are located within an area of the protein that attaches to ATP and is responsible for providing energy to the SWI/SNF complexes. These altered proteins are able to form SWI/SNF complexes, but these complexes are nonfunctional and cannot participate in chromatin remodeling. Disturbance of this regulatory process alters the activity of many genes, which likely explains the diverse signs and symptoms of Nicolaides-Baraitser syndrome.

2.2. Cancers

Common DNA variants (polymorphisms) that affect the *SMARCA2* gene have been found in certain types of cancer, particularly lung cancer in tobacco smokers and head and neck cancer. The changes that are associated with these cancers are described as germline, meaning that they are present from birth and found in all of the body's cells. (While the mutations that cause Nicolaides-Baraitser syndrome, which is described above, are also germline, there is no increased risk for cancer in individuals with that condition.) Two specific *SMARCA2* gene polymorphisms have been found to be associated with the development of these cancers. These changes occur in an area near the *SMARCA2* gene called the promoter region, which controls the production of the SMARCA2 protein. One change adds seven building blocks of DNA (nucleotides) at position -741 (insTATTTTT); the other adds six nucleotides at position -1321 (insTTTTAA) of the promoter. The incidence of lung cancer and head and neck cancer is increased only when both of these polymorphisms are present in both copies of the *SMARCA2* gene in each cell.

These polymorphisms impair the function of the promoter and reduce the expression of the *SMARCA2* gene. The reduced gene activity likely decreases or alters protein production, which would lead to changes in SWI/SNF complexes. These changes may impair normal cell differentiation, which leads to the overgrowth of certain cell types, causing cancer. Alternatively, abnormal SWI/SNF complexes may disrupt the regulation of genes that help control the growth and division of cells, which leads to cancer. It is unclear why these changes in the promoter region of the *SMARCA2* gene seem to be associated only with head and neck cancer and lung cancer in smokers.

3. Other Names for This Gene

- ATP-dependent helicase SMARCA2
- BAF190
- BAF190B
- BRG1-associated factor 190B
- BRM
- global transcription activator homologous sequence
- hBRM
- hSNF2a
- protein brahma homolog
- SNF2
- SNF2-alpha
- SNF2/SWI2-like protein 2
- SNF2L2
- SNF2LA
- Sth1p
- sucrose nonfermenting 2-like protein 2
- SWI/SNF-related matrix-associated actin-dependent regulator of chromatin a2
- SWI2

References

1. Liu G, Gramling S, Munoz D, Cheng D, Azad AK, Mirshams M, Chen Z, Xu W,Roberts H, Shepherd FA, Tsao MS, Reisman D. Two novel BRM insertion promotersequence variants are associated with loss of BRM expression and lung cancerrisk. Oncogene. 2011 Jul 21;30(29):3295-304. doi: 10.1038/onc.2011.81.
2. Sousa SB, Hennekam RC; Nicolaides-Baraitser Syndrome International Consortium.Phenotype and genotype in Nicolaides-Baraitser syndrome. Am J Med Genet C SeminMed Genet. 2014 Sep;166C(3):302-14. doi: 10.1002/ajmg.c.31409.Review.
3. Van Houdt JK, Nowakowska BA, Sousa SB, van Schaik BD, Seuntjens E, Avonce N,Sifrim A, Abdul-Rahman OA, van den Boogaard MJ, Bottani A, Castori M,Cormier-Daire V, Deardorff MA, Filges I, Fryer A, Fryns JP, Gana S, Garavelli L, Gillessen-Kaesbach G, Hall BD, Horn D, Huylebroeck D, Klapecki J,Krajewska-Walasek M, Kuechler A, Lines MA, Maas S, Macdermot KD, McKee S, MageeA, de Man SA, Moreau Y, Morice-Picard F, Obersztyn E, Pilch J, Rosser E, Shannon N, Stolte-Dijkstra I, Van Dijck P, Vilain C, Vogels A, Wakeling E, Wieczorek D,Wilson L, Zuffardi O, van Kampen AH, Devriendt K, Hennekam R, Vermeesch JR.Heterozygous missense mutations in SMARCA2 cause Nicolaides-Baraitser syndrome.Nat Genet. 2012 Feb 26;44(4):445-9, S1. doi: 10.1038/ng.1105.
4. Wong KM, Qiu X, Cheng D, Azad AK, Habbous S, Palepu P, Mirshams M, Patel D,Chen Z, Roberts H, Knox J, Marquez S, Wong R, Darling G, Waldron J, Goldstein D, Leighl N, Shepherd FA, Tsao M, Der S, Reisman D, Liu G. Two BRM promoterinsertion polymorphisms increase the risk of early-stage upper aerodigestivetract cancers. Cancer Med. 2014 Apr;3(2):426-33. doi: 10.1002/cam4.201.