

AIP gene

aryl hydrocarbon receptor interacting protein

Normal Function

The *AIP* gene provides instructions for making a protein called aryl hydrocarbon receptor-interacting protein (AIP). Although AIP's function is not well understood, it is known to interact with numerous other proteins, including one called the aryl hydrocarbon receptor. Through these interactions, AIP likely helps regulate certain cell processes, such as the growth and division (proliferation) of cells, the process by which cells mature to carry out specific functions (differentiation), and cell survival. This protein is thought to act as a tumor suppressor, which means it normally helps prevent cells from proliferating in an uncontrolled way.

Health Conditions Related to Genetic Changes

Familial isolated pituitary adenoma

Mutations in the *AIP* gene cause 15 to 25 percent of cases of familial isolated pituitary adenoma (FIPA), an inherited condition characterized by development of a noncancerous tumor in the pituitary gland (called a pituitary adenoma). This small gland at the base of the brain produces hormones that control many important body functions. There are several types of pituitary adenomas categorized by the hormone they produce. Affected individuals within the same family may develop the same type of pituitary adenoma or different types. People with a mutation in the *AIP* gene most commonly develop a type of pituitary adenoma called a somatotropinoma. FIPA tumors caused by *AIP* gene mutations usually occur at a younger age and are larger than those without *AIP* gene mutations.

Many kinds of mutations in the *AIP* gene have been identified in affected families. Some of these changes lead to an abnormally short protein or no protein at all. Other mutations change single protein building blocks (amino acids) in AIP. Although it is unclear how these mutations are involved in tumor development, researchers believe that the alterations disrupt interaction between AIP and one or more other proteins. The ability of AIP to control cell proliferation may be reduced, allowing pituitary cells to grow and divide unchecked and form a tumor. It is not known why the pituitary gland is specifically affected or why certain types of pituitary adenomas develop.

Even before FIPA was defined as a condition, doctors recognized that

somatotropinomas could occur in multiple members of a family. They referred to these tumors as isolated familial somatotropinoma. These tumors produce and release excess growth hormone (also called somatotropin), which promotes growth of the body. Because it can cause overgrowth of the hands, feet, and face (acromegaly), the condition is also referred to as familial isolated acromegaly. Later, researchers discovered that isolated familial somatotropinoma can be caused by mutations in the *AIP* gene, and these tumors are now considered part of FIPA.

Other disorders

Mutations in the *AIP* gene are found in a small percentage of individuals with sporadic macroadenomas, which are large (macro-) pituitary adenomas that occur in individuals with no history of the condition in their family. When caused by *AIP* gene mutations, the tumors occur at a relatively young age, usually before age 30. Although other family members are not affected, the gene mutation is often inherited from a parent who never developed an adenoma.

Other Names for This Gene

- AH receptor-interacting protein
- AIP_HUMAN
- ARA9
- FKBP16
- FKBP37
- HBV X-associated protein 2
- immunophilin homolog ARA9
- SMTPHN
- XAP-2
- XAP2

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of AIP ([https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=9049\[geneid\]](https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=9049[geneid]))

Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28%28AIP%5BTIAB%5D%29+OR+%28aryl+hydrocarbon+receptor+interacting+protein%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+720+days%22%5Bdp%5D%29%29%29>)

Catalog of Genes and Diseases from OMIM

- ARYL HYDROCARBON RECEPTOR-INTERACTING PROTEIN; AIP (<https://omim.org/entry/605555>)

Gene and Variant Databases

- NCBI Gene (<https://www.ncbi.nlm.nih.gov/gene/9049>)
- ClinVar ([https://www.ncbi.nlm.nih.gov/clinvar?term=AIP\[gene\]](https://www.ncbi.nlm.nih.gov/clinvar?term=AIP[gene]))

References

- Beckers A, Aaltonen LA, Daly AF, Karhu A. Familial isolated pituitary adenomas (FIPA) and the pituitary adenoma predisposition due to mutations in the arylhydrocarbon receptor interacting protein (AIP) gene. *Endocr Rev.* 2013Apr;34(2):239-77. doi: 10.1210/er.2012-1013. Epub 2013 Jan 31. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/23371967>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3610678/>)
- Cazabat L, Bouligand J, Salenave S, Bernier M, Gaillard S, Parker F, Young J, Guiochon-Mantel A, Chanson P. Germline AIP mutations in apparently sporadic pituitary adenomas: prevalence in a prospective single-center cohort of 443 patients. *J Clin Endocrinol Metab.* 2012 Apr;97(4):E663-70. doi:10.1210/jc.2011-2291. Epub 2012 Feb 8. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/22319033>)
- Daly AF, Vanbellinghen JF, Khoo SK, Jaffrain-Rea ML, Naves LA, Guitelman MA, Murat A, Emy P, Gimenez-Roqueplo AP, Tamburrano G, Raverot G, Barlier A, DeHerder W, Penfornis A, Ciccarelli E, Estour B, Lecomte P, Gatta B, Chabre O, Sabate MI, Bertagna X, Garcia Basavilbaso N, Stalder G, Colao A, Ferolla P, Wemeau JL, Caron P, Sadoul JL, Oneto A, Archambeaud F, Calender A, Sinilnikova O, Montanana CF, Cavagnini F, Hana V, Solano A, Delettieres D, Luccio-Camelo DC, Basso A, Rohmer V, Brue T, Bours V, Teh BT, Beckers A. Aryl hydrocarbon receptor-interacting protein gene mutations in familial isolated pituitary adenomas: analysis in 73 families. *J Clin Endocrinol Metab.* 2007May;92(5):1891-6. doi: 10.1210/jc.2006-2513. Epub 2007 Jan 23. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/17244780>)
- Heliovaara E, Raitila A, Launonen V, Paetau A, Arola J, Lehtonen H, Sane T, Weil RJ, Vierimaa O, Salmela P, Tuppurainen K, Makinen M, Aaltonen LA, Karhu A. The expression of AIP-related molecules in elucidation of cellular pathways in pituitary adenomas. *Am J Pathol.* 2009 Dec;175(6):2501-7. doi:10.2353/ajpath.2009.081131. Epub 2009 Oct 22. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/19850893>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2789606/>)
- Igreja S, Chahal HS, King P, Bolger GB, Srirangalingam U, Guasti L, Chapple JP,

Trivellin G, Gueorguiev M, Guegan K, Stals K, Khoo B, Kumar AV, Ellard S, Grossman AB, Korbonits M; International FIPA Consortium. Characterization of arylhydrocarbon receptor interacting protein (AIP) mutations in familial isolated pituitary adenoma families. *Hum Mutat.* 2010 Aug;31(8):950-60. doi:10.1002/humu.21292. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/20506337>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3065644/>)

- Leontiou CA, Gueorguiev M, van der Spuy J, Quinton R, Lolli F, Hassan S, Chahal HS, Igreja SC, Jordan S, Rowe J, Stolbrink M, Christian HC, Wray J, Bishop-Bailey D, Berney DM, Wass JA, Popovic V, Ribeiro-Oliveira A Jr, Gadelha MR, Monson JP, Akker SA, Davis JR, Clayton RN, Yoshimoto K, Iwata T, Matsuno A, Eguchi K, Musat M, Flanagan D, Peters G, Bolger GB, Chapple JP, Frohman LA, Grossman AB, Korbonits M. The role of the aryl hydrocarbon receptor-interacting protein gene in familial and sporadic pituitary adenomas. *J Clin Endocrinol Metab.* 2008 Jun;93(6):2390-401. doi: 10.1210/jc.2007-2611. Epub 2008 Apr 1. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/18381572>)
- Tichomirowa MA, Barlier A, Daly AF, Jaffrain-Rea ML, Ronchi C, Yaneva M, Urban JD, Petrossians P, Elenkova A, Tabarin A, Desailoud R, Maiter D, Schurmeyer T, Cozzi R, Theodoropoulou M, Sievers C, Bernabeu I, Naves LA, Chabre O, Montanana CF, Hana V, Halaby G, Delemer B, Aizpun JI, Sonnet E, Longas AF, Hagelstein MT, Caron P, Stalla GK, Bours V, Zacharieva S, Spada A, Brue T, Beckers A. High prevalence of AIP gene mutations following focused screening in young patients with sporadic pituitary macroadenomas. *Eur J Endocrinol.* 2011 Oct;165(4):509-15. doi: 10.1530/EJE-11-0304. Epub 2011 Jul 13. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/21753072>)
- Vierimaa O, Georgitsi M, Lehtonen R, Vahteristo P, Kokko A, Raitila A, Tuppurainen K, Ebeling TM, Salmela PI, Paschke R, Gundogdu S, De Menis E, Makinen MJ, Launonen V, Karhu A, Aaltonen LA. Pituitary adenoma predisposition caused by germline mutations in the AIP gene. *Science.* 2006 May 26;312(5777):1228-30. doi:10.1126/science.1126100. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/16728643>)

Genomic Location

The *AIP* gene is found on chromosome 11 (<https://medlineplus.gov/genetics/chromosome/11/>).

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