Tuberous sclerosis complex

Description

Tuberous sclerosis complex is a genetic disorder characterized by the growth of numerous noncancerous (benign) tumors in many parts of the body. These tumors can occur in the brain, kidneys, heart, skin, and other organs, in some cases leading to significant health problems. Tuberous sclerosis complex also causes developmental problems, and the signs and symptoms of the condition vary from person to person.

Tuberous sclerosis complex often affects the brain, with some affected individuals having benign growths in the outer surface of the brain (cerebral cortex) known as cortical tubers. Individuals with tuberous sclerosis complex often develop a pattern of behaviors called TSC-associated neuropsychiatric disorders (TAND). These disorders include hyperactivity, aggression, psychiatric conditions, intellectual disability, and problems with communication and social interaction (autism spectrum disorder). Additionally, individuals with tuberous sclerosis complex may have attention-deficit/hyperactivity disorder (ADHD) or seizures.

Kidney tumors are common in people with tuberous sclerosis complex; these growths can cause severe problems with kidney function and may be life-threatening in some cases. Additionally, tumors can develop in the heart (cardiac rhabdomyoma) and the light-sensitive tissue at the back of the eye (the retina). Some women with tuberous sclerosis complex develop lymphangioleiomyomatosis (LAM), which is a lung disease characterized by the abnormal overgrowth of smooth muscle-like tissue in the lungs that causes coughing, shortness of breath, chest pain, and lung collapse.

Virtually all affected people have skin abnormalities, including patches of unusually light-colored skin, areas of raised and thickened skin, and growths under the nails. Tumors on the face called facial angiofibromas are also common beginning in childhood. Sometimes, affected individuals have areas of bone or dental damage.

Frequency

Tuberous sclerosis complex affects 1 in 6,000 to 10,000 people.

Causes

Variants (also known as mutations) in the *TSC1* or *TSC2* gene can cause tuberous sclerosis complex. The *TSC1* and *TSC2* genes provide instructions for making the

proteins hamartin and tuberin, respectively. Within cells, these two proteins work together to help regulate cell growth and division (proliferation) and cell size. The proteins act as tumor suppressors, which normally prevent cells from growing and dividing too fast or in an uncontrolled way.

People with tuberous sclerosis complex are born with one altered copy of the *TSC1* gene or the *TSC2* gene in each cell. A variant in one copy of the *TSC1* gene prevents cells from making functional hamartin protein from that copy; a change in one copy of the *TSC2* gene prevents cells from making functional tuberin protein from the altered copy. However, enough protein is usually produced from the other, normal copy of the *TSC1* or *TSC2* gene to regulate cell growth effectively. For tumors to develop in tuberous sclerosis complex, a second change involving the other copy of the *TSC1* or *TSC2* gene must occur in cells during a person's lifetime.

Cells that have variants in both copies of the *TSC1* gene cannot produce any functional hamartin; cells with two altered copies of the *TSC2* gene are unable to produce any functional tuberin. The loss of either of these proteins allows the cell to grow and divide in an uncontrolled way to form a tumor. In people with tuberous sclerosis complex, a second variant in the *TSC1* or *TSC2* gene typically occurs in multiple cells over an affected person's lifetime. The absence of hamartin or tuberin in different types of cells leads to the growth of tumors in many different organs and tissues, as seen in tuberous sclerosis complex.

Learn more about the genes associated with Tuberous sclerosis complex

- TSC1
- TSC2

Inheritance

Tuberous sclerosis complex has an autosomal dominant pattern of inheritance, which means one copy of the altered gene in each cell is sufficient to increase the risk of developing tumors and other problems with development. In about one-third of cases, an affected person inherits an altered *TSC1* or *TSC2* gene from a parent who has the disorder. The remaining two-thirds of people with tuberous sclerosis complex are born with new variants in the *TSC1* or *TSC2* gene. These cases, which are described as sporadic, occur in people with no history of tuberous sclerosis complex in their family. *TSC1* gene variants appear to be more common in familial cases of tuberous sclerosis complex, while variants in the *TSC2* gene occur more frequently in sporadic cases.

Rarely, individuals with tuberous sclerosis complex do not have an identified variant in the *TSC1* or *TSC2* gene. Research suggests that in these cases the condition may be caused by a random variant in the *TSC1* or *TSC2* gene that occurs very early in development. As a result, some of the body's cells have a normal version of the gene, while others have the altered version. This situation is called mosaicism.

Other Names for This Condition

- Bourneville disease
- Bourneville phakomatosis
- Cerebral sclerosis
- Sclerosis tuberosa
- Tuberose sclerosis

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Tuberous sclerosis 1 (https://www.ncbi.nlm.nih.gov/gtr/conditions/C1854465/)
- Genetic Testing Registry: Tuberous sclerosis 2 (https://www.ncbi.nlm.nih.gov/gtr/conditions/C1860707/)

Genetic and Rare Diseases Information Center

- Tuberous sclerosis complex (https://rarediseases.info.nih.gov/diseases/7830/index)

Patient Support and Advocacy Resources

- National Organization for Rare Disorders (NORD) (https://rarediseases.org/)

Clinical Trials

- ClinicalTrials.gov (https://clinicaltrials.gov/search?cond=%22Tuberous sclerosis complex%22)

Catalog of Genes and Diseases from OMIM

- TUBEROUS SCLEROSIS 1; TSC1 (https://omim.org/entry/191100)
- TUBEROUS SCLEROSIS 2; TSC2 (https://omim.org/entry/613254)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=(Tuberous+Sclerosis%5BMAJR%5D)+AND+(tuberous+sclerosis%5BTI%5D)+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D)

References

- Crino PB, Nathanson KL, Henske EP. The tuberous sclerosis complex. N Engl JMed. 2006 Sep 28;355(13):1345-56. doi: 10.1056/NEJMra055323. No abstractavailable. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/17005952)
- Franz DN, Bissler JJ, McCormack FX. Tuberous sclerosis complex: neurological, renal and pulmonary manifestations. Neuropediatrics. 2010 Oct;41(5):199-208. doi: 10.1055/s-0030-1269906. Epub 2011 Jan 5. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/21210335) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4629839/)
- Hyman MH, Whittemore VH. National Institutes of Health consensus conference: tuberous sclerosis complex. Arch Neurol. 2000 May;57(5):662-5. doi:10.1001/archneur.57.5.662. No abstract available. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/10815131)
- Marom D. Genetics of tuberous sclerosis complex: an update. Childs Nerv Syst. 2020 Oct;36(10):2489-2496. doi: 10.1007/s00381-020-04726-z. Epub 2020 Aug 6. Citation on PubMed (https://www.ncbi.nlm.nih.gov/pubmed/32761379)
- Northrup H, Aronow ME, Bebin EM, Bissler J, Darling TN, de Vries PJ, Frost MD, Fuchs Z, Gosnell ES, Gupta N, Jansen AC, Jozwiak S, Kingswood JC, Knilans TK, McCormack FX, Pounders A, Roberds SL, Rodriguez-Buritica DF, Roth J, Sampson JR,Sparagana S, Thiele EA, Weiner HL, Wheless JW, Towbin AJ, Krueger DA; International Tuberous Sclerosis Complex Consensus Group. Updated InternationalTuberous Sclerosis Complex Diagnostic Criteria and Surveillance and ManagementRecommendations. Pediatr Neurol. 2021 Oct;123:50-66. doi:10.1016/j.pediatrneurol.2021.07.011. Epub 2021 Jul 24. Citation on PubMed (https://www.ncbi.nlm.nih.gov/pubmed/34399110)
- Northrup H, Koenig MK, Pearson DA, Au KS. Tuberous Sclerosis Complex. 1999 Jul13 [updated 2021 Dec 9]. In: Adam MP, Feldman J, Mirzaa GM, Pagon RA, Wallace SE,Bean LJH, Gripp KW, Amemiya A, editors. GeneReviews(R) [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2024. Available fromhttp://www.ncbi.nlm.nih.gov/books/NBK1220/ Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/20301399)
- Randle SC. Tuberous Sclerosis Complex: A Review. Pediatr Ann. 2017 Apr1;46(4):e166-e171. doi: 10.3928/19382359-20170320-01. Citation on PubMed (https://www.ncbi.nlm.nih.gov/pubmed/28414398)
- Salussolia CL, Klonowska K, Kwiatkowski DJ, Sahin M. Genetic Etiologies, Diagnosis, and Treatment of Tuberous Sclerosis Complex. Annu Rev Genomics HumGenet. 2019 Aug 31;20:217-240. doi: 10.1146/annurev-genom-083118-015354. Epub2019 Apr 24. Citation on PubMed (https://www.ncbi.nlm.nih.gov/pubmed/31018109)

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