Tuberous Sclerosis Complex

Subjects: Genetics & Heredity

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genetic conditions

1. Introduction

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 skin, brain, kidneys, 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.

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.

Tuberous sclerosis complex often affects the brain, resulting in 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). Some individuals with tuberous sclerosis complex have seizures or benign brain tumors that can cause serious or life-threatening complications.

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 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 cause coughing, shortness of breath, chest pain, and lung collapse.

2. Frequency

Tuberous sclerosis complex affects about 1 in 6,000 people.

3. Causes

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 likely work together to help regulate cell growth and 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 mutated copy of the *TSC1* or *TSC2* gene in each cell. This mutation prevents the cell from making functional hamartin or tuberin from the altered copy of the gene. However, enough protein is usually produced from the other, normal copy of the gene to regulate cell growth effectively. For some types of tumors to develop, a second mutation involving the other copy of the *TSC1* or *TSC2* gene must occur in certain cells during a person's lifetime.

When both copies of the *TSC1* gene are mutated in a particular cell, that cell cannot produce any functional hamartin; cells with two altered copies of the *TSC2* gene are unable to produce any functional tuberin. The loss 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 *TSC1* or *TSC2* mutation typically occurs in multiple cells over an affected person's lifetime. The loss of hamartin or tuberin in different types of cells leads to the growth of tumors in many different organs and tissues.

3.1 The genes associated with Tuberous sclerosis complex

- TSC1
- TSC2

4. 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 mutations 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* mutations appear to be more common in familial cases of tuberous sclerosis complex, while mutations in the *TSC2* gene occur more frequently in sporadic cases.

Rarely, individuals with tuberous sclerosis complex do not have an identified mutation in the *TSC1* or *TSC2* gene. Research suggests that in these cases the condition may be caused by a random mutation 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 mutated version. This situation is called mosaicism.

5. Other Names for This Condition

- Bourneville disease
- Bourneville phakomatosis
- cerebral sclerosis
- epiloia
- sclerosis tuberosa
- tuberose sclerosis

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