UT Southwestern Harold C. Simmons Comprehensive Cancer Center | NCI Designated Comprehensive Cancer Center

Tuberous Sclerosis Complex (*TSC1*, *TSC2* Gene Mutations)

What You Should Know About Tuberous Sclerosis Complex

Tuberous sclerosis complex (TSC) is caused by mutations in the *TSC1* and *TSC2* genes. TSC is an extremely variable disease that results in benign tumors forming throughout the body. The most common benign tumors occur in the skin, brain, kidneys, lungs, heart, and eyes. Although these tumors are benign, they can interfere with normal organ function and cause a range of health problems. Additionally, individuals with TSC do have an increased risk for kidney cancer.

Cancer/Tumor Risks, Other Features Associated with Tuberous Sclerosis Complex

- Skin: The majority of individuals (virtually 100%) with TSC have skin abnormalities. These can include light spots, known as hypomelanotic macules, as well as a variety of other benign tumors or lesions, including facial angiofibromas, shagreen patches, fibrous facial plaques, and ungual fibromas.
- Brain: Most individuals (up to 90%) with TSC have brain abnormalities, including subependymal nodules (SEN), cortical tubers, and benign tumors known as subependymal giant cell astrocytomas (SEGA). These brain abnormalities can results in seizures, cognitive impairment, and behavioral problems.
- Kidneys: Most individuals (approximately 80%) with TSC develop kidney disease. Kidney disease in TSC most commonly includes kidney cysts and benign tumors known as angiomyolipomas (AML). Rarely, individuals with TSC can also develop kidney cancer.
- Lungs: Approximately 30% of individuals with TSC develop lymphangiomyomatosis (LAM), a lung disease. LAM primarily affects females. For many individuals, LAM does not cause any significant symptoms, but it may result in lung collapse (pneumothorax) or fluid build-up in the lungs.
- Heart: Approximately 47-67% of individuals with TSC have cardiac rhabdomyomas, benign tumors of the heart. These tumors are present at birth and often remain stable or decrease in size over time. While most cardiac rhabdomyomas do not cause any symptoms, they can, in some instances, affect blood flow or cause abnormal heart rhythms.
- Eyes: Individuals with TSC can develop benign tumors of the retina known as hamartomas, and other eyes lesions. Most eye lesions are asymptomatic, but can cause retinal detachment, glaucoma, and vision loss.

Risks to Family Members

Mutations in the *TSC1* and *TSC2* genes are inherited in an autosomal dominant fashion. This means that children, brothers, sisters, and parents of individuals with a *TSC1/2* mutation have a 1 in 2 (50%) chance of having the mutation as well. Most individuals with TSC have new mutation not inherited from either parent, known as a *de novo* mutation. Most individuals with TSC develop at least one of the associated tumors/features, but the presentation of the condition can vary greatly among individuals. Both males and females can inherit a familial *TSC1/2* mutation and can pass that it on to their children.

Managing Cancer Risks

- Skin: Annual dermatologic examinations, and appropriate treatment of rapidly changing or symptomatic lesions.
- Brain: MRI every 1-3 years for asymptomatic individuals under age 25 years (more frequently for symptomatic individuals). Continued periodic surveillance is recommended after age 25 for individuals with SEGA.
- Kidneys: Abdominal MRI every 1-3 years, annual blood pressure monitoring and glomerular filtration rate (GFR) testing.
- Lungs: Baseline pulmonary function test (PFT) and high-resolution chest computed tomography (HCRT) for all females, and symptomatic males age 18 years and older at the time of diagnosis. Repeat HCRT every 5-10 years if baseline was normal. Individuals with lung cysts should have annual PFT, and HCRT every 2-3 years.
- Heart: Echocardiography at initial diagnosis, and minimally every 3-5 years thereafter for individuals with an asymptomatic cardiac rhabdomyoma (or every 1-3 years in children).
- Eyes: Opthalmologic exam at the time of diagnosis, and annually thereafter for symptomatic individuals
- mTOR inhibitors may be considered as a therapeutic option for skin lesions, SEGAs, kidney AMLs, and LAM.

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