STK11

The *STK11* gene is a tumor suppressor gene. Tumor suppressor genes slow down cell division, repair DNA mistakes, or tell cells when to die. When they don't work properly, cells can grow out of control, which can lead to cancer. The primary role of *STK11* is to slow down cell growth and production when the cell does not have enough energy and nutrients to grow and divide. *STK11* also helps the cell maintain its shape and aids in its ability to move.

Like most genes, each person has two copies of the *STK11* gene: one inherited from each parent. A mutation in a single *STK11* gene inherited from one parent causes Peutz-Jeghers syndrome (PJS), which is known to increase the risk of developing gastrointestinal polyps as well as certain cancers, including breast, ovarian, colorectal, stomach and others.

Mutations in *STK11* can be a risk factor for many non-cancerous findings. These include a high number of colon polyps that may lead to bowel obstruction; dark blue to dark brown pigmented spots on the fingers, around the mouth, eyes, nostrils, and anus, and inside of the cheeks that may fade in puberty and adulthood; non-cancerous ovarian tumors called sex cord tumors with annular tubules (SCTAT) and mucinous tumors; and non-cancerous testicular tumors called large calcifying Sertoli cell tumors (LCST). Some of these non-cancerous findings can have symptoms, while others will have no effect on health.

How common are mutations in the *STK11* gene?

Mutations in the *STK11* gene are rare—but approximately 80-94% of individuals with PJS have a pathogenic mutation in *STK11*.[1]

How mutations in this gene impact risk

Women

If a woman has a mutation in the *STK11* gene, her chances of developing breast, ovarian, colorectal, stomach, cervical, lung, pancreatic, small bowel, and uterine cancer are greater than that of the average US woman. This does not mean that she has a diagnosis of cancer or that she will definitely develop cancer in her lifetime.

[1] Aretz S, Stienen D, Uhlhaas S, et al. High proportion of large genomic STK11 deletions in Peutz-Jeghers syndrome. Hum Mut. 2005; 26(6):513–519.

Cancer by age 65 or 70	Average US woman[2]	With *STK11* mutation
Breast	7.1%	32-54%[3,4,5,6]
Ovarian	<1%	21%[5,6]
Colorectal	1.6%	39%[4,6]
Stomach	<1%	29%[5,6]
Cervical	<1%	Elevated[5,6]
Lung	2.1%	7-17%[3,5]
Pancreatic	<1%	11%[4]
Small bowel	<1%	13%[5,6]
Uterine	1.3%	9%[5,6]

Elevated: Risk is increased, but further research may clarify the exact risk figure.

Men

If a man has a mutation in the *STK11* gene, his chances of colorectal, lung, pancreatic, small bowel, stomach, and testicular cancer are greater than that of the average US man. This does not mean that he has a diagnosis of cancer or that he will definitely develop cancer in his lifetime.

Cancer by age 65 or 70	Average US man[2]	With *STK11* mutation
Colorectal	2%	39%[4,6]
Lung	2.5%	7-17%[3,5]
Pancreatic	<1%	11%[4,6]
Small bowel	<0.1%	13%[5,6]

[2] Surveillance, Epidemiology, and End Results (SEER) Program, National Cancer Institute. 2010-2012. DevCan software (http://surveillance.cancer.gov/devcan) V 6.7.0, Accessed June 2015.
[3] Lim W, Olschwang S, Keller JJ, et al. Relative frequency and morphology of cancers in STK11 mutation carriers. Gastroenterology. 2004;126(7):1788-94.
[4] Hearle N, Schumacher V, Menko FH, et al. Frequency and spectrum of cancers in the Peutz-Jeghers syndrome. Clin Cancer Res. 2006;12(10):3209-15.
[5] Giardiello FM, Brensinger JD, Tersmette AC, et al. Very high risk of cancer in familial Peutz-Jeghers syndrome. Gastroenterology. 2000;119(6):1447-53.
[6] van Lier MG, Wagner A, Mathus-vliegen EM, Kuipers EJ, Steyerberg EW, Van leerdam ME. High cancer risk in Peutz-Jeghers syndrome: a systematic review and surveillance recommendations. Am J Gastroenterol. 2010;105(6):1258-64.

Stomach	<1%	29%[5,6]
Testicular	<1%	Elevated[5,6]

Elevated: Risk is increased, but further research may clarify the exact risk figure.

Screening guidelines

Below is a summary of screening guidelines from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) established by experts at the National Comprehensive Cancer Network (NCCN).[7] They are for individuals who have a mutation in the *STK11* gene. If you have a mutation in this gene, your healthcare provider may use these NCCN Guidelines® to help create a customized screening plan for you.

Women

Breast[8]

- **Starting at age 25:** Breast exam by your provider every 6 months. Mammogram and breast MRI screening every year. Your provider may wish to alternate between these two screenings every 6 months.

Cervical, ovarian, and uterine cancer[8]

- **Starting at age 18-20:** Pelvic examination by your provider and Pap smear every year. Your provider may also discuss the benefits and limitations of a transvaginal ultrasound.

Colorectal cancer[8]

- **Starting in the late teens:** Colonoscopy every 2-3 years.

Stomach cancer[8]

- **Starting in the late teens:** Upper endoscopy every 2-3 years.

Lung cancer[8]

- Currently, there are no lung cancer screening guidelines from the NCCN specific to *STK11* mutation carriers. Your provider may discuss smoking cessation and symptoms of lung cancer.

Pancreatic cancer[8]

- **Starting at age 30-35:** Magnetic resonance cholangiopancreatography (MRCP) or endoscopic ultrasound (EUS) every 1-2 years.

[7] Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Genetic/Familial High-Risk Assessment: Colorectal V.2.2016. © National Comprehensive Cancer Network, Inc 2016. All rights reserved. Accessed October 25, 2016. To view the most recent and complete version of the guideline, go online to NCCN.org. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, NCCN GUIDELINES®, and all other NCCN Content are trademarks owned by the National Comprehensive Cancer Network, Inc.

[8] National Comprehensive Cancer Network. Genetic/Familial High-Risk Assessment: Breast and Ovarian. *NCCN Guidelines Version 1.2017.* Available at www.nccn.org. Published September 2016.

Small bowel cancer[8]

- **Starting at age 8-10:** Baseline small bowel visualization (CT or MRI enterography) with follow-up visualizations based on findings.
- **Starting at age 18:** Small bowel visualization (CT or MRI enterography) every 2-3 years, though this may be individualized.

Men

Testicular cancer[8]

- **Starting at age 10:** Annual testicular exam by a provider with observation for feminizing changes

Colorectal cancer[8]

- **Starting in the late teens:** Colonoscopy every 2-3 years.

Stomach cancer[8]

- **Starting in the late teens:** Upper endoscopy every 2-3 years.

Lung cancer[8]

- Currently, there are no lung cancer screening guidelines from the NCCN specific to *STK11* mutation carriers. Your provider may discuss smoking cessation and symptoms of lung cancer.

Pancreatic cancer[8]

- **Starting at age 30-35:** Magnetic resonance cholangiopancreatography (MRCP) or endoscopic ultrasound (EUS) every 1-2 years.

Small bowel cancer[8]

- **Starting at age 8-10:** Baseline small bowel visualization (CT or MRI enterography) with follow-up visualizations based on findings.
- **Starting at age 18:** Small bowel visualization (CT or MRI enterography) every 2-3 years, though this may be individualized.

Useful resources

Hereditary Colon Cancer Foundation

A nonprofit organization serving the hereditary colorectal cancer community.
www.hcctakesguts.org

Kintalk

An educational and family communication site for individuals and their families with hereditary cancer conditions
www.kintalk.org

Bright Pink
Focused on the prevention and early detection of breast and ovarian cancer in young women, while providing support for high-risk individuals.
www.brightpink.org

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