



Disease Information

Peutz-Jeghers Syndrome (PJS) is an autosomal dominant disorder characterized by the development of gastrointestinal hamartomatous polyps and melanin hyperpigmentation of the skin and mucous membranes. The gastrointestinal (GI) polyps, while benign, can result in chronic bleeding, secondary anemia, and contribute to recurrent obstruction and intussusceptions, often requiring surgical intervention. In addition to polyposis and mucocutaneous pigmentation, PJS patients are predisposed to a variety of tumors, most commonly gastroesophageal, small bowel, colorectal, and pancreatic.¹ With an estimated incidence of 1 in 120,000 births, individuals affected by PJS are also at increased risk for developing breast, ovarian, uterine, cervical, testicular, and lung cancer.^{2,3} Overall, individuals affected with PJS have an 81% risk of developing cancer by age of 70, with GI and breast cancers being the most common.^{4,5,6}

PJS is caused by mutations in the *STK11* gene (previously known as *LKB1*). Located on chromosome 19p13.3, *STK11* is comprised of 10 exons, only nine of which code for the serine threonine protein kinase-11.⁷ *STK11* is a tumor suppressor gene that helps in cell cycle arrest and growth suppression.⁸ *STK11* also interacts with the p53 tumor suppressor to regulate apoptosis. Polyps in PJS have been shown to have reduced numbers of apoptotic cells and lack *STK11* protein expression.⁹ Mutations in *STK11* result in a truncated protein that causes an inactivation of kinase domains.^{10,11}

Testing Benefits & Indications

Treatment options are available for disease management, including removal of polyps, as well as preventative screening and standard treatments for the associated cancers. Genetic testing enables identification of individuals who are at increased risk of cancers associated with *STK11* mutations.¹²

Test Description

This Ambry Test: Peutz-Jeghers AMPLIFIED includes concurrent gene sequence analysis and gross deletion/duplication analysis of the *STK11* gene. PCR-based double-stranded automated sequencing in the sense and antisense directions for exons 1-9 of the *STK11* gene, plus at least 20 bases into the 5' and 3' ends of all the introns and analysis for gross deletions/duplications of the *STK11* gene is performed by the Multiplex Ligation-Dependent Probe Amplification (MLPA) kit, developed by MRC Holland. Specific mutation analysis for individual *STK11* mutations known to be in the family is also available.

Mutation Detection Rate

Mutations in *STK11* have been identified in 100% of individuals with a family history of PJS, and 91% of those with a negative family history.¹¹ The Ambry Test: Peutz-Jeghers AMPLIFIED is capable of detecting >99% of identified mutations in *STK11*.

Turn-Around-Time

Peutz-Jeghers AMPLIFIED™	21 – 28 days
Gene sequence analysis	14 – 21 days
Deletion/duplication analysis	10 – 14 days
Specific mutation analysis	10 – 14 days

Specimen Requirements

Blood: Collect 3-5 cc from adult or 2 cc minimum from child into EDTA purple-top tube (first choice) or ACD yellow-top tube (second choice). Store at room temperature or refrigerate. Ship at room temperature.

Blood Spot: Call for availability.

Saliva: Collect 2 ml into Oragene™ DNA Self-Collection container. Store and ship at room temperature.

DNA: Send 20 µg in TE at 50-100 ng/µl. Store frozen and ship on ice or dry ice.

Prenatal: Prenatal testing is available. Please call an Ambry Genetic Counselor to discuss your case.

CPT Codes

Peutz-Jeghers AMPLIFIED™83891, 83894x9, 83898x8, 83904x17, 83900, 83901x11, 83909x16, 83912x2
STK11 Gene Sequence analysis83891, 83894x9, 83898x 8, 83904x16, 83909x16, 83912
STK11 Deletion/Duplication analysis83891, 83894, 83900, 83901x11, 83909, 83912x2
Gene sequence or specific mutation analysis83891, 83894x2, 83898, 83904x2, 83909x2, 83912

References

¹ Westerman AM et al. *Scand J Gastroenterol Suppl.* 1999; 230: 64-70.

² Giardiello FM et al. *Gastroenterology.* 2000; 119(6): 1447-53.

³ Marignani PA. *J Clin Pathol.* 2005; 58(1): 15-9.

⁴ Boardman LA et al. *Human Mutation.* 2000; 16(1): 23-30.

⁵ Spigelman AD et al. *Gut.* 1989; 30:1588-1590.

⁶ Lim W et al. *Gastroenterology.* 2004; 126:1788-1794.

⁷ Jenne DE et al. *Nat Genet.* 1998; 18(1): 38-43.

⁸ Tiainen M et al. *Hum. Mol. Genet.* 2002; 11(13): 1497-1504.

⁹ Karuman P et al. *Molecular Cell.* 2001; 7(6): 1307-1319.

¹⁰ Ylikorkala A et al. *Hum Mol Genet.* 1999; 8(1): 45-51.

¹¹ Aretz S et al. *Human Mutation.* 2005;26(6): 513-519.

¹² Hemminki A. *CLMS.* 1999; 55: 735-750.