STK11 Gene Analysis in Peutz-Jeghers syndrome

Disorder also known as: Peutz-Touraine-Jeghers Syndrome; Hamartomatous intestinal polyposis

Clinical Features:
Peutz-Jeghers syndrome (PJS) is characterized by the combination of gastrointestinal hamartomatous polyps and mucocutaneous pigmentation. Polyposis is most prevalent in the small intestine, but also presents in the stomach and large bowel in the majority of affected persons. The classic mucocutaneous stigmata include dark pigmented macules around the mouth, eyes, and nostrils, on the buccal mucosa, and in the perianal area, and hyperpigmented areas on the fingers. Affected females have increased risk to develop sex cord tumors with annular tubules (SCTAT), a benign ovarian neoplasm, as well as adenoma malignum of the cervix, a rare aggressive carcinoma. More infrequently, affected males can develop calcifying Sertoli cell tumors of the testes which may cause gynecomastia.

Inheritance Pattern/Genetics:
Autosomal dominant; more cases are sporadic than familial

Test Methods:
Analysis is performed by bi-directional sequencing of the coding regions (exons 1-9) and splice sites of the STK11 gene. Concurrently, multiplex ligation-dependant probe amplification (MLPA) is performed to evaluate for a deletion or duplication of one or more exons in this gene. Any variant is confirmed by repeat analysis using sequencing, restriction fragment analysis, qPCR, or other appropriate method.

Test Sensitivity:
DNA sequencing is estimated to identify roughly two-thirds of all STK11 variants, the only known gene associated with PJS. In a study of 56 individuals with classical PJS, Aretz et al. showed that 64% had small intragenic variants that would be detectable by sequencing methods.[1] Another 30% of the PJS patients had large deletions of one or more exons, which sequencing would not detect. In another study of 33 probands with the PJS diagnostic features of hamartomatous polyps and mucocutaneous pigmentation, 42% of patients who harbored a pathogenic variant had a full or partial deletion of STK11.[2] The sequencing approach used by GeneDx will identify >99% of existing small, intragenic variants in the STK11 gene. MLPA is expected to detect a complete STK11 gene deletion, as well as any partial gene deletion that involves one or more exons.

References:

1. Aretz, S. et al., High Proportion on Large Genomic STK11 Deletions in Peutz-Jeghers Syndrome. Human Mutation 12: 513-519, 2005.
2. Chow, E. et al. An updated mutation spectrum in an Australian series of PJS patients provides further evidence for only one gene locus. Clin Genet. 70:409-414, 2006.
3. Mehenni, H. et al. Molecular and clinical characteristics in 46 families affected with Peutz-Jehgers syndrome. Dig Dis Sci. 52:1924-1933, 2007.