Peutz-Jeghers Syndrome

Genetics

-Gene: STK11 (95% of PJS; Serine/threonine-protein kinase STK11; 19p13.3)

-AD

Clinical findings/Dysmorphic features

-GI polyposis + mucocutaneous pigmentation + cancer predisposition

-Hamartomatous polyps: most common in small intestine but also in stomach, large bowel, extraintestinal sites (renal pelvis, bronchus, gall bladder, nasal passages, urinary bladder, ureters) --> chronic bleeding, anemia, recurrent obstruction, intussusception

-Mucocutaneous hyperpigmentation: dark blue/brown macules around mouth, eyes, nostrils, perianal area, buccal mucosa

-Increased risk for epithelial malignancies: colorectal, gastric, pancreatic, breast, ovarian; Sertoli cell tumors of the testes, sex cord tumors with annular tubules (SCTAT)

Etiology

-Estimates range widely from 1:25,000 to 1:280,000

Pathogenesis

-Dysregulation of mTOR is common molecular pathway for hamartoma syndromes

-STK11 acts as suppressor for mTOR pathway by activating mTOR inhibitor TSC2 through (AMP-dependent protein kinase (AMPK)--> leading to accumulation/activation of mTOR --> protein synthesis and angiogenesis

-STK11 is multi-tasking tumor suppressor with roles in apoptosis, cell cycle arrest, cell proliferation, cell polarity, energy metabolism

Genetic testing/diagnosis

-STK11: Seq 81%, InDel 15%

Others

-PTEN also effects TSC2 and mTOR pathway via AKT1

-Rapamycin is mTOR inhibitor