Birt-Hogg-Dubé Syndrome
Clarification of diagnosis and concerns for SMS

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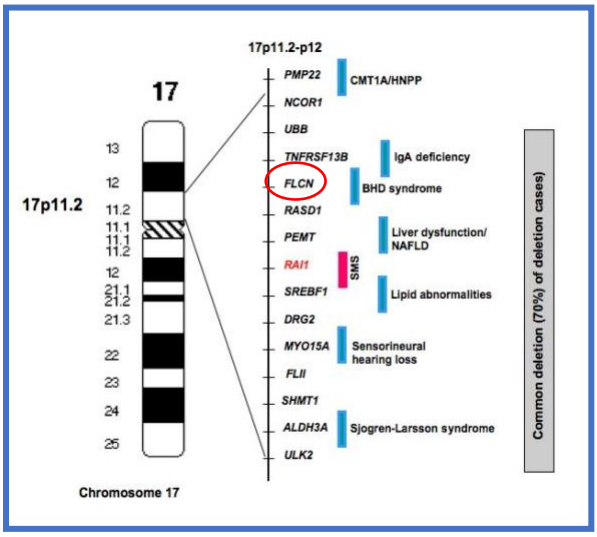
- Autosomal dominant; **adult onset**
- Caused by germline mutation of folliculin *(FLCN)* gene
- *FLCN* maps to chromosome 17p11.2 (within common SMS deletion)



Clinical features of BHD

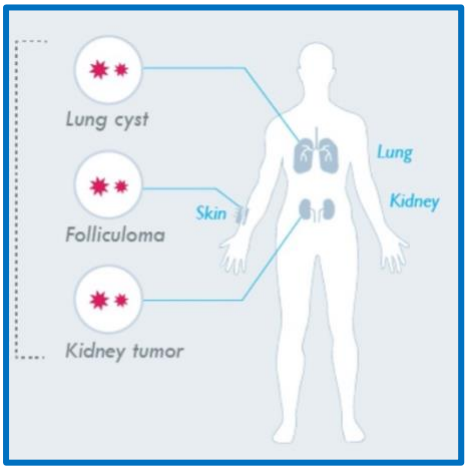
- Fibrofolliculomas (benign hair follicle tumors), after puberty, most common manifestation
- Lung cysts, adult onset, multiple; normal lung function
- Spontaneous pneumothorax, develops in 30% of those affected with BHD, average age 38 yrs
- Kidney cancer, develops in 12-34% of those affected with BHD, average age 49 yrs; requires mutation or deletion of 2nd copy of *FLCN* gene

Recommended surveillance and screening for BHD manifestations

- Dermatologic exam after puberty; biopsy to confirm fibrofolliculoma
- High resolution chest computed tomography (CT) to detect lung cysts at or after 21 years of age to establish baseline; repeat imaging not necessary
- MRI with contrast at 21 years of age to monitor for kidney tumors; repeat every 3yrs

Risk of developing BHD manifestations to individuals with SMS

- Individuals with SMS and chr17p11.2 deletion have 1 copy of *FLCN* gene.
  (❋ = del)
- Loss or mutation of remaining copy of *FLCN* gene can occur spontaneously and increase risk for developing kidney cancer.
  (✶ = 2nd hit)
- If 2nd copy of *FLCN* is inactivated (2nd hit), there is a 7-fold increased risk for kidney cancer.
- To date, only 2 individuals reported with SMS and kidney cancer (ages 45 and 50).
- Individuals with RAI1 mutations (10%) or uncommon deletions that do not encompass *FLCN* have same risk for kidney cancer as general population.



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