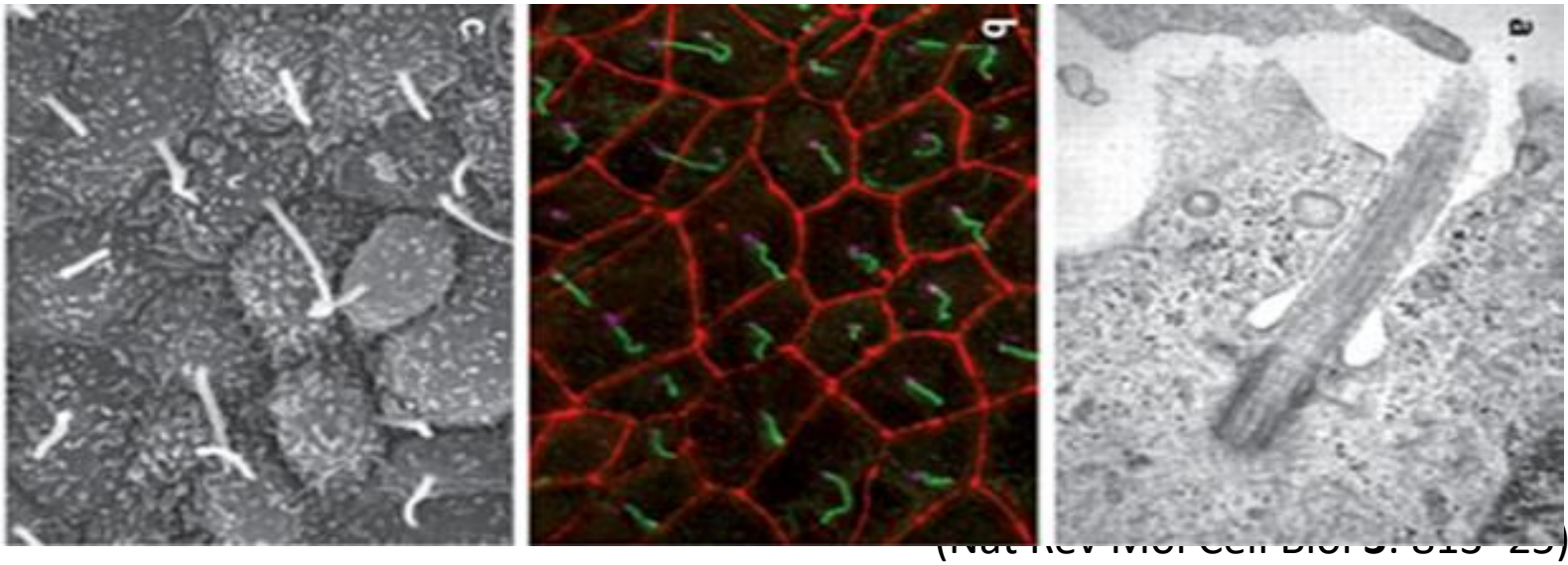


# Primary Cilium and Tumor Suppression

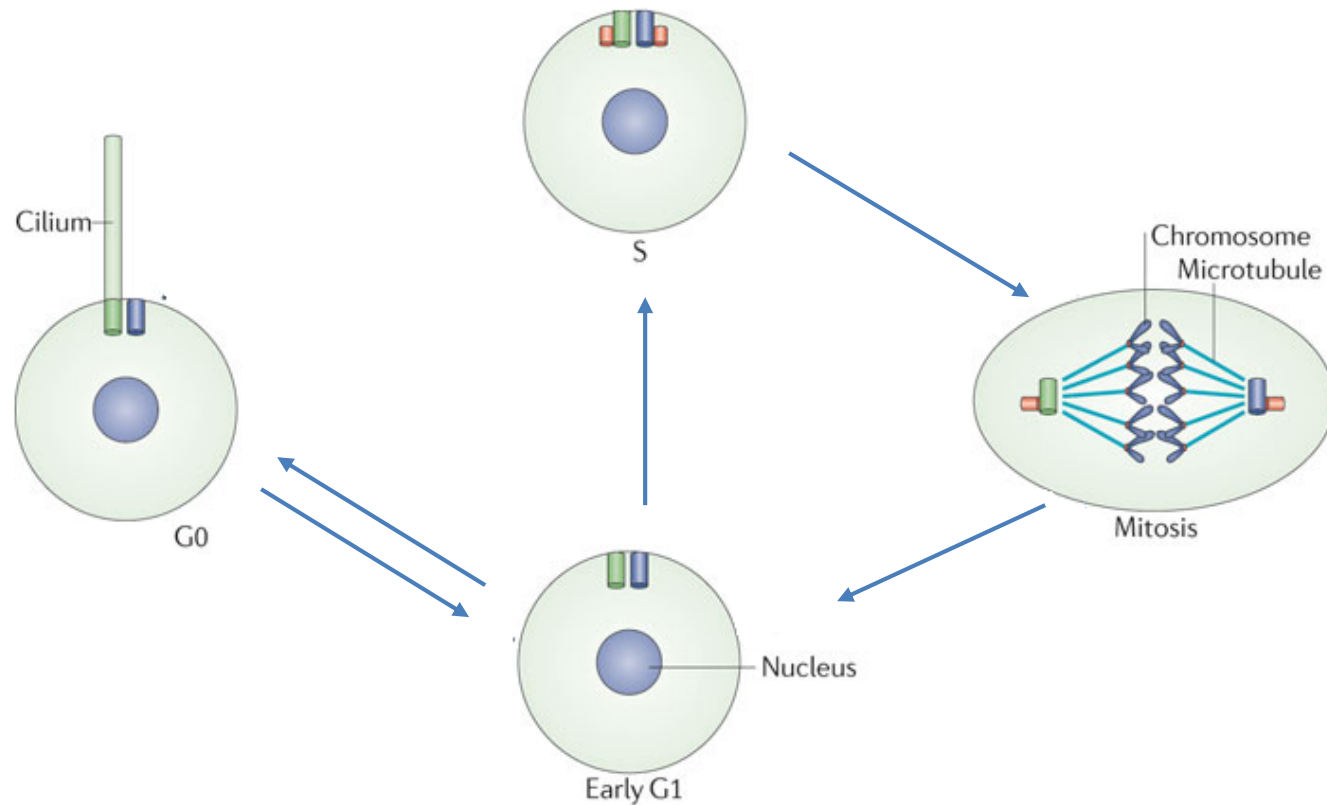
Yu Jiang, Ph.D.

Department of Pharmacology and Chemical Biology,  
University of Pittsburgh

# Primary Cilium



# Primary Cilium and Cell Cycle



Resting Phase

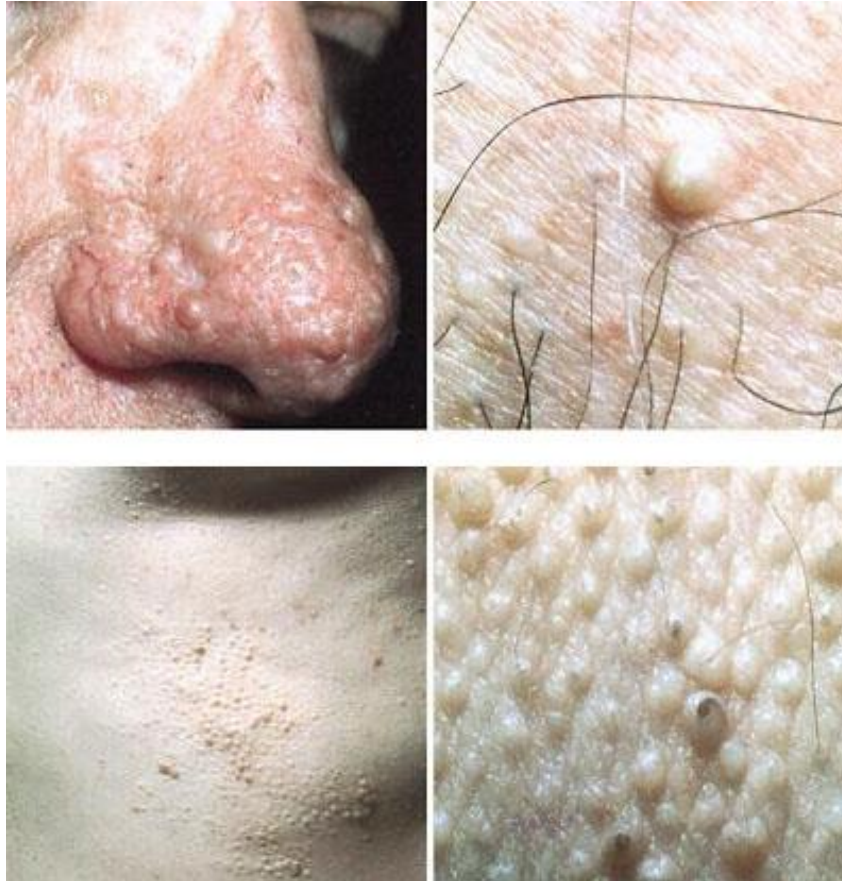
Cycling Phase

(Adapted from Nat Rev Mol Cell Biol **3**: 813–25)

# Birt Hogg Dube Syndrome

- A rare genetic disease predisposing patients to developing cystic kidney, renal cell carcinomas, fibrofolliculomas, spontaneous pneumothorax and lung cysts.
- The syndrome is caused by germline mutations in the BHD gene, which encodes the tumor-suppressor protein folliculin (FLCN).

## BHD Skin Lesions: Fibrofolliculomas



([www.bhdsyndrome.org](http://www.bhdsyndrome.org))

# Polycystic Kidneys in FLCN Deficient Mice

N (Bhd<sup>f/f</sup>)

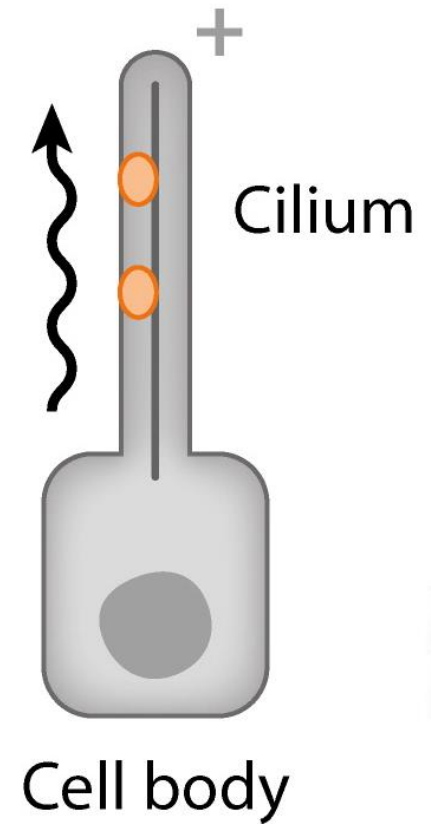
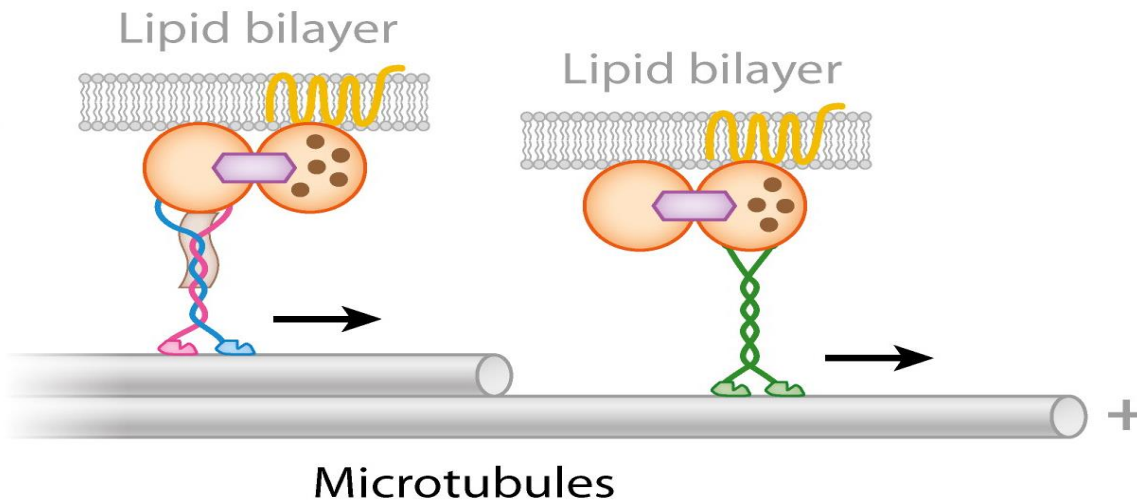
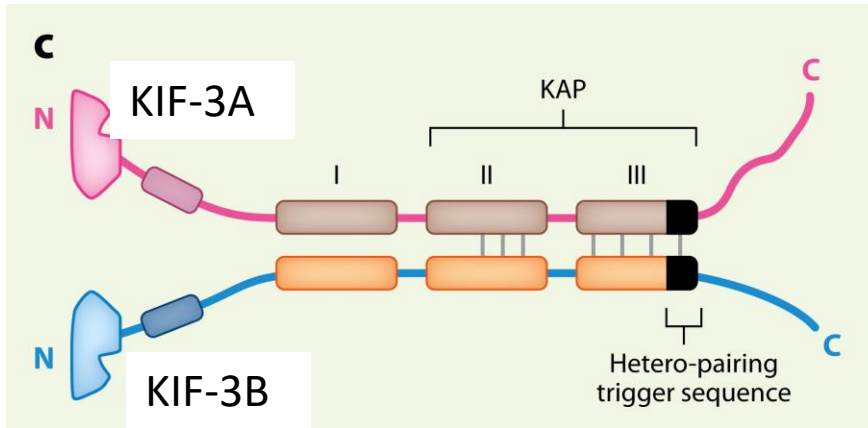


Bhd<sup>f/f</sup>/Sglt2-Cre



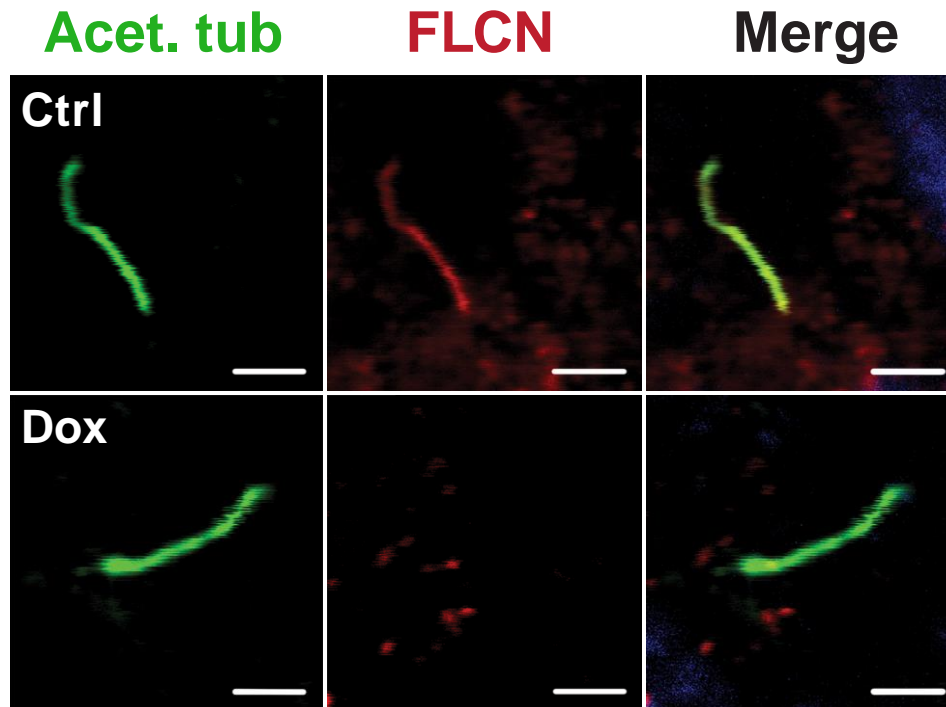
(Chen J et al. PLoS one. Oct 30. 2008)

# Kinesin 2



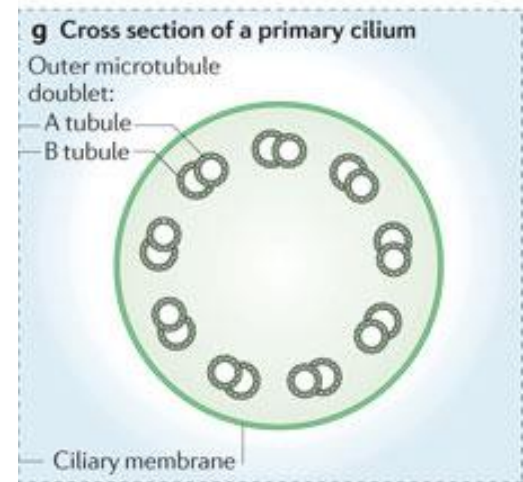
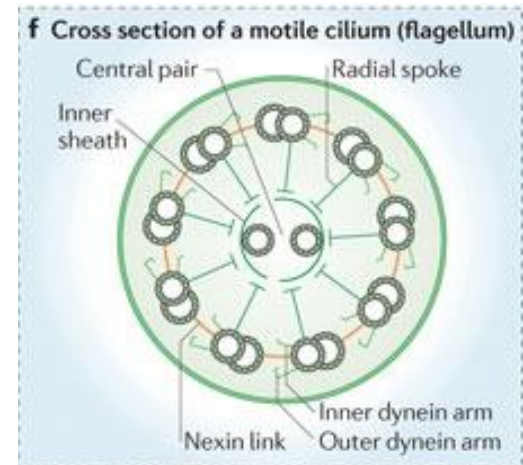
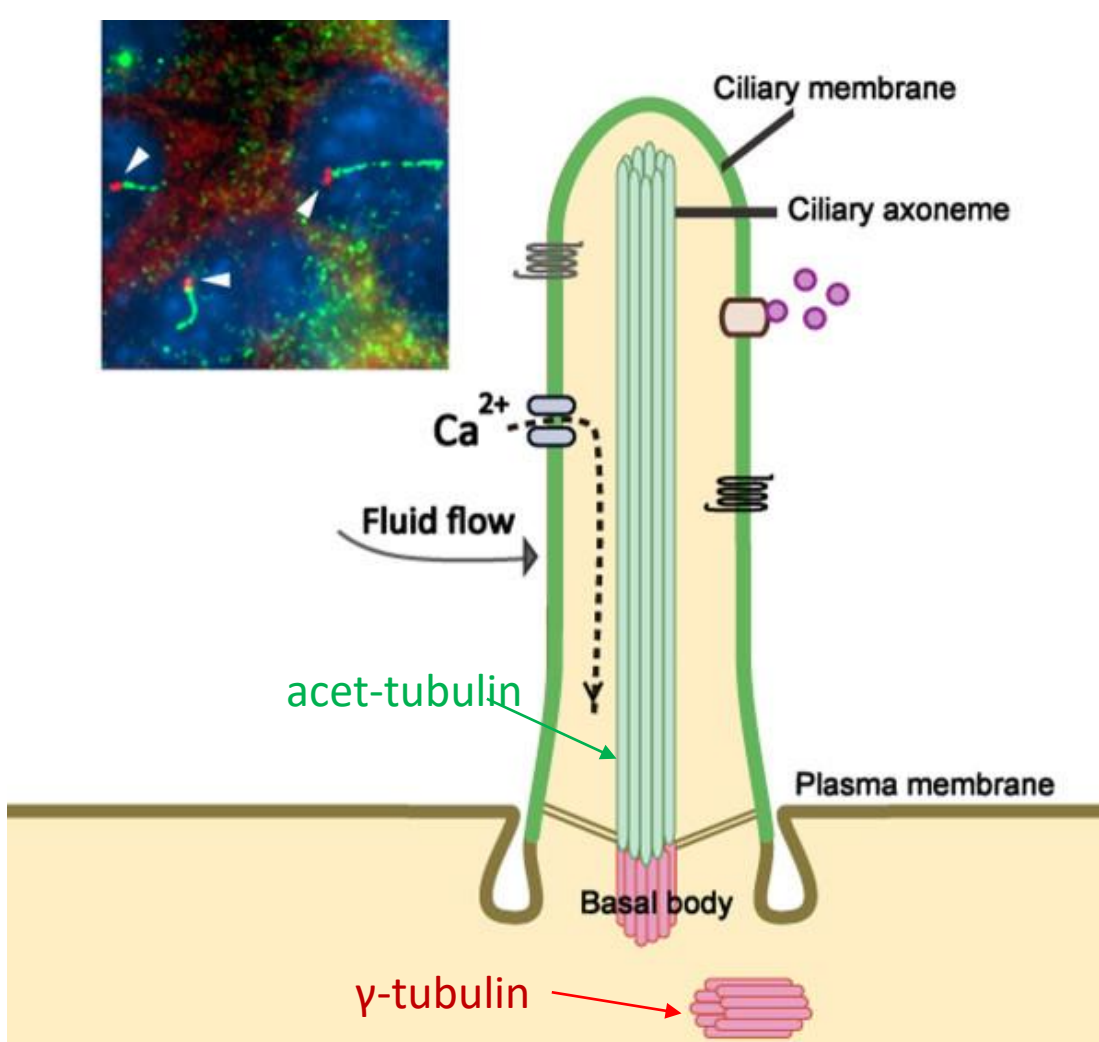


# Ciliary Localization of FLCN

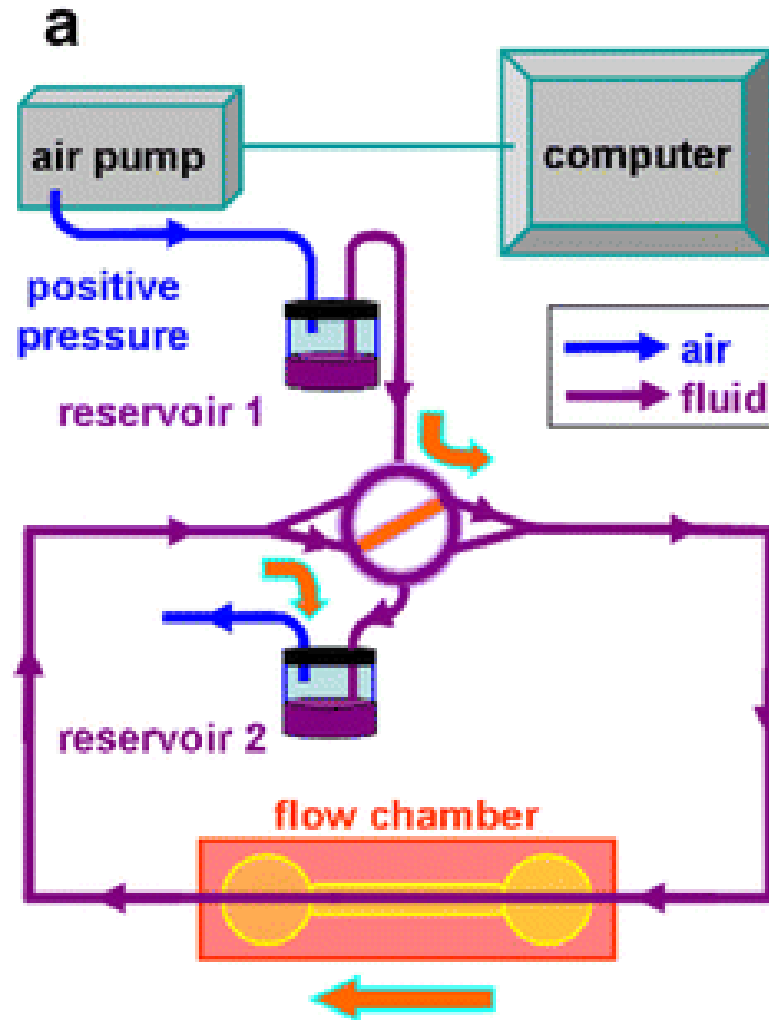




# Structure of Primary Cilium

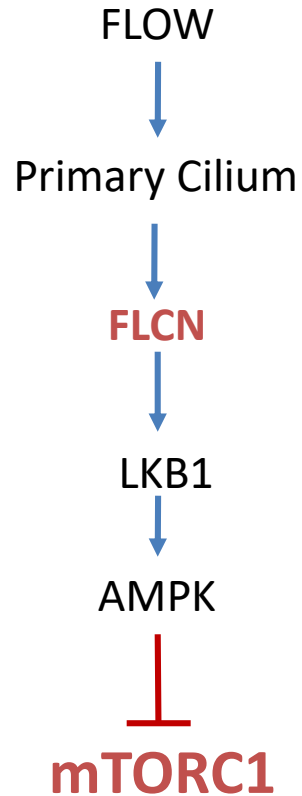


# Flow System

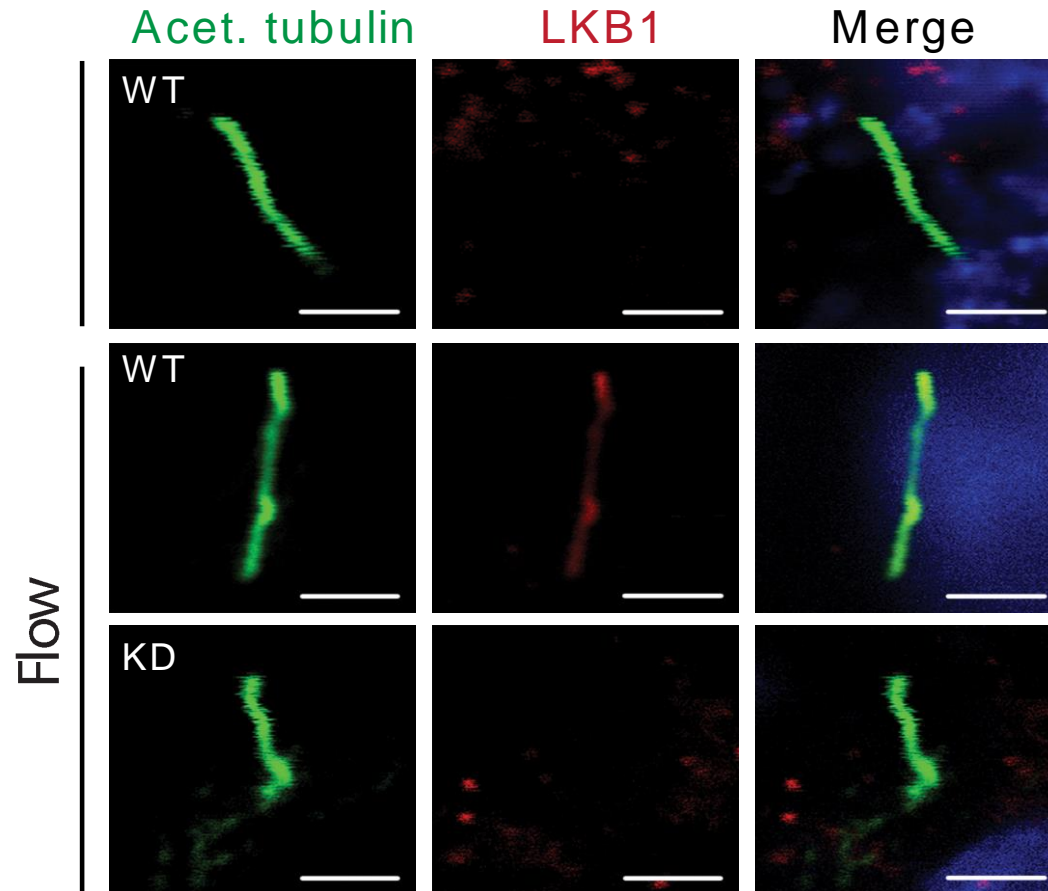


(Kotosis et al 2008 )

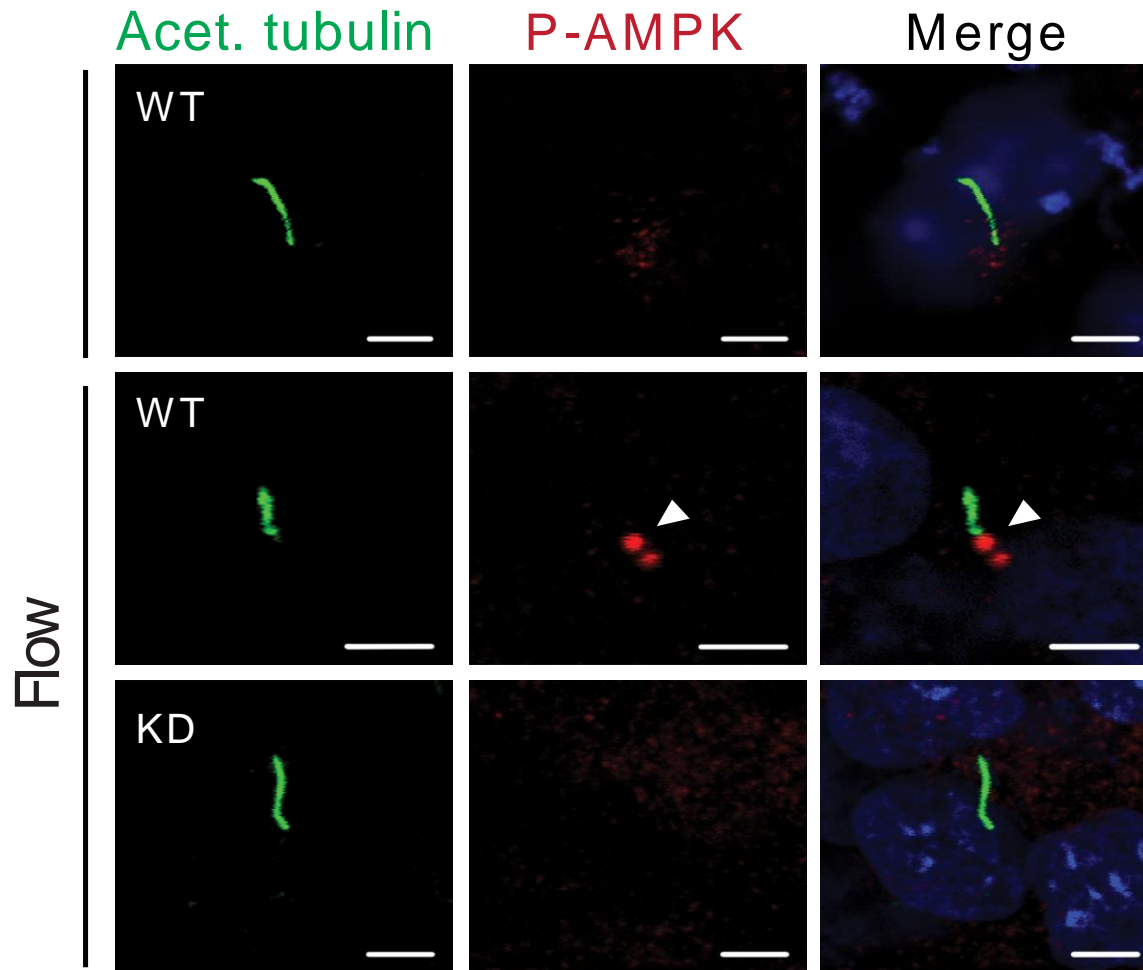
# FLCN inhibits mTORC1 activity through primary cilia in QUIESCENT cells



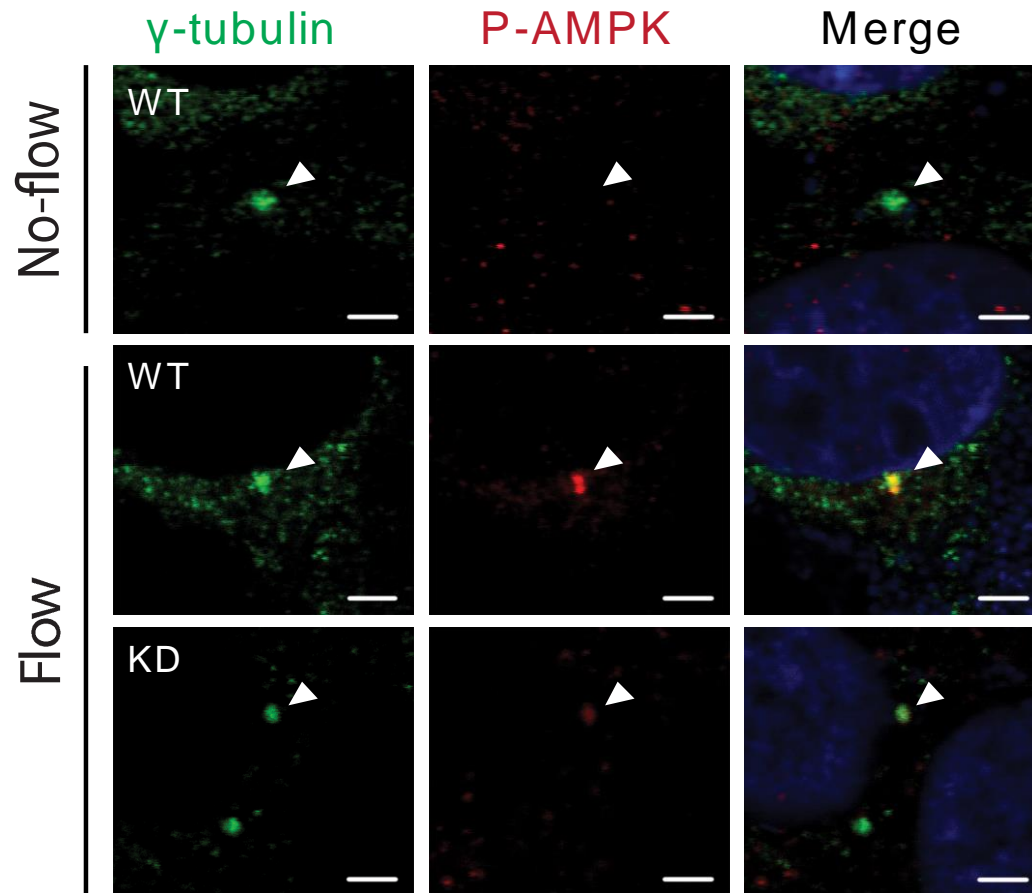
# FLCN recruits LKB1 to primary cilia in response to flow



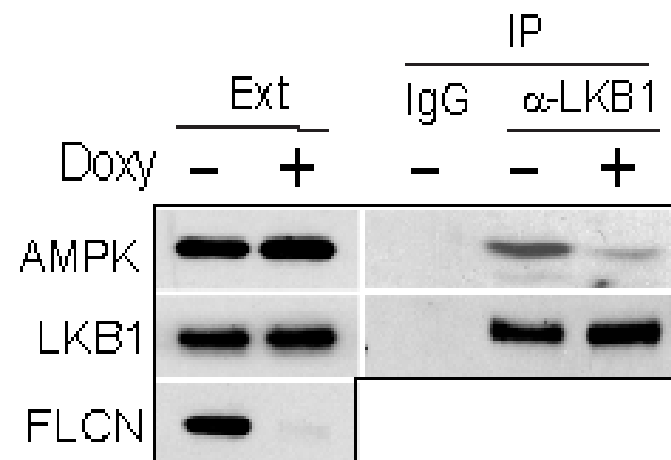
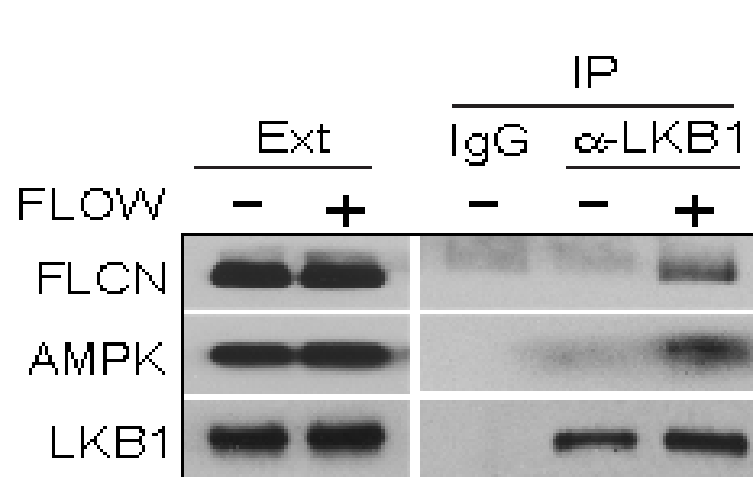
## FLCN is required for flow induced AMPK activation



# Flow activates AMPK on the basal body

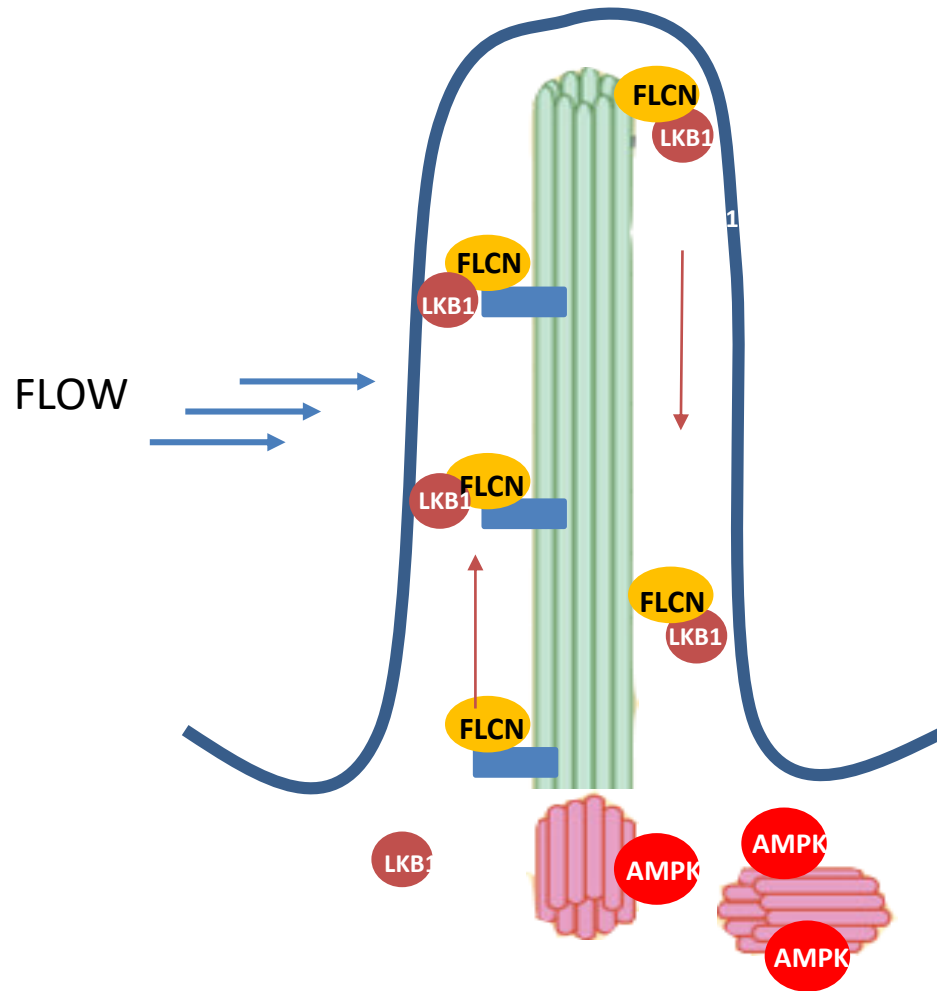


# Cilium-Dependent interaction of FLCN with LKB1

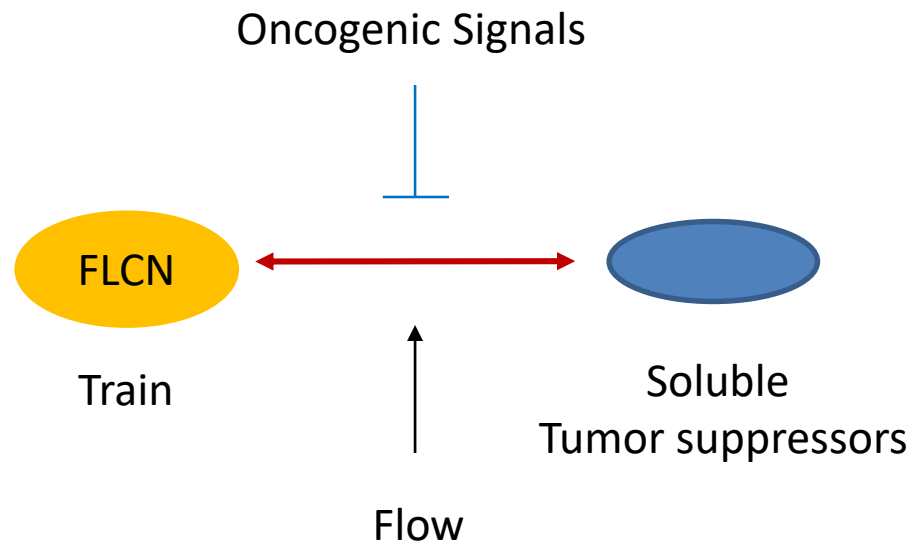




# Action of FLCN in Primary Cilia



## A Working Model for the Action of FLCN in Primary Cilia



# Acknowledgement

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