Nature Reviews Nephrology | Published online 23 May 2016; doi:10.1038/nrneph.2016.74

CILIOPATHIES

CPLANE regulates intraflagellar transport

> mutations in CPLANE components are associated with ciliopathies in patients and in mouse models

Recent research has identified a new protein complex with an important role in ciliogenesis and in human ciliopathies, including disorders that affect the kidney. John Wallingford and coworkers show that ciliogenesis and planar cell polarity effector (CPLANE), a complex formed by Inturned (Intu), Fuzzy and Wdpcp, recruits a specific subset of intraflagellar transport (IFT) proteins to the cilium and that mutations in CPLANE components are associated with ciliopathies in patients and in mouse models.

The researchers report that the CPLANE proteins form a physical and functional unit with the ciliopathy-associated protein Jbts17 and the small GTPase Rsg1. Jbts17 localizes CPLANE to the base of the cilium where the complex specifically recruits the peripheral proteins of the multiprotein IFT complex, IFT-A. "These data provide the first demonstration that cytoplasmic factors are specifically required for the recruitment and assembly of IFT particles," notes Wallingford.

In mice, mutations in CPLANE proteins led to developmental defects reminiscent of oro–facial–digital syndrome (OFD). Consistent with this finding, the researchers identified disease-associated mutations in *WDPCP* and/or *INTU* in the exomes of patients with ciliopathies (nephronophthisis, OFD and short-rib polydactyly syndrome) or ciliopathy features (cerebellar vermis hypoplasia, ataxia, and retinal dystrophy).

"What is remarkable is that none of the CPLANE proteins are particularly well-studied, which highlights the importance of the 'ignorome' — the huge body of proteins encoded by the human genome that remain poorly studied or even entirely unstudied," remarks Wallingford. Moving forward, the researchers' efforts will focus on the biochemical characterization of CPLANE and a broad and extensive search for CPLANE mutations in patients with ciliopathies.

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ORIGINAL ARTICLE Toriyama, M. *et al.* The ciliopathy-associated CPLANE proteins direct basal body recruitment of intraflagellar transport machinery. *Nat. Genet.* http://dx.doi.org/10.1038/ng.3558 (2016)