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> ciliary and nuclear import pathways use similar mechanisms

The construction and maintenance of cilia requires intraflagellar transport along axonemal microtubules by the heterotrimeric kinesin-2 family complex KIF3A–KIF3B–KAP and the homodimeric KIF17 motor. But how kinesin motors and their cargoes enter cilia is unknown. Dishinger *et al.* now uncover intriguing parallels between nuclear and ciliary import mechanisms by showing that ciliary entry of KIF17 is regulated by the nuclear import protein importin β2 and a ciliary–cytoplasmic gradient of the small GTPase RAN.

KIF17 was shown to accumulate in cilia in all mammalian cell lines tested, but deletion of the carboxy-terminal tail domain abolished ciliary localization of KIF17, suggesting that a ciliary localization signal (CLS) is present in this region. Surprisingly, constructs containing the tail region localized predominantly to the nucleus, which prompted the authors to look for a nuclear localization signal (NLS) in the KIF17 tail. They identified two putative NLSs, one of which could also act as a CLS and is necessary and sufficient for ciliary targeting of KIF17.

Given that nuclear import requires recognition of NLSs by importin proteins, translocation through the nuclear pore complex and dissociation of the NLS–importin complex in the nucleus by GTP-bound RAN, Dishinger *et al.* verified the presence of RAN–GTP in cilia. To test whether ciliary RAN–GTP regulates KIF17 import, they used a system for fast induction of RAN expression in the cytoplasm. Cytoplasmic expression of wild-type RAN or a RAN mutant that was unable to bind GTP did not affect the ciliary localization of KIF17, whereas expression of a constitutively active RAN–GTP mutant reduced the number of cells containing ciliary KIF17. The authors confirmed these findings by fluorescence recovery after photobleaching (FRAP) analysis of ciliary KIF17 in the presence or absence of the constitutively active RAN–GTP mutant. The FRAP data showed a drastic reduction in ciliary KIF17 recovery when levels of this RAN mutant were increased. Together, these findings suggest that cytoplasmic RAN–GTP abolishes ciliary entry of KIF17.

So, do importin proteins feature in the ciliary entry of KIF17? Indeed, importin β2 is present in the proximal region of the cilium and co-immunoprecipitates with KIF17 but not with a KIF17 mutant containing a defective CLS. This suggests that the interaction of KIF17 with importin β2 is necessary for ciliary import. Interestingly, no interaction between KIF17 and importin β1 was observed by immunoprecipitation, suggesting that importin β2 alone is responsible for ciliary entry of KIF17.

This study provides the first direct evidence that ciliary and nuclear import pathways use similar mechanisms, and expands the role of RAN in intracellular transport.

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ORIGINAL RESEARCH PAPER Dishinger, J. F. *et al.* Ciliary entry of the kinesin-2 motor KIF17 is regulated by importin-β2 and RanGTP. *Nature Cell Biol.* 6 Jun 2010 (doi:10.1038/ncb2073)
FURTHER READING Verhey, K. J. & Hammond, J. W. Traffic control: regulation of kinesin motors. *Nature Rev. Mol. Cell Biol.* **10**, 765–777 (2009)