INTRAFLAGELLAR TRANSPORT

Trainspotting in a cillum

A new imaging technique sheds light on how cilia regulate their length and growth.

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Cilia are antenna-like structures that protrude from many cells and perform a variety of roles: some help cells to move while others are involved in signaling. Faulty or disrupted cilia can lead to diseases known as ciliopathies that can affect multiple organs and cause symptoms ranging from blindness, kidney cysts and neurological problems to infertility and skeletal malformations (Reiter and Leroux, 2017).

Cilia are complex structures that contain over 600 proteins, all of which have to be transported to the cilium when it is being assembled. Moreover, all the proteins and receptors involved in signaling have to be shuttled into and out of the cilia as needed: this is done by an elaborate piece of molecular machinery called the intraflagellar transport system, or IFT for short (Lechtreck, 2015).

The tip of a cilium is a busy place and once the IFT trains have reached the tip and unloaded their cargo, they undergo major remodeling before returning to the base with their new cargo. However, until now existing microscopy techniques have not been able to reveal what happens during this remodeling. Now, in eLife, Ahmet Yildiz at the University of California Berkeley and colleagues – including Alexander Chien and Sheng Min Shih as joint first authors – report new insights into the behavior of IFT trains and motor proteins (Chien et al., 2017).

Chien et al. used a method called PhotoGate microscopy to image the tips of cilia in Chlamydomonas and to track individual IFT trains (Belyy et al., 2017). With this technique, most of the IFT complexes labeled with a fluorescent marker were ‘photobleached’ by moving a laser from the tip of the cilium to the base, leaving only a few selected complexes fluorescent. This way, the entire journey of individual trains to the tip of the cilium and back to the base could be tracked. Chien et al. found that the IFT trains stop at the ciliary tip for about three seconds, during which they undergo extensive remodeling. The trains split apart and mix with other ones to form new trains – a process that takes just over a second – and then wait for two seconds before departing. For every fluorescent train arriving at the tip, about 2.4 new fluorescent ones return to the base.

Next, Chien et al. tracked the movement of kinesin-II and dynein-1b and found that although these two motor proteins arrive together at the tip of the cilium, they depart independently of each other. While dynein-1b participates in the formation of new trains, kinesin-II rests at the tip of the cilium to transport cargo proteins along dedicated microtubule tracks (that run along the length of cilia) in different directions (Figure 1). Kinesin motor proteins move the IFT trains from the base of the cilium to the tip, while dynein motors move the IFT trains back to the base (Lechtreck, 2015).
for about two seconds and is not part of the new trains. Rather, kinesin-II seems to rely on passive diffusion rather than active transport to return to the base of the cilium, which means that it takes 10 times longer to return than dynein-1b.
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