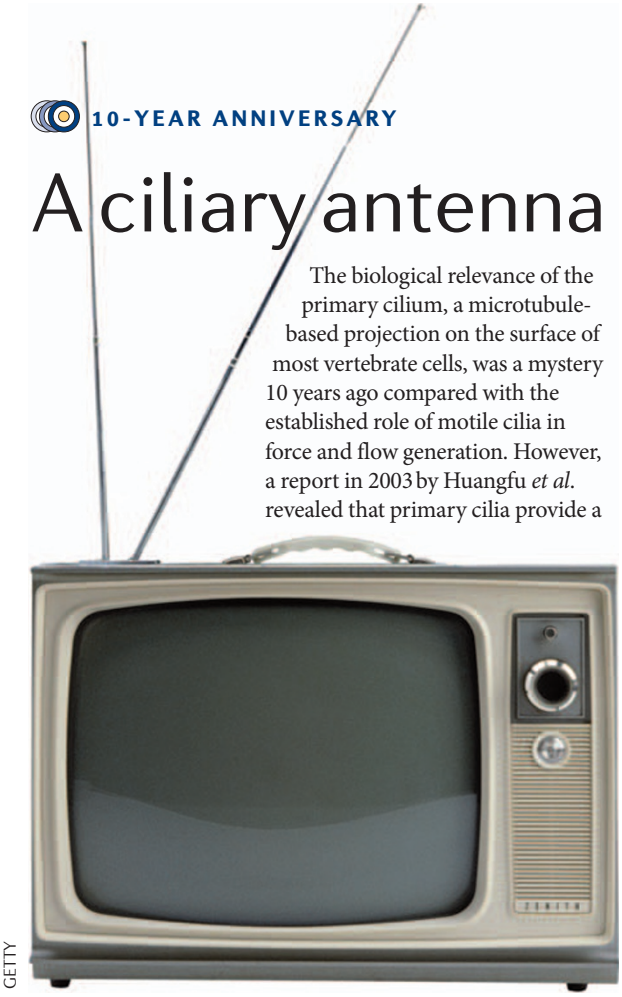
10-YEAR ANNIVERSARY

A ciliary antenna



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The biological relevance of the primary cilium, a microtubule-based projection on the surface of most vertebrate cells, was a mystery 10 years ago compared with the established role of motile cilia in force and flow generation. However, a report in 2003 by Huangfu *et al.* revealed that primary cilia provide a new way for cells to interact with their environment.

Huangfu *et al.* were carrying out a phenotypic study to identify embryonic patterning mutations in mice and observed that some of the mutants showed abnormalities that are typical of loss of Sonic Hedgehog (SHH) signalling. The genes mutated in these embryos encode the intraflagellar transport (IFT) proteins IFT88, IFT172 and KIF3A (part of the kinesin-2 motor), which are required for cilium maintenance and growth; this suggested a link between cilia and SHH signalling.

Further analysis revealed that IFT proteins are important in SHH signalling and that their loss interferes with the SHH pathway, leading to phenotypic abnormalities. Specifically, although embryos mutated for Patched 1 (the receptor for SHH, which inhibits SHH in the absence of ligand) showed increased levels of SHH signalling, the concomitant mutation of IFT proteins blocked SHH activation and resulted in embryos that were morphologically similar to those mutated for IFT proteins alone. This indicated that IFT proteins function downstream from Patched 1. Similarly, IFT proteins were found to act downstream of RAB23 (which acts downstream of Patched 1 and Smoothened and negatively regulates SHH signalling). By contrast, the authors showed that IFT proteins act upstream of the transcription factor GLI3 (which represses SHH target gene activation in the absence of ligand).

Several studies have since focused on how cilia contribute to vertebrate SHH signalling. Together, these reports have revealed that primary cilia function as signalling 'antennae', probing the extracellular environment for signalling components, and also as dynamic platforms for signalling, where signalling components localize and interact.

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ORIGINAL RESEARCH PAPER Huangfu, D. *et al.* Hedgehog signalling in the mouse requires intraflagellar transport proteins. *Nature* **426**, 83–87 (2003)

FURTHER READING Corbit, K. C. *et al.* Vertebrate Smoothened functions at the primary cilium. *Nature* **437**, 1018–1021 (2005) | Caspary, T. *et al.* The graded response to Sonic Hedgehog depends on cilia architecture. *Dev. Cell* **12**, 767–778 (2007)