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DEVELOPMENT

Knowing left from right

Left–right asymmetry is established early during embryonic development. In most vertebrates, symmetry breaking is mediated by a unidirectional fluid flow in the ventral node, a cavity at the midline that is filled with extra-embryonic fluid. Sensing of this flow occurs through cilia, and Yoshiba *et al.* now report that this requires the Ca^{2+} channel polycystin 2 (PKD2; also known as TRPP2).

It is known that mice lacking PKD2 exhibit left–right patterning defects. Moreover, they lose the left-sided expression of *Nodal*, which encodes a member of the transforming growth factor-β superfamily that is essential for the formation of the mesoderm and left–right specification.

To determine the site of PKD2 action, the authors tested whether expression of *Pkd2* in specific areas of the node could rescue the defects seen in *Pkd2*$^{-/-}$ mutant mice. Indeed, they found that expression of *Pkd2* specifically in crown cells (a type of ciliated cell in the node) rescued left-sided expression of *Nodal* in the lateral plate mesoderm (LPM). This suggests that PKD2 is required exclusively in crown cells for correct left–right determination. Furthermore, the main target of PKD2-mediated signalling here was *Cerl2* (cerberus-like 2; also known as *Dand5*), which encodes an inhibitor of Nodal signalling that is expressed by crown cells and is required for subsequent asymmetric expression of *Nodal* in the LPM.

Interestingly, the authors observed that *Pkd2*$^{-/-}$ mutant embryos have normal cilia and unperturbed flow. This suggests that the defects seen in *Pkd2*$^{-/-}$ mutant embryos are due the inability to sense such flow, which was confirmed by using Ca^{2+} signalling blockers that interfere with PKD2 signalling. Furthermore, although endogenous PKD2 localizes to cilia of both crown cells and pit cells (another type of ciliated cell in the node), PKD2 is required only in crown cells for the correct establishment of left–right asymmetry.

Last, Yoshiba *et al.* directly demonstrated that the cilia of crown cells function as sensors of nodal flow, as restoring cilium formation exclusively in crown cells of embryos that lack cilia was sufficient to induce left–right asymmetry. Moreover, these embryos could also respond to artificial flow.

This work indicates that fluid flow in the node is sensed by the cilia of crown cells via PKD2. Whether these cilia sense flow-transported chemicals or flow-generated mechanical cues for symmetry breaking remains to be determined, as is the pathway that links PKD2 to *Cerl2*.

Kim Baumann

“restoring cilium formation exclusively in crown cells of embryos that lack cilia was sufficient to induce left–right asymmetry”

ORIGINAL RESEARCH PAPER Yoshiba, S. *et al.* Cilia at the node of mouse embryos sense fluid flow for left-right determination via Pkd2. *Science* 13 Sep 2012 (doi:10.1126/science.1222538)