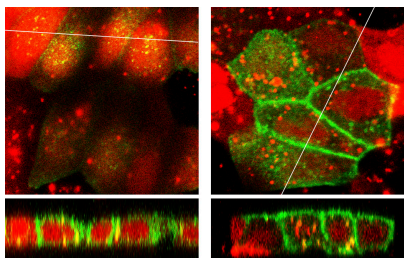


Cytosolic calcium increases in response to ciliary bending when TRPV4 is present (left), but not when it is absent (right).



Tagged Eg5 tetramers (white) move directionally where microtubules overlap (between red dotted lines).



When TM5b is knocked down (right), aquaporin (green) can reach the membrane even without phosphorylation. Lines show position of cross-sections shown in bottom panels.

TRPV4 shows TRPP2 the moves

You'd think that something as dramatic as a bending cilia would be easy to sense, especially if your own activity depended on it. But the ion channel TRPP2 is oblivious to the cilia movement that activates it, and depends on another channel to relay the information, [Köttgen et al. report](#).

In the kidney, bending of the cilia in response to the flow of fluid through the nephron tubule triggers intracellular calcium transients, setting off multiple response pathways. This cilia deflection-induced calcium increase requires the ion channel TRPP2. But TRPP2 is not itself a mechanosensor. That role, it turns out, is played by another channel called TRPV4.

TRPV4 is similar in sequence to a worm mechanosensory channel, is expressed in the kidney, and has been shown to associate with cilia. With that in mind, the authors investigated its relationship with TRPP2. They found that the two proteins both physically and functionally interacted and that blocking TRPV4 abrogated flow-triggered calcium transients.

Mutations in TRPP2 lead to cysts throughout the kidney, liver, and pancreas. It had been assumed that the primary step in polycystic disease pathogenesis was the loss of mechanosensation and downstream calcium transients. But while absence of TRPV4 abolished calcium increase, neither zebrafish nor mice deficient in TRPV4 developed cysts. This suggests that TRPP2 has an unknown function in addition to triggering calcium transients.

Köttgen, M., et al. 2008. *J. Cell Biol.* doi:[10.1083/jcb.200805124](#).

Two microtubules means one-way movement

For the microtubule motor Eg5, binding two microtubules gives it direction, say [Kapitein et al.](#)

Eg5, the vertebrate form of kinesin-5, moves along microtubules either randomly or directionally. In other kinesins, directionality is triggered when the motor binds to its cargo and to the microtubule track. But for Eg5, microtubules are both the track and the cargo, as both ends of the motor protein bind microtubules.

The authors showed that Eg5 moved predominantly randomly when bound to only one microtubule, but switched solely to plus end-directed movement when a second microtubule bound.

Eg5 is one of the main organizers of microtubules in the mitotic spindle, and its ability to slide antiparallel fibers along one another is crucial for pushing opposite poles apart. Alternatively, when encountering parallel fibers, it can "zip them together" if they are skewed, says co-PI Tarun Kapoor. He thinks the ability to move randomly on a single microtubule allows Eg5 to "explore" its environment for another microtubule, "dramatically increasing the efficiency of crosslinking."

Kapitein, L.C., et al. 2008. *J. Cell Biol.* doi:[10.1083/jcb.200801145](#).

Aquaporin clears its own path

Aquaporin takes charge of getting itself to the membrane, say [Noda et al.](#)

In the renal collecting duct, aquaporin channels increase permeability and are central to water homeostasis. The channel normally hangs out in the cytoplasm, but when the body needs to retain water, it relocates to the apical membrane, allowing water to flow from the tubule into the cell.

This relocation is under the control of antidiuretic hormone. The hormone activates protein kinase A (PKA), which in turn phosphorylates aquaporin. But once phosphorylated, how does aquaporin relocate? The only clue was the authors' previous study showing aquaporin can bind both actin and tropomyosin (TM5b).

Phosphorylation, the team found, dissociated aquaporin from G-actin molecules, but also destabilized F-actin. They speculated that this destabilization might be related to aquaporin's ability to bind TM5b, because TM5b is a known F-actin stabilizer.

Overexpression of TM5b indeed increased the amount of F-actin and prevented aquaporin from reaching the membrane. The authors thus propose a model whereby, upon phosphorylation, aquaporin detaches from G-actin and binds to TM5b, causing TM5b to lose its grip on F-actin. The F-actin then depolymerizes, opening the way for aquaporin to reach the membrane.

Because trafficking of numerous other channels is regulated by phosphorylation, and because channel–actin interactions have also been found elsewhere, Noda suggests that other channels may also promote their own relocation through this scheme. She also suggests TM5b may be an appropriate therapeutic target for diabetes insipidus, in which aquaporin’s ability to reach the membrane is impaired.

Noda, Y., et al. 2008. *J. Cell Biol.* doi:[10.1083/jcb.200709177](https://doi.org/10.1083/jcb.200709177).

Mitochondria split with a calcium hit

An influx of calcium into neurons causes mitochondrial fission, according to [Han et al.](#)

To respond to changing cellular needs, mitochondria move, fuse together, or undergo fission. Han et al. now reveal some of the proteins and signals that regulate fission in neurons.

The authors tested mitochondrial responses to an increase in potassium (K^+) levels, which mimics an action potential. The K^+ spike brought mitochondria to a halt and prompted their division, making them shorter and rounder. These changes depended on the opening of voltage-dependent calcium channels and the resulting Ca^{2+} gradient, which in turn activates the Ca^{2+} /calmodulin-dependent protein kinase (CaMKI α). A CaMKI α antagonist blocked K^+ -triggered changes in mitochondrial shape.

In their search for CaMKI α substrates, the authors turned to Drp1 (dynamin-related protein 1), which promotes mitochondrial fission and whose sequence suggested it could be phosphorylated. And the authors found that it was, in fact, a CaMKI α substrate. K^+ treatment not only led to Drp1 phosphorylation, but caused cytoplasmic Drp1 to rapidly relocate to mitochondria and associate with another fission protein, Fis1. Together, these results indicate that a calcium influx is an important trigger for mitochondrial fission, and that Drp1 is a final effector of the fission signal.

Lead investigator Masayuki Matsushita says there is much more to discover about how calcium controls mitochondrial dynamics, including other roles for CaMKI α : “We think it may have other substrates as well, also involved in mitochondrial morphology.”

Han, X.-J., et al. 2008. *J. Cell Biol.* doi:[10.1083/jcb.200802164](https://doi.org/10.1083/jcb.200802164).

Egg P bodies protect maternal mRNA

P bodies (processing bodies) are cytoplasmic granules that, in somatic cells, store and degrade mRNAs. But P bodies in the worm egg protect mRNA, according to a study by [Boag et al.](#) In a separate study [Noble et al.](#) observed that worm eggs have different flavors of P bodies depending on developmental stage.

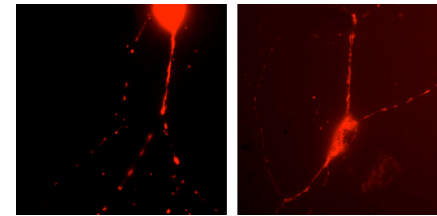
Boag et al. showed that P bodies in eggs lack an mRNA decapping protein called Pat1 that in somatic cells promotes mRNA degradation. So if egg P bodies aren’t degrading mRNA, what are they doing? A core P body component called CGH-1 holds mRNAs at P-bodies in both somatic cells and egg cells. When the authors removed CGH-1 from eggs, mRNAs were mislocalized and destabilized. “We think CGH-1 acts like a chaperone for a protective mRNA-protein complex,” says PI Keith Blackwell. The oocyte contains large numbers of maternally derived mRNAs, which are all transcribed and packaged at once, but then used in a specific temporal pattern for proper development. The protective complex may keep them safe until they are expressed.

Noble et al. showed that eggs in fact have a whole range of specialized P bodies. They identified at least three types of P bodies arising at different stages of egg development, and a fourth type in embryos, each with a distinct set of proteins. During early meiosis, “germ granules” associate with germ nuclei, while grP (germline RNP) bodies accumulate in the syncytial (multinucleate) cytoplasm. Neither type carried the RNA decapping enzyme DCAP-2, suggesting they do not degrade mRNA, in line with the observations of Boag et al. As mononucleate oocytes formed and then entered an arrested stage, dcP bodies appeared, which did contain DCAP-2, but, interestingly, didn’t contain measurable amounts of CGH-1. Finally, during early embryogenesis, more canonical P bodies form, carrying CGH-1 and decapping enzymes.

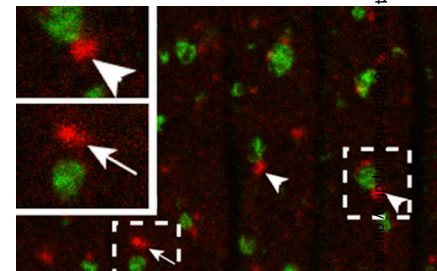
Although the different types of P bodies most likely have different functions, they do appear to interact with one another, indicating that they exchange mRNAs. Thus, sorting out which P bodies do what will be a challenging next step.

Boag, P.R., et al. 2008. *J. Cell Biol.* doi:[10.1083/jcb.200801183](https://doi.org/10.1083/jcb.200801183).

Noble, S.L., et al. 2008. *J. Cell Biol.* doi:[10.1083/jcb.200802128](https://doi.org/10.1083/jcb.200802128).



Mitochondrial fragmentation in response to K^+ stimulation (left) is blocked by preventing phosphorylation of Drp1 (right).



In oocytes, DCAP-2 (red) resided in granules that were distinct (arrows and arrowheads) but often adjacent (arrowheads) to CGH-1 granules (grP bodies) (green).