

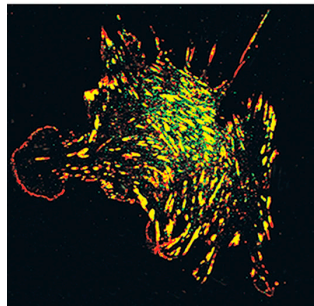
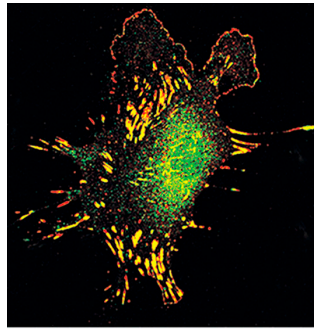
ICAP for sensing matrix density

Competition for the cytoplasmic tail of an integrin allows cells to read different matrix densities, say [Millon-Frémillon et al.](#)

The tail region of $\beta 1$ integrin is tiny—only 47 amino acids long. That doesn't leave much room for the binding of cytoplasmic accessory proteins that help control the integrin's activation state. When talin holds this position, it flips open integrin as a first step toward full activation. Active integrins then cluster into patches called focal adhesions, which stick a cell to its surface. Signals from the adhesions then relay matrix information to the rest of the cell.

In the new paper, the authors show that talin's competitor for integrin binding—a protein called ICAP-1—ensures that integrin activation does not occur prematurely. They found that fibroblasts and osteoblasts that lack ICAP-1 had overzealous focal adhesions: the adhesions were larger, more widespread, and formed more rapidly than those of normal cells grown on the $\beta 1$ integrin substrate fibronectin.

In the mutant cells, talin was recruited to integrins prematurely. Their integrins were thus



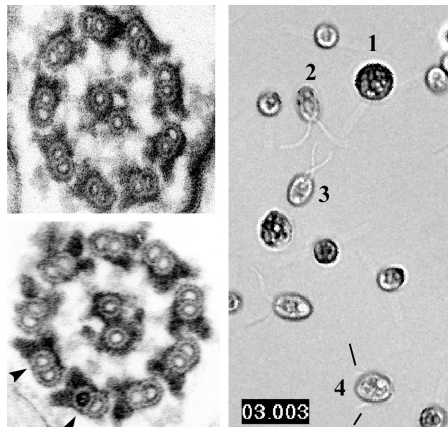
Clusters of integrin (green) grow and adhesions (yellow) are redistributed in fibroblasts lacking ICAP-1 (bottom).

more adhesive, fooling cells into sensing a denser matrix than was actually present. The ICAP-1 mutant cells spread and migrated on lower densities of fibronectin and collagen (another $\beta 1$ integrin substrate). The authors reproduced these effects by artificially activating $\beta 1$ integrins in wild-type cells.

Matrix sensing is important for determining migration speed, cell spreading, and lineage specification in progenitor cell lines. The authors previously showed that mice lacking ICAP-1 have structural bone defects but are viable. Evidently, some cell types—such as bone forming osteoblasts, which start out on a smooth, flexible substrate that later hardens—are more sensitive to their environment than others.

Although delayed by ICAP-1, talin must eventually make its way onto the integrin tail for adhesions to form. The authors are now searching for signals that trigger the dismissal of ICAP-1, allowing talin to take its place. **JCB**

Reference: Millon-Frémillon, A., et al. 2008. *J. Cell Biol.* 180:427–441.



Normal flagellar structure (left, top) is only slightly perturbed by the lack of HSP40 (left, bottom), but the mutants (right) beat their flagella erratically.

Spokes coordinate flagella

Like a good relationship, communication is key for properly beating flagella. According to results from [Yang et al.](#), coordinated movements require the radial spoke, which keeps the center of the flagellum in touch with its outer parts.

Most flagella have a pair of central microtubules surrounded by nine outer microtubule doublets. The central pair is transiently connected to each outer pair by a protein complex called the radial spoke. But not all flagella have spokes and a central pair, leaving scientists to wonder just what these structures do.

The creation of mutant flagella to address this question has been less than successful. Most of the flagellum assembles in units, so loss of one protein demolishes a chunk of the structure and leaves it paralyzed. Yang et al. averted this problem by getting rid of a protein that is added on its own, late in spoke assembly. The latecomer, a chaperone assistant called HSP40, hooks onto the spoke. Using RNAi, the group fully depleted HSP40 from *Chlamydomonas* and created mutants with only subtle structural defects in the spoke, near the central pair.

The loss of HSP40 resulted in herky-jerky flagella that paused sporadically midstroke and occasionally switched directions prematurely. The authors conclude

that the spoke helps time the beating movements.

For *Chlamydomonas*, this timing coordination probably entails the sequential activation—from flagellum base to tip—of dynein motors along outer doublets. Dyneins slide one doublet past another to drive bending. The team imagines that mechanical or molecular signals travel along the spoke from the outer doublet to the central pair, then back out to the outer pair, and so forth. Near the head of the spoke, HSP40 is well-positioned to stabilize other spoke proteins into a rigid structure that might transduce these signals.

Flagella that naturally lack the central pair have a different beating pattern and evidently use an alternative coordination system. The nodal flagella that establish left-right asymmetry, for example, move in a swirling pattern rather than the more powerful breaststroke-like movements of *Chlamydomonas* flagella. Spoke-driven coordination might thus be the basis for this extra power. **JCB**

Reference: Yang, C., et al. 2008. *J. Cell Biol.* 180:403–415.