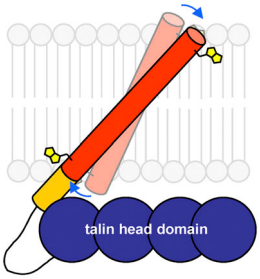
In This Issue

Text by Mitch Leslie
mitchleslie@comcast.net

Talin gives integrins a nudge



Talin binding pushes both ends of the β3 integrin's transmembrane domain (red) farther into the plasma membrane.

Kim et al. show how the cytoskeletal adaptor protein talin activates integrins.

Activating integrins, or making them stickier, helps control cell migration and adhesion and construction of the extracellular matrix. Researchers know that activation involves the protein talin, which clamps onto the cytoplasmic tail of the β subunit of an integrin. But they aren't certain how that interaction alters the adhesiveness of the integrin's extracellular end. One possibility is that talin attachment tilts the membrane-spanning domain of the β subunit, separating the transmembrane portions of the β and α subunits and switching the integrin on. Alternatively, talin might induce a piston-like motion, pushing the transmembrane domain farther out or retracting it.

Kim et al. tested these two explanations by implanting the membrane-spanning section of the β3 integrin into tiny membrane "nanodiscs." To determine whether talin caused tilting or sliding, they attached a fluorophore to the intracellular or extracellular end of the fragment. The more hydrophobic its surroundings, the brighter the fluorophore glows. Talin attachment increased the glow from a fluorophore linked to the extracellular tip, indicating that this end of the fragment sinks into the membrane. After talin binding, a fluorophore attached to the cytoplasmic end of the transmembrane domain also shone brighter. Thus, both ends of the fragment bury themselves in the membrane, suggesting that talin binding alters the angle of the β subunit rather than causing a piston-like movement. However, the researchers caution that they can't rule out the possibility that talin binding rotates rather than tilts the β integrin.

Kim, C., et al. 2012. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201112141.

Recycling endosomes feed autophagy

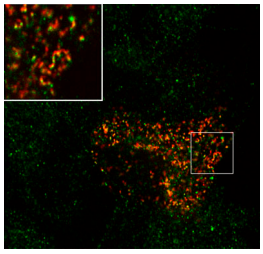


IMAGE COURTESY OF ANDREA LONGATTI

TBC1D14 (red) tubulates recycling endosomes that carry the ULK1 protein (green).

By identifying a protein that hampers membrane trafficking within the cell, Longatti et al. provide evidence that recycling endosomes supply membrane to growing autophagosomes.

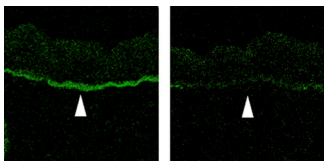
When cells are stressed or hungry, they often eat some of their contents through the process of autophagy, in which a membrane compartment called an autophagosome forms and scoops up cytoplasmic material for digestion. Autophagy's early steps remain a puzzle, however. Previous studies have identified several origins for the autophagosome membrane, including the ER and mitochondria. Longatti et al. identify a new source—recycling endosomes, which shuttle cargo from early endosomes to the cell membrane.

The researchers started out by searching for proteins that control the early stages of autophagy. They screened potential inhibitors of Rab GTPases, which help manage membrane movement within the cell and are essential for several steps of autophagosome development. The team then tested which of the 11 inhibitors they identified linked up with the autophagosome protein ULK1. One protein, TBC1D14, combined with ULK1 on recycling endosomes.

Longatti et al. discovered that a Rab GTPase on recycling endosomes, Rab11, promotes autophagy. TBC1D14 blocked autophagy by binding to Rab11 and deforming the recycling endosomes into tubes that cannot dispatch membrane to an autophagosome. When a cell is starving, TBC1D14 relocates from the recycling endosomes to the Golgi apparatus, allowing autophagy to proceed.

Longatti, A., et al. 2012. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201111079.

Unfinished basement membrane spurs developmental disorder



α8β1 integrin (green) binds to skin from a control mouse (left), but little attaches to skin from a mouse lacking QBRICK (right).

The integrin-binding protein QBRICK holds another integrin ligand in position, Kiyozumi et al. show, suggesting how defects in QBRICK lead to a rare developmental disorder.

Children with the inherited disorder Fraser syndrome suffer from severe, often fatal, birth defects. Mutations in four genes trigger the syndrome. Three of these genes encode proteins, including QBRICK, that localize to the basement membrane between an organ's outer epithelial cells and the mesenchymal cells beneath. During development of an organ such as the kidney, epithelial and mesenchymal cells interact with the basement membrane, and without this interplay the organ can't form properly. For mesenchymal cells, the α8β1 integrin serves as the basement membrane receptor.

Kiyozumi et al. tested whether QBRICK is the binding partner of the α8β1 integrin. Mouse embryos that lacked QBRICK showed reduced binding between the α8β1 integrin and the basement membrane, suggesting that QBRICK and the integrin interlock. However, rodents that carried a version of QBRICK that can't latch onto the integrin were healthy and had normal α8β1 integrin binding, indicating that a direct interaction between the two proteins isn't necessary for development. Instead, the researchers found, QBRICK helps anchor another basement membrane protein, nephronectin, which connects to α8β1 integrin and promotes interactions between mesenchymal cells and the basement membrane.

Mice lacking QBRICK produce normal amounts of nephronectin. But the researchers suspect that without QBRICK to detain them in the basement membrane, the nephronectin molecules become unstable and are destroyed.

Kiyozumi, D., et al. 2012. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201203065.