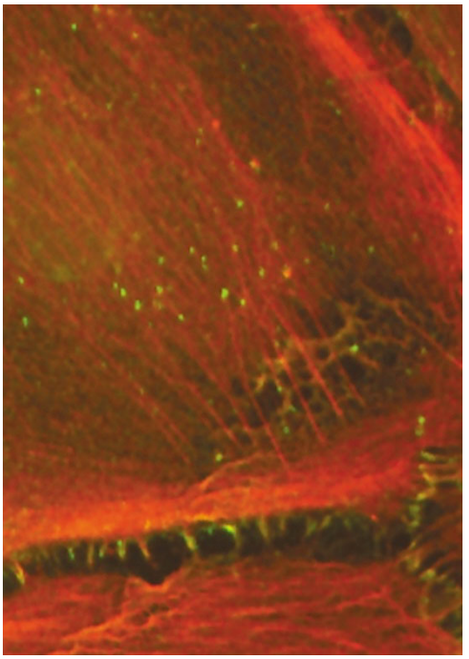

From the study of these mice and cells, it seems that desmoplakin is fundamentally important for organizing desmosomal proteins into functional adhesion structures and for maintaining the structure of the adherens junction. Once adherens junctions are formed and adhesive connections are made, desmosomes act to clamp the neighbouring cells together. This allows adhesion to be 'zipped up' through membrane sealing. Without desmosomes, neighbouring membranes cannot maintain strong adherens junctions or organization of the actin cytoskeleton. Both of these processes are necessary for cells to seal their membranes with their neighbours. Far from being the second-class citizens in intercellular adhesion, desmosomes must now stand shoulder-to-shoulder in our thinking on how our cells generate bonds with their neighbours.

Sarah Greaves, Senior Editor,
Nature Cell Biology

References and links

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FURTHER READING Green, K. J. & Gaudry, C. A. Are desmosomes more than tethers for intermediate filaments? *Nature Rev. Mol. Cell Biol.* **1**, 208–216 (2000) | Tepass, U., Truong, K., Godt, D., Ikura, M. & Peifer, M. Cadherins in embryonic and neural morphogenesis. *Nature Rev. Mol. Cell Biol.* **1**, 99–100 (2000)

WEB SITE

Elaine Fuchs' laboratory: http://www.hhmi.org/research/investigators/fuchs.html

Plating CD25–β3-expressing cells on anti-CD25-coated surfaces led to substrate-localized integrin 'clustering' which, in turn, prevented apoptosis, leading Cheresh and colleagues to propose that integrin ligation by physiological ligands similarly prevents death.

So, what's the molecular mechanism behind IMD? IMD was not prevented by inhibiting stress-mediated caspase signalling, but inhibiting the action of initiator caspases did offer protection from IMD. However, this was independent of death receptors. After observing that caspases and unligated integrins co-localized on the cell surface, the authors identified caspase-8 as being involved in this process by analysing lysates for biotinylated proteins after cells undergoing IMD were labelled with biotinylated caspase inhibitors.

But if death receptors aren't involved, then how do unligated integrins induce apoptosis? They do this, apparently, by recruiting caspase-8 — either directly or indirectly — to the membrane, 'clustering' and thereby activating it. Whether or not accessory molecules regulate this interaction isn't yet known. For now, we can only build on the model that, in the absence of the appropriate extracellular matrix, integrins can activate caspase-8, thereby inducing apoptosis, and that this process is prevented when appropriate ligands are present. Such a model is likely to be important in many physiological situations when cells find themselves in inappropriate surroundings.

Katrin Bussell

References and links

ORIGINAL RESEARCH PAPER Stupack, D. G. *et al*. Apoptosis of adherent cells by recruitment of caspase-8 to unligated integrins. *J. Cell Biol.* **155**, 459–470 (2001)

WEB SITES

Encyclopedia of Life Sciences: http://www.els.net/Integrin superfamily

David Cheresh's laboratory: http://www.scripps.edu/imm/cheresh/

IN BRIEF

CYTOSKELETON

Phosphorylation of γ-tubulin regulates microtubule organization in budding yeast.

Vogel, J. *et al. Dev. Cell* **1**, 621–631 (2001)

In this study, γ-tubulin — an essential component of microtubule-organizing centres — is found to be regulated by phosphorylation. The authors show that Tub4, the budding yeast γ-tubulin equivalent, is phosphorylated in a cell-cycle-dependent manner, phosphorylation being maximal during G1. Mutation of a tyrosine residue (Tyr445) to aspartate increases the assembly rate of microtubules, causing yeast cells to arrest before anaphase. This indicates that modification of γ-tubulin is important for regulating microtubule organization and function during the yeast cell cycle.

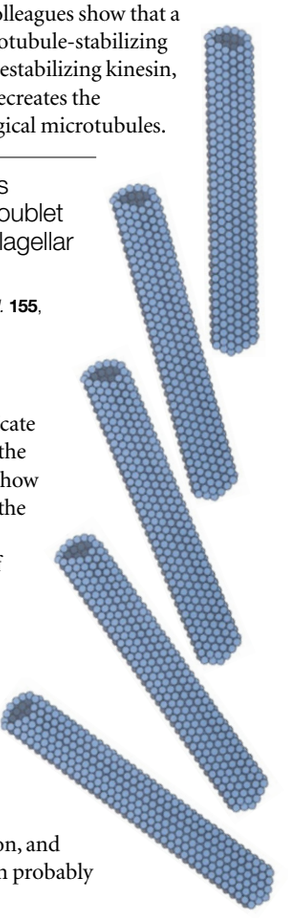
Reconstitution of physiological microtubule dynamics using purified components.

Kinoshita, K. *et al. Science* **294**, 1340–1343 (2001)

The addition and loss of αβ-tubulin dimer subunits from the ends of microtubules is required for the microtubule cytoskeleton to function effectively. Microtubules must polymerize more rapidly and move between polymerized and depolymerized states more frequently than has so far been achieved using purified tubulin *in vitro*. Here, Hyman and colleagues show that a three-component mixture — a microtubule-stabilizing protein, XMAP215, a microtubule-destabilizing kinesin, XKCM1, and tubulin — effectively recreates the characteristic behaviour of physiological microtubules.

Intraflagellar transport balances continuous turnover of outer doublet microtubules: implications for flagellar length control.

Marshall, W. F. & Rosenbaum, J. L. *J. Cell Biol.* **155**, 405–414 (2001)



Historically, ciliar and flagellar microtubules were considered static structures, but more recent data indicate that they do turn over. In this paper, the authors propose a model explaining how the length of flagella is controlled in the unicellular alga *Chlamydomonas reinhardii*. By visualizing turnover of tubulin, the authors show that microtubule polymerization takes place at the tip of the flagellum, and that it occurs through intraflagellar transport — the anterograde movement of large protein complexes driven by kinesin-II. Polymerization is balanced by continuous depolymerization at the same location, and the resulting steady-state equilibrium probably controls the length of the flagellum.