Anchoring microtubules to adherence junctions

Adhesion between epithelial cells is mediated by E-cadherin, which concentrates in adherence junctions and binds to β-catenin and 120-catenin in the cytoplasm. The epithelial cell sheet contains polarized non-centrosomal microtubules with their minus ends oriented apically, but their function remains unclear. Takeichi and colleagues (*Cell*, doi:10.1016/j.cell.2008.09.040) now show that microtubule minus ends are tethered to the apical-most part of adherence junctions, the zonula adherens (ZA), by the previously uncharacterized protein Nezha in colon carcinoma cells. In a search for p120-interacting proteins, the authors found PLEKHA7 and subsequently identified Nezha as a PLEKHA7 binding partner in the ZA. Interestingly, the authors found microtubules growing from minus ends anchored by Nezha in PLEKHA7-rich regions in the ZA. Thus, Nezha and PLEKHA7 link the E-cadherin/p120-catenin complex to microtubules. Depletion of either Nezha or PLEKHA7 disrupts the localization of the other, as well as that of E-cadherin, showing that the complex is required for ZA integrity. Furthermore, the kinesin motor KIFC3, which is recruited to the ZA via microtubules in a PLEKHA7- and Nezha-dependent manner, is required for ZA integrity. It remains to be investigated whether KIFC3 transports molecules needed for ZA maintenance. CKR

Cleaving histones

David Allis and colleagues report on a mode of post-translational regulation of histones — proteolytic cleavage of histone H3 during mouse embryonic stem cell (ESC) differentiation (*Cell* **135,** 284–294; 2008). The authors first noticed a faster migrating species of H3 in extracts from differentiating mouse ESCs that seemed to lack a short stretch of amino acids from the extreme amino terminus. Mass spectrometry confirmed that H3 was indeed proteolytically processed and identified the cleavage sites. Remarkably, cathepsin L, a protease long thought to function in the lysosome, seems to be the protease-cleaving H3. Indeed, the cleavage site in H3 showed sequence features characteristic of cathepsin L substrates. Mutating this consensus site abolished cleavage *in vitro*. Recombinant cathepsin L also cleaved recombinant H3 *in vitro* at the same sites at which H3 was proteolysed *in vivo*. Loss-of-function analysis provided conclusive evidence that cathepsin L is indeed the H3 protease *in vivo*. Interestingly, the authors found that histone acetylation and methylation can modulate cleavage efficiency *in vitro* and that proteolytic processing of H3 reduces the binding of its effectors, such as the Polycomb transcriptional repressor complex. Although H3 cleavage almost certainly modulates its function *in vivo*, precisely how remains a question for future study. SS

Tracking early development of zebrafish

Tracing the 671 cells of *Caenorhabditis elegans* through development earned the 2002 Nobel Prize. Now, Keller, Wittbrodt and colleagues (*Science*; doi:10.1126/science.1162493) have developed a variant of light sheet microscopy called DSLM, where a laser scanner rapidly scans a specimen horizontally and vertically, to allow time-lapse recording of the 16,000 cells of an early zebrafish embryo. Three-hundred and fifty images of H2B–eGFP-labelled nuclei were collected every 90 s over the 24 h period from early cleavages to the beating-heart stage.

Phototoxicity was markedly lower, compared with alternative techniques and the data were processed to allow the automatic detection of nuclei. Seven 'digital embryo' datasets comprising 55 million nuclei follow the positions and sizes of 92% of an embryo's nuclei, allowing the spatiotemporal tracking of individual cell movement and the polarity of cell divisions. The data are available as a free online resource (www.embl-heidelberg.de/digitalembryo).

An early symmetry-breaking event, where radial waves of division originating at the embryonic centre are disrupted by two peripheral waves, coincides with the nuclear localization of β-catenin at the 512-cell stage before zygotic transcription; this event defines the orientation of the body axis. Furthermore, the authors present a new model of germ-layer formation.

DSLM should allow analysis ranging from mechanical forces and gene expression dynamics to normal organ development and mutant phenotypes, and it may provide developmental blueprints for other model organisms. BP

RBP control of mRNAs goes large

RNA-binding proteins (RBPs) regulate many aspects of gene expression at the post-transcriptional level. Several hundred RBPs have been identified but so far, RNA targets of most of these are unknown. Brown and colleagues systematically identified mRNAs associated with 40 of the 600 RBPs present in *Saccharymyces cerevisiae* and found that they bind specific sets of mRNAs that seem to share related functions or locations in the cell (*PLoS Biol.* **6,** 2297-2313; 2008). The authors immunoprecipitated tagged versions of 40 RBPs and identified associated mRNAs using microarrays. Most RBPs had unique profiles of mRNA partners, and most mRNAs identified were bound by multiple RBPs, suggesting the existence of multidimensional and combinatorial control, similar to the transcription factor networks that regulate gene expression. Surprisingly, RBPs often associate with mRNAs that share common gene ontology terms, indicating that they may regulate the fates of functionally related RNAs. For 16 of the RBPs, the authors looked for potential recognition elements that were enriched in their targets and identified sequence or structural motifs in diverse positions along the mRNAs. Given that the authors found that 70% of the yeast mRNAs associate with at least one RBP, and that each mRNA is bound by three RBPs on average, this analysis offers a first glimpse of an extensive combinatorial network that acts at the post-transcriptional level. NLB

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