Any which way but loose

A back-to-back arrangement of kinetochores is not needed for correct alignment on the mitotic spindle, as shown by Hilary Dewar, Tomoyuki Tanaka (University of Dundee, UK), and colleagues.

Sister chromatids are glued together by cohesin such that their kinetochores face opposing poles. This arrangement might thus prevent both chromatids from attaching to spindle microtubules from the same pole. But Tanaka’s group shows that even when geometry fails, a tension-sensitive mechanism fixes any mistakes.

The authors messed with the usual geometry in two ways. First, they confronted yeast cells with a nonreplicating dicentric minichromosome. Its two kinetochores are not held in any fixed relative orientation, yet were efficiently attached to opposing poles. Second, normal chromosomes in cohesin mutants (which have attachment defects), were roughly linked by inhibiting topoisomerase II. This restored bipolar attachments. Thus, any connection that can produce tension is enough to ensure biorientation.

The tension-sensitive correction depends on the Ipl1 kinase, whose mammalian homologue, Aurora B, prevents monopolar attachments. This suggests that Ipl1 activity knocks off attachments until tension somehow stops it—which by turning off the kinase, turning on a counteracting phosphatase, or pulling substrates away from the kinase.

Reference: Dewar, H., et al. 2004. Nature. 10.1038/nature02328.

A dynamite intercellular highway

Long, delicate tubes are a new trade route for the intercellular exchange of goods, as shown by Amin Rustom, Hans-Hermann Gerdes (University of Heidelberg, Germany), and colleagues.

Rustom noticed these actin-rich extensions, which the group calls tunneling nanotubes (TNTs), while looking for secretory granules near the plasma membrane. The membrane dye that he used revealed long thin tubes, up to several cell diameters long but only ~100 nm wide, linking some of the plated cells. “They are extremely sensitive,” says Gerdes. “Even light exposure disrupts them. Maybe because of [this sensitivity], this is the first time we realized these unique structures are there.” The group has seen the connectors in kidney and neurosecretory cell lines and primary neuroendocrine cultures, but other cell types could be similarly linked.

The TNTs are made when filopodia contact a distant cell. Once it becomes contiguous with the new partner, the extension establishes a one-way conveyor belt—like system through which one cell (probably the one that sent out the filopodia) dispatches endosomal-like vesicles to the other.

Smaller soluble molecules, however, are blocked from entry into the TNTs. The actin bundle at the base of the TNT, wrapped tightly by the surrounding membrane, may act like a plug to prevent passive diffusion of small molecules. If TNTs exist in vivo, then theoretically anything packaged into endosomes, such as morphogens or immunogenic components, could be used to signal between otherwise unconnected cells.

Reference: Rustom, A., et al. 2004. Science. 303:1007–1010.

Teeny tiny rafts

Tiny but dynamic domains define the elusive lipid raft, based on results from Madan Rao, Satyajit Mayor (National Centre for Biological Science, Bangalore, India), and colleagues.

Describing the structure and components of rafts—membrane domains enriched in specific lipids and proteins—has been a long-standing challenge for cell biologists. In this new report, the authors use FRET, photobleaching, and theoretical modeling to get the closest look yet at raft components called GPI-APs (GPI-anchored proteins). They show that lipid rafts contain small clusters (four or fewer molecules) of very tight-knit GPI-APs packed into an ~4-nm-wide space.

About a third of any given GPI-AP species is found in rafts. The rest remain as monomers. This percentage holds true across multiple expression levels, which is inconsistent with equilibrium-based formation. “It means rafts have to be actively maintained,” says Mayor. “And within these regions, the GPI proteins form clusters.”

Different types of GPI-APs are found within a cluster, and the clusters are dynamic—cross-linking of one species removes it from the cluster, and another species readily takes its place. The cross-linked GPI-APs formed larger groups that were endocytosed by the clathrin-mediated pathway, rather than the route responsible for uptake of raft GPI-APs. Thus, ligation of a receptor could change its fate by altering its lipid environment.

Reference: Sharma, P., et al. 2004. Cell. 116:577–589.