**Helicobacter breaks down junctions**

Bacteria can break apart cell junctions that link neighboring stomach cells, based on the work of Manuel Amieva, Roger Vogelmann, Stanley Falkow (Stanford University, Stanford, CA), and colleagues. Although the bacteria may do it to gain access to tasty chemicals that leak out, the results for humans may include stomach ulcers and gastric cancer.

The link from cell junctions to stomach ailments may, say the researchers, lie in tissue repair. Injury to the stomach triggers cell division and migration to plug the gap. The chiefs in charge of these processes may well lie in cell junctions—ideally placed, as they would be, to sense whether there is a breach in the epithelium. If bacterial proteins interfere with that process, the persistent gaps could lead to ulcers. And if the bacterial proteins push the repair process into inappropriate overdrive then cancerous growths might arise.

Such pathways remain the stuff of speculation. But what the Stanford team has shown is that CagA, a protein that the ulcer-associated bacterium *Helicobacter pylori* injects into gastric epithelial cells, can associate and interfere with junctional proteins. Some of the tight junction scaffolding protein ZO-1 is lured away from junctions to associate with attached bacteria, and still more ZO-1 colocalizes with intracellular CagA at the remaining tight junctions, which are now leaky.

Others have demonstrated that CagA can bind signaling proteins such as SHP2 and Grb2 and increase spreading of isolated cells driven by the c-Met receptor. Although these effects are initially resisted in monolayers, the cells eventually succumb, perhaps when CagA induces inappropriate signaling from what is left of the cell junctions.

Reference: Amieva, M.R., et al. 2003. *Science*. 300:1430–1434.

---

**Commuting to mitosis**

There is a time for caution and a time for committing. For the cell cycle, a halt before mitosis is an appropriate response to ionizing radiation or inhibition of DNA replication. But once mitosis is underway the cell is better off just carrying on regardless of DNA-damaging insults. Dmitry Bulavin, Albert Fornace (National Cancer Institute [NCI], Bethesda, MD), and colleagues now report on a double phosphorylation switch that keeps irradiated mitotic cells from bouncing unexpectedly out of mitosis.

The switch is in one of the Cdc25 phosphatases—proteins that remove an inhibitory phosphate from Cdc2, thus allowing entry into mitosis. Cdc25C is itself phosphorylated during interphase. First, a constitutive kinase and then an irradiation-induced kinase hit Ser 216 on Cdc25, thus keeping the phosphatase inactive. The NCI team now show that this Ser 216 phosphorylation is replaced in mitotic cells by phosphorylation of Cdc25C on Ser 214, and that the new Ser 214 phosphorylation blocks reestablishment of the earlier Ser 216 phosphorylation. Thus, Cdc25C is locked on in mitotic cells, and does not respond to irradiation.

The mitosis-reinforcing function of the Ser 214 is clear from a Ser 214 to Ala mutant, which delays entry into mitosis in mammalian cells and reinstates a DNA damage replication checkpoint that is normally absent in early embryonic frog extracts. The Ser 214 residue is probably phosphorylated by Cdc2 itself, but it is unclear how the inactive Cdc25C and Cdc2 might jumpstart each other—other Cdc25 isoforms or polo kinase are possibilities. Meanwhile, the authors suspect that pairs of mutually exclusive phosphorylation sites will turn up in other regulatory complexes. Either way, Sawin believes that the next step will be more biochemistry to determine just what happens when tea1p is dropped off at the ends.

Reference: Snait, H.A., and K.E. Sawin. 2003. *Nature*. 423:647–651.

---

**Anchored by feedback**

A pair of proteins, each individually incapable of maintaining a polar distribution, can convince each other to stay put at the ends of a fission yeast cell, according to Hilary Snait and Ken Sawin (University of Edinburgh, Edinburgh, Scotland).

Polarity studies in fission yeast have focused on the tea1p protein. It can be seen hitching a ride on growing microtubules as they speed toward the two ends of the cell—the only sites where growth takes place in fission yeast. Now, Snait and Sawin have found a protein called mod5p that is localized to cell ends and helps to keep the arriving tea1p anchored to those same sites. Cells lacking mod5p delivered tea1p as usual but failed to keep it localized at the cell ends. Mod5p, in turn, was found all around the plasma membrane when tea1p was no longer present. Thus, the authors believe that tea1p and mod5p feedback on each other to ensure immobility.

There is preliminary evidence to suggest an indirect physical link between tea1p and mod5p. This linkage may cement both proteins in a complex that is big enough to be inherently immobile, thus anchoring them near the site where tea1p arrives. Alternatively, the association of the two proteins may trigger a biochemical change in the complex that fixes the complex in place. Either way, Sawin believes that the next step will be more biochemistry to determine just what happens when tea1p is dropped off at the ends.

Reference: Snait, H.A., and K.E. Sawin. 2003. *Nature*. 423:647–651.