Research Roundup

BARS takes Golgi apart

Cristina Hidalgo Carcedo, Alberto Luini, Daniela Corda, and colleagues (Consorzio Mario Negri Sud, Santa Maria Imbaro, Italy) suggest that Golgi membranes are chopped up by a protein called BARS before mitosis can occur. Their cell culture studies contrast, however, with results from genetic knock-out experiments.

BARS is closely related to the CtBP family of transcriptional repressors needed for normal embryonic development in mouse and fly. Corda and Luini previously found that, in rat cells, BARS is what brefeldin A might target with its ADP ribosylation activity when it inhibits Golgi trafficking. Their subsequent work suggested that BARS is needed for the fission of vesicles during trafficking.

The new report indicates that BARS also cuts up the Golgi into vesicles and small tubules to be shared by daughter cells. The authors removed BARS activity from cultured rat cells using anti-sense methods or from an in vitro Golgi fission assay by immunodepletion or dominant-negative mutants. In all cases, Golgi stacks disassembled into a tubular network, but were not fragmented further into vesicles. The BARS-depleted cells did not enter mitosis, a known side effect of the failure to break down the Golgi.

How BARS might induce fission is unclear. Its acyl transferase activity modifies lipids such as LPA and might thus induce a needed structural change in the membrane. However, mutation of this activity reduced but did not abolish its fission activity in vitro.

Mice CtBP mutants have developmental problems, but cell cultures can be made from these lines, and architectural Golgi defects have not yet been found. “We think that BARS is the main mechanism for Golgi fission during mitosis,” says Corda, “and that there are other redundant mechanisms that can take over where BARS fails.” Fail-safes might include dynamin, which has also been proposed to cleave the Golgi.

Reference: Hidalgo Carcedo, C., et al. 2004. Science. 305:93–96.

With their dying breath

Cells gasping for air call out to progenitor cells for help, according to results from Daniel Ceradini, Geoffrey Gurtner, and colleagues (NYU School of Medicine, New York, NY).

Stem cells and progenitor cells do not start making new tissue just anywhere—most often, they are recruited to injury sites. The chemokine SDF-1 is known to trigger this recruitment, but what causes injured tissues to make SDF-1 was unclear.

Gurtner’s group shows that SDF-1 expression is activated by HIF-1, a transcription factor known to be stabilized at low oxygen levels. Tissues with low oxygen and high SDF-1—either injury sites or bone marrow, where progenitors normally hang out—were hot spots for endothelial progenitor cells (EPCs) carrying the SDF-1 receptor, CXCR4. These EPCs adhered better to endothelial cells expressing SDF-1, and they also migrated toward SDF-1 gradients in vitro. Disruption of SDF-1 interactions with CXCR4 prevented EPC homing and blocked vascular regeneration in mice.

Progenitors for other cell types (neurons, muscle, etc) might also respond to SDF-1, but Gurtner focused on EPCs because new vasculature can both repair and prevent injury. “Endothelial cells downstream of a [partial] blood vessel blockage become hypoxic and make SDF-1,” he says. “This marks them like a barcode that says this is an area of injury. Often, nothing cataclysmic happens because new vessels form natural bypasses around the blockage.”

HIF-1 was already known to induce sprouting of existing blood vessels through the induction of the growth factor VEGF. But hypoxia and HIF-1 were not known to recruit circulating progenitors.

Reference: Ceradini, D., et al. 2004. Nat. Med. doi:10.1038/nm1075.

SDF1 (red) calls progenitor cells to endothelial cells (green) lacking oxygen.

Gurtner/Macmillan