E-cadherin immobilizes cells from the inside

As invasive cells, metastatic tumor cells must be free-roaming—able to detach from the extracellular matrix and neighboring cells. So when E-cadherin, a cell–cell adhesion molecule, was found to suppress invasion, it was logical to attribute this ability to its adhesive properties. But results by Wong and Gumbiner on page 119 indicate that E-cadherin uses an adhesion-independent mechanism to inhibit the invasiveness of human cancer cells.

The authors studied the effects of various E-cadherin constructs on two invasive cell lines derived from breast and prostate cancers. They found that intracellular signaling, not adhesion, mediated E-cadherin’s tumor suppressor function. The adhesive portion of E-cadherin, its extracellular domain, was neither necessary nor sufficient to stop invasive behavior. In contrast, constructs containing E-cadherin’s cytoplasmic tail, in particular the β-catenin–interacting domain, inhibited the invasive phenotype of the cells.

β-Catenin, as part of the Wnt signaling pathway, activates transcription of a set of target genes that induce cell motility, including a matrix metalloproteinase. E-cadherin can suppress β-catenin action by sequestering the protein from its target genes, and indeed the authors found that loss of β-catenin also stopped invasion.

Golgi united are also divided

Golgi bodies do not need to disassemble to divide, according to results from Uchiyama et al. on page 1067.

In mammalian cells, the Golgi apparatus disassembles into vesicles and short tubules before mitosis. Golgi breakdown requires that two membrane fusion pathways necessary for Golgi reassembly after mitosis be temporarily inhibited. For one, the NSF pathway, this inhibition is achieved by Cdc2-mediated phosphorylation of an NSF-associated factor at early mitosis. But how the cell cycle regulates the second, the p47/p97 pathway, was not known.

Uchiyama et al. have determined that Cdc2-mediated phosphorylation also inhibits the p47/p97 pathway. p97 is an ATPase that binds to the Golgi through its associated factor, p47. Uchiyama et al. find that p47 is phosphorylated by Cdc2 upon entry into mitosis. Phosphorylated p47 bound to p97 in mitotic cells and had a decreased binding affinity for Golgi membranes, thus releasing the complex from the Golgi.

Addition of a phosphorylation-insensitive version of p47 to mitotic cells blocked Golgi breakdown. However, the mutant did not impair proper separation of the Golgi into the daughter cells. How the Golgi can partition without first disassembling in mammalian cells is unclear. Furthermore, it is unclear if Golgi disassembly occurs in other organisms.

NRG-1 talks back to neurons

On page 1133, Bao et al. demonstrate that a neuronal growth factor signals to neighboring cells while also communicating back to the nucleus of its own cell. This two-way signaling is necessary to maintain neuronal survival.

The Nrg-1/erbB partnership is well known to control responses in the erbB-expressing cells, such as epithelial cell motility and proliferation, through MAP kinase pathways. Now, the target cells are shown to talk back to neurons that express membrane-bound Nrg-1 via the same erbB–Nrg-1 complex.

Bao et al. show that treatment with soluble erbB protects Nrg-1–expressing neurons from cell death in vitro. The protective activity appears to stem from Nrg-1’s ability to regulate transcription of apoptotic genes, including BAK and RIP, whose expression levels were repressed by treatment with erbB. Membrane-bound Nrg-1 was cleaved by a γ-secretase–like activity in response to erbB treatment, thus releasing the Nrg-1 intracellular domain, which moved to the nucleus. Although Nrg-1 has not been shown to bind to DNA, the authors demonstrate that it does have transcription-activating activity on a reporter construct, and preliminary evidence indicates it may interact with zinc finger–containing transcription factors.