The NPC, in detail

The nuclear pore complex (NPC) is a huge cylindrical assembly that transports material to and from the nucleus. In a biological tour de force, researchers have determined the positions of all 456 proteins of the NPC, providing structural insights of unprecedented detail. Among other discoveries, Svetlana Dukudovskaya, Liesbeth Veenhoff, Michael Rout, Brian Chait (Rockefeller University, New York, NY), Frank Alber, Andrej Sali (University of California, San Francisco, CA), and colleagues show that the large, complicated NPC is formed by only a few, structurally similar modules, including 16 repeated columns.

The researchers combined data on the size, shape, structure, and neighbors of every NPC protein to create a set of positional probabilities, or “restraints,” which were then analyzed and optimized to produce a final structure. Rout compared it in principle to solving a crossword puzzle, in which partial knowledge of one word restrains the possibilities for many others. “If you have tens of thousands of these restraints,” he says, “you can pare down until a protein is restrained to a volume of its own size.”

Previous characterizations of the NPC structure did not resolve the positions of its individual components. Nine years of work went into the generation and analysis of the data, although future studies of other cell structures should be faster.

The new structure is highly symmetrical. “It’s very clear that the underlying architecture of the NPC is modular,” says Rout, “and likely arose from several rounds of gene duplication.” Each column is paired with an adjacent one of related proteins; the pairs give rise to eight identical spokes that make up the NPC. Gene duplication may also have given rise to the prominent inner and outer rings, which circle within the NPC like concentric belts.

The structure is not the last word on the subject; it gives a protein-level but not atomic-level picture. It also does not include the fine structure of the basket, which projects into the cytoplasm and is believed to aid nuclear transport. The team is now working on solving these structures. JCB

References: Alber, F., et al. 2007. Nature. 450:683–694.
Alber, F., et al. 2007. Nature. 450:695–701.

Cells within cells (within cells)

One tumor cell can burrow its way entirely inside another. Now, Michael Overholtzer, Joan Brugge (Harvard Medical School, Boston, MA), and colleagues report that, while its fate is usually met in the host’s lysosome, in some cases the burrowing cell can divide or pop back out, or even go along for the ride as the host burrows into yet another cell.

Such “cell-in-cell” structures are common in tumors, but the mechanism of invasion was unknown. By labeling human breast cancer cells with different colors, the authors showed that 25% of cells contained other cells within 12 hours of detachment from their substrate. While apoptosis of one cell can drive phagocytosis by another, blockade of either process did not diminish the rate of invasion.

Invasion was suppressed, however, by stopping actin–myosin II contraction in the internalized cell. “The process requires activity of the invading cell,” Brugge says. The group found no evidence that the host initiates the process, and contraction blockade in the host had no effect. Cadherins, which link epithelial cells together, were required and were densest at contacts between the two cells during internalization.

Both cadherins and actin–myosin contraction feature prominently in epithelial compaction, through which multiple layers of attached cells condense into a dense monolayer. The authors suggest that the cell invasion process, which they christened “entosis,” may be epithelial compaction gone awry, with the invader tugging so hard it pulls the other cell right around it. The malaria parasite performs a roughly similar trick when invading its host.

Once inside, most cells were degraded by lysosomes, but about 15% were released apparently unharmed. A few divided inside their hosts, and some hosts apparently turned into invaders themselves, giving rise to a cell within a cell within a cell.

Entosis is not just a novelty of the lab bench: 1–2% of metastatic breast tumor cells contained other cells. Whether entosis promotes tumorigenesis by increasing aneuploidy or inhibits it by killing invasive cells and whether noncancerous cells undergo entosis during development remain to be seen. JCB

Reference: Overholtzer, M., et al. 2007. Cell. 131:966–979.