New model of a nuclear pore complex is based on crystal structure of its key component

Everything that goes in and out of a cell's nucleus must pass through one of its nuclear pores. In the second nuclear pore study to come out of Rockefeller University in as many months, researchers have determined the crystal structure of one of the pore's main components and used it to propose an overall structure for the circular pore, rings of alternating protein complexes that fit together like two sides of a zipper.

In research published in the journal Cell, a team of scientists from Günter Blobel's Laboratory of Cell Biology describes how they crystallized a central component of the nuclear pore that provided a tantalizing glimpse of the pore's structure in its entirety. Building on this component, the team has proposed a new molecular model of the nuclear pore.

Visualizing the nuclear pore complex is a particularly tricky endeavor: It's such a large, pliant structure that traditional methods just don't work. So researchers have had to get creative. Just a month ago, two Rockefeller professors published the first complete model of a nuclear pore complex created through a combination of biochemical, spectrometry and computer-modeling techniques. Blobel's team — Kuo-Chiang Hsia, Peter Stavropoulos, Blobel and André Hoelz — used an approach that was quite different: x-ray crystallography to visualize a core piece of the pore and determine how it bound to a neighboring complex, then puzzle-solving to deduce how the rest of the structure fit together. In the end, the researchers' results differed, too. But the new findings were consistent with research published by the Blobel lab last spring, which proposed a ring-like arrangement of sliding subunits.

Using the high-resolution structures they've uncovered, Hoelz says, the lab is working to build a model of the nuclear pore complex that's constructed piece by piece. He and Blobel found that their complex — called Sec13-Nup145C — crystallized into two distinct shapes that came together to form a bent rod. From there, they devised a molecular architecture for the pore that consists of eight of these rods, placed vertically, linking four stacked rings of alternating protein complexes in a pattern akin to houndstooth. Hoelz, a research associate, and Blobel, John D. Rockefeller Jr. Professor and a Howard Hughes Medical Institute investigator, propose that this structure may represent one of the four concentric cylinders that, according to their previous research, may make up the core of the nuclear pore. "Clearly more work will be required to test these two proposals," Blobel says.

The nuclear pore is the center of so much attention because everything that goes in and out of the nucleus has to pass through. But apart from a few binding sites, "the structure is essentially a black box," Hoelz says. "And if we don't know how it looks and how it is constructed in atomic detail, then we have no way to figure out how this large transport machine works."

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