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Assembling yeast complexes

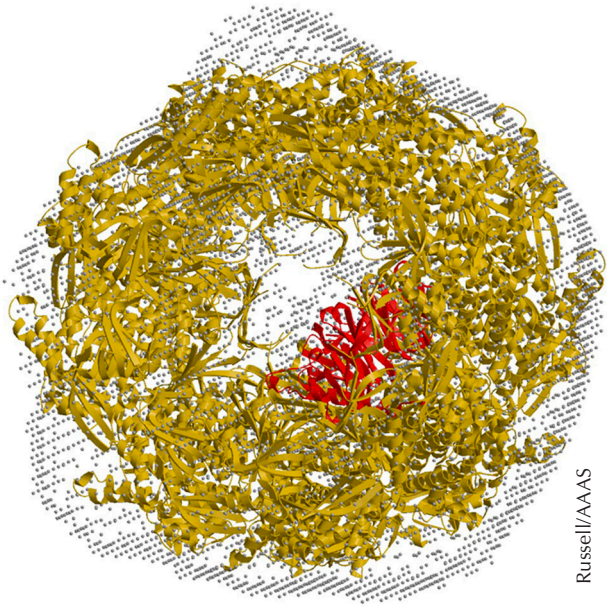
The machine that is a cell is more than the sum of its protein parts. A large step toward understanding how those parts are so effectively put together has been taken by Patrick Aloy, Rob Russell (EMBL, Heidelberg, Germany), and colleagues. Their work has identified ~100 yeast protein complexes and predicted interactions within and among many of them.

"We were working on a large scale to model as many complexes as possible," says Aloy. Proteins that purified together were assigned to functional groups. The authors built three-dimensional models for as many proteins in these groups as possible, based on known structures and protein homologies. They then predicted which proteins interact directly, and subsequently modeled the structures of complexes containing multiple proteins.

Additional structural data came from EM analyses of the complexes that purified with sufficient quality. "We figured out not just who interacts with whom, but how," says Aloy. "Understanding function requires structure. At the end of the day it's what gives you the biochemistry."

Using known two-hybrid interactions and estimates based on homology, the group also predicted communications between complexes. Some were unexpected connections, such as those between transcription and translation components. Although the accuracy of many of their cross-talk predictions is unknown, the structures suggest suitable sites for mutagenesis by any group interested in a particular interaction pair.

So far, the authors have a good idea of the structure of about a quarter of the estimated total protein complexes in yeast (~400) and has nearly complete structures for 42 complexes. "Our final goal," says Aloy, "is to model all the associations of all the complexes or organelles at a molecular level." More structural information should be forthcoming once the group is able to improve their EM using tomographic techniques. ■


Russell/AAAS

EM data (gray) and known structures of a chaperonin (gold) and its inhibitors (red) help build a model for the full complex.

Reference: Aloy, P., et al. 2004. *Science.* 303:2026–2029.

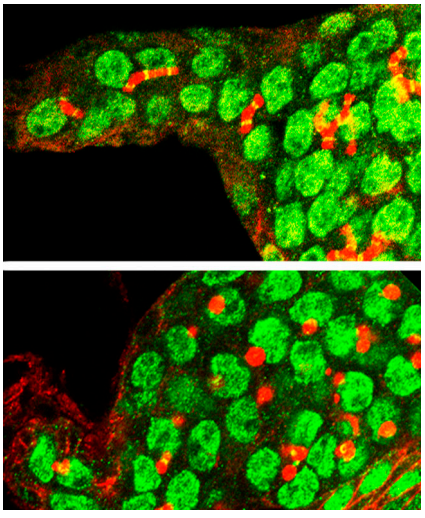
Mass dedifferentiation

Germline stem cells (GSCs) on their way to differentiation can change their minds and return to pluripotency, according to Toshie Kai and Allan Spradling (Carnegie Institution of Washington, Baltimore, MD). Such a return is a long-sought goal for those hoping to create pluripotent cells for transplantation.

GSCs in the adult fly reside in a niche where they receive Dpp signals telling them to remain undifferentiated. Upon division, one daughter escapes the niche (and the realm of Dpp) and expresses *Bam*. The freed cell thus differentiates into a cyst–a set of up to 16 cells interconnected by incomplete cytokinesis and a cytoskeletal structure called the fusome.

Kai and Spradling show that these steps toward differentiation can be undone with Dpp. They overexpressed *Dpp* in flies to form many GSCs, then induced a transient burst of *Bam* to produce cysts. Hours later, when *Bam* was gone, the cysts broke down into single cells resembling GSCs.

Using larvae, the group shows that the resulting cells are functional GSCs. As in the adult, transient *Bam* caused cysts to form, and again these cysts individualized. The resulting single cells developed into normal GSCs as the larvae grew into adults. Reversion of cyst cells may repopulate GSCs depleted by injury or age, for example, although how this choice might be regulated is unknown.


Spradling/Macmillan

Dpp makes multicellular cysts (red, top) dedifferentiate into single cells (bottom).

Although other cell types (such as liver) are thought to dedifferentiate on rare occasions, Spradling is excited about the frequency of reversion in cysts. "All the germ cells in the larval ovary become cysts and then, seemingly, all become stem cells again," he says. So the system should lend itself to finding the factors that direct this backward step. Like cysts, dividing germ cell precursors are transiently linked by a fusome. Spradling wonders whether the severing of this connection is the trigger to stemness. ■

Reference: Kai, T., et al. 2004. *Nature.* 10.1038/nature02436.