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A molecular chain gang at work in maturing ribosomes

Study finds interconnected molecules that reorganize preribosomes.

A motor protein on immature ribosomes connects to a network of other molecules within the nascent organelles, Baßler et al. reveal (1). The motor might help an assembling ribosome get into shape by tugging some of its components into position.

A ribosome contains four types of rRNA and around eighty kinds of proteins, so piecing together a working molecular machine from these raw materials is a tricky task. Roughly two hundred different proteins collaborate to orchestrate ribosome assembly and maturation (2). Not only do they have to construct the two main ribosome components, the 60S and 40S subunits, but they have to shape features such as the peptidyl transferase center (PTC), where transfer RNAs hand off their amino acids to the growing peptide chain. The functions of many of these assembly and maturation factors remain a mystery. One protein that scientists have made some headway on is Rea1, a motor protein related to dynein. Rea1 sits on the immature 60S subunit, and researchers initially speculated that it might help move the partly completed ribosome out of the nucleus. Instead, they found that Rea1's power stroke tugs another protein, Rsa4, out of the ribosome (3, 4). However, it wasn't clear whether removing Rsa4 caused additional changes to the ribosome's organization.

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To answer this question, Baßler et al. first searched for ribosomal proteins that bind to Rsa4. They found that a short segment of the protein Nsa2 fastened onto Rsa4. When they crystallized this section of the protein along with Rsa4's C-terminal region, which is shaped like an eight-bladed propeller, they found that a 10-amino-acid section of Nsa2 fits neatly into a slot in Rsa4's propeller.

Focal Point

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(Left to right) Jochen Baßler, Helge Paternoga, Elisar Barbar, Ed Hurt, Irmi Sinning, and colleagues (not pictured) reveal that a chain of molecules connects directly and indirectly to Rea1, a motor protein on the surface of maturing ribosomes. Rea1 links to Rsa4, which in turn attaches to Nsa2. This image, based on the team's crystal structures, shows a segment of Nsa2 (red) inserted into the propeller-shaped C-terminal domain of Rsa4 (blue).

To test whether the interaction between Rsa4 and Nsa2 was crucial for ribosome assembly, the researchers created a mutated form of Nsa2 that can't bind to its partner. Yeast cells carrying this version couldn't assemble functional 60S ribosome subunits. Several proteins that normally depart the assembling ribosome remained attached in the mutants, including two enzymes that work to construct the PTC.

Before this study, researchers only had a rough idea where Rsa4 resides in the incipient 60S subunit. Baßler et al. not only characterized Rsa4's interactions with Nsa2 but also nailed down the locations of the two proteins and discovered further connections to other ribosomal components. For example, two blades of Rsa4's C-terminal propeller attach to a structural feature called the central protuberance, which helps hold the two ribosomal subunits together. The connection between Rsa4 and a protuberance protein called Rpl5 is necessary for yeast cells to survive, the team showed. The researchers also found that Nsa2 contacts helix 89 of the ribosomal RNA that forms part of the PTC but is out of place in the unfinished 60S subunit.

Thus, when Rea1 yanks on Rsa4, it does more than remove its partner from the nascent ribosome. Because Rea1 links to a network of interconnected molecules, the study suggests that its actions reshape the organelle. "It tells us how mechanical energy can be used for restructuring the preribosome," says senior author Ed Hurt. For example, Rea1 could help arrange the PTC through its indirect connection to rRNA helix 89. In the immature ribosome, the 5S RNA and proteins of the central protuberance are twisted 180° out of their final orientation, and pulling by Rea1 might be required to straighten them out.

The researchers now want to obtain structures for different stages in ribosome maturation so they can track how the rearrangements occur. And it's possible that Rea1 has a bigger impact on ribosome structure. Early in ribosome maturation it links to a different partner, Ytm1, and thus it also might shift other ribosome components.

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4. Ulbrich, C., et al. 2009. *Cell*. 138:911–922.