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Journal club

RIBOSOME CYCLE EMERGES FROM DNA REPLICATION

Ribosomes are composed of two subunits, but into the late 1960s, the reason for their universal bipartite construction remained elusive. Were subunits necessary simply to assemble these mega complexes or did they have a function in protein synthesis?

Arriving for my postdoc in Matt Meselson's laboratory at Harvard, I set out to investigate whether the two bacterial ribosomal subunits are associated permanently or come apart during cell growth. To test this, I used heavy isotope transfer, adopting the pioneering approach taken by Meselson and Stahl in their seminal paper, which revealed semi-conservative replication of *Escherichia coli* DNA through the use of density equilibrium centrifugation analysis in caesium chloride.

> "Using this rare yeast in heavy isotope transfer experiments, ribosomal subunit exchange could be detected readily"

In the high salt environment of caesium chloride, however, the ribosomes dissociated completely into their protein and RNA components, precluding the use of this method. We overcame the problem by using velocity sedimentation through shallow sucrose gradients to resolve intact heavy ribosomes from light ribosomes. Two reciprocal heavy–light hybrid species emerged promptly, whereas heavy ribosomes disappeared, thereby demonstrating that bacterial ribosomes continuously undergo subunit exchange.

The question then became whether eukaryotic cells used the same or a different ribosome cycle. To answer this question, it was necessary to find a eukaryote that was able to grow on heavy isotopes. Fortunately, Matt had held onto an exceptional yeast that was isolated from a cactus in Texas, which managed to multiply when fed the lysate of algae that had been grown on heavy isotopes. I had this unidentified strain typed as *Candida krusei* (Castellani) Berkhout.

Using this rare yeast in heavy isotope transfer experiments, ribosomal subunit exchange could be detected readily, validating that eukaryotic ribosomes also dissociate unceasingly into their two subunits and reform — an observation that is now a cornerstone of translation initiation. I flew to London and handed the manuscript to the editor of *Nature*, where it was accepted the next day.

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ORIGINAL ARTICLES Meselson, M. & Stahl, F. W. The replication of DNA in *Escherichia coli*. *Proc. Natl Acad. Sci. USA* **44**, 671–682 (1958) | Kaempfer, R. Ribosomal subunit exchange in the cytoplasm of a eukaryote. *Nature* **222**, 950–953 (1969)