Biochemistry
Cite This: Biochemistry XXXX, XXX, XXX−XXX
Viewpoint
pubs.acs.org/biochemistry

In Which the Deity Attempts To Make a Ribose-Free Ribosome

Peter B. Moore*

Department of Chemistry, Yale University, New Haven, Connecticut 06520-8107, United States

Mitochondria and chloroplasts are believed to be the descendants of eubacteria that took up residence in the cytoplasm of eukaryotic cells billions of years ago. Both have since become obligate symbionts, but they retain genomes of their own, albeit much reduced in size, as well as the apparatus needed for gene expression, including organelle-specific ribosomes.

Chloroplast and mitochondrial ribosomes have never been easy to work with because they are much less abundant than cytoplasmic ribosomes, and preparations uncontaminated by cytoplasmic ribosomes are hard to obtain. Nevertheless, it has long been evident that while chloroplast ribosomes are closely similar to those found in modern eubacteria, mitochondrial ribosomes have diverged a lot, and moreover, there is a lot of species to species variability.

The first atomic-resolution ribosome structures to appear were all prokaryotic. From 2000 to ∼2015, the number of high-resolution structures available for the cytoplasmic ribosomes from eukaryotes was modest, and chloroplast and mitochondrial ribosomes were terra incognita. These gaps began to fill when the "resolution revolution" in cryo-electron microscopy (cryo-EM) got underway ∼2013, and we now have atomic-resolution cryo-EM structures for the cytoplasmic ribosomes from several eukaryotes, for chloroplast ribosomes (e.g., ref 1), and for three different kinds of mitochondrial ribosomes: yeast (e.g., ref 2), human (e.g., ref 3), and *Trypanosoma brucei*.[4] The *T. brucei* structure, which was determined recently by Ban and his co-workers, is the subject of this commentary, and the data displayed in Table 1 show why it deserves attention. Compared to other ribosomes, it is gigantic, larger even than mammalian cytoplasmic 80S ribosomes [molecular weight (MW) of ∼3.8 × 10^6], and it is phenomenally rich in protein.

When you look at images of this structure, you quickly realize that the small ribosomal subunit of the mitochrondrial ribosome from *T. brucei* (Tb-mit-SSU) is not so small. In most ribosomes, the molecular weight of the SSU is approximately half that of the large ribosomal subunit (LSU), but in these particles, the molecular weights of the two subunits are roughly equal. In addition, the Tb-mit-SSU is ∼92% protein by weight. Thus, instead of being an RNA assembly stabilized by proteins, like the SSUs and LSUs from all other ribosomes, it is a protein assembly slightly contaminated with RNA. Nevertheless, it retains the head, shoulder, and body organization typical of SSUs.

The Tb-mit-LSU is somewhat less rich in protein than the Tb-mit-SSU, but it too is protein-dominated. Nevertheless, once again, its overall morphology resembles that of other LSUs. Crudely, it is a hemisphere, the (more or less) flat side of which contacts the SSU when the two subunits join to make a complete ribosome, and as usual, three protrusions extend from that surface. It is only when you look closer that it becomes apparent how profoundly this LSU has diverged from the eubacterial norm. The protrusion that in other LSUs consists of an RNA stalk capped with uL1 is made entirely of protein, and its central protrusion is also an all-protein assembly, instead of being a composite structure that includes 5S rRNA. (There is no 5S rRNA in these particles.) Finally, the RNA components of the two subunits are so positioned that when the subunits join to form a complete ribosome, a viruslike structure that consists of an RNA-rich core surrounded by a thick protein coat emerges.

The rRNAs in these particles are radically reduced versions of those found in eubacterial ribosomes (see Table 1). Included in the little that remains are the components of SSU rRNA that support decoding and the parts of domain V of LSU rRNA that form the peptidyl transferase center (PTC) of the ribosome. Evidently, the Almighty has not yet figured out a way to dispense with them. The nucleotide sequence in the decoding region of the Tb-mit-SSU differs significantly from the eubacterial consensus but appears likely to function the same way. Little can be said about the three-dimensional structure of the PTC in these particles because it is so disordered that it can barely be seen in cryo-EM maps. The PTC is nowhere near as disordered in any of the other known ribosomes, but the implications of this difference in dynamics are completely obscure.

This structure raises many questions. Why do the structures of mitochondrial ribosomes deviate so much from the eubacterial norm? Why is there so much variation from

Table 1. Chemical Compositions of Some Types of Ribosomes[a]

	E. coli	yeast mitochondria	human mitochondria	*T. brucei* mitochondria
LSU rRNA (no. of nucleotides)	2309	3296	1559	1179
SSU rRNA (no. of nucleotides)	1539	1649	954	621
protein number (average MW)	55 (16000)	75 (23000)	81 (25000)	145 (33000)
particle MW	2.16 × 10^6	3.32 × 10^6	2.86 × 10^6	5.39 × 10^6
% protein	39	51	71	89

[a]Particle compositions and molecular weights were obtained using data deposited in the Protein Data Bank (4U1U, 5MRC, 3J9M, and 6HIV). The molecular weights provided refer only to the macromolecular components of the particles in question. Protein compositions were estimated assuming that the average molecular weight of the ribonucleotides in rRNAs is 330.

DOI: 10.1021/acs.biochem.8b01191
Biochemistry XXXX, XXX, XXX−XXX

species to species? Do these weird ribosomes promote protein synthesis exactly the same way as ordinary eubacterial ribosomes, which is what the conventional wisdom would have us believe?

AUTHOR INFORMATION

Corresponding Author

*E-mail: peter.moore@yale.edu.

ORCID

Peter B. Moore: 0000-0002-8538-2276

Notes

The author declares no competing financial interest.

REFERENCES

(1) Bieri, P., Leibundgut, M., Saurer, M., Boehringer, D., and Ban, N. (2017) Structure of the 70S chloroplast ribosome. *EMBO J. 36*, 475−486.

(2) Desai, N., Brown, A., Amunts, A., and Ramakrishnan, V. (2017) Structure of the yeast mitchondrial ribosome. *Science 355*, 528−531.

(3) Amunts, A., Brown, A., Toots, J., Scheres, S. H. W., and Ramakrishnan, V. (2015) Structure of the human mitochondrial ribosome. *Science 348*, 95−98.

(4) Ramrath, D. J. F., Niemann, M., Leibundgut, M., Bieri, P., Prange, C., Horn, E. K., Leitner, A., Boehringer, D., Schneider, A., and Ban, N. (2018) Evolutionary shift toward protein-based architecture in trypanosomal mitochrondrial ribosomes. *Science 362*, 422.

DOI: 10.1021/acs.biochem.8b01191
Biochemistry XXXX, XXX, XXX−XXX