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Advances in Pharmacoepidemiology & Drug Safety

ISSN: 2167-1052

Commentary

A Nonamer is what the Protoribosome can do

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DESCRIPTION

The protoribosome was proposed by Ada Yonath's group shortly after the structure of the large ribosomal subunit was revealed [1]. It contains about 180 nt of rRNAs with a 2-fold rotational symmetry at the peptidyl center of the ribosome. This symmetry is defined by structural rather than sequence similarity. It is also the oldest component of the current ribosome, based on sequence comparative analysis and A-minor interaction mapping [2-4]. However, experimental evidence that demonstrates the ligase activity of a pure ribozyme is still lacking [5,6]. In Xu and Wang's recent publication, a nonamer lysine peptide was synthesized in the presence of only rRNA fragments [7]. The ribozyme consisted of 2-pieces: one piece contained helices H91-93, and the other contained H74-5, H80 and H89. Single molecule FRET (smFRET) experiments revealed that these two pieces can dimerize as well as bind to short aminoacyl tRNA fragments, which were prepared by Rnase T1 digestion of lysine-tRNAlys. The combination of these three components in the presence of 15 mM MgCl2 generated species whose masses were consistent with a nonamer-lysine attached to short tRNA fragments. Compared to previous experiments, two new features were implemented. One feature was the use of smaller RNA fragments to form the enzyme after self-folding, as the highly conserved peptidyl transfer center of approximately 180 nt may not fold properly if transcribed *in vitro* in one piece. The second feature was the application of sensitive methods such as smFRET and Maldi mass spectrometry. These new technologies are significantly more sensitive than conventional methods, such as radiation counting and Gel or TLC separations.

Demonstration of the protoribosome's enzyme activity is essential to studying the origin of the ribosome. It is surprising that the very primitive protoribosome is capable of synthesizing 9-mer oligos, which could mean that RNA and protein evolved simultaneously, rather than a pure "RNA world" evolving into the protein dominant environment of today [8]. Why were oligos longer than di-peptide not detected before? To my best knowledge, many experiments took the advantage of puromycin as tRNA analogs, which prevented continuous peptide formation [9-12]. In contrast, our experiments only utilized aminoacylated tRNA fragments, which do not terminate the peptidyl transfer reaction.

Further experiments are necessary to obtain more specific information. For example, because of the highly sensitive detections, the yield and efficiency of the identified ribozyme is unclear. Ribozyme optimization and peptide quantification are needed. In addition, only 9-mer oligos were detected. This could be due to the stability of the oligo, or the narrow mass range that was scanned. Nevertheless, because the reaction components were simple and the isotopic shifting results are robust, there is no doubt that nonamer-lysine was covalently generated. However, the actual atomic structure of the oligo is not yet clear: Is the oligo cyclic or linear? Could both amino groups be involved in bonding? Are rRNA aggregates greater than dimers possible? Although smFRET demonstrated close distance between the monomers, it does not rule out the formation of higher orders of aggregates. These are the questions currently under investigation in our lab.

REFERENCES

1. Agmon I, Auerbach T, Baram D, Bartels H, Bashan A, Berisio R, et al. On peptide bond formation, translocation, nascent protein progression and the regulatory properties of ribosomes. Derived on 20 October 2002 at the 28th FEBS Meeting in Istanbul. Eur J Biochem. 2003;270: 2543-2556.
2. Bokov K, Steinberg SV. A hierarchical model for evolution of 23S ribosomal RNA. Nature. 2009;457: 977-9780.
3. Fox GE. Origin and evolution of the ribosome. Cold Spring Harb Perspect Biol. 2010;2: a003483.
4. Mears JA, Cannone JJ, Stagg SM, Gutell RR, Agrawal RK, Harvey SC. Modeling a minimal ribosome based on comparative sequence analysis. J Mol Biol. 2002;321: 215-34.
5. Noller HF, Hoffarth V, Zimniak L. Unusual resistance of peptidyl transferase to protein extraction procedures. Science. 1992;256: 1416-1419.
6. Noller HF, Kop J, Wheaton V, Brosius J, Gutell RR, Kopylov AM, et al. Secondary structure model for 23S ribosomal RNA. Nucleic Acids Res. 1981;9: 6167-6189.
7. Xu D, Wang Y. Protein-free ribosomal RNA scaffolds can assemble poly-lysine oligos from charged tRNA fragments. Biochem Biophys Res Commun. 2021;544: 81-85.

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Received: May 26, 2021; **Accepted**: June 11, 2021; **Published**: June 18, 2021

Citation: Wang Y (2021) A Nonamer is what the Protoribosome can do. Adv Pharmacoepidemiol Drug Saf.10:235.

8. Gilbert W. Origin of life: The RNA world. Nature. 1986; 319-618.
9. Anderson RM, Kwon M, Strobel SA. Toward ribosomal RNA catalytic activity in the absence of protein. J Mol Evol. 2007;64: 472-483.
10. Zhang B, Cech TR. Peptide bond formation by in vitro selected ribozymes. Nature. 1997;390: 96-100.
11. Khaitovich P, Tenson T, Mankin AS, Green R. Peptidyl transferase activity catalyzed by protein-free 23S ribosomal RNA remains elusive. RNA. 1999;5: 605-608.
12. Nitta I, Ueda T, Watanabe K. Possible involvement of Escherichia coli 23S ribosomal RNA in peptide bond formation. RNA. 1998;4: 257-67.