Enzymatic activity of ribosomal RNA

The discovery that the RNA molecule, the cellular intermediate in protein biosynthesis, under certain conditions and in certain species can catalyse its own cleavage reaction is undoubtedly one of the turning points in biochemistry. The overthrow of the dogma that enzymatic activity is an exclusive prerogative of proteins has stimulated a worldwide search for similar activity in diverse systems. Indeed, the rapidity with which the importance of the discovery of ribozymes was recognized by the Nobel Committee, which awarded the 1989 Chemistry prize to T. Cech and S. Altmann only a few years after publication of their results[1,2], is remarkable. However, the most abundant RNA in a cell is ribosomal RNA, which is not an intermediate in protein synthesis and is structurally stable. It is now known that ribosomal RNA exists, at least in some parts, as a double stranded RNA molecule with Watson–Crick type of base complementarity, bearing a similarity to an *A* DNA conformation. Although it has generally been felt that catalytic RNA may have wider implications in the functioning of ribosomal RNA, firm experimental support has not been available. The reasons for this are manifold. Firstly, the abundance and stability of ribosomal RNA make it a poor candidate to act as an enzyme. Secondly, a purely structural role has been ascribed to ribosomal RNA which apparently acts as a scaffold to assemble fifty odd ribosomal proteins over it and generate ribosome particles, the factory for protein synthesis or translation. In fact, various steps like aminoacylation, peptidyl transferase action, translocation, etc. the minimum activities necessary to synthesize peptide bonds over the ribosomal surface have already been assigned to specific positions on the ribosome particle. The group of ribosomal proteins available at such locations has also been identified and is thought to be associated with these activities.

In the June 5th issue of *Science*, H. F. Noller and his group from the University of California, Santa Cruz report a remarkable finding[3]. They demonstrate that the peptidyl transferase activity of ribosomes is resistant to protein extraction from the ribosome in the thermophilic organism *Thermus aquaticus*. Careful experiments which remove all the proteins from the ribosome particle, yet do not disturb the secondary conformation of ribosomal RNA do not destroy peptidyl transferase activity, clearly indicating that ribosomal RNA is the main catalytic site for peptide bond formation during protein biosynthesis. This observation, according to many, is one of the most fascinating findings in molecular biology in recent times and will lead to the understanding of various aspects of RNA catalysis in the near future. Interestingly, their paper is modestly (and cautiously) entitled "Unusual resistance of peptidyl transferase to protein extraction procedures". The authors mention that any such experiments with *Escherichia coli*, the most popular prokaryotes for molecular biology researchers, have failed so far and this, they suggest, is probably due to the loss of *E. coli* RNA secondary structure during protein extraction.

To keep the record straight, I would like to emphasize that a group of Indian researchers (D. P. Burma and his group at Banaras Hindu University) had predicted much earlier that the biological activities performed by the *E. coli* ribosome can indeed be expressed by the complex of ribosomal RNA, provided if only three proteins out of about 50 ribosomal proteins are added to the RNA complex. This work has duly been acknowledged by Noller *et al.* in their *Science* paper. Burma and his group showed first that ribosomal RNA fragments form a stoichiometric complex[4] like the *E. coli* ribosome and later demonstrated that ribosomal activities can be mimicked by this complex provided a few proteins are added[5]. Unfortunately, the function of the added proteins, may have been only to restore the ribosomal RNA structure to a functionally active form. However, the fact that Burma *et al.* performed the experiment in *E. coli* is of special significance.

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4. Burma, D. P., Nag, B. and Tewari, D. S., *Proc. Natl. Acad. Sci. USA*, 1983, **80**, 4875–4878.
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