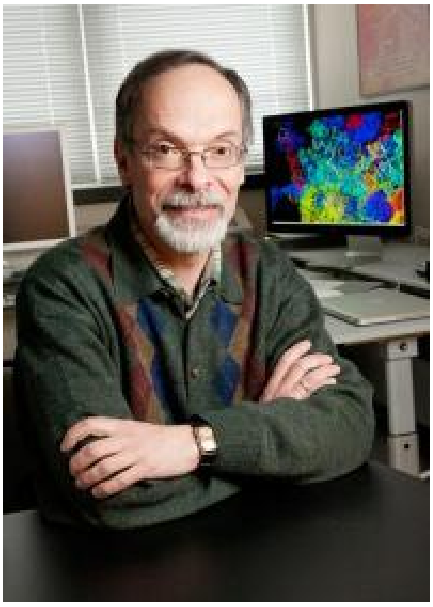
Study of ribosome evolution challenges 'RNA World' hypothesis

12 March 2012



In a new study that challenges the "RNA World" hypothesis, researchers constructed an evolutionary history of the RNA (left) and protein (right, shown with the ribosomal RNA) components of the ribosome. Older components are shown in red; more recent ones are blue. The two timelines "showed great congruence" and suggest that ribosomal proteins co-evolved with ribosomal RNAs. Credit: Derek and Gustavo Caetano-Anollés

In the beginning - of the ribosome, the cell's protein-building workbench - there were ribonucleic acids, the molecules we call RNA that today perform a host of vital functions in cells. And according to a new analysis, even before the ribosome's many working parts were recruited for protein synthesis, proteins also were on the scene and interacting with RNA. This finding challenges a long-held hypothesis about the early evolution of life.

The study appears in the journal *PLoS ONE*.

The "RNA world" hypothesis, first promoted in 1986 in a paper in the journal *Nature* and defended and elaborated on for more than 25 years, posits that the first stages of molecular evolution involved RNA and not proteins, and that proteins (and DNA) emerged later, said University of Illinois crop sciences and Institute for Genomic Biology professor Gustavo Caetano-Anollés, who led the new study.

"I'm convinced that the RNA world (hypothesis) is not correct," Caetano-Anollés said. "That world of nucleic acids could not have existed if not tethered to proteins."

The ribosome is a "ribonucleoprotein machine," a complex that can have as many as 80 proteins interacting with multiple RNA molecules, so it makes sense that this assemblage is the result of a long and complicated process of gradual co-evolution, Caetano-Anollés said. Furthermore, "you can't get RNA to perform the molecular function of protein synthesis that is necessary for the cell by itself."

Proponents of the RNA world hypothesis make basic assumptions about the evolutionary origins of the ribosome without proper scientific support, Caetano-Anollés said. The most fundamental of these assumptions is that the part of the ribosome that is responsible for protein synthesis, the peptidyl transferase center (PTC) active site, is the most ancient.

In the new analysis, Caetano-Anollés and graduate student Ajith Harish (now a post-doctoral researcher at Lund University in Sweden) subjected the universal protein and RNA components of the ribosome to rigorous molecular analyses - mining them for evolutionary information embedded in their structures. (They also analyzed the thermodynamic properties of the ribosomal RNAs.) They used this information to generate timelines of the evolutionary history of the ribosomal RNAs and proteins.

These two, independently generated "family trees" of ribosomal proteins and ribosomal RNAs showed "great congruence" with one another, Caetano-Anollés said. Proteins surrounding the PTC, for example, were as old as the ribosomal RNAs that form that site. In fact, the PTC appeared in evolution just after the two primary subunits that make up the ribosome came together, with RNA bridges forming between them to stabilize the association.

The timelines suggest that the PTC appeared well after other regions of the protein-RNA complex, Caetano-Anollés said. This strongly suggests, first, that proteins were around before ribosomal RNAs were recruited to help build them, and second, that the ribosomal RNAs were engaged in some other task before they picked up the role of aiding in protein synthesis, he said.

"This is the crucial piece of the puzzle," Caetano-Anollés said. "If the evolutionary build-up of ribosomal proteins and RNA and the interactions between them occurred gradually, step-by-step, the origin of the ribosome cannot be the product of an RNA world. Instead, it must be the product of a ribonucleoprotein world, an ancient world that resembles our own. It appears the basic building blocks of the machinery of the cell have always been the same from the beginning of life to the present: evolving and interacting proteins and RNA molecules."

"This is a very engaging and provocative article by one of the most innovative and productive researchers in the field of protein evolution," said University of California at San Diego research professor Russell Doolittle, who was not involved in the study. Doolittle remains puzzled, however, by "the notion that some early proteins were made before the evolution of the ribosome as a protein-manufacturing system." He wondered how - if proteins were more ancient than the ribosomal machinery that today produces most of them - "the amino acid sequences of those early proteins were 'remembered' and incorporated into the new system."

Caetano-Anollés agreed that this is "a central, foundational question" that must be answered.

"It requires understanding the boundaries of emergent biological functions during the very early stages of protein evolution," he said. However, he said, "the proteins that catalyze non-ribosomal protein synthesis - a complex and apparently universal assembly-line process of the cell that does not involve RNA molecules and can still retain high levels of specificity - are more ancient than ribosomal proteins. It is therefore likely that the ribosomes were not the first biological machines to synthesize proteins."

Caetano-Anollés also noted that the specificity of the ribosomal system "depends on the supply of amino acids appropriately tagged with RNA for faithful translation of the genetic code. This tagging is solely based on proteins, not RNAs," he said. This suggests, he said, that the RNA molecules began as co-factors that aided in protein synthesis and fine-tuned it, resulting in the elaborate machinery of the ribosome that exists today.

Provided by University of Illinois at Urbana-Champaign