PATTERNS OF COAXIAL HELICAL STACKING IN RIBOSOMAL RNA SUPPORT A MODEL OF MOLECULAR GROWTH THAT IS INCOMPATIBLE WITH AN ORIGIN OF THE RIBOSOME IN THE PEPTIDYL TRANSFERASE CENTER D. Caetano-Anollés1,2 and G. Caetano-Anollés1,1 Department of Cell and Developmental Biology, and 2Evolutionary Bioinformatics Laboratory, Department of Crop Sciences, University of Illinois, Urbana, IL 61801, USA.

Background: The structure of complex macromolecules must originate from simpler primordial substructures that gradually ‘transform’ into modern counterparts [1,2]. Phylogenetic reconstruction of the history of ribosomal proteins and RNA suggests that the ribosome unfolded by gradual accretion from structures supporting RNA decoding and ribosomal mechanics [3-6]. However, a recent study that compared atomic structural models of bacterial and eukaryotic ribosomes revealed that new eukaryote-specific segments inserted into old common core regions of the large subunit (LSU) of rRNA without significantly perturbing local helical conformations [6]. Assuming that the ancient ribosomal core evolved via similar mechanisms, a series of putative insertions of ‘branch’ helices onto preexisting coaxially stacked ‘trunk’ helices were proposed, which appeared to originate in the peptidyl transferase center (PTC) [7]. Here we analyze coaxial helical stacking patterns and insertion data and find that the claim that the ribosome originated in structures supporting protein biosynthesis is unwarranted. Instead, the analysis reveals possible primordial episodes of substructural grafting of core rRNA segments that confirm the previously proposed importance of decoding and ribosomal mechanics [3-6].

Results: Analysis of coaxial helical stacking present in LSU rRNA was guided by careful annotations of coaxial helical stacking regions that are present in ribosomal junctions [8-10]. Analysis of a ‘family A’ 3-way junction connecting a long helical coaxial branch that supports the PTC to a trunk (H76-H79) subtending the L1 stalk and its translocation functions reveals a branch-to-trunk insertion assignment that is in conflict with the PTC-centered accretion model. Instead, the insertion supports the ancestral origin of the crucial L1 translocation structure (Fig. 1). Similarly, insertions linkings terminal coaxial trunks that subtend the L7-12 stalk (H41-H45) and structures of the central ribosomal protuberance (H37-H38) to a 7-way junction of the molecule again question the early origin of the PTC. These trunks are particularly important to both ribosomal translocation and energetics. The comprehensive analysis of all coaxial stacked helices reveal that ribosomal accretion does not always occur via apical growth of terminal helices. Instead, basipetal growth appears also common. The data suggests a frustrated interplay of acropetal-basipetal dynamics that, in the absence of phylogenetic information, compromises the construction of an unequivocal insertion-based model of macromolecular accretion. Instead, coaxial helical stacking patterns suggest scenarios of grafting of extensive rRNA segments or accretion from a primordial core composed of multiple growing rRNA molecules.

Conclusions: Coaxial helical stacking patterns fail to support models of apical growth of a branching and expanding core ribosomal structure. Instead, patterns support both acropetal and basipetal ribosomal growth, which are compatible with an origin of the complex in ribosomal mechanics. Results prompt careful integration of phylogenetic and structure-based models to address ribosomal growth and evolutionary constraints acting on ribosomal structure.


Fig. 1. Radial views of three coaxial helical stacks that subtend translocation functions in LSU rRNA. Putative primordial insertions of branches (colored tan) did not significantly perturb trunk conformations (red). However, their branch-to-trunk directionality crucially falsify the claim that the ribosome originated in the PTC. Similar patterns of coaxial helical stacking exist in centrally located segments of the LSU rRNA structure that are buried deep inside the molecule and are in conflict with models of apical and layered growth [7].