An ancient nuclease cuts a path through "Life's Dark Ages"

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Introduction: Evolutionary models based on structural comparison of ribosomes have extended the reach of top-down approaches beyond LUCA, to "Life's Dark Ages"[1-4]. The approaches used to develop these models of early ribosome evolution can also be used to investigate the deep evolutionary history of non-ribosomal RNAs, some of which also preceded LUCA. These ancient non-ribosomal RNAs include transfer RNA, the signal recognition particle RNA, and Ribonuclease P (RNase P) RNA. Among these RNAs, RNase P represents the only ribozyme. Arguably, it is the only extant enzyme, besides the ribosome, with direct lineage extending back to a time prior to translation. The RNase P lineage may even extend farther back in time than the peptidyl-transferase center of the ribosome.

RNase P evolution through accretion, deletion, and substitution: We have developed a model of RNase P evolution that examines its evolutionary history from the Dark Ages of pre-LUCA life to the light of modern biology. This model of RNase P evolution combines extensive phylogenetic and structural analyses of the ribosome and RNase P. We will describe this model and highlight similarities and differences in the evolution of these two ancient ribozymes.

Accretion events are a feature common to the ribosome and RNase P. Like the ribosome, RNase P retains evidence of insertion events that expanded the structure and introduced new structural elements while preserving pre-existing functional structures. Based on insertion fingerprints we can identify specific expansion elements that were inserted into ancestral forms (Figure 1). The relative timing of these events can be established in part based on tertiary interactions within the RNA structure, with A-minor interactions playing an important role in determining the chronology of insertion events.

Deletion and substitution are a distinguishing feature of RNase P evolution. Unlike the ribosome, deletion of large structural elements plays a substantial role in the evolution of RNase P. In multiple instances proteins in complex with the remaining RNA have taken the place of RNA structures that were lost during RNase P evolution. Additionally, in some eukaryotic lineages, the entire RNase P RNA and its associated proteins have been replaced by unrelated protein nucleases.

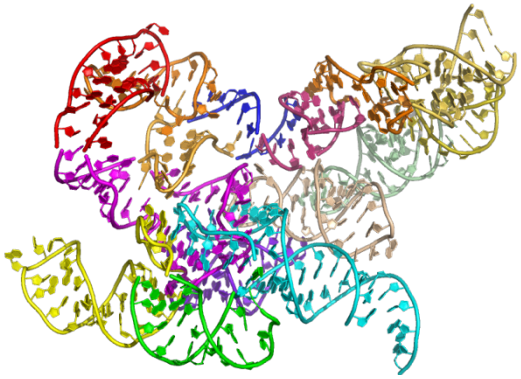

Figure 1. Ancestral expansion sequences predicted by our model are shown mapped on to a structure of RNase P. Each expansion sequences is represented by a different color with the oldest expansion sequences shown in the lower half and left hand side of the image in cyan, green, yellow, and magenta.

Experimental constructs provide a functional test for our evolutionary model. In our model, the catalytic domain of RNase P evolved prior to the addition of the specificity domain. It has been shown that the isolated catalytic domain, which roughly approximates an ancestral form predicted by this model, is catalytically active. We are testing our model by generating experimental constructs that represent stages of RNase P evolution as predicted by the model. Functional assays provide a means of experimentally testing the model and provide an opportunity to resolve ambiguities in the model that cannot be resolved based on structural and phylogenetic analyses alone.

References:

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