The Plausibility of an Iron-Sulfur Linked pre-RNA

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The structure and origin of the first genetic material remains a longstanding problem for origin of life research. Several RNA precursors (i.e. pre-RNAs) have been proposed [1]; however, the polymerization of their monomers, much like RNA, has yet to be demonstrated under plausible prebiotic conditions. Given the relative ease with which metallic bonds form, break, and reform, a pre-RNA composed of metal-linked monomers may be plausible. Iron is arguably the most relevant metal for the origin of life: Earth's earliest oceans were iron-rich and the redox activity of iron-sulfur minerals and clusters has led many to speculate that they may have been one of the first catalyts utilized by life [2-4]. However, surprisingly little work has been done investigating whether iron and sulfur may have been incorporated into primitive genetic material. In this study, we evaluated the plausbility of a novel pre-RNA composed of thionucleosides linked by iron-sulfur clusters.

First, using UV-Vis, electron paramagnetic resonance, and Mössbauer spectroscopy we found that 1-thioglucose readily forms [2Fe-2S] clusters within 30 minutes of being incubated with 0.2 mM sodium sulfide and 0.5 mM ferric(III)chloride at room temperature; within 4 hours [4Fe-4S] clusters also form. We then investigated mechanisms for the prebiotic synthesis of thiosugars via formose reactions and Miller-Urey spark discharge experiments conducted in sulfide-rich solutions: for example, analysis of the formose mixture by high-resolution mass spectrometry shows that polythiols readily form. Together, these results suggest that thiosugar containing Fe-S clusters may have formed alongside oxic sugars on early Earth. The reactivity of such Fe-S clusters could then have facilitated the formation of Fe-S clusters with thionucleoside ligands.

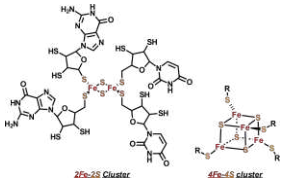

Figure 1. Proposed structure of an Fe-S linked pre-RNA.

[1] Robertson and Joyce (2012) *Cold Spring Harb Perspect Biol* 4:a003608. [2] Walker and Brimblecombe (1985) *Precambrian Res.* **28**, 205-222. [3] Wächtershäuser (1990) *Orig. Life Evol. Biosph.* **20**, 173-176. [4] Scintilla *et al.* (2016) *Chem. Commun.* **52**, 13456-13459.