The Potential Emergence of "Homogeneous" RNA from "Heterogeneous-Backbone" Pre-RNA Scaffolds.

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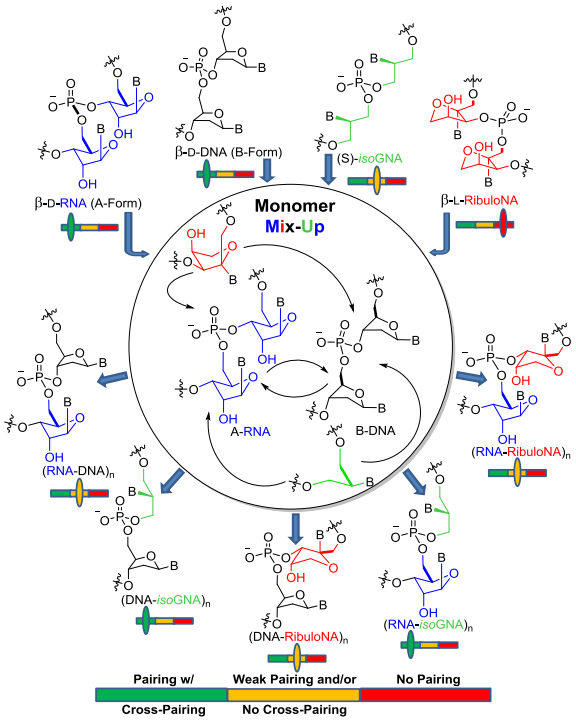
Introduction: The synthesis of extant ribonucleosides and their homogeneous polymeric forms (RNA) under prebiotic conditions, still remains enigmatic. Given the likelihood of the "prebiotic clutter", we herein present a model which introduces the possibility that RNA emerged from polymers which were heterogeneous in both their nucleobase and sugar composition.



Results from the Formose reaction[1] and the 'Glyoxylate Scenario',[2] both suggest that pentulose sugars could have existed in greater quantities than pentose sugars on prebiotic Earth. With a focus on the sugar moiety, we have synthesized and characterized alternative nucleoside analogs based on the pentulofuranose sugar, *β*-L-ribulose, and its acyclic analog known as *iso*GNA.[3] Although preliminary investigations determined that homogeneous polymers consisting of these alternative nucleic acids demonstrate limited to no Watson-Crick pairing,[3, 4] synthetic chimeric oligonucleotides designed with *ribulo*NA- or *iso*GNA-based nucleosides strategically positioned within RNA oligomers exhibit unique base-pairing properties and structural conformations. Our results illustrate the importance of the backbone's influence on base pairing, and lend credence to the possibility that a homogeneous-backbone informational system such as RNA, could have emerged from pre-RNA polymers with heterogeneous backbones.[5, 6]

References: [1] Butlerow, A. (1861) *C. R. Acad. Sci.*, *53*, 145-147. [2] Sagi, V. N., Punna, V., Hu, F., Meher, G., Krishnamurthy, R. (2012) *J. Am. Chem. Soc.*, *134*, 3577-3589. [3] Karri, P., Punna, V., Keunsoo, K., Krishnamurthy, R. (2013) *Angew. Chem. In. Ed.*, *52*, 5840-5844. [4] Stoop, M., Meher, G., Karri, P., Krishnamurthy, R. (2013) *Chem. Eur. J.*, *19*, 15336-15345. [5] Krishnamurthy, R. (2015) *Israel J. Chem.*, *55*, 837-850. [6] Gavette, J. V., Stoop, M., Hud, N., Krishnamurthy, R. (2016) *Angew. Chem. In. Ed.*, *55*, 13204-13209.

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