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Parallel prebiotic origin of canonical and non-canonical purine nucleosides

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Introduction: Due to its catalytic activity and information storage properties, RNA is believed to have been the key molecule during chemical evolution.[1] Next to the canonical bases, RNA contains more then 120 known modifications, which are critical for regulating diverse biological processes.[2] Without modified nucleosides life as we know it would not be possible. It is an open question of how the essential non-canonical bases evolved that are found today in all three kingdoms of life. It might be possible that some of the most central modifications could have been formed on an early Earth, while others especially the more complex modified nucleosides, might have been the result of biological evolution. Therefore we investigated if there is a chemical pathway that would allow a parallel prebiotic origin of canonical and non-canonical purine nucleosides.

Based on the chemistry reported here, we can conclude that some of the ubiquitously abundant modified RNA purine nucleosides can readily form under conditions compatible with early Earth geochemical models. Their synthesis is possible in parallel to the canonical purine bases by a unified reaction pathway via formamidopyrimidines (FaPys).[3] This shows that these non-canonical nucleosides had a chance to appear together with the canonical ones on the early Earth. Consequently, they would have been part of the prebiotic nucleoside pool and therefore participated in the chemical evolution process that presumable established an RNA world. These non-canonical bases might have been necessary for correct folding of catalytic RNA or facilitating RNA/RNA interactions, giving modified RNA a superior functionality. We assume that the modifications available through our FaPy pathway took over crucial functions and were therefore conserved until today, making them fossils of an early Earth.

References:

[1] L. Orgel (2004) *Critical Reviews in Biochemistry and Molecular Biology* 39:99–123.[2] T. Carell et al. (2012) *Angewandte Chemie International Edition* 51:7110-7131 [3] S. Becker et al. (2016) *Science* 352:833-836.

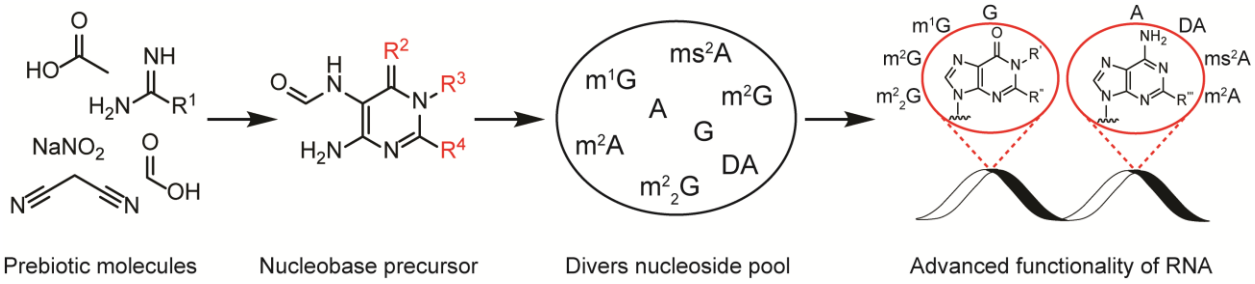

Figure 1 – Scheme of the prebiotic origin of canonical and non-canonical nucleosides. Simple prebiotic molecules can assemble into Formamidopyrimidines (FaPy) as nucleobase precursors. Reaction of the FaPy compounds with ribose provides a divers set of purine nucleosides. From the pool of RNA building blocks, the first RNA polymer must have been assembled. These modified bases might have improved RNAs functionality, leading to a superior RNA molecule that was able to undergo Darwinian evolution.