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Prebiotic Synthesis: Selection Overcoming Clutter

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Introduction: Living organisms are highly complex chemical systems that exploit a small constellation of universally conserved metabolites. The chemical unity of these metabolites provides compelling evidence that a simple set of predisposed reactions predicated the appearance of life on Earth.[1-5]

Prebiotic Selection from Complex Mixtures: Non-enzymatic syntheses of both nucleic acids and amino acids are essential to elucidating the origins of life, however overcoming the "*clutter wrought by prebiotic chemistry*"[1] to select the specific palette of metabolites exploited by life is widely cited as the chief obstacle to understanding the origins of life. Now, through the application of a systems chemical analysis of canonical nucleotide and proteinogenic amino acid syntheses, we have discovered that 2-aminothiazole–a hybrid product of prebiotic nucleotide and amino acid syntheses–delivers unprecedented efficiency and selectivity in directing prebiotic synthesis of the canonical metabolites essential for life from complex mixtures.[2] Our results emphasize the importance of holistic systems analysis.

Divergent Purine and Pyrimidine Nucleotide Synthesis: Although remarkable progress has been made toward understanding prebiotic nucleotide synthesis, to date all syntheses account separately for the pyrimidine and purine ribonucleotides.[3] Here, we present a novel divergent synthesis of pyrimidine and purine nucleotides from a common prebiotic precursor.[4] The generational and constitutional relationship between pyrimidine and 8-oxo-purine nucleotides suggests that 8-oxo-purine ribonucleotides may have played a significant role in early evolution.[4]

Triose Glycolysis and Nature's Highest-Engery Phosphate: Triose glycolysis is one of the most-central and highly conserved pathways in metabolism. We present a novel α-phosphorylation controlled reaction network that gives access to glyceric acid 2-phosphate, glyceric acid 3-phosphate, phosphoenol pyruvate, pyruvate, and phosphoserine.[5] The results presented demonstrate that mild, prebiotically plausible conditions can efficiently furnish all of the key components of a core metabolic pathway that is central to energy transduction, as well as amino acid, sugar, nucleotide, and lipid biosyntheses.[5]

References: [1] Joyce G. F. (2002) *Nature* **418**, 214–221. [2] Islam, S. et al. (2017) *Nat. Chem.* DOI: 10.1038/nchem.2703. [3] Islam, S. and Powner, M.W. (2017) *Chem* DOI 10.1016/j.chempr.2017.03.001. [4] Stairs, S. et al. (2017) *Nat. Commun.* accepted. [5] Coggins, A.J. and Powner, M.W. (2017) *Nat. Chem.* **9**, 310–317.