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Which Came First, Proteins or Cofactors? Recreating Metabolic Reactions of the Early Earth

T. R. Maltais[1], D. VanderVelde[2], D. LaRowe[3], A. D. Goldman[4] and L. M. Barge[1,5]

[1]NASA Jet Propulsion Laboratory, California Institute of Technology, 4800 Oak Grove Drive, Pasadena CA 91109 , [2]Department of Chemistry, California Institute of Technology, 1200 E. California Blvd, Pasadena, CA, 91125, USA , [3]Department of Earth Sciences, University of Southern California, 3651 Trousdale Pkwy, Los Angeles, CA 90089, [4]Department of Biology, Oberlin College, Science Center K123, 119 Woodland St. Oberlin, OH, 44074, [5]NASA Astrobiology Institute Icy Worlds Team.
* laura.m.barge@jpl.nasa.gov

Very little is known about the emergence of metabolic pathways in the early Earth environment. Two prominent theories propose that the first catalytic protein cofactors may have acted as pre-protein catalysts prior to the evolution of protein synthesis, or that metabolic pathways arose from nonprotein catalysts producing chains of reactions with lower rate enhancements than modern proteins [1,2]. However, these theories have not been systematically tested. Examining enzymatic reactions that are considered to be ancient, and determining if the protein cofactor alone can promote proto-enzymatic reactions in an early Earth environment is paramount to testing these hypotheses. We chose Coenzyeme A (CoA), the cofactor central to synthesizing citrate with the enzyme citrate synthase in the citric acid cycle, as a target for beginning such examinations of cofactor activity without its protein enzyme (Figure 1). By monitoring with NMR spectroscopy, we tested whether citrate synthesis from oxaloacetate and acetate, or the acetyl group from acetyl-CoA, could occur in aqueous solutions at pH values relevant to Earth's early oceans and/or hydrothermal fluids (~5-10). We also tested the effect of the presence of dissolved carbon dioxide as bicarbonate, which could act as a carbon source as well as a base to drive reactions under prebiotic ocean conditions. The stability of citrate would also be a factor in prebiotic environments, since it can decay into a variety of products depending on the chemical/geochemical conditions [3]. These results will test the hypothesis that cofactors can promote parts of core metabolic pathways, and could have implications in the search for life on other worlds by offering predictive potential about which environments could have supported such reactions.

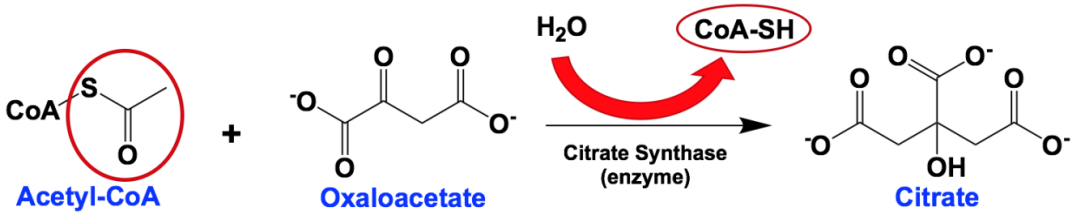

Figure 1: The citrate synthase reaction driven by a protein enzyme and ACoA.

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