De novo synthesis and functional study of primitive polypeptides in the prebiotic Protein World

Kosuke Fujishima 1,2, Kendrick Wang 3, Raphael Ferreira3, 4, and Lynn Rothschild 1

1 NASA Ames Research Center
2 University Affiliated Research Center (UARC), University of Santa Cruz
3 Stanford University
4 Synthetic & Systems Biology, Sorbonne Paris – Diderot University, ParisTechParis University - Diderot

DNA, RNA and proteins within a lipid-bound membrane are the core components of life, but the order of their appearance during the origin of life is still under debate. The widely accepted "RNA World" hypothesis states that RNA likely emerged prior to proteins and DNA since RNA can serve both replicative and catalytic roles. While biochemists have reproduced the synthesis, polymerization, and replication of nucleotides and RNA under controlled prebiotic conditions, it is clear that such complex organic molecules were are not present in significant amounts in the the starting prebiotic material on Earth either from endogenous production or meteoritic input. In contrast, amino acids are naturally abundant in various prebiotic contexts such as carbonaceous chondrites and Urey-Miller type experiments, and many studies have demonstrated that under plausible prebiotic conditions amino acids could condense or polymerize to give rise to short peptides. These findings support the basis of a "Protein World" hypothesis for life, however little has been done to study the functions of such primitive peptides. Here we present our novel synthetic biology-based approach to the *de novo* synthesis of billions of primitive peptides/proteins derived from a limited set of naturally abundant proteinogenic amino acids such as glycine, alanine, aspartic acid, glutamic acid, valine and serine. Of these peptides, the ones with divalent metal-binding capability are of particular interest and will be screened and identified. Certain divalent metals were likely present in prebiotic environments. Not only do they coordinate well with amino acids, but they also catalyze reactions, which are difficult to achieve in organic chemistry. Since D-chiral and non-proteinogenic amino acids are also abundant in the universe and may provide insight into the pathway by which life developed, we will also discuss methods to analyze primitive peptides consisting of these amino acids and D-chiral and non-proteinogenic amino acids. By understanding this naturalistic pathway, we will be able to better understand how life developed here on Earth. Since these amino acids are abundant in universe, this work provide insight into pathways by which life developed on Earth and, by extension, the probability of life arising elsewhere.