Dynamic Polymerization of Prebiotic Depsipeptides Allows Selection of Stable Structures

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A long-standing challenge of origins of life research is to find a plausible prebiotic route for the formation of peptides. Although the synthesis of various amino acids by prebiotic reactions is now generally accepted, their subsequent oligomerization into peptides is more difficult to explain. Recently, a simplified route for prebiotic peptide formation has been reported, which involves subjecting a mixture of hydroxy acids and amino acids, both of which were likely present on the prebiotic Earth, to repetitive wet-cool/dry-hot cycles [1,2]. It has been proposed that the resulting depsipeptides, containing both ester and amide linkages, might have constituted part of the primordial proto-peptides population.

We hypothesize that depsipeptides possess characteristics that would have facilitated their selection by chemical evolution, namely a propensity for self-assembly, a chemical stability sufficient for functionality, as well as a susceptability to hydrolysis that allows regular recycling and exploration of sequence space. To demonstrate these properties, we have synthesized an OH-capped peptide library, ranging from dimers to octamers, which contain an N-terminal glycolic acid (the hydroxy acid analog of glycine) that, upon polymerization via ester bond formation, would produce depsipeptides with regularly spaced ester and amide linkages.

We have found that applying dry-hot conditions drives oligomerization of these OH-capped peptides. Analysis of depsipeptide length, monomer composition, and assemblies reveals a structural shift that coincides with polymer growth. We have also found that shorter OH-capped peptides polymerize more readily than the longer OH-capped peptides. We will discuss investigations of depsipeptide stability and self-assembly propensity by a variety of spectroscopy- and microscopy-based methods, such as circular dichroism and electron microscopy. Additionally, we were able to find pronounced differences in the chemical stability of certain OH-capped peptides over others, and we have used these differences as a basis to show selection of certain OH-capped peptides in complex depsipeptide mixtures.