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Self-Assembly of Plausible Proto-Peptides

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A primary 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 under prebiotic conditions is now generally accepted, their subsequent oligomerization into peptides is more difficult to explain. Recently, a simplified route to the formation of peptides 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 have chemically synthesized short depsipeptides and are now testing if these oligomers possess the characteristics that would have allowed them to be selected by chemical evolution based on self-assembly propensity, stability and functionality. Specifically, we have synthesized a simple depsipeptide library, ranging from dimers to octamers, which contain an *N*-terminal glycolic acid (the hydroxy acid analog of glycine) in order to promote polymerization via ester bond formation.

We have found that applying dry-hot conditions drives oligomerization and we were able to show a structural shift that coincides with polymer growth. We have also found that there is a negative correlation between peptide length and polymerization rate. 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.

References: [1] Forsythe JG, Yu SS, Mamajanov I, Grover MA, Krishnamurthy R, et al. (2015) *Angew Chem Int Ed Engl* 54: 9871-9875. [2] Yu SS, Krishnamurthy R, Fernandez FM, Hud NV, Schork FJ, et al. (2016) *Phys Chem Chem Phys* 18: 28441-28450.

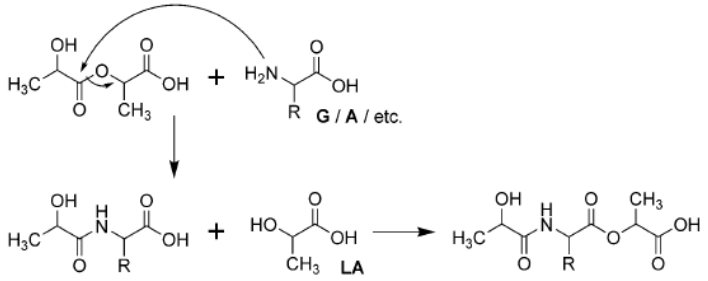

Figure 1 – Proposed reaction scheme for hydroxy acid–mediated peptide bond formation and depsipeptide elongation by ester-amide exchange [1] .