PR0049

Membraneless Polyester Microdroplets as a Window into the First (Proto)cells on Earth

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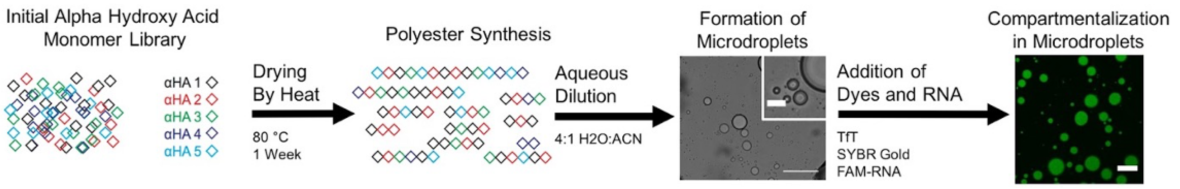
While it is often believed that the origins of life required participation of early biomolecules, "non-biomolecules" could have also played a part. In particular, recent research has highlighted the various ways by which polyesters, could have played a major role during the origins of life. Polyesters could have been synthesized readily on early Earth through simple dehydration reactions at mild temperatures involving abundant "non-biological" alpha hydroxy acid (AHA) monomers. This dehydration synthesis process results in a polyester gel, which upon further rehydration, can assemble into membraneless droplets proposed to be protocell models. These protocells can provide functions to a primitive chemical system such as analyte segregation, which could have further led to chemical evolution from prebiotic chemistry to nascent biochemistry (**Fig. 1**).

Figure 1. Synthesis and assembly of polyester protocells



Here, we first demonstrate polyester synthesis by dehydration of neutral AHA monomers at mild temperatures over one week, confirmed by MALDI-MS, and subsequent microdroplet assembly by rehydration. These microdroplets were able to differentially segregate various small molecule dyes, nucleic acids, and proteins, while also being able to interact with lipids, suggesting their compatibility with modern biologies. Next, we increased the chemical diversity of the initial AHA library by introducing basic monomers as a means to increase functional diversity, followed by incorporation into cationic polyesters *via* dehydration synthesis. These polyesters could also assemble into membraneless microdroplets which showed a greater propensity to segregate nucleic acids, while also acquiring autofluorescent character. Finally, we applied various spectroscopic and biophysical methods to further analyze emergent functions of polyester microdroplets, which can selectively partition salt cations, leading to differential microdroplet coalescence due to ionic screening effects reducing electrostatic repulsion forces between microdroplets. By understanding the assembly, structure, and function of membraneless polyester microdroplets, we hope to provide a window to the first proto(cells) on Earth.

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