July 16-21, 2017 at UC San Diego, CA, USA

Dynamic Chemical Assembly of Peptide Nucleic Acids

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Introduction: The origin of life was marked by the transformation of simple chemical building blocks into increasingly complex systems. A remarkable example of this was the conversion of prebiotic feedstock molecules into the first informational polymers. Important strides have been made in the laboratory to identify mechanisms by which prebiotic informational polymers could have arisen de novo. Even so, there remains a great need to experimentally demonstrate the non-enzymatic assembly of small building blocks into informational oligomers with functionally competent sequences capable of basic life activities, such as replication. We have developed dynamic peptide nucleic acids (PNA) that efficiently assemble via reversible covalent reactions from simple peptides and nucleobase units. These PNA can undergo dynamic sequence adaptation and template mismatch correction. We demonstrate that, because of their unique structures, the PNA can assemble from relatively simple building blocks via mechanisms that are not available to other PNA or oligonucleotides. In one instance, a tetrapeptide building block is shown to polymerize to give peptides up to >30 residues in length that serve as backbones for the dynamic PNA. Further, we describe the development of a PNA that can reversibly self assemble and undergo dynamic sequence selection, and then spontaneously lock into a given sequence to preserve the contained information content. Our findings highlight an intriguing aspect of dynamic informational oligomers with respect to prebiotic chemistry- the synthesis of their backbones is chemically decoupled from the attachment of nucleobases to the molecule. This greatly simplifies the process of generating lengthy oligomers with specific sequences because the backbone can polymerize in a first step, while the sequence can be selected (reversibly, with the capacity for mismatch repair) in a second step.