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Chenical Evolution Routes to Functional Peptide-Nucleic Acid Chimeras

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One major challenge for scientists keen to understand the origin of life has to do with the pre-LUCA (last universal common ancestor) transition from the chemistry of single molecular families (e.g., RNA, peptides or lipids) into today's DNA-RNA-proteins triad that drives replication and evolution in cells. According to the Central Dogma of biology, the information encoding all living matter is stored in DNA gene sequences and managed by proteins at every level.[1] This synergism is made possible by the ribosome, which translates RNA sequences into proteins. The stunning structural and functional mutualism between nucleic acids and proteins exhibited by the ribosome is a primary guiding inspiration to search for similar synergies within structurally much simpler nucleic-acid-peptide (NA-pep) or nucleobase-peptide chimeras.

In this presentation, we will describe our current effort towards the design, synthesis and structural and functional analysis of a new family of nucleic acid peptide conjugates. Particularly, we have been studied dynamic self-assembly in a prebiotically relevant system consisting of simple peptides amenable to form fibrils and two NA-pep chimeras. The DNA domain of the latter conjugates are complementary to each other, and the peptide domain sequence derived from a family of peptides containing repetitive Glu-Phe dyads previously studied by our group. Such peptides can readily assemble into fibrils effective as catalysts[2] and replicators[3], and even for charge transport.[4] Studies on the putative trajectory leading to self-assembly of peptide fibrils seeded with variable amounts of ssDNA-pep conjugates, or dsNA-pep conjugates, revealed a plethora of different supramolecular structures. Remarkably, we find that dsDNA-pep assemblies (Fig. 1) are more chemically and physically stable than their DNA or peptide alone counterparts, and furthermore that these assemblies are useful for encapsulating small molecules of relevance to prebiotic chemistry, as well as for therapeutically relevant delivery to cells.

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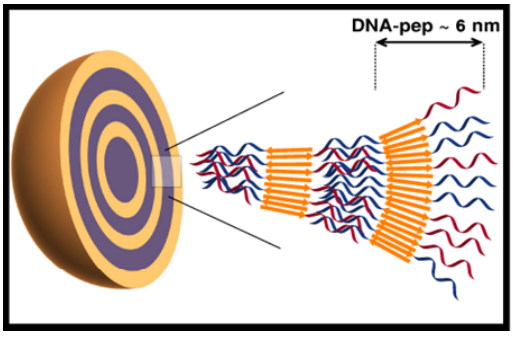

Figure 1 – Nanometric spheres formed via self-assembly of dsDNA-pep conjugates. The layered structure found useful to protect the DNA against thermal and chemical degaradation and for binding small molecules.