Enzyme Intructed Self Assembly of Guanosine Derivatives

The development of advanced supramolecular devices requires a precise control over their structure and dynamics. This responsive behavior can be achieved by modulating the interactions of amphiphilic systems with the surrounding water molecules where an increased hydrophobicity enhances the propensity for self-assembly. This modulation is achievable via physical (e.g., heat, light), chemical (e.g., acid/base reactions), or biochemical stimuli like enzymatic transformations. The latter strategy, also known as enzymatic instructed self-assembly (EISA), has successfully been applied systems ranging from amphiphilic peptides and carbohydrates, to synthetic polymers. To the best of our knowledge, however, there has been no reports of using EISA to promote the hierarchical self-assembly of supramolecular guanosine (G)-quadruplexes (SGQs). Our group has previously shown that SGQs could be triggered to form colloidal particles termed supramolecular hacky sacks (SHS) via thermal and/or chemical (i.e., pH) stimuli. In this project we will develop a new family of SGQs that respond to enzymatic transformations, specifically, via phosphorylation/dephosphorylation by protein tyrosine kinase/phosphatases. To accomplish this, we designed and synthesized G-derivatives containing the 4-hydroxyphenyl moiety characteristic of L-tyrosine, via addition of tyramine using a Suzuki coupling. We will evaluate the suitability of these derivatives for enzymatic phosphorylation by ABL protein tyrosine kinase and the subsequent in situ self-assembly into SGQs as determined by water suppression proton NMR. Subsequent addition of alkaline phosphatase will result in the formation of SHS particles that will be studied by dynamic light scattering and microscopy (i.e., SEM, CLSM). These results should open the door for the enzymatically triggered formation of SHS in cells, which in turn could lead to their use as artificial organelles as tools for biological studies and, in the longer term, as novel therapeutics.