Hybrid polypeptide-DNA nanomaterials for biomedicine

*Nicholas Stephanopoulos**

Biodesign Center for Molecular Design and Biomimetics
1001 S. McAllister Ave
Arizona State University
Tempe, Arizona, USA
nstepha1@asu.edu

One of the central goals of nanotechnology is to create functional materials for biology and medicine. Areas like drug delivery and tissue engineering require simultaneous control over morphology, size, surface chemistry, and biomolecule functionalization at the nanoscale. DNA is one particularly attractive building block for biomaterials due to the programmability afforded by Watson-Crick pairing. However, DNA nanomaterials are generally not bioactive, and require modification with proteins or peptides to imbue them with cell-signalling functions. We describe a novel category of hybrid peptide-DNA and protein-DNA materials that merge the structural programmability of oligonucleotides with the functional and chemical diversity of proteins. We will first describe DNA-modified hydrogels and biomaterial surfaces, where the DNA can serve as a reversible crosslinker or an addressable handle. The stiffness and ligand presentation of these materials can be tuned independently of one another, and in a reversible fashion, by using strand displacement reactions. We will also demonstrate spatiotemporal control of signals through photopatterning of the biomaterials with multiple DNA handles. In all these approaches, peptide-DNA and protein-DNA chemical hybrids—synthesized through site-specific bioconjugation reactions—will be used to impart specific bioactivity for applications in stem cell differentiation and cancer metastasis studies. We will next describe a hybrid protein-DNA nanoscale cage with potential applications in drug delivery or artificial vaccines. A homotrimeric protein building block modified with DNA was modified with DNA, and co-assembled with a triangular DNA to create a tetrahedral cage. The dimensions of the cage can be tuned through the size of the DNA, and we explored two different chemical approaches for building the protein-DNA conjugates. These hybrid nanostructures represent the first protein-DNA cages from chemically-conjugated constituents, and will find diverse applications in several areas of biomedicine. Taken together, our work shows the promise of peptide/protein-DNA hybrids for building functional materials for advanced applications in biology and medicine.