Programming Protein Patterns on DNA Nanostructures With Pyrrole-Imidazole Polyamides

Thesis by

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For my family

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Abstract

Molecular recognition of DNA has important applications for gene regulation, molecular biology, and DNA nanotechnology. Pyrrole-Imidazole polyamides are a unique class of molecules with the ability to bind to DNA in a programmable manner. These small molecule analogues of distamycin A can be programmed to target virtually any DNA sequence with high affinity and specificity. Originally characterized for their ability to bind to B-form DNA, polyamides are also able to target DNA in architectures such as the nucleosome core particle (NCP) and two-dimensional DNA nanostructures including DX-arrays and DNA origami. In addressing DNA nanostructures, polyamide-biotin conjugates can be used to create nanoscale molecular assemblies in a bottom-up approach to self-assembly. The ability to address unique sequences on a DNA nanostructure with different polyamides makes it possible to create unique arrangements of protein on a single 2-dimensional DNA template. Polyamides targeted to the NCP can be used for a variety of exciting applications including NCP-templated ligation reactions, gene regulation, and as tools for X-ray crystallography. The programmability of polyamides makes them an ideal tool for addressing a variety of DNA architectures for varying applications.

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