

To my Family

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Abstract

Polyamides are a class of synthetic small molecules that recognize DNA in a sequence-specific fashion through a network of hydrogen bonds formed with bonding partners in the floor of the minor groove. The binding affinity of polyamides is comparable to that of numerous DNA-binding proteins, and polyamides have been shown to displace DNA-binding proteins. As such, they present a powerful opportunity to modulate expression levels of genes vital to human health. The cellular permeability and biological activity of polyamides has presented an impediment in moving from *in vitro* to *in vivo* work that was partially removed by the discovery that fluorescein dyes facilitate cell entry. The work described here details recent advances in modifications to the C-terminal polyamide linker, linkage and tail groups that improve the endogenous inducible gene regulation activity of polyamides in cell culture.

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