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Massive changes to the biophysical properties of DNA upon binding antiviral polyamides

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N-methyl-pyrrole and imidazole-derived polyamides (PAs), acting as DNA minor groove binders, are higher homologs of natural products such as distamycin A. PAs show attractive biomedical properties and draw interest from many groups. A series of long hairpin polyamides was designed to target the high risk human papillomavirus types 16, 18 and 31, and shows antiviral activity in cell and tissue culture. With our designed PA library we found that large size (containing ≥14 rings, with a binding size ≥10 bp of DNA) was necessary for activity. Antiviral activities varied from highly active to complete inactive between the molecules with the same cognate DNA recognition properties. Antiviral activities also show little correlation to PA/DNA binding affinity. It has been since pursued the mechanism of action of antiviral polyamides, and polyamides in general with collaborators at NanoVir. It was mapped large regions of HPV16 and 18 genomes by DNase I and hydroxyl radical affinity cleavage with lead compounds (20% for HPV16 and 12% for HPV18). It was also investigated active PA-DNA-interactions via UV-Vis and Circular Dichroism. Active PAs show dramatically different thermodynamic and kinetic properties from commonly-used 6 to 8 ring PAs. Recently, for the purpose of biodistribution and metabolic stability studies, it was developed two independent synthetic routes for specific incorporation deuterium at one position. Stability studies of unlabeled compound were also carried out at several temperatures.

Biography

Gaofei He completed his PhD from Carnegie Mellon University and his postdoctoral studies at University of Missouri-St. Louis, where he has recently begun teaching as well as conducting research. He has published more than 13 papers in reputed journals.

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