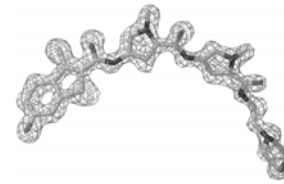


W0070

Structure of an Antimicrobial Compound in Complex with AT-rich DNA at 0.95 Å Resolution. Yuan Lin, Shanthi R. Paranawithana, Clara L. Kielkopf. Johns Hopkins Univ., Bloomberg School of Public Health, Baltimore, MD.

We present the ultra-high resolution structure of a representative ‘Small Molecule AnTi-microbial’ (SMAT) polyamide in complex with 5'-CCAITACTGG-3' at 0.95Å resolution (current R_{work} 16.5%, R_{free} 19.3%). For comparison, the unliganded DNA counterpart has been determined at 1.4Å resolution (current R_{work} 22.5%, R_{free} 27.2%). An unanticipated polyamide dimer is slipped towards one end of the AT-rich binding site. Tight packing of sulfur and fluorine atoms within the DNA minor groove provides a structural basis for the improved DNA affinity of SMATs compared with distamycin-A and related polyamides. The structure reveals unprecedented details of local disorder, hydration, hydrogen bonds, and polyamide stacking previously unavailable for a polyamide/DNA complex. The bromine multiwavelength anomalous dispersion experiment used to solve the SMAT/DNA structure provides excellent experimental electron density ($\langle m \rangle = 0.46$ to 1.1Å resolution). This freedom from the influence of any crystallographic model provides the first stringent test for theories of DNA disorder and solvation in general.



*Experimental Electron Density
at 1.1Å Resolution*

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