

STRUCTURE OF AN ANTIGEN-BINDING FRAGMENT BOUND TO STEM-LOOP DNA AND CRYSTALLIZATION OF RECOMBINANT HAEMOPHILUS INFLUENZAE e(P4) ACID PHOSPHATASE

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ABSTRACT

DNA-1 and 11F8 are anti-ss DNA antibodies derived from autoimmune lupus-prone mice. They are very similar to each other in terms of CDR sequence and preference for binding T-rich ssDNA. G1-17 is an oligonucleotide identified by *in vitro* selection experiments and binds with high affinity and specificity to Fab 11F8. G5-14 is a synthetic oligonucleotide with the ten-nucleotide sequence identical to the stem-loop portion above the bulge of G1-17. The 1.95 Å resolution DNA-1/G5-14 structure shows that the two DNA strands dimerize to form a double-stranded DNA dumbbell and have a large conformational change including the breaking and reformation of hydrogen bonds. The most striking feature of the Fab/DNA interactions is the use of extensive π - π stacking of the DNA bases and the protein side chains. These results provide insights into the specific recognition model of anti-DNA Abs and the potential challenges in structure based drug design to treat autoimmune diseases.

The second part of this thesis describes purification and crystallization of *Haemophilus influenzae* class C acid phosphatase P4, and acquisition of a 1.7 Å resolution native X-ray diffraction data set. The space group of the crystals is $P4_22_12$ with $a = 65.6$, $c = 101.4$ Å, one protein molecule per asymmetric unit and 37 % solvent content. This is the first report of crystallization of a class C acid phosphatase.