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The Interactions of Amino Acids and Peptides with DNA

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The Interactions of Amino Acids and Peptides with DNA

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DNA cleavage agents have received considerable attention for multiple purposes, such as the strategy for site-selective inhibition of gene expression. Small molecules with DNA cleavage activity are used as research tools for the investigation of nucleic acids structures. Examples of oxidative cleavage catalysts have been reported. Recently, much effort has been devoted to the development of DNA hydrolysis catalysts. More artificial catalysts for the hydrolysis of DNA are desirable for the extreme hydrolytic stability of the phosphodiester bonds of DNA.

In order to find new DNA hydrolyzing agents, we try to mimic the catalytic mechanism of nature enzyme. The interactions of amino acids (serine and histidine) that usually locate at the active sites of many enzymes, and dipeptides (seryl-histidine and histidyl-serine) with DNA were studied. It was found that only Ser-His could cleave DNA. The presence of histidine will inhibit the cleavage activity of Ser-His on DNA. The mechanism was proposed to be involved both the imidazole and the hydroxyl groups. The imidazole group acts as general acid to interact with the ionize phosphodiester. The interaction enables the phosphorus to be easily attacked by the hydroxyl group on serine residue, which acts as the fifth coordinator to the phosphorus, enabling the formation of the penta-coordinate phosphorus transition state through which the phosphodiester bond is hydrolyzed.

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