

**P001** Biomolecular Simulation Studies of Anti-Cancer Mechanism by a DACA Derivative.

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DNA Holliday Junctions are intermediate products in homologous recombination and has multiple functional roles of gene shuffling and replication fork repair, in a normal cell. It was found over expressed in most of the breast cancer patients and thus believed to promote excessive cell proliferation in cancerous state. Thus acts as a potential and novel target for anti-cancer therapies.

Our group's recent crystallographic studies of the stabilisation of a novel DACA dimeric derivative – DNA Holliday junction revealed the drug's recognition for DNA Holliday junctions and showed key movements involving flipping off two adenine bases symmetrically in order to sit into the core of the Holliday junction and stabilise it. We performed several bio-molecular simulations using Amber9 & Cerius2 softwares to study the drug – DNA binding interactions and the drug induced conformational changes in the DNA Holliday junction.

An initial, partially restrained molecular mechanics optimisation of a plain DNA Holliday junction with the sketched DACA dimeric derivative (using DREIDING force field) flipped off two adenine bases near the junction, similar to the movements seen in crystallographic studies. Further extensive solvated molecular dynamics simulations in the presence of Na<sup>+</sup> cations and periodic boundary conditions to ~5ns revealed the structural distortions induced by the drug binding.