DNA Crystallography: Exploring Small-Molecule Interactions With DNA for a Novel Nanoscale Drug Delivery Platform

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Nanomedicine is a rapidly growing field, however limited understanding of molecular mechanisms hinders the development of next generation gene-targeting drugs. Ethidium bromide (EB) is a common small-molecule utilized in comparative fluorescence assays, the primary method for determining drug/DNA binding locations. However, no methods in the field offer structural data necessary for visualizing binding interactions. EB can also serve as a model molecule in drug delivery studies due to its structural resemblance to chemotherapeutics such as doxorubicin. Caffeine is known to trigger the release of EB from DNA, demonstrating the potential of DNA for drug delivery. This study presents DNA crystallography, the creation and diffraction of DNA nanocrystals, both as a novel framework for investigating drug/DNA interactions and functionalization as a nanoscale drug delivery platform. Specifically designed DNA strands were mixed at certain molar ratios and incubated to self propagate into a 3D crystal lattice structure with EB. All crystals were diffracted and data was used to solve crystal structures. EB exhibit signs of being a major/minor groove binder despite previous studies, casting heavy doubt on the accuracy of comparative fluorescence assays that do not account for EB's non-interbase binding. Caffeine solutions were added to crystals with EB and were then subject to fluorescence imaging to investigate drug release. The increase of crystal fluorescence emission intensity peaks demonstrate signs of caffeine-induced EB release, proving DNA nanocrystals to be a promising platform for nanoscale drug delivery.

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