Ben-Gurion University of the Negev
אוניברסיטת בן-גוריון בנגב

Graduate Students Seminar

Department of Chemistry

Sunday, June 04th, 2023
Time 14:30
Bldg. 43 Room 015

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Under the supervision of Prof. Yossi Weizmann

Mimicking Biological Functionality Using Artificial DNA Topology for the Design of a Topoisomerase Activity Assay

Topoisomerases regulate DNA topology, enabling crucial processes such as replication and transcription, that are vital for the cell's survival[1]. Thus, they have become a powerful target for drugs designed to destroy pathogenic cells, e.g., bacterial infections and cancer[2]. Traditional assays, such as gel electrophoresis[3] and fluorescence-based methods[4,5], have been commonly employed to evaluate topoisomerase activity and identify new candidates for drug development. However, these assays possess inherent limitations that make them unsuitable for high-throughput screening (HTS) technologies. To address this challenge, our research objective was to develop a novel assay for topoisomerase activity. This innovative approach utilizes artificial topological DNA nanostructures, which effectively mimic the biological function of topoisomerases *in vitro*. To ensure fast and real-time data acquisition, we apply nucleic acid amplification techniques. We have specifically engineered various DNA topologies[6,7], among them a single-stranded trefoil knot structure measuring 15 nm in size. Leveraging the remarkable properties of nucleic acids, we have successfully achieved precise control over the desired shape. These nanostructures function as exceptionally specific substrates for the bacterial topoisomerase IA enzyme. By coupling real-time PCR amplification techniques, with our artificial topological structures, we have developed an assay ideal for HTS. This platform could facilitate the identification of candidates for topoisomerase-targeted antibiotics.

References:

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