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Biophysical and structural investigations into CAGAGG repeats associated with cancer

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(CAGAGG)n repeats are difficult-to-replicate sequences in the mouse genome, with n frequently greater than 100. Such sequences were shown to promote the collapse of DNA replication forks, contributing to the breakpoints and translocations that cause cancer.1 We hypothesize that (CAGAGG)n folds into a secondary structure which stalls DNA polymerase during replication. The structure and stability of (CAGAGG)n repeats (where n = 2-15) as well as their variants and mutants were investigated using a panel of complementary biophysical methods including circular dichroism, UV-vis and fluorescence spectroscopy, gel electrophoresis, thermal stability, and analytical ultracentrifugation. Fluorescence of 2-aminopurine incorporation into specific regions of the DNA was also used to assess the secondary structure. The DNA sequences were studied under a variety of conditions: 1) variance in the presence and concentration of cations, K+, Li+, Na+, Mg2+, Zn2+, and Pb2+ 2) changes in pH; and 3) the presence of secondary-structure modifying small molecules. X-ray crystallography was used to investigate the atomic details of (CAGAGG)n structure.

Date: Wed, Sept. 11, 2019

Time: 4:30-5:30 pm

Location: 208 Clark Hall