Rothmund-Thomson Syndrome Helicase and Its DNA Binding Preferences

Cechova, Barbora

Our DNA is constantly exposed to mutagens generating damage in the polynucleotide chain. If not repaired, these DNA lesions can lead to genomic instability and potentially to cancer. Fortunately, hundreds of proteins, including RecQ helicase family, have evolved in several pathways that repair various DNA lesions. This research focuses on the human RECQ4 – the least characterized protein among this family with its role being unknown. Additionally, mutations in the RECQ4 gene are linked to hereditary disease called Rothmund-Thomson syndrome. The aim of this study was to reveal the main role of RECQ4 during DNA repair by characterizing its DNA binding properties. Two protein truncations of N-terminus of RECQ4 [RECQ4(1-269) and RECQ4(269-400)] were produced using biochemical and molecular-biology techniques. These were tested for their affinity to Holliday junction structure (HJs) and ssDNA substrate using electrophoretic mobility shift assay. The acquired results showed that N-terminus of RECQ4 exhibited high affinity and specificity to HJs. The domain responsible for this binding is located within the region of 269-400 amino acids. The results imply that RECQ4 plays a crucial role in the processing of HJs arising as intermediates during the DNA replication and repair. These results further allow understanding of the exact role of RECQ4 in DNA repair and thus decipher molecular basis of the Rothmund-Thomson syndrome. Furthermore, RecQ helicases showed promising potential in anticancer therapy, and, therefore studies of this protein family are highly demanding.

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