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Understanding substrate specificity of activation induced cytidine deaminase

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Activation Induced Cytidine Deaminase (AID) is a crucial enzyme for the adaptive immune response. It is a member of the Zn dependent AID/APOBEC superfamily and is expressed in B cells where it initiates secondary antibody diversification by mutating antibody genes. AID acts in vitro on single stranded DNA structures such as stemloops, bubbles and R-loop regions and its activity in vivo is proportional to transcription activity at a locus. It has also been shown that AID prefers to mutate cytidines situated in WRC (W=A/T, R=A/G) motifs. However, several studies have shown that AID demonstrates multiple stochastic targeting along the DNA sequence. Therefore, the relationship between its processive nature and multimeric forms and DNA target preference are not clearly understood. Here we examined AID's enzymatic properties using complex DNA structures and sequences in order to better understand the basis for AID targeting. We compared AID activity on a number of substrates. We found that generally structure shapes supersede sequence in dictating target choice for AID. We also investigated the activity of AID on various modified DNA bases. We found that many commonly modified bases in DNA can drastically affect the activity of AID. Since mistargeted deamination could lead to oncogenesis, a thorough examination of AID's sequence targeting and its enzymatic characteristics is imperative for understanding why AID selectively targets certain genes.

Biography

Hala Abdouni graduated from Memorial University of Newfoundland with a Bachelor of Science (major: Biochemistry) in 2011. She worked as a Research Assistant for three years and in 2013 was a first co-author in a paper published in NAR (Nucleic Acids Research). She was accepted into the Master's of Science in Medicine program in January 2014 and is currently conducting her research on the biochemical characteristics of AID (Activation Induced cytidine Deaminase).

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