Analysis of Structural Changes on Functional Domains of WRN Gene Responsible for Werner Syndrome

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Werner syndrome is a premature aging disorder that may serve as a model of normal human aging. This defect is on a gene that codes DNA helicase and it is located on the short arm of 8th chromosome. It is an autosomal recessive disorder caused by mutation at the WRN gene (8p12-p11.2) which belongs to the family of RecQ helicases. WRN is a bipartite and bifunctional enzyme as it has helicase activites as well as functional exonuclease domain. Like all helicases, the basic activity of wrn is unwinding of DNA, in 3'-5' direction. Exonuclease helps in DNA repair mechanism. Through Simple alignment and other structural studies four defined regions of WRNp are identified. They are, exonuclease domains I, II, and III in the N-terminal region; RecQ-type helicase domains I, Ia, II, III, IV, V, and VI in the central region; a RecQ conserved motif immediately following the helicase motifs; and a helicase ribonuclease D C-terminal (HRDC) conserved motif in the C-terminal regions. More than 20 different mutations on this gene cause the defect known as Werner syndrome. Many of these mutations result in an abnormally shortened Werner protein. This altered protein is not transported into nucleus, where it normally interacts with DNA. Here is an *insilico* approach for showing maximum possible mutations on these domains, and the impact on predicted 3D structures due to these mutations. We identified different hazardous mutations on four different domains of wrn gene and predicted their subsequent mutated structure by superimposing them with normal templates. Since no specific treatment is available for this disease, this molecular approach will at least help to understand the structural changes on the functional region and their impact on the metabolism.