Correlation between Function and Oligomeric State of Human RECQ1 Helicase Revealed by Biochemical and Cryo-EM Analysis

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DNA helicases are DNA unwinding enzymes that play an important role in cellular events such as replication, recombination, repair [1]. Human RecQ helicases are involved in the maintenance of chromosome stability, although their exact function is under investigation Five members of the RecQ family are present in humans: RECQ1, BLM, WRN, RECQ4 and RECQ5. Mutations in BLM, WRN, and RECQ4 cause syndromes characterized by genomic instability, and cancer predisposition [2]. Our work focus on RECQ1 the first helicase of the family to be discovered in human cells, but also one of the less characterized in terms of its functional properties.

RECQ1 is a 3' to 5' helicase capable of unwinding short dsDNA substrates but also to promote strand annealing of complementary ssDNA molecules. These processes are modulated by nucleotide binding which alters RECQ1 protein conformation. We demonstrated that nucleotide binding inhibits the strand annealing activity of RECQ1 probably by inducing a change in the oligomeric state of the protein. The 3D structure of RECQ1 has been determined from a heterogeneous image population using cryo-electron microscopy. Our results indicated that RECQ1 forms hexameric rings in the presence of ATPγS and Mg^{2+}, while it remains as a dimer in the presence of Mg^{2+}. Moreover, EM data collected in the presence of DNA showed that its addition narrows the central channel of the hexameric ring. These results provide the first information on the structure of the RECQ1 helicase in the presence and absence of DNA opening a wide range of hypothesis concerning the role of RECQ1 in DNA metabolism.

[1] Hickson I.D., *Nat Rev Cancer,* 2003, **3**, 169. [2] Opresko P.L., Cheng W.H., Bohr V.A., *J Biol Chem.,* 2004, **279**, 18099.

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