Yuliang Wu, Transcriptomics 2017, 5:2 (Suppl)
DOI: 10.4172/2329-8936-C1-012

KH domain in DEAD-box helicase: An old wine in a new bottle

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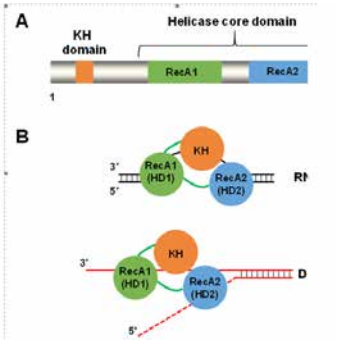
The K-homology (KH) domain is a nucleic acid–binding domain present in many proteins, but has not been reported in helicases. DDX43, also known as HAGE (helicase antigen gene), is a member of the DEAD-box protein family. It contains a helicase core domain in its C-terminus and a potential KH domain in its N-terminus. DDX43 is highly expressed in many tumors, and is therefore considered a potential target for immunotherapy. Despite its potential as a therapeutic target, little is known about its activities. Here, we purified recombinant DDX43 protein to near homogeneity and found that it exists as a monomer in solution. Biochemical assays demonstrated that it is an ATP-dependent RNA and DNA helicase. Although DDX43 was active on duplex RNA regardless of the orientation of the single-stranded RNA tail, it preferred a 5' to 3' polarity on RNA and a 3' to 5' direction on DNA. Truncation mutations and site-directed mutagenesis confirmed that the KH domain in DDX43 is responsible for nucleic acid binding. Compared with the activity of the full-length protein, the C-terminal helicase domain had no unwinding activity on RNA substrates and had significantly reduced unwinding activity on DNA. Moreover, the full length DDX43 protein, with single amino acid change in the KH domain, had reduced unwinding and binding activates on RNA and DNA substrates. Our results demonstrate that DDX43 is a dual helicase and the KH domain is required for its full unwinding activity.



Biography

Yuliang Wu has obtained his BSc and MSc from Zhejiang University, China in 1995 and 1998 respectively, and PhD from International Centre of Genetic Engineering and Biotechnology (ICGEB), Delhi, India in 2002. In the following eight years, he has completed his Post-Doc training at the University of Alberta, Canada and the National Institute on Aging-NIH, where he studied the molecular and cellular basis of human genetic diseases characterized by genomic instability. He has joined the Department of Biochemistry at the University of Saskatchewan, Canada in May 2011. His lab focuses on DNA repair proteins, including helicase, single strand DNA binding protein, and recombinase. Through structural and functional studies of these DNA repair proteins, we try to understand the molecular mechanisms underlying genomic instability.

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