Relax and unwind

The RecQ DNA helicase family

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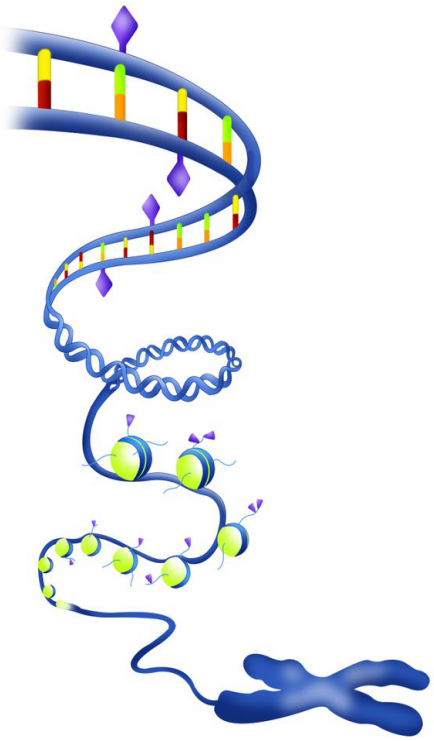
When people go on holiday or travel for a conference, fitting all their clothes, books and a laptop into a small suitcase often presents a challenge. For eukaryotic cells, packing their lengthy genomic DNA into their relatively small nucleus presents a similar challenge. To pack more efficiently, eukaryotic cells wrap their DNA around histone proteins and pack them into the condensed structure that constitutes chromatin. Although this packing approach helps the cells overcome the space constraint issue, it also provides an obstacle when unpacking and unwinding during events such as DNA replication and recombination. Before DNA replication or recombination can proceed, histone proteins have to be shifted or removed and DNA has to be relaxed and unwound. This unwinding process is facilitated by a group of proteins called helicases[1].



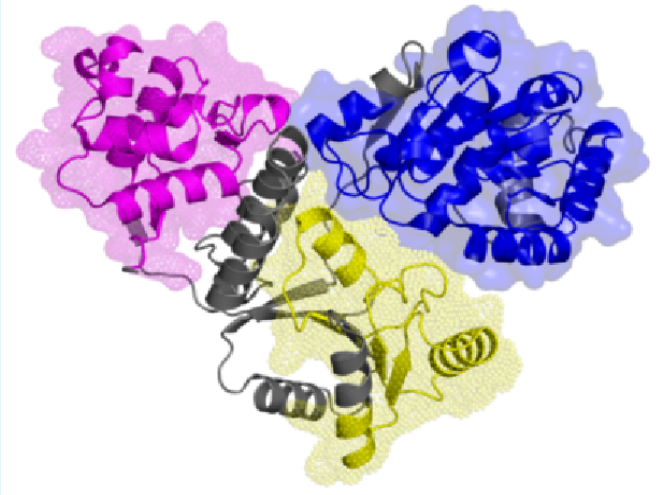
Picture provided by the National Institute of General Medical Sciences

RecQ helicase is a family of helicases that have the function of maintaining genome stability. Humans have at least five RecQ helicases[1]. Mutations in three of these: BLM, WRN and RECQ4, are associated with heritable human diseases. The syndromes of these diseases include cancer predisposition, premature ageing and chromosomal instability[2,3,4].

From the literature, we know that the RecQ family is defined by a highly conserved helicase domain, which is essential for ATP binding and hydrolysis[5]. To gather more information on this family and the domains associated with it, we can use the InterPro classification and sequence analysis database.

We can find the RecQ family entry (IPR004589) in InterPro either by searching with the keyword “RecQ” directly or by searching with the sequences from a RecQ family member. For instance, by searching InterPro with the human BLM protein sequence (UniProt Accession: B7ZKN7), we can also find the link to the RecQ family entry.

InterPro's overview of this helicase family tells us that RecQ is involved in genome maintenance and that all RecQ homologues tested have been shown to be able to unwind paired DNA. It also details that the BLM budding yeast homologue, Sgs1p, acts both as a 'sensor' for DNA damage during replication and a 'resolvase' for structures that arise at paused forks. The structure of the RecQ helicase catalytic core (*E. coli*) can be seen via a link to the Protein Data Bank[6] (Fig.1).



- DEAD/DEAH box helicase domain is in blue (N-terminal)
- Helicase conserved C-terminal domain is in yellow
- RQC domain is in magenta

Figure 1. The crystal structure of *E. coli* RecQ helicase catalytic core from PDB (1OYW).

Overall, InterPro predicts that over 6,000 proteins belong to the RecQ family. Only a single family member is found in unicellular organisms, such as *E. coli* and budding yeast (*S. cerevisiae*), while several family members are found in multicellular organisms, such as humans and mice. We can also compare the protein domain organisation among some of these family members using the information provided by InterPro (Fig. 2).

Species	Accession	Name	Domain Organisation	Length (aa)
E. coli	P15043	RecQ		609
S. cerevisiae	P35187	Sgs1		1447
Homo sapiens	P46063	RECQ1		649
	P54132	BLM		1417
	Q14191	WRN		1432
	O94761	RECQ4		1208
	O94762	RECQ5		991

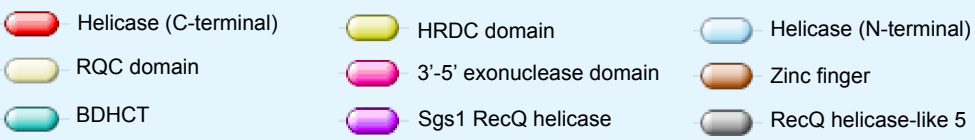


Figure 2. The domain architectures of RecQ family members from InterPro.

As expected, the helicase domain is conserved in all RecQ proteins examined. However, there are some differences - for instance, the RQC domain is absent in human RECQ4, and the HRDC domain is absent in human RECQ1, RECQ4 and RECQ5. The inclusion of an exonuclease domain as an extension element in WRN indicates that this protein has an exceptional function.

It has been suggested that the single RecQ helicase in bacteria and yeasts may play specialized roles that are also performed by the multiple human RecQ family members[7]. Therefore, protein information on the RecQ homologues could be crucial for revealing the mechanisms behind RecQ related diseases. Gathering information about protein homologues, domains, structures and functional sites can be time consuming, but as we have seen with the RecQ family, InterPro can help to speed up this process. So let InterPro take care of some of the hard work for you, while you relax, unwind, and enjoy your journey!

References

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3. Hickson I. D., 2003. RecQ helicases: caretakers of the genome. Nat. Rev. Cancer 3:169-178.
4. Ozgenc A., Loeb L. A., 2005. Current advances in unraveling the function of the Werner syndrome protein. Mutat. Res. 577: 237-251.
5. Bernstein D. A. and Keck J. L., 2003. Domain mapping of *Escherichia coli* RecQ defines the roles of conserved N- and C-terminal regions in the RecQ family. Nucleic Acids Research 31: 2778-2785.
6. Bernstein D. A., Zittel M. C. and Keck J. L., 2003. High-resolution structure of the *E. coli* RecQ helicase catalytic core. EMBO J. 22:4910-4921.
7. Bachrati C. Z. and Hickson I. D., 2003. RecQ helicases: suppressor of tumorigenesis and premature aging. Biochem. J. 374: 577-606.

Useful Links

InterPro
http://www.ebi.ac.uk/interpro/

RecQ family (InterPro)
http://www.ebi.ac.uk/interpro/search?q=IPR004589

UniProt
http://www.uniprot.org/

Human BLM (UniProt)
http://www.uniprot.org/uniprot/b7zkn7

E. coli RecQ helicase catalytic core structure (PDB)
http://www.ebi.ac.uk/pdbe-srv/view/entry/1oyw/summary

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