WEB WATCH

Human Protein Reference Database

• http://www.hprd.org

Browse, query or BLAST? Or why not view one of the available protein-interaction networks? It's up to you. The Human Protein Reference Database (HPRD) is a user-friendly resource that lets you do it all. However you find your protein of choice, information on every possible feature — alternative names, function, sequence, domains, motifs, interactions, expression, localization, post-translational modifications, substrates and any disease association — is just a click away.

Couple all of this with links to external resources, such as the OMIM, Swiss-Prot, LocusLink and Unigene web sites, and this really is a unified protein bioinformatics platform.

Almost all of the information that is included in the HPRD has been obtained manually by biologists who read hundreds of thousands of publications and interpreted and analysed the data. Every protein is reviewed twice, but should you spot any errors, they can be reported online. The HPRD ontology should soon be fully compliant with that of the Gene Ontology consortium, and the HPRD data will eventually be downloadable.

This resource is a joint venture between Akhilesh Pandey's laboratory (http://pandeylab.bs.jhmi.edu) and the Institute of Bioinformatics (http://www.ibioinformatics.org), but contributions from 'the outside world' are also encouraged — so how about becoming a 'molecule authority' for your favourite protein? And if your protein of interest cannot be found, then let the curators know and they will annotate it for you.

With more than 3,000 proteins in the HPRD already, and that number expected to reach 10,000 by the end of 2003, this really is a great resource for anyone who is interested in the human proteome!

Natalie Wilson

DNA REPAIR

Controlled crossing over

In meiosis, homologous recombination (HR) events frequently lead to crossover recombinants. By contrast, mitotic crossing over is rare, which indicates that there is probably a regulatory mechanism in place. Indeed, James Haber and colleagues, reporting in *Cell*, now show that two helicases — Srs2 and Sgs1 — regulate the proportion of HR-associated crossovers, versus non-crossovers, in mitosis.

The Haber group used an ectopic-HR assay to study crossing over in budding yeast. An inducible endonuclease generates a double-strand break (DSB) that is repaired by a homologous sequence — which cannot be cleaved — on a different chromosome. The authors analysed the effect of deleting several DNA-repair and -recombination genes, and found that cell viability was reduced in cells lacking the helicases Srs2 or Sgs1, the latter of which is a homologue of the human Bloom's syndrome (BLM) and Werner syndrome (WRN) helicases. Deletion of either gene increased the proportion of crossover products by two- to threefold, as shown by Southern blot analysis — so, the helicases suppress crossover events. Indeed, overexpression of Srs2 caused an almost complete absence of crossover events.

The authors noticed that in cells lacking Srs2, the overall DNA-repair efficiency was reduced, and that the absolute number of crossovers was, in fact, unchanged compared to wild-type cells. This indicated that when Srs2 is lacking, a repair pathway leading to non-crossovers is affected. When they then overexpressed Rad51 in Srs2-deficient cells, the non-crossover pathway was nearly eliminated. On the basis of additional data, Haber and colleagues suggest that Srs2 might remove Rad51 to allow the non-crossover pathway to repair DSBs. This is consistent with two recent papers in *Nature*, which showed that Srs2 can displace Rad51 from single-stranded DNA *in vitro*.

As was previously shown in meiosis, Haber and co-workers found evidence for two kinetically distinct DSB-repair pathways in mitosis — one that leads primarily to non-crossover products and one to both crossover and non-crossover products. Crossovers appeared more slowly, about 30 minutes after the formation of non-crossovers. Interestingly, in the *srs2*Δ strain there was no difference in the kinetics of gene conversions, and all events took place at the time that crossover products are normally formed. This confirms that the deletion of Srs2 mainly affects the non-crossover pathway.

The authors suggest, on the basis of previous studies, that the non-crossover pathway is probably a

synthesis-dependent strand-annealing (SDSA) mechanism, and that the second pathway, which leads to both crossover and non-crossover events, involves Holliday-junction intermediates.

Unlike Srs2, the absence of Sgs1 does not affect the efficiency of DSB repair or the kinetics of product formation. Haber and co-workers did mutational analysis of Sgs1 and found that both the helicase domain and the amino-terminal domain, which interacts with topoisomerase III (Top3), are required for the suppression of crossover events. The authors propose that Sgs1–Top3 can remove Holliday-junction structures, which results in non-crossover events. Incidentally, Shirleen Roeder and colleagues have recently found that an *sgs1* mutant increases meiotic crossing over in budding yeast.

Whether BLM and WRN helicases have similar functions in recombination events in humans, and how this relates to genome instability in Bloom's and Werner syndrome, requires further studies.

Arianne Heinrichs

References and links

ORIGINAL RESEARCH PAPER Ira, G. *et al*. Srs2 and Sgs1–Top3 suppress crossovers during double-strand break repair in yeast. *Cell* **115**, 401–411 (2003)
FURTHER READING Krejci, L. *et al*. DNA helicase Srs2 disrupts the Rad51 presynaptic filament. *Nature* **423**, 305–309 (2003) | Veaute, X. *et al*. The Srs2 helicase prevents recombination by disrupting Rad51 nucleoprotein filaments. *Nature* **423**, 309–312 (2003) | Rockmill, B. *et al*. The Sgs1 helicase regulates chromosome synapsis and meiotic crossing over. *Curr. Biol.* **13**, 1954–1962 (2003)