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Damage in worms

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The DNA damage response (DDR) is essential for normal cell function and for tumour suppression. In the January 4 *Science*, Simon Boulton and researchers at the Dana-Farber Cancer Institute, Boston, report a strategy to identify novel DDR genes (*Science* 2002, **295**:127-131). They combined functional genomics approaches, namely protein-protein interaction mapping and high-throughput phenotype analysis, to investigate DDR in *Caenorhabditis elegans*. They chose 75 worm genes representing orthologs of proteins involved in nucleotide-excision repair (NER), mismatch repair (MS), base-excision repair (BER) or non-homologous end joining (NHEJ), and tested them in the yeast two-hybrid protein-protein interaction assay. They confirmed interactions observed in other species and found new interacting partners. Proteome-wide interaction screening identified a large number of 'interologs', enabling Boulton *et al.* to construct a DDR protein-interaction map. They validated candidate genes using the 'RNAi by feeding' method, and looked for DDR phenotypes following irradiation. This combined approach led them to identify 12 DDR orthologs in worms and 11 novel DDR-related genes. The authors propose that similar strategies, integrating high-throughput protein interaction screens and RNAi phenotype analysis, could generate genomic maps for DDR and other biological processes in mammalian cells.

References

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