

the short-allele carriers is probably due to increased neuronal activity that, in turn, might be caused by increased synaptic levels of serotonin. These results imply that there is a direct genetic link between serotonin receptor function and the response of a particular part of the brain to emotional information. Serotonin has been previously linked to depressive and suicidal behaviour, and the authors suggest that the amygdala might also mediate these behaviours. Such an approach could prove to be powerful in future investigations of the potential links between behavioural differences and genetic polymorphisms.

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References and links

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loss of one of the two visible markers in *P(wHy)* that are on either side of *hobo*. A broad set of genomic deletions — which can be up to 400 kb but with the highest density ~60 kb — can be generated in this way, all of which, importantly, start at one end of the hybrid element.

This deletion technique is not the first gene disruption method known in flies: RNA interference and targeted gene knockouts have been used by many labs over the past few years. What makes the *P(wHy)* deletion system so appealing, however, is that it can be applied globally to the genome. Moreover, as the components of *P(wHy)* have their equivalents outside *Drosophila*, it might not be long before this phenotypic analysis tool takes a leap into other eukaryotes.

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FURTHER READING Kornberg, T. Another arrow in the *Drosophila* quiver. *Proc. Natl Acad. Sci. USA* **99**, 9607–9608 (2002)

IMMUNOGENETICS

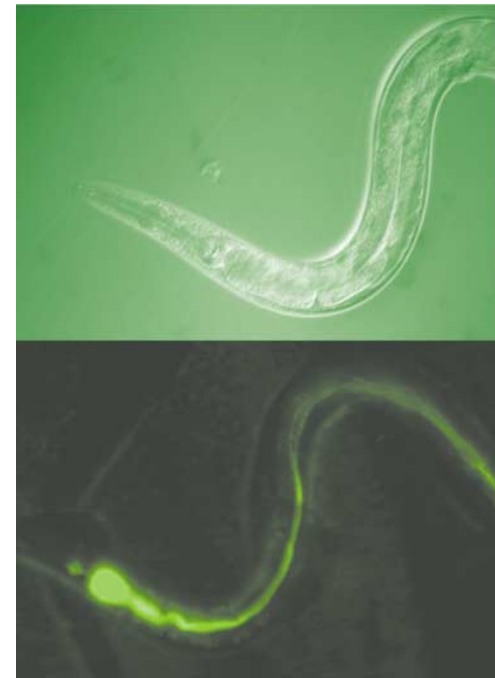
C. elegans — an innate choice?

Much of what we know about innate immunity — an organism's immediate response to pathogen infection — comes from studies in *Drosophila*, which have shown that the components of innate immunity are highly conserved. Two papers now illustrate how *Caenorhabditis elegans*, another genetically tractable organism, might also be a useful model for studying innate immunity. Their results show that *C. elegans* has an inducible response to pathogen infection and that this response shares many features with innate immunity in other organisms.

Kim *et al.* assayed the progeny of mutagenized worms, which had been exposed to the bacterium *Pseudomonas aeruginosa* for enhanced susceptibility to pathogen (*esp*) infection. From a screen of 14,000 haploid genomes, they isolated two mutants, *esp2* and *esp8*, that die much faster on exposure to *P. aeruginosa* than wild-type worms do. High-resolution SNP mapping revealed the chromosomal locations of the mutant genes, which were identified by phenotypic rescue — the *esp2* mutant was rescued by the gene *sek-1*, and *esp8* by *nsy-1*.

sek-1 encodes a MAP kinase kinase (MAPKK) homologue of mammalian MKK3/MKK6 and MKK4, and *nsy-1* encodes an orthologue of the mammalian MAPKKK ASK1. Because these kinases activate the p38 kinase family and the JNK MAP kinases in mammals, the authors tested the role of p38 and JNK in the *C. elegans* defence response. The *esp2* and *esp8* mutants had markedly reduced levels of p38 MAPK activity. Moreover, the knockdown of *pmk-1*, one of two *C. elegans* p38 orthologues, by RNA interference produced a strong *esp* phenotype. Knockdown of *pmk-2* and a *jnk* mutation, however, produced no enhanced susceptibility to *P. aeruginosa* infection. Together these results show that the p38 MAPK pathway is required for innate responses to pathogen infection, which is an important discovery as this signalling pathway is also crucially required in mammals for inflammatory and innate-immune response signalling pathways.

Mallo *et al.* used an expression screen to look for *C. elegans* genes upregulated in response to infection by the bacterium *Serratia marcescens*. Of 7,500 cDNAs surveyed, several were induced



An *esp2* mutant worm, after exposure to GFP-labelled *P. aeruginosa*. Nomarski (top) and fluorescence (bottom) images, courtesy of Dennis Hyong-Kun Kim, Frederick Ausubel and Rhonda Feinbaum.

over twofold, most of which encoded lectins, which function in innate immunity in other organisms. Also upregulated was lysozyme 1. As lysozymes have been implicated in innate-immune responses, Mallo *et al.* overexpressed *lys-1* in worms to see if this would enhance their resistance to *S. marcescens*. It did, although only against a less pathogenic strain of the bacterium, possibly because this strain does not produce proteases that degrade the enzyme, whereas the more pathogenic strain does. The authors also assayed *Dbl-1* mutants for their susceptibility to *S. marcescens* infection, because *Dbl-1* — a TGF- β -related gene — regulates some of the genes induced in the screen. *Dbl-1* mutants were extremely susceptible to *S. marcescens* infection and, surprisingly, also to infection by the *E. coli* strain OP50, which *C. elegans* is often cultured on.

So, 30 years after its discovery in *Drosophila*, these studies show that *C. elegans* also has an innate-immune response — the components of which are conserved in other organisms — and the ease with which this response can be investigated genetically in worms.

Jane Alfred

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