INNATE IMMUNITY

imd unveiled

Although they lack an adaptive immune system, *Drosphila* are armed with a battery of highly effective antimicrobial peptides. In response to infection, antibacterial and antifungal peptides are induced by independent recognition pathways, initially defined by *imd* and *Toll* mutants, respectively. Remarkably, these basic signalling pathways are highly conserved in humans, making *Drosophila* immunity an extremely useful model of mamalian innate immunity. Although *imd* mutants were described 6 years ago, the gene had not been characterized. But now, Georgel *et al.*, reporting in *Developmental Cell*, have identified the elusive *imd*.

Previous studies mapped the *imd* gene to a defined interval containing many genes. To pinpoint *imd*, the authors fine-mapped this region using a panel of mutants generated by transposase-induced male recombination — a relatively new technique which introduces traceable deletions. The mutants were then screened for complementation of the *imd* mutation. This approach showed that *imd* is a single gene encoding a 30-kDa protein. Importantly, *imd* has a carboxy-terminal death domain, a protein–protein interaction module that is involved in apoptotic and immune signalling pathways.

Although there is no human homologue of *imd*, its death domain is remarkably similar to that of mamalian RIP (receptor-interacting protein), an adaptor molecule involved in NF-κB activation and apoptosis. *imd* was known to act upstream of an NF-κB-like molecule, but it had not been implicated in apoptosis. Surprisingly, overexpression of *imd* during development is lethal, and several clues indicated that *imd* might activate apoptosis, including the resistance of *imd* mutant flies to UV-induced apoptosis.

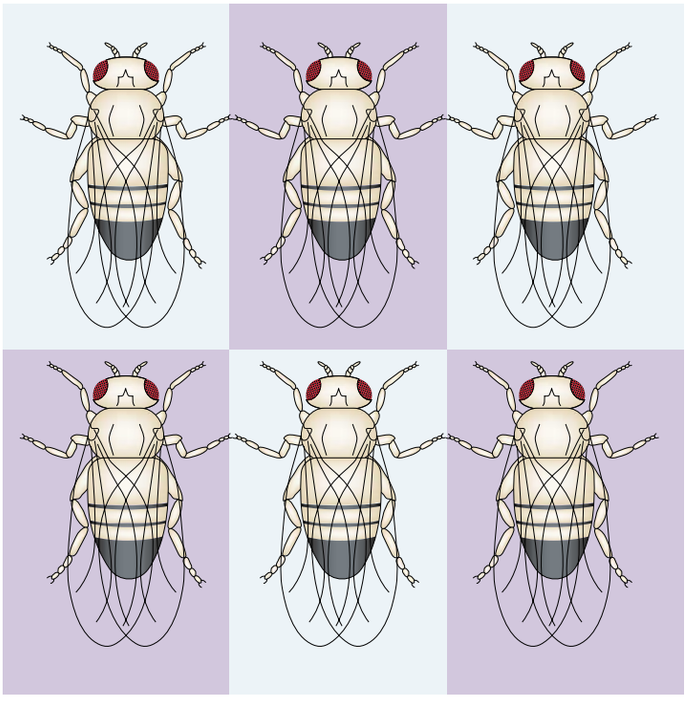
This study, then, fills a key gap in the Imd pathway and indicates for the first time that antibacterial and apoptotic pathways in *Drosophila* might intersect.

Jen Bell

References and links

ORIGINAL RESEARCH PAPER Georgel, P. *et al.* *Drosophila* immune deficiency (IMD) is a death domain protein that activates antibacterial defense and can promote apoptosis. *Dev. Cell* **1**, 503–514 (2001)

FURTHER READING Medzhitov, R. Toll-like receptors and innate immunity. *Nature Rev. Immunol.* **1**, 135–145 (2001)



IN BRIEF

T-CELL ACTIVATION

OX40 promotes Bcl-xL and Bcl-2 expression and is essential for long-term survival of CD4 cells.

Rogers, P.R., Song, J., Gramaglia, I., Killeen, N. & Croft, M. *Immunity* **15**, 445–455 (2001)

Optimal T-cell activation occurs when a T cell receives a signal from the T-cell receptor and a signal from a co-stimulatory receptor, for example CD28. CD28 signalling enhances T-cell proliferation, cytokine secretion and expression of anti-apoptotic proteins. This paper provides direct evidence that OX40 acts synergistically and at a later stage than CD28, and promotes T-cell survival by increasing expression of the anti-apopototic molecules Bcl-xL and Bcl-2.

T-CELL DEVELOPMENT

Epigenetic silencing of *CD4* in T cells committed to the cytotoxic lineage.

Zou, Y. *et al. Nature Genet.* **29**, 332–336 (2001)

The development of immature double-positive thymocytes into mature single-positive $CD4^+$ and $CD8^+$ T cells requires the termination of expression of either the CD4 or CD8 co-receptor. The first intron of the *CD4* gene contains a silencer element that represses *CD4* transcription. Zou *et al.* used the Cre/*loxP* system to show that the *CD4* silencer is only required at distinct stages of development. Once a cell is committed to the $CD8^+$ lineage, the *CD4* locus remains silent even if the silencer element is removed.

T-CELL SIGNALLING

Deficiency of small GTPase Rac2 affects T cell activation.

Yu, H., Leitenberg, D., Li, B. & Flavell, R.A. *J. Exp. Med.* **194**, 915–925 (2001)

Yu *et al.* investigated the function of Rac2, a haematopoietic-specific Rho GTPase, in T-cell signalling. $Rac2^{-/-}$ T cells responded poorly to T-cell-receptor stimulation, showing reduced proliferation, Ca^{2+} mobilization and activation of ERK1/2 and p38. Actin polymerization and cap formation were also decreased in these cells in comparison with wild-type cells. These results show that Rac2 mediates both transcriptional and cytoskeletal changes during T-cell activation.

INNATE IMMUNITY

Subsets of human dendritic cell precursors express different Toll-like receptors and respond to different microbial antigens.

Kadowaki, N. *et al. J. Exp. Med.* **194**, 863–869 (2001)

Dendritic cells (DCs) can prime naive T cells and direct the development of immune responses. Yong-Jun Liu's group investigated the expression of Toll-like receptors (TLRs) — which recognize specific molecular patterns on microbial pathogens — on human DC subsets. The results show that DC subsets express distinct sets of TLRs, supporting the view that DC subsets have evolved to recognize different microbial pathogens.