Chasing Flies because Time Flies

In this issue of the *Journal of Innate Immunity*, Rafael Cantera and Rosa Barrio [1] describe the relationship between neurodegeneration and innate immune responses in humans by referring to studies on *Drosophila*. At first glance, when reading the title and the abstract of the review, the reader may wonder whether the authors' conclusions are fictional. However, decades ago, pioneer work performed by Boman et al. [2] and Lemaitre et al. [3] set the fundament for this area of research, showing that the basic function of the immune system in insects evolved into the complex regulation of host defenses found in humans. So long ago, these researchers already reported that *Drosophila* has an inducible antibacterial defense system [2] and that Toll-like receptors regulate immunity against fungi [3]. Both findings have provided a basis for our understanding regarding critical innate defense mechanisms that are both phylum-independent and evolutionarily conserved. More recent investigations of innate defense mechanisms in *Drosophila*, e.g. the induction of antimicrobial peptides [4], the activation of the IMD pathway [5], antimicrobial autophagy [6] and host responses in epithelial barriers [7] are in line with these findings, supporting the concept that many principles of innate immunity in the animal kingdom originated very early on and have an important function in vertebrates still today. This also applies to the article by Cantera and Barrio [1], who present convincing evidence that in neurodegenerative processes, it is not only that the same immune genes are employed in *Drosophila* and *Homo sapiens*, but also that the transcription of these genes is regulated in a similar manner. It is therefore not surprising

that the authors conclude that *Drosophila* can be used as an instrumental model to elucidate the role of immune response as regulators of neuroprotection.

In addition to *Drosophila*, much has been learnt from studying the zebrafish (*Danio rerio*), appearing as an early vertebrate during evolution. The zebrafish has become an important organism for exploring defense mechanisms in innate immune responses, such as in a model of *Candida albicans* infection [8]. The list of animal types to be studied is continuously growing and also contains more exotic species including the lophotrochozoan snail *Biomphalaria glabrata* [9] and the African clawed frog (*Xenopus laevis*) [10]. These examples show that a great deal of our knowledge about innate immune processes has been achieved by studying invertebrates and early vertebrates. However, one should not forget that invertebrates can also act as pathogens and actually cause disease. For instance, the *Journal of Innate Immunity* recently published that γ -tocopherol supplementation can suppress house dust mite allergies [11] or that serine proteases in the German cockroach can regulate chemokine production and dendritic cell recruitment [12]. Such interactions also contribute to increasing our knowledge about innate immunity. Together, the examples show that mechanisms of innate immunity and virulence occurred early on in the evolution of animals. Studies on invertebrates have contributed tremendously to our current understanding of the molecular mechanisms underlying host-parasite interactions.

Heiko Herwald, Lund
Arne Egesten, Lund

References

- 1 Cantera R, Barrio R: Do the genes of the innate immune response contribute to neuroprotection in *Drosophila*? *J Innate Immun* 2015;7:3–10.
- 2 Boman HG, Nilsson I, Rasmuson B: Inducible antibacterial defence system in *Drosophila*. *Nature* 1972;237:232–235.
- 3 Lemaitre B, Nicolas E, Michaut L, Reichhart JM, Hoffmann JA: The dorsoventral regulatory gene cassette *spätzle*/Toll/cactus controls the potent antifungal response in *Drosophila* adults. *Cell* 1996;86:973–983.
- 4 Vonkavaara M, Pavel ST, Holz K, Nordfelth R, Sjostedt A, Stoven S: *Francisella* is sensitive to insect antimicrobial peptides. *J Innate Immun* 2013;5:50–59.
- 5 Karlsson J, Oldenvi S, Fahlander C, Daenthanasanmak A, Steiner H: Growing bacteria shed elicitors of *Drosophila* humoral immunity. *J Innate Immun* 2012;4:111–116.
- 6 Moy RH, Cherry S: Antimicrobial autophagy: a conserved innate immune response in *Drosophila*. *J Innate Immun* 2013;5:444–455.
- 7 Davis MM, Engstrom Y: Immune response in the barrier epithelia: lessons from the fruit fly *Drosophila melanogaster*. *J Innate Immun* 2012;4:273–283.
- 8 Kuo ZY, Chuang YJ, Chao CC, Liu FC, Lan CY, Chen BS: Identification of infection- and defense-related genes via a dynamic host-pathogen interaction network using a *Candida albicans*-zebrafish infection model. *J Innate Immun* 2013;5:137–152.
- 9 Portela J, Duval D, Rognon A, Galinier R, Boissier J, Coustau C, Mitta G, Theron A, Gourbal B: Evidence for specific genotype-dependent immune priming in the lophotrochozoan *Biomphalaria glabrata* snail. *J Innate Immun* 2013;5:261–276.
- 10 Grayfer L, Robert J: Colony-stimulating factor-1-responsive macrophage precursors reside in the amphibian (*Xenopus laevis*) bone marrow rather than the hematopoietic subcapsular liver. *J Innate Immun* 2013;5:531–542.
- 11 Geiser M, Lay JC, Bennett WD, Zhou H, Wang X, Peden DB, Alexis NE: Effects of ex vivo gamma-tocopherol on airway macrophage function in healthy and mild allergic asthmatics. *J Innate Immun* 2013;5:613–624.
- 12 Day SB, Ledford JR, Zhou P, Lewkowich IP, Page K: German cockroach proteases and protease-activated receptor-2 regulate chemokine production and dendritic cell recruitment. *J Innate Immun* 2012;4:100–110.