



Immune adaptation in flies

DOI:

10.1038/nri2065

One of the defining characteristics of vertebrate immunity is the development of an adaptive immune response to an invading pathogen. By contrast, it was thought that the immune system of invertebrates was completely innate and could not adapt to infection. Now, new research published in *PLoS Pathogens* shows that the innate immune system of *Drosophila melanogaster* can adapt to infection by modulating its response to subsequent challenges.

Pham *et al.* primed flies with a non-lethal dose of live or heat-killed *Streptococcus pneumoniae*, followed 1 week later by a lethal dose of the same bacteria. Surprisingly, they found that *S. pneumoniae*-primed flies survived the subsequent lethal challenge. An examination of the bacterial load in primed flies compared with naive controls showed that the survival difference was due to enhanced *S. pneumoniae* killing in the primed flies. This protection

against subsequent infection persisted throughout the life of the fly.

Although a priming-induced protective response was not observed for all pathogens examined, priming with the natural fly pathogen *Beauveria bassiana* also provided protection against a subsequent challenge with the same pathogen. Interestingly, priming with either *S. pneumoniae* or *B. bassiana* did not protect against lethal infections with other pathogens, indicating that the priming response is specific and not due to the general activation of the immune response.

Fly immunity involves two main pathways, the Toll pathway and the Imd pathway. Flies with loss-of-function mutations in either pathway were susceptible to infection with *S. pneumoniae*. However, flies with mutations in the Imd pathway, but not the Toll pathway, were protected by a priming dose of heat-killed *S. pneumoniae*. Therefore, both pathways are needed

to fight infection but the Toll pathway is necessary for the primed response. In addition, inhibition of phagocytosis in primed flies resulted in susceptibility to subsequent infection, with the same death rate as naive flies. The authors conclude that priming with *S. pneumoniae* allows phagocytes to respond and kill the bacteria more efficiently during a subsequent challenge.

So, the data indicate that the innate immune response in *D. melanogaster* has adaptive characteristics, modulating its response to subsequent challenges following the first exposure to a particular pathogen. It will be of interest to determine whether the innate immune system of vertebrates shares a similar characteristic.

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ORIGINAL RESEARCH PAPER Pham, L. *et al.* Specific primed immune response in *Drosophila* is dependent on phagocytes. *PLoS Pathog.* **3**, e26 (2007)

