Genetic dissection of the pathogenesis of intracellular parasites in Drosophila

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We use the fruit fly as a model insect to study host pathogen interactions. We are interested in the role phagocytes play in removing sporozoites from the hemolymph of an infected mosquito. We use intracellular pathogens such as Listeria monocytogenes, Mycobacterium marinum and Salmonella typhimurium as a tool to study phagocyte biology. In vertebrates, these pathogens have been shown to actively manipulate the biology of the host to improve the chance of survival of the bacteria. We have found that this is also true in the fly and these manipulations point to immune mechanisms outside the widely studied Toll and imd pathways.

Death by infection is often due to the host's reaction to the infecting organism, not the direct result of microbial action. We have found that in Drosophila melanogaster infected with Salmonella enterica var. typhimurium, genes in both the host and pathogen are involved in the pathogenesis of the infection. We demonstrated that S. typhimurium causes a lethal systemic infection when injected into the hemocoel of D. melanogaster. Deletion of either of two secreted bacterial effectors, SspH1 or SlrP, changes an acute and lethal infection to one that is persistent and more benign. We propose a model in which Salmonella secreted effectors irritate the fly and thus causes an immune response that is damaging both to the fly and the bacteria. In support of this model, we show that mutations in a fly gene can delay the lethality of Salmonella infection. This suggests that the flies are dying from a condition that resembles toxic shock in vertebrates.