

The 2009 Patton Lecture

Drosophila intestinal response to bacterial infection: Activation of host defense and stem cell proliferation

Professor Bruno Lemaitre, École Polytechnique Fédérale de Lausanne, Switzerland

The gut is the major interface between microbes and their animal hosts and constitutes the main entry route for pathogens. As a consequence the gut must be armed with efficient immune defenses to combat invasion and colonisation by pathogens. However, the gut also harbors commensal bacteria, which may benefit the host, and must be tolerated without activating a chronic and harmful immune response. In recent years, *Drosophila* has served as a powerful model to dissect host-pathogen interactions, leading to the paradigm of antimicrobial peptide regulation by the Toll and Imd signaling pathways. The strength of this model derives from the availability of powerful and cost effective genetic and genomic tools, as well as the high degree of similarities to vertebrate innate immunity. However, in spite of growing interest in gut mucosal immunity, little is known about the immune response of the *Drosophila* gut. To address this, we are using integrated approaches to dissect not only the gut immune response, but also gut homeostasis in the presence of the commensal microbiota, as well as strategies used by pathogens to circumvent these defenses. Recently, we reported a global analysis of the changes in gene expression that occur in the *Drosophila* gut in response to infection by a Gram-negative bacterium, *Erwinia carotovora carotovora* 15 (Buchon et al. 2009). This study demonstrated that bacterial infections trigger expression of a combination of immune, stress, and developmental signaling pathways. Surprisingly, we observed that ingestion of *E. carotovora* 15 strongly stimulates stem cell division, promoting a rapid turnover of the gut epithelium. These results highlighted an unexpected link between oral bacterial infection and epithelial renewal. They also suggested that, following infection, gut homeostasis is maintained through a balance between cell damage induced by the infection and epithelial repair by stem cell activation. We believe that the fundamental knowledge generated on *Drosophila* gut immunity will serve as a paradigm of epithelial immune reactivity and inform our comprehension of animal defense mechanisms. This has particular relevance to insects, as oral ingestion is the main entry route of many human pathogens to their insect vector hosts.