

The *Drosophila* antimicrobial response: deconstructing the immune effector program using CRISPR/Cas9 technology

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While neglected during the decades where adaptive immunity captured most of the attention, innate immune mechanisms have become central to our understanding of immunology. The recent emphasis on innate immunity has, however, mostly focused on the first two phases of the immune response: recognition and signaling. In contrast, how innate immune effectors individually or collectively contribute to host resistance has not yet been investigated to the same extent. The existence of multiple effectors that redundantly contribute to host resistance has hampered their functional characterization by genetic approaches. As a consequence, the logic underlying the role of effectors is only poorly defined, and exactly how immune parameters contribute to survival is not well characterized. To fill this gap, we are currently studying the deployment of the immune response with a focus on immune effectors taking advantage of the CRISPR/Cas9 editing approach. To carry out this ambitious program, we systematically inactivate putative immune effector genes and generate compound mutants with mutations in various effector genes. This approach allows us to overcome functional redundancy, and to disentangle the respective contribution of each effector to host resistance. We are currently characterizing the role of antimicrobial peptides in immunity and beyond infection, notably aging. We are also studying the metabolic and physiological landscape required to mount an effective immune response while preserving vital host functions. Collectively, our study aims at providing a high-resolution map of the *Drosophila* immune response by deciphering the relative contribution of each immune effector to combat infectious microbes. Taking into consideration the key role that the immune system plays in many processes including microbiota control, neurodegeneration, and aging, our study is likely to have a global impact.