Mutliple roles of Peptidoglycan Recognition proteins in Drosophila

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In Drosophila, two pathways regulate the expression of antimicrobial peptides in response to bacteria infection. The Toll pathway is activated by gram-positive bacteria, while the Imd pathway responds to gram-negative bacteria. The activation of these two pathways relies on the detection of peptidoglycan (PGN), a component of the bacterial cell wall, by a conserved family of proteins, the Peptidoglycan Recognition Proteins (PGRPs). The secreted PGRP, PGRP-SA and SD function upstream of the Toll pathway in the sensing of peptidoglycan from gram-positive bacteria while two other PGRP, -LC and LE activate the Imd pathway upon recognition of PGN from gram-negative bacteria. In addition to these recognition PGRPs that can bind and recognize PGN, genome analysis points to the existence of a second class named catalytic PGRPs (PGRP-SC1/2, SB1/2, and LB) that can degrade PGN. No functional data was available on catalytic PGRPs. A combination of biochemical and genetic approaches allowed us to determine two important functions for catalytic PGRPs. First, we shown that PGRP-LB is a secreted protein regulated by the Imd pathway, which specifically degrades gram-negative bacterial PGN into non-immunostimulatory fragments. We demonstrated that the regulation of *PGRP-LB* by the Imd pathway provides a negative feedback regulation to tightly adjust immune activation to infections. Second, we demonstrated in vivo an essential bactericidal function for PGRP-SB1. We have shown that this enzyme is strongly induced by the Imd pathway after an infection and is secreted into the hemolymph, where it participates in the elimination of bacteria. Collectively, our work indicates that PGRPs are essential components of the Drosophila host defense that act not only in the sensing of microbes but also as regulators and effectors of the antibacterial response.