

Webinar

Blood cells link immunity to wound response in flies

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Innate immunity provides the first line of defense against invading organisms. Organisms sense pathogens using specific signatures called microbe-associated molecular patterns (MAMPs) found in microbes such as lipopolysaccharide, peptidoglycan, and lipoproteins. Upon recognizing these signatures, the host activates signaling cascades that cause immune effectors and regulators' expression. Animals have acquired the capacity to recognize signals called damage-associated molecular patterns (DAMPs). DAMPs are associated with tissue damage and wounding, and are involved in activating specific pathways involved in repair or in inflammation. Numerous DAMPs have been identified in mammals, which include cellular components such as ATP, uric acid, nucleic acids, and the components of actin cytoskeleton. However, the pathway and effector mechanisms that are activated by DAMPs and the cellular response to these cues are poorly understood.

When damage occurs in adult *Drosophila*, not only is there a local response of the injured tissue, but a coordinated action across different tissues is elicited to help the organism overcome the deleterious effect of an injury. In our recently published work, we show that the production of hydrogen peroxide from a wound activates flies blood cells (also known as hemocytes). In some ways, hydrogen peroxide acts as a DAMP signal to help home hemocytes damage and activate them. Hemocytes contribute to increasing levels of hydrogen peroxide near the wound by producing it using an oxidase called DUOX. We provide evidence that production of the cytokine Upd3 involves the accumulation of intracellular ROS in hemocytes, which is facilitated by the diffusion of hydrogen peroxide through a newly identified channel protein, Prip. Thus, levels of ROS inside hemocytes appear as a critical mechanism that regulates the inflammatory response of hemocytes. The innate immune pathway Toll is also induced on injury and protects flies. This Toll pathway activation following a wound protects flies from subsequent infection with a bacterium like *Enterococcus faecali*.

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