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# Ex vivo genome-wide RNAi screening of the *Drosophila* Toll signaling pathway elicited by a larva-derived tissue extract

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## KEY WORDS

*Drosophila*, Innate immunity, Sterile inflammation, Toll pathway, Danger signals

## HIGHLIGHTS

The *Drosophila* larva-derived tissue extract activates the Toll pathway.

The extract activates Toll without Spz or bacterial components.

Genome-wide RNAi screening revealed damage-related signaling factors.

## ABSTRACT

Damage-associated molecular patterns (DAMPs), so-called “danger signals,” play important roles in host defense and pathophysiology in mammals and insects. In *Drosophila*, the Toll pathway confers damage responses during bacterial infection and improper cell-fate control. However, the intrinsic ligands and signaling mechanisms that potentiate innate immune responses remain unknown. Here, we demonstrate that a *Drosophila* larva-derived tissue extract strongly elicits Toll pathway activation via the Toll receptor. Using this extract, we performed *ex vivo* genome-wide RNAi screening in *Drosophila* cultured cells, and identified several signaling factors that are required for host defense and antimicrobial-peptide expression in *Drosophila* adults. These results suggest that our larva-derived tissue extract contains active ingredients that mediate Toll pathway activation, and the screening data will shed light on the mechanisms of damage-related Toll pathway signaling in *Drosophila*.

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