

## Original Research

# Protection of insects against viral infection by apoptosis-dependent phagocytosis

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Running title: Phagocytosis of virus-infected cells in insects

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## Abstract

We investigated whether phagocytosis participates in the protection of insects from viral infection using natural host-virus interaction between *Drosophila melanogaster* and *Drosophila C* virus (DCV). We first found that *Drosophila* S2 cells became susceptible to phagocytosis upon DCV infection accompanied by reduction in viral proliferation. Phagocytosis partly depended on caspase activity in S2 cells as well as the engulfment receptors Draper and integrin  $\beta v$  in phagocytes. To validate the *in vivo* situation, adult flies were abdominally infected with DCV followed by the analysis of fly death and viral growth. The data showed that DCV infection killed flies in a dose-responding manner, and viral virulence was exaggerated when flies lost the engulfment receptors. Furthermore, early death of engulfment receptor-deficient flies was accompanied by the augmented proliferation of virus. Finally, phagocytosis of DCV-infected cells *in vitro* was inhibited by phosphatidylserine-containing liposome, and DCV-infected flies died early when a phosphatidylserine-binding protein was ectopically expressed. Collectively, our study demonstrates that the apoptosis-dependent, phosphatidylserine-mediated phagocytosis of virus-infected cells plays a role in innate immune responses against viral infection in *Drosophila*.

**Keywords:** apoptosis / *Drosophila* / innate immunity / phagocytosis / viral infection