

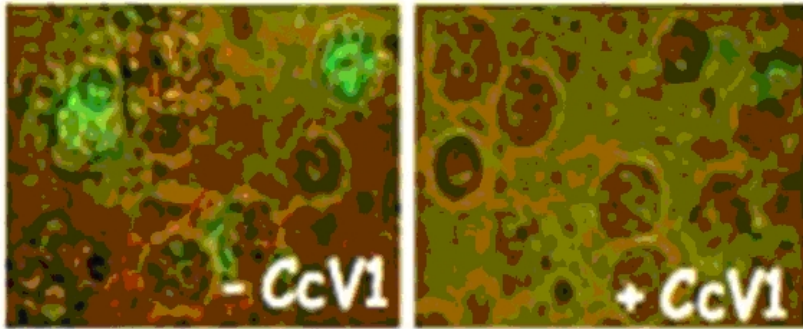
Lepidopteran insects are parasitized by hymenopteran parasitoids (wasps) which results in immunosuppression and physiological changes of the lepidopteran larvae. The parasitoid survival within the host (lepidopteran larvae) depends on viral particles, the wasp endosymbiotic polydnaviruses (PDV) that are injected along with parasitoid eggs in the host's body. Our studies concern the relationship between *Cotesia congregata* bracovirus, CcBV, the endosymbiotic bracovirus of the *Cotesia congregata* (Hymenoptera) wasp and the hemocytes of *Manduca sexta*, the host, in order to understand the role(s) of CcBV proteins in the suppression of immune responses against the parasitoid wasps. In our studies we use the virally encoded gene products expressed in lepidopteran cell lines in order to explore their functional properties in the disruption of the host cellular and humoral defence response.

Objectives

- Interactions of viral proteins with proteins from host hemocytes
- Functional characterization of polydnavirus CcBV proteins.
- The role of ankyrin repeat proteins (IkB α -like) in transcriptional regulation of immune related genes and signalling pathways.
- Identification of new agents for control of insect pest populations

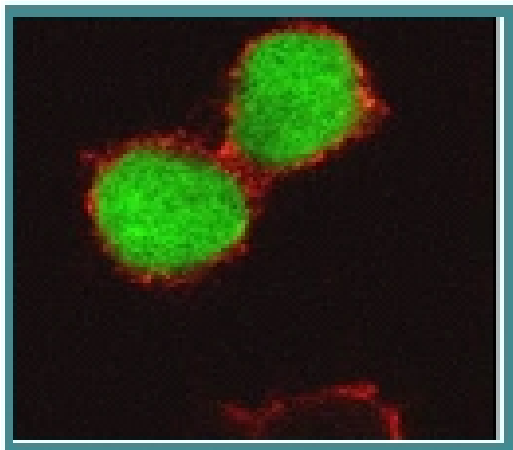
1. Viral protein interactions with host proteins.

Our previous results on the investigation of the viral CcV1 protein showed that this protein interacts with the host protein, hemolin. Hemolin belongs to the immunoglobulin-like protein family and is the most abundant immune induced protein after microbial infection in *Manduca sexta*. The binding of CcV1 to hemolin was shown to inhibit known hemolin functions including binding to lipopolysaccharides (LPS) and its ability to cause bacterial agglutination. The viral protein and hemolin co-localized on the cell surface suggesting interference with the function of hemolin as a pattern recognition molecule. CcV1 protein was also found to inhibit phagocytosis of *E. coli* bacteria by lepidopteran hemocytes or hemocyte-like cells (**Figure1**). Current investigation focuses on the role of CcV1 protein in the melanization process, another important defence mechanism in insects and the interaction of viral gene products with serine protease inhibitors, serine protease homologues and transferrin molecules of the host, found to interact with CcV1 in the yeast two hybrid system.

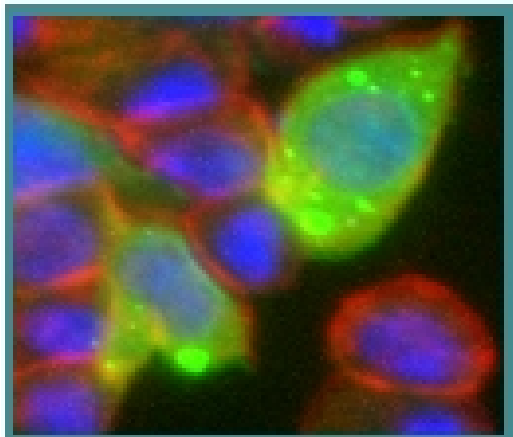


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Expression of OcBV Ank proteins



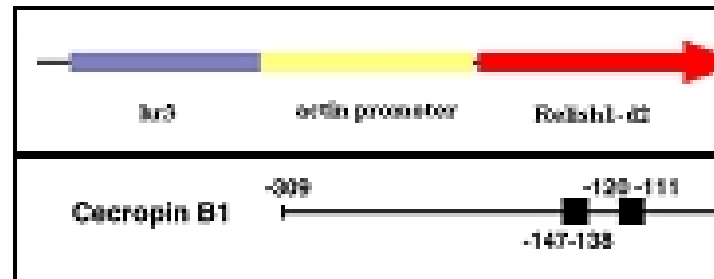
Ank3-myc Phalloidin



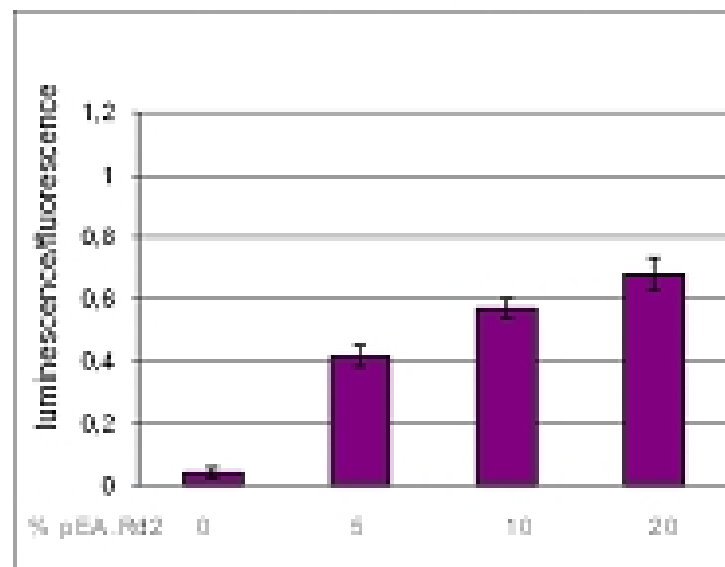
Ank2-myc DAPI Phalloidin

Confocal microscopy showing the subcellular localization of OcBV Ank-proteins in transfected insect cells.

Transcriptional activation



The *Bombyx mori* NF- κ B/Rel transcription factor control of actin promoter and the luciferase gene of *Bombyx mori* antimicrobial peptide cecropin.



Induction of *Bombyx mori* cecropin antimicrobial peptide expression by increasing amounts of Bm Relish1-d2 transcript.

Relevant publications

1. Labropoulou, V., Douris, V., Stefanou D., Magrioti C., Swevers L., and Iatrou, K. (2008). "Endoparasitoid wasp bracovirus-mediated inhibition of hemolin function and lepidopteran host immunosuppression". *Cell. Microbiol.* 10: 2118-28.
2. Douris, V., Swevers, L., Labropoulou, V., Andronopoulou E., Georgioussi, Z. and Iatrou, K. (2006). Stably transformed insect cell lines: tools for expression of secreted and membrane-anchored proteins and high throughput screening platforms for drug and insecticide discovery. *Adv. in Virus Res.*, 68: 113-156

3. Lapointe, R, Wilson, R., Vilaplana, L., O'Reilly, D.R., Falabella, P., Douris, V., Bernier-Cardou, M., Pennacchio, F., Iatrou, K., Malva, C., and Olszewski J.A. (2005). Expression of a *Toxoneuron nigriceps* polydnavirus (TnBV) encoded protein, TnBV1, causes apoptosis-like programmed cell death in lepidopteran insect cells. *J. Gen. Vir.* 86, 963-971.
4. Espagne, E., Douris, V., Lalmanach, G., Provost, B., Cattolico, L., Iatrou, K., Drezen, J.M., and Huguet, E. (2005). A virus required for hymenopteran parasite survival into lepidopteran host expresses genes encoding cystatins. *J Virol.*;79(15):9765-76.