Manipulation of Programmed Cell Death by intracellular bacteria in insects

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Programmed Cell Death (PCD) is a central mechanism in host-pathogens interactions, especially when the pathogen has an intracellular phase in its cycle. On one hand, infected host cells can respond to pathogen attack by initiating PCD preventing infection to spread within the whole body. On the other hand, the pathogen can manipulate the PCD of its host either to escape the host defense (inhibition of PCD), or to increase its dissemination within the host tissues (activation of PCD). This applies to a wide variety of pathogens including viruses, bacteria and protozoa.

While host's response and microbes' manipulations mediated by PCD have been well studied in vertebrates, virtually nothing is known in invertebrates with the exception of viral infections. This is surprising given that invertebrates are hosts and vectors to a variety of intracellular pathogens that cause severe diseases in humans. Examples include *Plasmodium, Chlamydia* and many members of the group of the Rickettsiales (*Anaplasma, Ehrlichia, Orientia* and *Rickettsia*). Among the factors that might explain this lack of studies are the fastidious requirements for studying interactions between invertebrates and the pathogens they vector and the lack of model systems to tackle these questions. However, understanding interactions occurring between pathogens and their invertebrate hosts could open new avenues for limiting the occurrence of infectious agents in the vector, and thus their dissemination and threat to animal and human populations.

The objective of the project is to develop a model system for studying the interactions between PCD and intracellular bacteria in invertebrates. The project is based on recent results that the common intracellular symbiont of insect *Wolbachia*, which belongs to the Rickettsiales, is able to manipulate its host PCD in the hymenoptera *Asobara tabida*. In addition, because *Wolbachia* infection occurs naturally in *Drosophila* species, among which *D. melanogaster*, and that *Wolbachia* can be maintained in insect cell lines, generalization of manipulation of PCD by *Wolbachia* could provide a very useful model for unraveling the mechanisms of manipulation of PCD by intracellular bacteria in invertebrates. The information provided could then be used on pathogens, some being closely related to *Wolbachia*, to develop new strategies to control them within their vectors.