Umeå University Medical Dissertations, New Series No 1741

Activation of the Cellular Immune Response in *Drosophila melanogaster* Larvae

Ines Anderl

Akademisk avhandling
som med vederbörligt tillstånd av Rektor vid Umeå universitet för avläggande av filosofie doktorsexamen framläggs till offentligt försvar i Major Groove, Byggnad 6L,
måndagen den 7 september, kl. 12:30.
Avhandlingen kommer att försvaras på engelska.
Fakultetsopponent: Senior Lecturer, Paul Badenhorst,
School of Immunity and Infection, Institute of Biomedical Research,
University of Birmingham, Birmingham, United Kingdom.

Department of Molecular Biology
Umeå University
Umeå 2015

Organization
Umeå University
Department of Molecular Biology

Document type
Doctoral thesis

Date of publication
17. August 2015

Author
Ines Anderl

Title
Activation of the Cellular Immune Response of *Drosophila melanogaster* Larvae

Abstract
During the last 40 years, *Drosophila melanogaster* has become an invaluable tool in understanding innate immunity. The innate immune system of *Drosophila* consists of a humoral and a cellular component. While many details are known about the humoral immune system, our knowledge about the cellular immune system is comparatively small. Blood cells or hemocytes constitute the cellular immune system. Three blood types have been described for *Drosophila* larvae. Plasmatocytes are phagocytes with a plethora of functions. Crystal cells mediate melanization and contribute to wound healing. Plasmatocytes and crystal cells constitute the blood cell repertoire of a healthy larva, whereas lamellocytes are induced in a demand-adapted manner after infection with parasitoid wasp eggs. They are involved in the melanotic encapsulation response against parasites and form melanotic nodules that are also referred to as tumors.
In my thesis, I focused on unraveling the mechanisms of how the immune system orchestrates the cellular immune response. In particular, I was interested in the hematopoiesis of lamellocytes.
In Article I, we were able to show that ectopic expression of key components of a number of signaling pathways in blood cells induced the development of lamellocytes, led to a proliferative response of plasmatocytes, or to a combination of lamellocyte activation and plasmatocyte proliferation.
In Article II, I combined newly developed fluorescent enhancer-reporter constructs specific for plasmatocytes and lamellocytes and developed a "dual reporter system" that was used in live microscopy of fly larvae. In addition, we established flow cytometry as a tool to count total blood cell numbers and to distinguish between different blood cell types. The "dual reporter system" enabled us to differentiate between six blood cell types and established proliferation as a central feature of the cellular immune response. The combination flow cytometry and live imaging increased our understanding of the tempo-spatial events leading to the cellular immune reaction.
In Article III, I developed a genetic modifier screen to find genes involved in the hematopoiesis of lamellocytes. I took advantage of the gain-of-function phenotype of the Tl^{10b} mutation characterized by an activated cellular immune system, which induced the formation blood cell tumors. We screened the right arm of chromosome 3 for enhancers and suppressors of this mutation and uncovered *ird1*.
Finally in Article IV, we showed that the activity of the Toll signaling pathway in the fat body, the homolog of the liver, is necessary to activate the cellular immune system and induce lamellocyte hematopoiesis.

Keywords
Drosophila melanogaster, immunity, blood cells, hematopoiesis, flow cytometry, *in vivo* imaging, genetic screens, Tl^{10b}, fat body, Toll signaling

Language
English

ISBN
978-91-7601-317-5

ISSN
0346-6612-1741

Number of pages
52 + 4 papers