REGULATING RESILIENCE: THE PLASTICITY AND DIFFERENTIATION POTENTIAL OF *DROSOPHILA* HEMOCYTES

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The immune defense of *Drosophila melanogaster* relies on the cooperation of humoral and cell-mediated components. The cellular immune reactions are carried out by specialized immune cells, the hemocytes. The differentiation of immune cells begins in early embryonic stages: two mesodermal segments give rise to two independent hemocyte lineages. These lineages form the larval hematopoietic compartments: the circulation, the sessile tissue and the lymph gland.

The cellular arm of the *Drosophila* immune response comprises morphologically and functionally distinct hemocyte classes. Plasmatocytes are phagocytic cells, which are mainly responsible for engulfing invading microbes. Crystal cells contain crystallized proenzymes, which, upon induction, are released into the hemolymph and through toxic intermediers result in melanization. The lamellocytes appear upon immune induction and form capsules around large foreign particles, which include tumors and eggs of parasitic wasps. Our earlier studies revealed that efficient encapsulation and the subsequent melanization require the mobilization of every hemocyte compartment. Also, we recently discovered that a portion of phagocytic plasmatocytes is capable of transforming into encapsulating lamellocytes during this process.

Our goal was to further understand the plasticity of the hemocyte lineages in the *Drosophila* larva. To investigate this phenomenon, we used a combination of *in vivo* lineage tracing transgenes and our molecular marker panel.

We demonstrated that although plasmatocytes can differentiate into lamellocytes following immune induction, crystal cells (marked by *lozenge* lineage tracing) are unable to do so. However, the overexpression of certain activating factors by a lineage tracing transgene in the crystal cell lineage led to both lineage autonomous and non-lineage autonomous lamellocyte differentiation.

Our experiments revealed that the regulation of lamellocyte differentiation consists of at least two levels: an upstream, *non-cell autonomous* induction and a downstream (*cell autonomous*) response. Our results also suggest that the ability of hemocytes to transform into lamellocytes differs in the plasmatocytes and crystal cell lineage. We theorize that this is possibly due to the lack of certain upstream factors in the crystal cells, which is also underlined by our finding that circumventing these factors by activated forms of downstream elements triggers the differentiation of lamellocytes from this cell type as well.