TITLE: Studying the signaling and metabolic factors involved in hemocyte progenitor maintenance and differentiation in *melanogaster*

Abstract: One of the most intriguing questions in developmental and stem cell biology is how cells adopt their fate. With an aim to correlate the factors associated with cell fate specification, we performed an RNAi mediated knockdown based genetic screen.

For our studies, we employed the genetically tractable organism melanogaster as the model organism and chose hematopoiesis as the developmental process to study cell fate specification. larval hemocyte progenitors are the specific cell type on which this genetic screen was focused and their maintenance and differentiation were the read out of the genetic screen. The *hemocyte* progenitors found in larvae are akin to the vertebrate common myeloid progenitors (CMP). They are quiescent, have high levels of ROS, lack differentiation markers, are multipotent, and give rise to all blood lineages.

First part of the study focussed on the strategic details and outcomes of the genetic screen. Out of the various outcomes of the genetic screen, three major cohorts, a) metabolism cohort, b) cell adhesion cohort mediated by integrin signaling and c) Hippo signaling pathway were chosen for further in-depth analysis and characterization.

Second part of the study focussed on the detailed characterization and analysis of fatty acid metabolism as regulators of hemocyte progenitors.
It is intriguing to note that early instar progenitors when self-renewing have high glucose utilization whereas, glucose utilization in late quiescent and differentiating progenitors is very less, at the same time when we knock down fat metabolism components, their quiescence is compromised and differentiation is disrupted. This suggests at the possibility that there is a switch from glucose to fat metabolism when hemocyte progenitors move from self-renewal to quiescence and then to differentiation.

Next part of the study focussed on cell adhesion complex mediated control of cellular fate via regulating metabolism. Integrins control the mitochondrial function and biogenesis thus contributes to differentiation of the hemocyte progenitors. Integrin mediates the production of ROS, which has been shown to induce differentiation in hemocyte progenitors by instigating JNK-Foxo signaling cascade.

This study also points out the requirement of hippo signaling effector yorkie in hemocyte progenitor survival, proliferation and differentiation and the concomitant requirement of hippo signaling in formation of adult hematopoietic hubs.

Our findings not only find new players involved in blood progenitor maintenance but also uncover a new aspect of requirement of metabolism in progenitor quiescence and differentiation.