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Title: Insulin signaling dependent Glycolysis supports hemocyte progenitor maintenance in Drosophila

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Abstract:

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Drosophila hematopoiesis takes place through two distinct waves of hematopoiesis. The second wave or the definitive wave of hematopoiesis gives rise to mature hemocytes that populate the organism during the larval and the adult stages. These hemocytes emerge from hematopoietic progenitors housed in an organ called Lymph gland. The hematopoietic progenitors have recently been shown to require Fatty-Acid β Oxidation (FAO) to stay in quiescence and later, to differentiate. Interestingly, we found that these progenitors are initially proliferative and then turn quiescent. We asked whether the early and late progenitors have distinct metabolic landscapes, which in turn manifests as two different cellular states in these cells. We found that early progenitors exhibit extensive glycolysis in stark contrast to the late progenitors which rely majorly on FAO. Our results indicate that, the role of an extrinsic signal is essential for regulating glycolysis in the early stage in order to help these progenitors divide and subsides as these progenitors become quiescent. In conclusion, the work conducted describes a metabolic basis of how the organ generates the required stem cell/ progenitor pool in early stages in collaboration with a cellular signaling and later shuts this metabolic program in order to differentiate and become functional. The long-term goal of this project would be to find out how the cellular signaling affects the production of ROS and to specifically investigate whether it abrogates mitochondrial physiology or it enhances the activity of cellular ROS scavengers. It would be also interesting to investigate how this signaling is affected in various pathophysiological conditions in order to modulate hematopoiesis. During infection, progenitors have to differentiate precociously, it would be interesting to further note, whether a metabolic dynamism is required to elicit immune responses.

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