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Title: Fatty acid b-oxidation is required for the differentiation of larval hematopoietic progenitors in

drosophila

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Keywords: Hematopoietic organ

Fatty acid b-oxidation

Drosophila

Issue Date: 2020

Publisher: eLife Sciences Publications

Citation: eLife, 9, pp.1-35.

Abstract:

Cell-intrinsic and extrinsic signals regulate the state and fate of stem and progenitor cells. Recent advances in metabolomics illustrate that various metabolic pathways are also important in regulating stem cell fate. However, our understanding of the metabolic control of the state and fate of progenitor cells is in its infancy. Using Drosophila hematopoietic organ: lymph gland, we demonstrate that Fatty Acid Oxidation (FAO) is essential for the differentiation of blood cell progenitors. In the absence of FAO, the progenitors are unable to differentiate and exhibit altered histone acetylation. Interestingly, acetate supplementation rescues both histone acetylation and the differentiation defects. We further show that the CPT1/whd (withered), the rate-limiting enzyme of FAO, is transcriptionally regulated by Jun-Kinase (JNK), which has been previously implicated in progenitor differentiation. Our study thus reveals how the cellular signaling machinery integrates with the metabolic cue to facilitate the differentiation program.

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