The Hepatocyte-like Oenocyte of the Host, as a Central Hub for Systemic Lipid Metabolism, is Altered by Tumor Progression and Cachexia.
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1. Introduction

- According to the American Cancer Society, cancer continues to be the second leading cause of death in the US, after heart disease.
- Cancer is a complex and dynamic cellular mechanism that leads to the over-proliferation of cells within the body.
- Cachexia, or wasting syndrome, is defined as a general state of weakness caused by muscle and weight loss.
- This study focuses on the interaction between tumor and host metabolism, where the hepatocyte-like oenocyte serves as a central hub for systemic lipid metabolism, contributing to the unraveling of the mechanisms of organ wasting induced by tumors.
- Oenocytes are large, specialized cells found along the cuticle of insects that are involved in the metabolism of very long chain fatty acids (VLCFA), hormone synthesis, and detoxification processes.

Figure 1 Drosophila platforms to study cancer and its metabolism. (A), Corresponding tissues/organisms regarding their structures and functions between Drosophila and humans. (B), The GAL4/UAS system enables induction of genes of interest in target fly tissues.

2. Methods

- Cachexia was induced in adult female flies by transplanting Actin>NICD tumors. The flies were allowed to remain at room temperature for 8-12 hours following injection.
- Flies were then incubated at 29°C for 10-14 days before being dissected and stained.
- Four different genotypes of flies were injected with tumors in this study:
  - wild type (Bloomington Line: W1118)
  - PromE>GFP
  - PromE>GFP x UAS-mCherry-Atg8a (Bloomington Line: 37750)
  - PromE>GFP x UAS-Spin-BFP.
- Host flies were cultured at 25°C and allowed to mature to adulthood before being injected with the tumor.

3. References

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4. Results

I. Tumor presence causes cellular membrane expansion in the oenocyte.

A. GFP expressed in the cellular membrane shows cachexia host flies (right) exhibit a thicker oenocyte cellular membrane when compared to control flies (left).
B. Nuclear fragmentation is believed to be a sign of cellular death and/or malfunction.

II. Nuclear warping is not a signal of cell death.

A. Nuclear warping is believed to be a sign of cellular death and/or malfunction.

III. Cachexia leads to a decrease in lysosome and autophagy activity.

A. DAPI staining shows nuclear warping in the oenocyte cells of host flies.

IV. Cachexia requires an increase in the number and activity of mitochondria.

A. Mitotracker staining showed greater mitochondrial activity in cachexia tumor-host flies when compared to control flies.

5. Conclusion

- Cancer cachexia causes membrane expansion and an increase in mitochondrial activity, but a decrease in autophagy and lysosome activity.
- Earlier stages of cachexia may have increased lysosome and autophagy activity, but this study only looked at the later stages of the disease.
- Lipid metabolism is also a significant metabolic indicator in the oenocyte which should be studied further.
- We do know that cachexia causes organism-wide metabolic dysregulation.
- This study requires further research as cancer and cachexia are very dynamic processes.

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