Drosophila embryos spatially sort their nutrient stores to facilitate their utilization

Marcus D. Kilwein, Matthew R. Johnson, Jonathon M. Thomalla, Anthony P. Mahowald and Michael Welte

DOI: 10.1242/dev.201423

Editor: Irene Miguel-Aliaga

Review timeline

Original submission:	4 November 2022
Editorial decision:	10 January 2023
First revision received:	14 January 2023
Accepted:	23 January 2023

Original submission

First decision letter

MS ID#: DEVELOP/2022/201423

MS TITLE: Drosophila embryos spatially sort their nutrient stores to facilitate their utilization

AUTHORS: Marcus Daniel Kilwein, Matthew R Johnson, Jonathon M Thomalla, Anthony P Mahowald, and Michael Welte

I have now received all the referees reports on the above manuscript, and have reached a decision. The referees' comments are appended below, or you can access them online: please go to BenchPress and click on the 'Manuscripts with Decisions' queue in the Author Area.

The overall evaluation is positive and we would like to publish your manuscript in Development, but I would like to kindly request that you incorporate the reference suggested by reviewer 2 in your revised manuscript, as well as providing a response to the comment regarding LD rings raised by reviewer 1. I will not send the manuscript back to the reviewers, but feel nonetheless that this comment should be addressed in your revised discussion of this experiment, even if no new experiments are required to do so.

Reviewer 1

Advance summary and potential significance to field

I agree with the comment that establishing the localization pattern of nutrient bodies during early embryogenesis is essential for any future follow-up work and thus an important contribution to understanding development.

Comments for the author

However, in my view, this manuscript by itself is still preliminary and insufficient conceptual advance to be published in Development.

I do not agree with the response related to Figures 5A-B. I appreciate that there are LD rings not associated with GGs as indicated by the arrow and this is likely YVs. However, there are several LD rings surround GGs. One can interpret this image as LDs equally associate with YVs and GGs.

Reviewer 2

Advance summary and potential significance to field

The submitted manuscript by Kilwein and colleagues examine the spatial distribution and movement of macromolecular energy stores during embryogenesis of the fruit fly Drosophila melanogaster. Their approach although largely descriptive, represents an important advance in our understanding of how embryonic metabolism is regulated during the course of development. To place their results in context, most previous studies used bulk biochemical methods to determine how the steady state pools of triglycerides, glycogen and small polar molecules change during the course of embryonic development. Kilwein et al reveal that these previously described biochemical studies overlooked dynamic changes in the spatial distribution of lipid droplets, glycogen granules, and yolk vesicles. In this regard, their observation that lipid droplets are physically separated from glycogen granules and yolk vesicles should of particular interest to anyone studying the intersection of metabolism and developmental biology, as it hints at unknown phenomena - that embryonic development might be precisely coordinated with movement of macromolecular energy stores. Overall, I imagine this manuscript represent the foundation of a new line of inquiry for the field of developmental metabolism.

Comments for the author

I found the paper a joy to read, and the experimental analysis was well executed. My only minor suggestion would be that the authors add a small discussion section commenting any correlations between changes in embryonic amino acid abundance and yolk protein distribution. While these changes have been described in a few modern publications, the original observations can be found in the following manuscript:

Crone-Gloor, U., 1959 Quantitative untersuchung der Freien Aminosäuren und Polypeptide während der Embryonalentwicklung von Drosophila melanogaster. J. Insect Physiol. 3: 50–56.

First revision

Author response to reviewers' comments

Response to Reviewer 1:

>I agree with the comment that establishing the localization pattern of nutrient bodies during >early embryogenesis is essential for any future follow-up work and thus an important >contribution to understanding development.

We thank the reviewer for feedback on these subgenres of nutrient utilization and spatial organization during development.

>However, in my view, this manuscript by itself is still preliminary and insufficient conceptual >advance to be published in Development.

We again thank the reviewer for the sincere feedback. We believe that this work is at the forefront of a new area of study; that leaves this manuscript without sister studies that can be cited as part of a broader conceptual framework. Nevertheless, we are convinced that understanding how nutrients are spatially sorted is an overlooked, yet critical aspect of developmental metabolism as it sets the stage for how nutrients are utilized during development and that inquiries into the spatial organization of nutrients will be critical for assembling a complete conceptual framework of embryogenesis.

>I do not agree with the response related to Figures 5A-B. I appreciate that there are LD rings >not associated with GGs as indicated by the arrow and this is likely YVs. However, there are >several LD rings surround GGs. One can interpret this image as LDs equally associate with >YVs and GGs.

The crux of our argument on the data in 5A-B is that the *mauve* mutants do not display the dimpled GGs found in the *Jabba* nulls where LDs are physically embedded in GGs and thus necessarily have to move with GGs during nutrient sorting. As the reviewer mentioned, *mauve* mutants do display rings around YVs, unlike *Jabba* nulls. We have updated the text to highlight these points.

Response to Reviewer 2:

>The submitted manuscript by Kilwein and colleagues examine the spatial distribution and >movement of macromolecular energy stores during embryogenesis of the fruit fly Drosophila >melanogaster. Their approach, although largely descriptive, represents an important advance >in our understanding of how embryonic metabolism is regulated during the course of >development. To place their results in context, most previous studies used bulk biochemical >methods to determine how the steady state pools of triglycerides, glycogen, and small polar >molecules change during the course of embryonic development. Kilwein et al reveal that these >previously described biochemical studies overlooked dynamic changes in the spatial >distribution of lipid droplets, glycogen granules, and yolk vesicles. In this regard, their >observation that lipid droplets are physically separated from glycogen granules and yolk >vesicles should of particular interest to anyone studying the intersection of metabolism and >developmental biology, as it hints at unknown phenomena – that embryonic development >might be precisely coordinated with movement of macromolecular energy stores. Overall, I >imagine this manuscript represent the foundation of a new line of inquiry for the field of >developmental metabolism.

We are very appreciative of the enthusiastic and insightful review of our work

>I found the paper a joy to read, and the experimental analysis was well executed. My only >minor suggestion would be that the authors add a small discussion section commenting any >correlations between changes in embryonic amino acid abundance and yolk protein >distribution. While these changes have been described in a few modern publications, the >original observations can be found in the following manuscript:

We sincerely appreciate this feedback. We have taken the suggestion and added the reference and a brief discussion on amino acids and YV spatial organization during development. It is our hope that there will be further investigations into the mobilization of YV-stored amino acids as they are undoubtedly contributing to overall embryonic metabolism.

Second decision letter

MS ID#: DEVELOP/2022/201423

MS TITLE: Drosophila embryos spatially sort their nutrient stores to facilitate their utilization

AUTHORS: Marcus Daniel Kilwein, Matthew R Johnson, Jonathon M Thomalla, Anthony P Mahowald, and Michael Welte
ARTICLE TYPE: Research Article

I am happy to tell you that your manuscript has been accepted for publication in Development, pending our standard ethics checks.