Understanding molecular motors regulation

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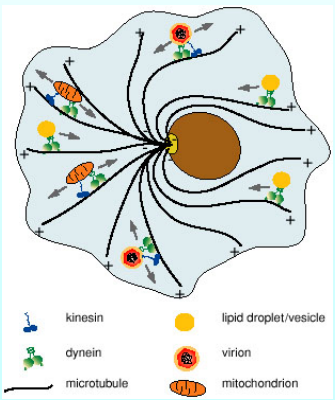
Background

Microtubule-based transport



Microtubules (MTs) are polar tracks on which vesicles and organelles are transported. Molecular Motors move cargos along microtubules and are responsible for their correct location within the cell. How such transport is regulated remains poorly understood. Nonetheless, understanding regulation of transport is extremely important to clarify diseases where impaired transport is observed, such as Alzheimer's and other neurodegenerative conditions, and epidemic diseases, such as obesity and diabetes, where intracellular transport has been associated to metabolism regulation.

Many cargos move bi-directionally

The cell controls the net transport of cargos by coordinating opposite polarity motors: when the plus-end motors are active, the minus-end motors are inactive, and viceversa. Accessory proteins play a role in mediating this coordination.

Big question

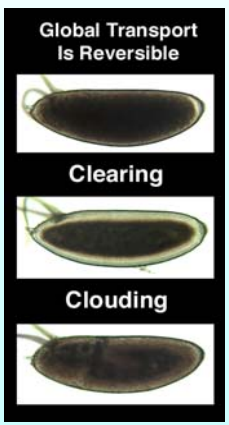
Which proteins are relevant for motors coordination?

So far, many aspects of motors regulation have been difficult to study but the Drosophila lipid droplets system is ideal to address the challenge

Experimental procedures

Model System

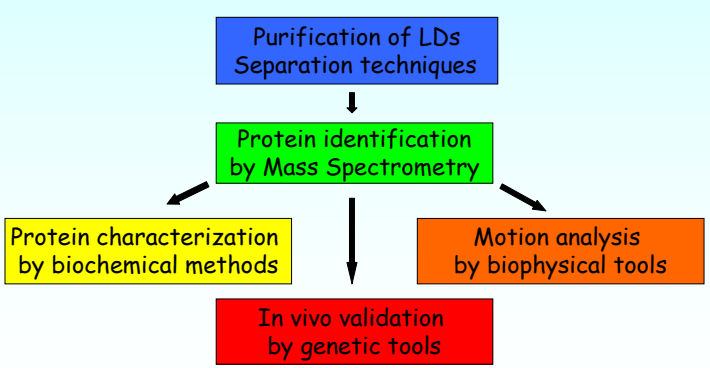
Lipid droplets in Drosophila embryos



Lipid droplets are blobs of fat coated by associated proteins. They move bi-directionally along MTs and their distribution change twice during early stages of development resulting in clearing and clouding states.
Understanding regulation of droplets' motion will increase our understanding of other bi-directionally moving cargos and will also clarify a likely link between droplet motion and metabolism.

Drosophila lipid droplets features allow a combination of different procedures to investigate droplet motion

- High index of refraction: to quantify and analyze motion by biophysical tools (optical tweezer and particle tracking)
- Buoyant properties: to isolate LDs and analyze proteins by biochemical methods
- Genetic manipulation: Drosophila is an ideal organism to modify protein levels by genetic approaches



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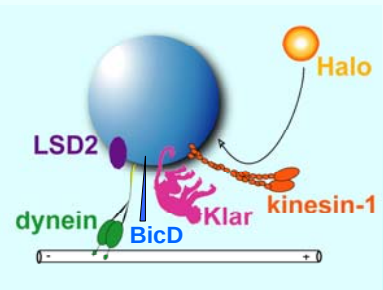
Results

Many proteins contribute to the regulation of lipid droplet motion



The importance of a few proteins, such as dynein, Klar and Halo, in the regulation of lipid droplet transport was well established. Recently, other players were added to the list of primary regulators, i.e. LSD2[1], Kinesin-1[2], BicD[3] by using this combination of multidisciplinary approaches.

In addition, our proteomic study[4] revealed that lipid droplets sequester large amount of histone proteins showing a new aspect of the biology of these organelle related to their function as protein sequestration sites.

Summary

- Our proteomic study found that the proteins present on *Drosophila* droplets are largely the same as those found on mammalian droplets, confirming the utility of using the *Drosophila* system to better understand the medically relevant processes of droplet transport and regulation of droplets metabolism in mammals.
- The droplet-associated protein, LSD2 regulates both droplet transport and lipid metabolism, supporting the connection between the two processes.
- Our proteomic approach have laid the groundwork for investigating coordination/regulation of motors at a molecular level

References
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