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# MONDAY SEMINAR

**Monday, October 15th, 2018 – 12h15**
Department of Physiology, Bugnon 7, 1005 Lausanne
Seminar room, 6th floor

## Molecular Mechanisms of Lipid Droplet Biogenesis

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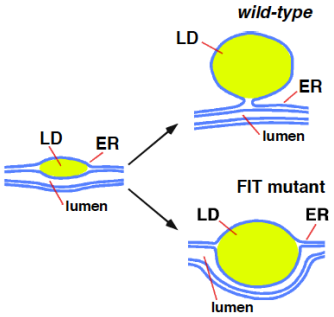
**Host** : Prof. Christian Widmann




- A conserved family of proteins called fat storage-inducing transmembrane (FIT) proteins is necessary for proper budding of LDs from the ER
- Remarkably, deletion of FIT proteins in higher eukaryotes (worm, flies, mice) is lethal
- Lipid droplet emergence is controlled by ER phospholipid intrinsic curvature

Lipid droplets (LDs) are found in all cells and play critical roles in lipid metabolism. De novo LD biogenesis occurs in the endoplasmic reticulum (ER) but is not well understood. We imaged early stages of LD biogenesis using electron microscopy and found that nascent LDs form lens-like structures that are in the ER membrane. We found that a conserved family of proteins, fat storage-inducing transmembrane (FIT) proteins, is required for proper budding of LDs from the ER. Elimination or reduction of FIT proteins in yeast and higher eukaryotes causes LDs to remain in the ER membrane. Deletion of the single FIT protein in *Caenorhabditis elegans* is lethal, suggesting that LD budding is an essential process in this organism. Our findings indicated that FIT proteins are necessary to promote budding of nascent LDs from the ER. Theoretical modeling indicated that the intrinsic molecular curvatures of ER phospholipids can determine whether LDs remain embedded in or emerge from the ER; lipids with negative intrinsic curvature such as diacylglycerol (DAG) and phosphatidylethanolamine favor LD embedding, while those with positive intrinsic curvature, like lysolipids, support LD emergence. This prediction was verified by altering the lipid composition of the ER in *S. cerevisiae* using mutants and the addition of exogenous lipids. We found that FIT2 homologs become enriched at sites of LD generation when biogenesis is induced. DAG accumulates at sites of LD biogenesis, and FIT2 proteins may promote LD emergence from the ER by reducing DAG levels at these sites. Altogether, our findings suggest that cells regulate LD integration in the ER by modulating ER lipid composition, particularly at sites of LD biogenesis and that FIT2 proteins may play a central role in this process

*References:*
***Choudhary et al., 2018, Current Biology;*** *Architecture of Lipid droplets in the ER is determined by phospholipid intrinsic curvature*
***Choudhary et al., 2015, Journal of Cell Biology;*** *A conserved family of proteins facilitates nascent lipid droplet budding from the ER*