Principles of organelle spatial organization and interactions

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Organelles compartmentalize biochemical reactions and allow controlled distribution of molecules within eukaryotic cells. Maintaining organelle identity and interorganelle communication requires sophisticated machinery. Newest advances in the field were discussed in the Minisymposium on the "Principles of Organelle Spatial Organization and Interactions."

Jonathon Nixon-Abell from CIMR (Cambridge, UK) discussed the dynamics of membrane proteins in the endoplasmic reticulum (ER) using ultrafast single molecule live-cell imaging. Focused on the protein VAP, he showed that disease-causing mutations sample larger ER regions perturbing the formation of ER–mitochondria contact sites. Although the functional significance is not yet clear, restricted localization appears to be a general feature of ER membrane proteins, especially when they engage in interorganelle contact.

Ya-Cheng Liao from the Lippincott-Schwartz lab showed that Annexin A11 (ANXA11) contributes to contacts between membrane-less RNA granules and lysosomes (Liao *et al.*, 2019). She showed that in axons RNA granules traffic with lysosomes along microtubules, a process that requires ANXA11. Mutations in ANXA11 that cause amyotrophic lateral sclerosis disrupted the interaction with lysosomes and rendered RNA granules immobile. Future work will address which particular cellular functions are perturbed by the defect in RNA granule trafficking.

Martin Jonikas from Princeton University presented proteomic and microscopic analysis of the pyrenoid, a membrane-less organelle in chloroplasts of *Chlamydomonas reinhardtii* (Mackinder *et al.*, 2017). The pyrenoid matrix and peripheral starch sheets were visualized by electron microscopy. Highly curved membrane tubules of the associated thylakoid membranes traverse the pyrenoid layers and interact tightly with its components. Jonikas focused on the function of EPYC1 and SAGE in organizing the pyrenoid and speculated on translating these insights into higher plants to improve crop yield.

Roxan Stephenson from the Welte lab discussed the significance of the lipid droplet (LD) localization of H2A, H2Av, and H2B histones. LD-localized histones rapidly exchange on the LD surface. Loss of LD-localized histones did not affect DNA replication or chromatin biogenesis. Instead, LDs appear to regulate the histone nuclear import by buffering their free concentration in the cytoplasm, which is critical for embryonic development.

Robin Klemm from the University of Zurich discussed how the mitochondrial protein MIGA2 acts at the interface between mitochondria, lipid droplets, and the ER in white adipocytes (Freyre *et al.*, 2019). MIGA2 promotes the synthesis of fatty acids and increases cellular triacylglycerols. Klemm's data indicated that enhanced lipid biosynthesis is part of a positive feedback to the transcriptional program driving adipogenesis. Inhibiting de novo lipogenesis perturbed several aspects of adipocyte function, possibly explaining fat loss observed in the MIGA2 knockout mouse.

Mike Henne from UT Southwestern showed evidence for at least two distinct LD populations in the fly fat body (Ugrankar *et al.*, 2019): a centrally located LD population formed by de novo lipogenesis requiring functional fatty acid synthase and peripheral LDs dependent on fatty acids from the hemolymph and requiring sorting nexins and cortical actin. How the two LD populations are functionally connected and how they relate to the LD populations previously found in yeast cells remains to be investigated.

Yifan Ge from Luke Chao's lab at Massachusetts General Hospital, Boston, focused on the inner mitochondrial membrane-fusing machinery. A dynamin-like GTPase called Opa1 exists in a long and a short isoform. In contrast to previous models Ge showed in in vitro experiments that the short isoform is necessary for productive fusion events controlling the formation and expansion of the fusion pore (Ge *et al.*, 2020). The correct ratio between the two isoforms is a prerequisite for efficient fusion kinetics and is likely relevant for well-organized fusion in vivo.

Jonathan Friedman from UT Southwestern talked about the role of MICOS, a megadalton protein complex that organizes mitochondrial cristae. Jonathan's results suggest a function of subunits of the translocase of the outer mitochondrial membrane (TOM) complex in MICOS organization. Mic60, a subunit required for proper MICOS localization, is present at ER–mitochondria contacts, suggesting that coordinated assembly of contacts sites on both sides of the mitochondrial outer membrane is important to cristae biogenesis.

Pedro Carvalho of the University of Oxford discussed a protein quality control system operating in a specialized ER domain, the inner nuclear membrane (INM) and that is defined by the Asi ubiquitin ligase complex. Carvalho showed that INM quality

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control prevents accumulation of over-stoichiometric subunits of ER membrane complexes by promoting their degradation (Natarajan *et al*., 2019). It was proposed that restriction of quality control of unassembled subunits to the INM protects complex subunits from premature degradation in the ER.

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