

## **Lamellar bodies: the Good, the Bad and the Ugly**

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Lamellar bodies (LBs) are membrane surrounded, specialized lipid storage and secretory organelles of diverse cells with variable size (0.1 – 2.5  $\mu\text{m}$ ) and unique chemical composition that reflects their function.

Essential formation of LBs occurs in many physiological processes (“the Good”). The LBs of type-II pneumocytes (surfactant bodies) have been investigated most extensively, as they nearly exclusively consist of dipalmitoyl-phosphatidylcholine for alveolar surfactant to prevent lung collapse. Epidermal LBs (Odland bodies), containing cholesterol, ceramides, glucosylceramides, complex sphingolipids and traces of glycerophospholipids, play a key role in delivering of polar lipids from keratinocytes (mortar) of stratum granulosum into the extracellular matrix (bricks) of stratum corneum, and therefore in formation and maintenance of the cutaneous permeability barrier protecting against transepidermal water loss.

Pathological accumulation (“the Bad”) of endolysosomal LBs can be observed in several cells in drug-induced phospholipidosis, and in congenital or acquired deficiencies of endolysosomal lipid degrading enzymes or their regulatory proteins. Characteristic hallmarks for these errors are (1) loss of the acidic luminal endolysosomal pH, parallel with (2) accumulation of bis(monoacyl)glycerophosphate, the anionic signature polyglycerophosphate of the acidic compartment, together with (3) impaired autophagy and/or lipophagy.

Lamellar bodies are also “Ugly” as they were largely ignored and viewed as non-functional “cellular dust” or “fixation artifacts” by early investigators, since most lipids of LBs are poorly preserved by conventional fixatives and washed out during the embedding procedure, leaving translucent, empty vacuoles, or shrunken, amorphous structures in light microscopic sections. New insights, however, suggest that LBs are far more than trash, and recently many specific lipid-interacting and -converting proteins have been identified, contributing to regulated formation and metabolism of LBs.

The presentation will provide an overview of LBs, their composition, intracellular trafficking and function in different cells. In addition, the contribution of multi-omics (e.g. lipidomics, proteomics, transcriptomics) and microscopic methods in the precise characterization of LBs will be discussed.

Representative electron micrographs of lamellar bodies (LBs) in different cells: (A) A human alveolar macrophage filled with different ingested lipid-rich materials. Inset: A fingerprint-like LB within the macrophage. (B) Accumulation of LBs in ACTH-stimulated rat adrenocortical cells in response to cycloheximide treatment. The LBs, in intimate contact with the outer phospholipid layer of lipid droplets, as well as membranes of endoplasmic reticulum and mitochondria, are indicated with red arrows. The green arrow indicates a profile of damaged endoplasmic reticulum without multilamellar whorls.

