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Leukocyte lipid bodies regulation and function: Contribution to allergy and host defense

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Abstract

Lipid bodies are lipid-rich organelles found in the cytoplasm of a variety of cells, including leukocytes. Lipid body morphology, its ability to interact with other organelles and its functions are dictated by its lipid arrangement, as well as its protein composition. Both may vary according to the cell type and with the specific lipid body biogenic stimulatory pathways. Nascent lipid bodies, which are formed in vivo in the course of a variety of immunopathological conditions, are sites of enzyme localization, eicosanoid production, as well as, sites for cytokine storage in inflammatory leukocytes, suggesting that lipid bodies function as inducible intracellular platforms for spatial segregation and organization of signaling leading to inflammatory mediator secretion during inflammation. The emerging role of lipid bodies as inflammatory organelles raises lipid body status to critical regulators of different inflammatory diseases, key markers of leukocyte activation and attractive targets for novel anti-inflammatory therapies.

Keywords: Lipid droplets; Innate immunity; Acquired immunity; Signaling; Eicosanoids; Leukocyte

Contents

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1. Introduction

Cytoplasmic lipid bodies are lipid-rich organelles present in virtually all organisms, including plants, yeast, prokaryotes and both non-mammalian and mammalian animal cells. Lipid bodies are comprised of an outer monolayer of phospholipids, which have a unique fatty acid composition, a neutral lipid-rich core, and variable protein composition. Although in the past the presence of lipid bodies in cells has been largely associated with lipid storage and transport, it has become apparent that lipid bodies are dynamic and functionally active organelles.

Here we will review several aspects of lipid body structure and function: their structural features, intracellular interaction abilities, highly regulated biogenesis, lipid and protein composition and relationship with immunopathologies. All these characteristics vary according to the leukocyte type, activation state and inflammatory environment. Major recent advances have established that leukocyte lipid bodies are specialized, inducible intracellular domains that function as signaling platforms in activated leukocytes (i) to regulate lipid metabolism and trafficking; (ii) to control the synthesis and secretion of inflammatory mediators; (iii) to respond to infections; (iv) to orchestrate allergic inflammation; and therefore, appears as attractive target candidate for therapeutic intervention of both innate and acquired immunopathologies.

1.1. Lipid body morphology in resting and activated cells

The organization of lipids within distinct cytoplasmic sites is a feature of many (if not all) cell types (Murphy, 2001; Martin & Parton, 2005). Lipid bodies are specific microenvironments distributed in the cytoplasm as roughly spherical organelles lacking a delimiting classical bilayer membrane (Dvorak et al., 1983; Weller et al., 1991a; Murphy, 2001; Tauchi-Sato et al., 2002). Because lipid bodies can be destroyed by drying or fixation and staining with alcohol-based reagents, there are consequently some methodological limitations to their study. For instance, May-Grunwald-Giemsa staining causes dissolution of lipid bodies (Fig. 1A) (Pacheco et al., 2002). Using appropriate fixation with paraformaldehyde (DiDonato & Brasaemle, 2003) and staining with osmium (Fig. 1B) (Weller et al., 1991b; Bozza et al., 1996b), Nile Red (Fig. 1C) (Fowler & Greenspan, 1985; Fukumoto & Fujimoto, 2002; Jackson et al., 2004) or fluorescent hydrophobic lipids (DiDonato & Brasaemle, 2003) (Fig. 1D), lipid bodies can be identified readily in the cytoplasm.

At the ultrastructural level, lipid bodies appear as variably osmiophilic organelles composed of amorphous material (Dvorak, 1991). Moreover, they often display either a complete or partial investiture with more dense material at their periphery (Dvorak, 1991) (Fig. 2A). This shell varies in thickness and does not display the trilaminar structure of true membranes (Dvorak, 1991) (Fig. 2A).

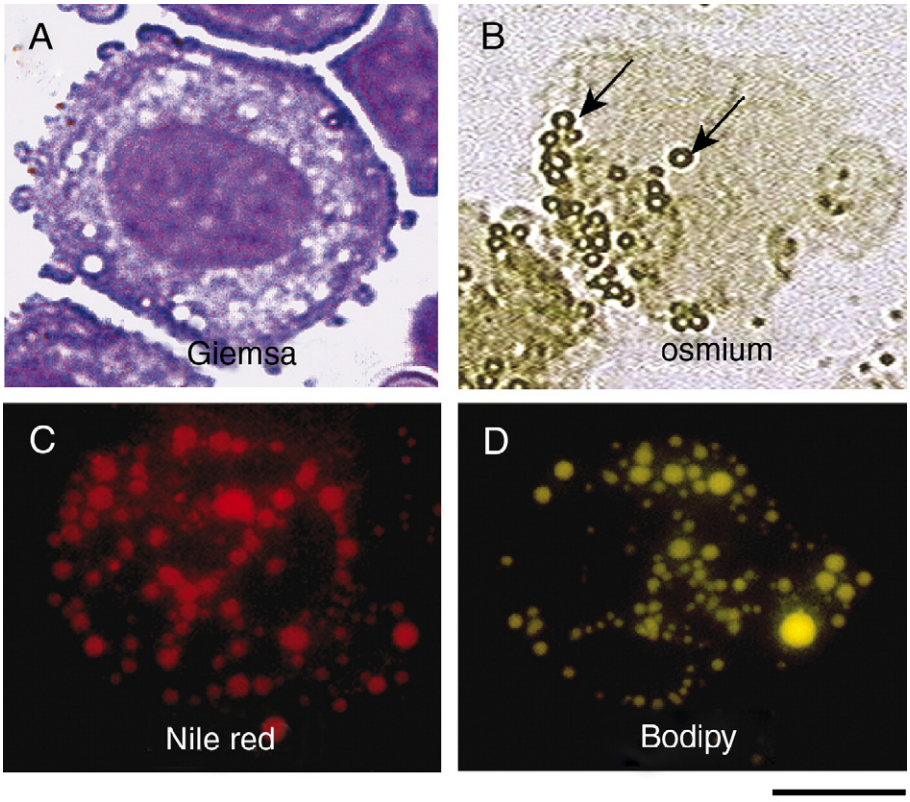

Fig. 1. Lipid bodies within macrophages imaged by bright-field (**A**, **B**) or fluorescence (**C**, **D**) microscopy after staining with May-Grunwald-Giemsa (**A**), osmium (**B**), Nile red (**C**) or BODIPY™ (**D**). Lipid bodies appear as spherical organelles that are blank unfilled cytoplasm spaces (**A**), dark rings (**B**) or fluorescent structures (**C**, **D**) distributed throughout the cytoplasm. Macrophages were activated by in vivo *M. bovis* BCG infection as described (D'Avila et al., 2006). Arrow=lipid body. Scale bar, 6 μm.