Mechanisms and Functions of Lipid Droplets in Cell Signaling, Inflammation and Cancer

Patricia T. Bozza

Immunopharmacology Laboratory, Instituto Oswaldo Cruz, FIOCRUZ, Rio de Janeiro, RJ – Brazil.

Lipid droplet accumulation within leukocytes and other cells is a common feature in both clinical and experimental infectious, neoplastic and other inflammatory conditions. Our findings demonstrate that lipid droplet biogenesis is a highly regulated process that is cell and stimuli specific, and culminate in the compartmentalization of a specific set of proteins and lipids, that place lipid droplets as inducible organelles with roles in cell signaling, regulation of lipid metabolism and control of the synthesis and secretion of inflammatory mediators. Pertinent to the roles of lipid droplets in inflammation and cell signaling, enzymes involved in eicosanoid synthesis are localized at lipid droplets and lipid droplets are sites for eicosanoid generation in cells during pathogen-infection and cancer. Moreover, inhibition of lipid droplet formation has roles in the modulation of host response to infection and in the inhibition of PGE$_2$ synthesis in colon cancer cells with implications to cancer cell growth. Protein kinases including PI3K, ERK, JNK, mTOR and p70S6k localize at lipid droplets in leukocytes and epithelial cells during inflammatory or neoplastic conditions. Moreover, lipid droplets are regulated during cell cycle, and this regulation is altered in transformed cells. Collectively, lipid droplets are emerging as dynamic and functional active organelles, critical regulators of different inflammatory diseases, and attractive targets for novel anti-inflammatory therapies.

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