The Eicosanoid Research Division

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Keywords
Cytokines. Lipid metabolism. Lipid signalling. Metabolic syndrome. Phospholipases.

State of the art
Numerous signal transduction processes involve lipids as signalling molecules. Many of these molecules are generated by phospholipases, enzymes that cleave ester bonds within phospholipids, and our aim is to get a better understanding of their regulation, particularly in relation to inflammation and obesity. At the Eicosanoid Research Division we combine a wide range of chemical, biochemical, biophysical, and molecular cell biology techniques to study relevant problems pathophysiologically.

Main lines of research
Signalling pathways involved in eicosanoid biosynthesis in obesity and inflammation.
Biosynthesis and degradation of lipid droplets.
Lipid metabolite analysis by mass spectrometry (lipidomics & metabolipidomics).
Spatiotemporal regulation of phospholipid-metabolic enzymes, as studied by advanced microscopy techniques.

Areas of expertise
Lipid chemistry and biochemistry: separation, identification and quantification of glycerolipids and sphingolipids by liquid chromatography/mass spectrometry.
Molecular cell biology: the use of fluorescent tagged proteins related to lipid metabolism for subcellular localization studies utilizing confocal microscopy.
Enzymology and pharmacology: manipulation of the activity of lipid signalling enzymes both *in vivo* and *in vitro* by utilizing structurally defined compounds.

Achievements in 2009
The discovery of key regulatory roles for c-jun N-terminal kinases (JNK) in lipid droplet formation and inflammatory signalling in human white cells.
The discovery of a novel cross-talk mechanism of regulation of lipid mediator biosynthesis during inflammatory signalling.

Future challenges
To establish pathway-oriented profiling of lipid mediators in adipose tissue and circulating white blood cells.
To characterize the role of lipins (magnesium-dependent phosphatidate phosphatases) in regulating the formation and/or degradation of lipid droplets.
To study the putative signalling roles of acyltransferases and their relevance to glycerolipid metabolism.

Publications
Original article
Gubern A, Barceló-Torns M, Barneda D, López JM, Masgrau R, Picatoste F, Chalfant CE, Balsinde J, Balboa MA, Claro E. JNK and ceramide kinase govern the biogenesis of lipid droplets through activation of group IVA phospholipase A2. *J Biol Chem*, **284**, 32359-32369 (2009)

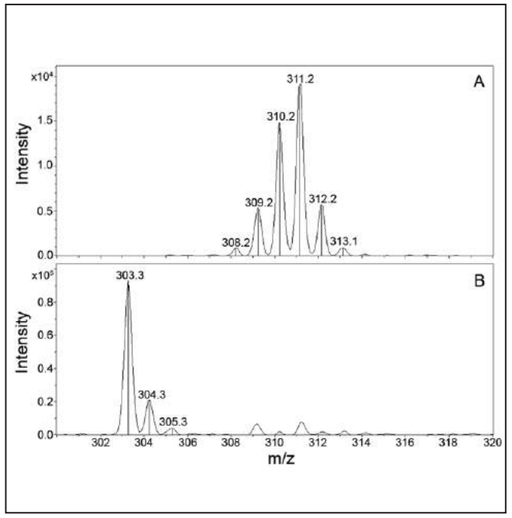
Gubern A, Barceló-Torns M, Casas J, Barneda D, Masgrau R, Picatoste F, Balsinde J, Balboa MA, Claro E. Lipid droplet biogenesis induced by stress involves triacylglycerol synthesis that depends on group VIA phospholipase A2. *J Biol Chem*, **284**, 5697-5708 (2009)

Ruipérez V, Astudillo AM, Balboa MA, Balsinde J. Coordinate regulation of TLR-mediated arachidonic acid mobilization in macrophages by group IVA and group V phospholipase A2s. *J Immunol*, **182**, 3877-3883 (2009)

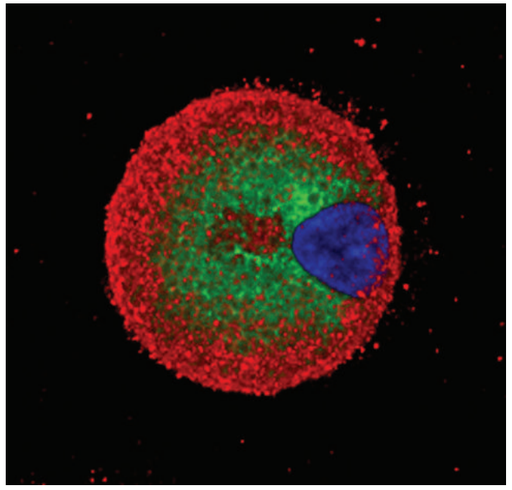
Review
Pérez-Chacón G, Astudillo AM, Balgoma D, Balboa MA, Balsinde J. Control of free arachidonic acid levels by phospholipases A2 and lysophospholipid acyltransferases. *Biochim Biophys Acta*, **1791**, 1103-1113 (2009)

Book chapter
Balsinde J, Dennis EA. «Role of phospholipase A2 forms in arachidonic acid mobilization and eicosanoid generation», in Handbook of Cell Signaling, 2nd Edition. *Bradshaw RA and Dennis EA eds*, 1213-1218 (2009)

Research networks and grants
CIBERDEM project
Adult adipose tissue-derived progenitor cells: influence



Detection of free arachidonic acid by mass-spectrometry. A) Deuterated arachidonic acid (from commercial sources); B, naturally-ocurring arachidonic acid.



Human macrophages transfected with a lipin1a-GFP construct (green fluorescence), immunostained with an antibody against adipophilin (red fluorescence), and labelled with DAPI (nuclear blue fluorescence) as analysed by confocal microscopy. The image shows a tridimensional reconstruction of fluorescence obtained from 20 different stacks from a single cell. Lipid droplets that are more distal in the cell have more prominent staining with adipophilin, while internal lipid droplets have a stronger expression of lipin1a.

of the clinical phenotype and adipose depot origin in their biological properties
STEMOB: 2009-2010
Principal Investigators: Jesús Balsinde, Anna Maria Gómez Foix, Margarita Lorenzo, Eduard Montanya, Rafael Simó, Manuel Vázquez-Carrera, Joan J Vendrell, Antonio Zorzano
Project coordinator: Joan J Vendrell

National project
Una aproximación de lipidómica al estudio de la respuesta inmune innata: mecanismos que gobiernan la disponibilidad y metabolismo oxidativo de ácido araquidónico en macrófagos
Ministerio de Ciencia e Innovación, BFU2007-67154: 2007-2010
Principal Investigator: Jesús Balsinde

Inflamación y obesidad: dos procesos metabólicos regulados por una misma enzima; la fosfatasa de ácido fosfatídico dependiente de magnesio
Ministerio de Ciencia e Innovación, SAF2007-60055: 2007-2010
Principal Investigator: María A Balboa

Autonomous Community project
Role of Calcium-independent Phospholipase A_2 in Oxidative Stress
Junta de Castilla y León, CSI09A08: 2008-2010
Principal Investigator: Jesús Balsinde ■