LESCH NYHAN DISEASE
JOSE MANUAL LÓPEZ BLANCO

PROFILE

José M. López obtained his PhD in Biological Sciences in 1994 at Hospital Clinic i Provincial de Barcelona, Facultat de Medicina, Universitat de Barcelona. Then, he was a Postdoctoral Research Associate at University of California, Irvine, USA, in the laboratory of Dr. Timothy F. Osborne, working in the transcriptional control of cholesterol and fatty acid biosynthesis. Coming back to Spain he worked as Postdoctoral Research Associate at Departament de Ciències Fisiològiques Humanes i de la Nutrició, Universitat de Barcelona, in the laboratory of Dr. Diego Haro; as Associate Professor at Departament de Ciències Fisiològiques II, Universitat de Barcelona in the laboratory of Dr. Joan Gil investigating cell death mechanisms for the treatment of Chronic Lymphocytic Leukemia; and as Postdoctoral Researcher Associate at Centro de Regulación Genómica (CRG), in the laboratory of Raúl Mendez, where he studied the mechanisms of translational control mediated by cytoplasmic polyadenylation. In 2004, he obtained a "Ramón y Cajal" contract at Institut de Neurociències, Universitat Autònoma de Barcelona, as a Group Leader. From 2011 he is Assistant Professor at Departament de Bioquímica i Biología Molecular, Universitat Autònoma de Barcelona, where he is teaching in the Medicine and Physiotherapy Degrees.

RESEARCH

RESEARCH INTERESTS

We are interested in how cell metabolism, signalling pathways, and gene expression are rewired in pathological conditions such as Lesch-Nyhan disease, a metabolic illness with severe neurological manifestations, or in cells submitted to hyperosmotic shock, a common stress that cells have faced during millions of years since their emergence.

STRATEGIC OBJECTIVES

We study the cellular abnormalities in Lesch-Nyhan disease and the potential treatments to revert these alterations. We also aim to understand the mechanisms that regulate osmostress-induced apoptosis and meiotic progression, and the role of stress protein kinases in these processes.

MAIN RESEARCH LINES

1) Purine nucleotides and cellular alterations in Lesch-Nyhan disease

Lesch-Nyhan disease is an illness with severe neurological manifestations, including dystonia, spasticity, cognitive deficit, and self-injurious behavior. The illness is caused by a deficiency in the purine savage enzyme hypoxanthine-guanine phosphoribosyltransferase (HGprt). How a simple alteration in the purine metabolism produces dramatic effects in human behaviour is still a mystery. HGprt deficiency is associated with a relatively selective dysfunction of brain dopamine systems. Different hypotheses have been suggested, some of them claiming for purine abnormalities and/or the accumulation of a toxic metabolite in the brain. We propose that ATP depletion and ZMP accumulation can induce cellular alterations accounting for brain dysfunction. We are investigating the cellular changes induced by HGprt deficiency and how to revert these alterations.

2) Role of stress protein kinases in cell death and meiosis

The aim of this project is to determine the role of the stress protein kinases AMPK, JNK and p38 during oocyte death induced by hyperosmotic shock and during meiotic

progression induced by progesterone. We use Xenopus oocytes as a model system, which have great advantages for biochemical manipulation.

LAB FEATURED PUBLICATIONS:

López JM, Outtrim EL, Fu R, Sutcliffe DJ, Torres RJ, Jinnah HA. *Physiological levels of folic acid reveal purine alterations in Lesch-Nyhan disease.* Proc Natl Acad Sci U S A. 117: 12071-12079, 2020.

Yue J, López JM. *Understanding MAPK Signaling Pathways in Apoptosis*. Int J Mol Sci. 21: 2346, 2020.

Yue J, López JM. *JNK does not regulate meiotic progression in Xenopus oocytes: The strange case of pJNK and pERK.* Dev Biol. 416: 42-51, 2016.

Yue J, Ben Messaoud N, López JM. *Hyperosmotic Shock Engages Two Positive Feedback Loops through Caspase-3-dependent Proteolysis of JNK1-2 and Bid.* J Biol Chem. 290: 30375-89, 2015.

Ben Messaoud N, Katzarova I, López JM. *Basic Properties of the p38 Signaling Pathway in Response to Hyperosmotic Shock.* PLoS One. doi: 10.1371/journal.pone.0135249, 2015.

Ben Messaoud N, Yue J, Valent D, Katzarova I, López JM. *Osmostress-induced apoptosis in Xenopus oocytes: role of stress protein kinases, calpains and Smac/DIABLO*. PLoS One. doi: 10.1371/journal.pone.0124482, 2015.

López JM.*Digital kinases: A cell model for sensing, integrating and making choices.* Communicative & Integrative Biology. 3: 146-150, 2010.

Martiáñez T, Francès S, López JM. *Generation of digital responses in stress sensors.* Journal of Biological Chemistry. 284: 23902-23911, 2009.

Piqué M, López JM, Sylvain F, Guigó R, Méndez R. *A combinatorial code for CPE-mediated translational control.* Cell. 132: 434-448, 2008.

Iglesias-Serret D, Piqué M, Gil J, Pons G, López JM.*Transcriptional and translational control of Mcl-1 during apoptosis.*Archives of Biochemistry and Biophysics. 417: 141-152, 2003.

López JM*, Campàs C*, Barragán M, Bellosillo B, Colomer D, Gil J.*Acadesine activates AMPK and induces apoptosis in B-cell chronic lymphocytic leukemia cells but not in T lymphocytes.*Blood. 101: 3674-3680, 2003.*Both should be considered as first author.

López JM, Santidrian AF, Campàs C, Gil J.*5-Aminoimidazole-4-carboxamide riboside induces apoptosis in Jurkat cells, but the AMP-activated protein kinase is not involved.*Biochemical Journal.370: 1027-1032, 2003.

López JM, Bombi JA, Valderrama R, Giménez A, Parés A, Caballería J, Imperial S, Navarro S. *Effects of prolonged ethanol intake and malnutrition on rat pancreas.*Gut. 38: 285-292, 1996.

López JM, Bennett MK, Sanchez HB, Rosenfeld JM, Osborne TF. Sterol regulation of acetyl CoA carboxylase provides a mechanism for coordinate control of cellular lipid. Proceedings of the National Academy of Sciences of the United States of America. 93: 1049-1053, 1996.

López JM*, Bennett MK*, Sanchez HB, Osborne TF. *Sterol regulation of fatty acid synthase promoter: coordinate feedback regulation of two mayor lipid pathways.* Journal of Biological Chemistry. 270: 25578-25583, 1995. *Both should be considered as first author.

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