Prof. Sima Lev

Regulatory mechanisms of membrane traffic and their implications in human disease

Our Research

Membrane trafficking pathways are mediated by a network of proteins and lipids that coordinately function to efficiently and rapidly transport proteins, lipids, and sugars to their final cellular destinations. The tight regulation of membrane transport events is not only fascinating but also fundamental for normal cell function and survival.

The major goal of our studies is to gain a novel insight into cellular mechanisms controlling membrane trafficking, and to extrapolate our knowledge to pathological situations involved in human diseases.

Current projects focus on:

i. Molecular mechanisms controlling **lipid transport** and their influence on membrane trafficking events and cellular lipid homeostasis (Read more)
ii. Mechanisms controlling the Golgi-glycosylation machinery and their implication in human diseases known as **Congenital disorders of glycosylation (CDG)** (Read more)
iii. Mechanisms regulating membrane traffic in professional secretory cells, such as the insulin-producing pancreatic β cells, and their implication in **diabetes**

We apply multidisciplinary experimental approaches including advanced biochemical and molecular biology techniques, advanced imaging techniques using confocal and electron microscopy, as well as basic lipidology.

Selected Publications

- **Lev, S.**, Hernandez, J., Martinez, R., Chen, A., Plowman, G.D., and J. Schlessinger. (1999) Identification of a novel family of targets of PYK2 related to Drosophila Retinal Degeneration B (rdgB) protein. **Mol. Cell. Biol.**, 19, 2278-2288.
- Tian, D., Litvak, V. and **Lev, S.** (2000) Cerebral ischemia and seizures induce tyrosine phosphorylation of PYK2 in neurons and microglial cells. **J. Neurosci.**, 20, 6478-6487.
- Tian, D., Litvak, V., Toledo-Rodriguez, M., Carmon, S., and **Lev, S.** (2002) Nir2, a novel regulator of cell morphogenesis. **Mol. Cell. Biol.**, 22, 2650-2288.
- Tian, D., and **Lev, S.** (2002) Cellular and Developmental Distribution of Human Homologues of the Drosophilia rdgB Protein in the Rat Retina. **Invest. Ophthalmol. Vis. Sci.**, 43(6), 1946-1953.
- Litvak, V., Tian, D., Carmon. S, and **Lev, S.** (2002) Nir2, a human homolog of the Drosophila rdgB, is essential for cytokinesis. **Mol. Cell. Biol.**, 22, 5064-5075.
- Litvak, V., Shaul, D.Y., Shulewitz, M., Amarilio, R., Carmon, S., and **Lev, S.** (2002) Targeting of Nir2 to lipid droplets is regulated by a specific threonine residue within its PI-transfer domain. **Current Biology**, 12 (17), 1513-1518.
- Litvak, V., Argov, R., Dahan, N., Ramachandran, S., Amarilio, R., Shainskaya. A, and **Lev, S.** (2004) Mitotic phosphorylation of the peripheral Golgi protein Nir2 by Cdk1 provides a docking mechanism for Plk1 and affects cytokinesis completion. **Molecular Cell.**, 14, 319-330.
- **Lev, S.** (2004) The role of the Nir/rdgB protein family in membrane trafficking and cytoskeleton remodeling. **Exper. Cell Res.**, 297(1), 1-10.
- Amarilio, R., Ramachandran, S., Sabanay, H., and **Lev, S.** (2005) Differential regulation of ER structure through VAP-Nir protein interaction. **J. Biol. Chem.**, 280(7), 5934-5944.
- Litvak, V., Dahan, N., Ramachandran, S,. Sabanay, H., and **Lev, S.** (2005) Maintenance of the diacylglycerol level in the Golgi apparatus by the Nir2 protein is critical for Golgi secretory function. **Nature Cell Biology**, 7(3), 225-234.
- **Lev, S.** (2006) Lipid Homeostasis and Golgi Secretory Function. **Biochem. Soc. Trans.**, 34(Pt 3):363-366.
- Peretti, D., Dahan, N., Shimoni, E., Hirschberg, K., **Lev, S.** (2008). Coordinated lipid transfer between the endoplasmic reticulum and the Golgi complex requires the VAP proteins and

is essential for Golgi-mediated transport. **Mol. Biol. Cell.**, 19(9):3871-3884.

- **Lev, S.**, Ben Halevy, D., Peretti, D., Dahan, N. (2008) The VAP protein family: from cellular functions to motor-neuron disease. **Trends Cell Biology**, 18, 282-290.
- Laufman O, Kedan A, Hong W and **Lev S.** (2009) Direct interaction between the COG complex and the SM protein, Sly1, is required for Golgi SNARE pairing. **EMBO J.**, 28: 2006-2017.
- Kim, S., Leal, S.S., Ben Halevy, D., Gomes, C.M., and **Lev, S.** (2010) Structural requirements for VAP-B oligomerization and their implication in ALS-associated VAP-B(P56S) neurotoxicity. **J. Biol. Chem.** In press.