IJAE
Vol. 119, n. 1 (Supplement): 150, 2014
ITALIAN JOURNAL OF ANATOMY AND EMBRYOLOGY

From interaction to function: Phospholipase C beta 1 protects cells from stress-induced apoptosis

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The phosphoinositide-dependent signal transduction pathway has been implicated in the control of a variety of biological processes, such as the regulation of cellular metabolism and omeostasis, cell proliferation and differentiation. One of the key player in the regulation of inositol lipid signaling is phospholipase C beta 1 (PI-PLCβ1), which hydrolyses PtIns(4,5)P2, giving rise to the second messengers IP3 and DAG.

The complete mapping of the PI-PLCβ1 interactome was undertaken, to understand its diverse functions within the nuclear compartment and to determine its contribution to physiological and pathological processes. Affinity purification-mass spectrometry (AP-MS) allowed for the identification of 160 proteins present in association with PI-PLCβ1 in the nucleus of erythroleukemia cells. Co-immunoprecipitation analysis of selected proteins confirmed the data obtained from mass spectrometry. Of particular interest was the identification of proteins involved in nuclear trafficking, as well as factors involved in hematological malignancies and several anti-apoptotic proteins (Piazzi et al., 2013).

PI-PLCβ1 has been associated with the regulation of several cellular functions, some of which are not yet fully understood. In particular, it has been reported that PI-PLCβ1 protects murine fibroblasts from oxidative stress-induced cell death, through signaling events which remain unclear. Reactive oxygen species (ROS) have been shown to regulate major epigenetic processes causing the silencing of tumor suppressors and enhancing the proliferation of leukemic cells under oxidative stress. Investigation of the role for ROS and their signaling mediators in the pathogenesis of leukemia might, therefore, outline innovative approaches for the improvement of pharmacological therapies to treat leukemia.

We demonstrate that in acute lymphoid leukemia cells (pro-B cells), treated with 250 μM of hydrogen peroxide (H2O2), PI-PLCβ1b conferred resistance to cell death, promoting cell cycle progression and cell proliferation. Interestingly, we found that, upon H2O2 exposure, the expression of PI-PLCβ1b affects the activity of several protein kinases, in particular it completely abolished the phosphorylation of Erk1/2 MAP kinases, down-regulated PTEN and up-regulated the phosphorylation of Akt; thereby sustaining cellular proliferation.

Reference

[1] Piazzi M et al. (2013). Phosphoinositide-specific phospholipase C β 1b (PI-PLCβ1b) interactome: affinity purification-mass spectrometry analysis of PI-PLCβ1b association with nuclear proteins. Mol Cell Prot 12:2220-35.