INTRACELLULAR SIGNALS TRANSDUCED BY STRESS INDUCIBLE PROTEIN 1 DEPENDS ON ENDOCYTIC ACTIVITY

Lopes, M. H.[1]; Andrade, F.C[2]; Hajj, G.[1];Linden, R.[3];Martins, V.R[1] and Prado, M.A.M.[2].

[1]Ludwig Institute for Cancer Research, SP; [2] Programa em Farmacologia Molecular, ICB, Universidade Federal de Minas Gerais, MG;[3]Universidade Federal do Rio de Janeiro, RJ, Brazil.

Stress inducible protein 1 (STI1), a co-chaperone molecule, whose interaction with the cellular prion protein (PrPc, a cell surface protein) in hippocampal neurons promotes neuroprotection and neuritogenesis through distinct signaling pathways. Herein, we examined STI1 cellular trafficking and signal transduction using neuronal cells (SN-56, an immortalized cell line, and hippocampal primary cultures). STI1 is rapidly internalized by endosomal vesicles containing flotillin, a lipid-raft component, in neuronal cells. SN56 cells bind specifically to STI1 and this interaction triggers the internalization of PrPc. Moreover, SN56 cells respond to STI1 by increasing mitogen-activated protein kinase (MAPK) phosphorylation..Supressioin of endocytosis by high-sucrose impairs MAPK activation by STI1. These results indicate that endocytosis of STI1 or PrPc might be a required step for intracellular signaling in response to PrPc engagement by STI1. .Supported by FAPESP, CNPq and HHMI.