

In vitro morphofunctional role of Bag3

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BAG3 (Bcl2-associated athanogene 3) belongs to the BAG protein family and was identified by yeast two-hybrid screens using the ATPase domain of heat shock protein (Hsc/Hsp70) it is, like the other members of the family, a co-chaperone that, through its BAG domain (110–124 amino acids), binds to Hsc70/Hsp70ATPase domain and modulates their activity in polypeptide folding. Furthermore, BAG3 protein contains also a WW domain and a proline-rich repeat (PXXP) that binds to the SH3 domain of PLC γ_1 and forms an epidermal growth factor (EGF)-regulated complex. Further BAG3 molecular partners are HspB8, Bcl2 (B-cell lymphoma 2), Raf1 kinase and the cytosolic chaperonin CCT. BAG3 is a 74 kDa cytoplasmatic protein, particularly concentrated in the rough endoplasmic reticulum; a slightly different molecular weight or a doublet form can be observed in some cell types and/or following cell exposure to stressors. A synaptosome associated form of 40 kD has recently been described

In humans, *bag3* gene expression is constitutive in myocytes, a few other normal cell types and several tumours: leukemia and lymphoma, myeloma, pancreas and thyroid carcinomas, melanoma, osteosarcoma. It is instead induced in different normal cell types as leukocytes, epithelial and glial cells by stressors, such as oxidants, high temperature, heavy metals and HIV-1 infection. BAG3 silencing by small interfering RNA diminishes cell migration influencing the availability of correctly folded monomeric actin.

It is likely that BAG3 influences several cell processes, such as apoptosis, autophagy and cell motility by interacting with more than one molecular partner. We investigated "in vitro" the mechanisms and the biological roles carried out by BAG3 using western blotting, confocal and transmission immuno-electron microscopy, on human umbilical vein endothelial cells HUVEC, MCF/7 and MDA231 human breast cancer cells and a monocyte cell line.

Key words

BAG3, PLC γ_1 , HUVEC, MCF7, MDA231