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GRP78 expression beyond cellular stress; a biomarker for tumor manipulation

Hardy Britta, Raiter Annat

#### Abstract

Physiological stress takes place in the endoplasmic reticulum (ER) of cells where activation and up-regulation of genes and proteins are primarily induced to enhance pro-survival mechanisms such as the unfolded protein response (UPR). A dominant protein in the UPR response is the heat shock GRP78 protein. Although GRP78 is primarily located in the ER, under certain conditions it is transported to the cell surface, where it acts as a receptor inducing pathways of cell signaling such as proliferation or apoptosis. In the prolonged chronic stress transportation of the GRP78 from the ER to the cell membrane is a major event where in addition to the presentation of the GRP78 as a receptor to various ligands, it also marks the cells that will proceed to apoptotic pathways. In the normal cell that under stress acquires cell surface GRP78 and in the tumor cell that already presents cell surface GRP78, cell surface GRP78 is an apoptotic flag. The internalization of GRP78 from the cell surface in normal cells by ligands such as peptides will enhance cell survival and

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