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Endoplasmic Reticulum Stress and Cancer

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Abstract—*Endoplasmic reticulum (ER) is an essential organelle in the eukaryotic system associated with diverse functions such as protein folding, calcium ion storage and lipid biogenesis. The folding of protein mainly occurs in lumen, which is assisted by molecular chaperons like Grp78, Grp94 and various folding enzymes. Subsequently folded protein is packaged to Golgi apparatus for its sorting and distribution to specific site. Alteration in the micro-environmental conditions leads to deregulation in the protein folding which results in accumulation of protein aggregates. Misfolded proteins retained in the lumen disturb the cellular homeostasis and cause structural stress on the cell known as the endoplasmic reticulum stress. Cell induces a defense mechanism to combat this stress related effect by activating the unfolded protein response (UPR), which comprises of three inter-dependent branches namely IRE1α, PERK and ATF-6. Unfolded/misfolded proteins are either restored to their proper conformation or are degraded by proteasomes through apoptosis. Excess of this stress may also lead to cell death. Rapid cell proliferation and poor vascularization in the tumor cells display ER stress and UPR activation. Cancer cells adopt various ways of inhibiting these branches like chromatin remodeling to escape apoptotic effects and adopt a survival strategy. These signaling pathways from the ER may be used as a novel therapeutic target for various cancers.*

Keywords*: ATF-6, ER stress, IRE1α, Molecular chaperons, PERK, Protein folding, UPR*