Endoplasmic reticulum proteostasis in glioblastoma - From molecular mechanisms to therapeutic perspectives

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Cellular stress induced by the accumulation of misfolded proteins at the endoplasmic reticulum (ER) is a central feature of secretory cells and is observed in many tissues in various diseases, including cancer, diabetes, obesity, and neurodegenerative disorders. Cellular adaptation to ER stress is achieved by the activation of the unfolded protein response (UPR), an integrated signal transduction pathway that transmits information about the protein folding status at the ER to the cytosol and nucleus to restore proteostasis. In the past decade, ER stress has emerged as a major pathway in remodeling gene expression programs that either prevent transformation or provide selective advantage in cancer cells. Controlled by the formation of a dynamic scaffold onto which many regulatory components assemble, UPR signaling is a highly regulated process that leads to an integrated reprogramming of the cell. In this Review, we provide an overview of the reg