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Manuscript Type: EDITORIAL

**Endoplasmic reticulum stress-mediated pathways to both apoptosis and autophagy: significance for melanoma treatment**

Mohamed Hassan, Denis Selimovic, Matthias Hannig, Youssef Haikel, Robert T Brodell, Mossaad Megahed

**Abstract**

Melanoma is the most aggressive form of skin cancer. Disrupted intracellular signaling pathways are responsible melanoma's extraordinary resistance to current chemotherapeutic modalities. The pathophysiologic basis for resistance to both chemo- and radiation therapy is in altered genetic and epigenetic mechanisms that destroy cell death machinery and/or excessive activation of cell growth and survival-dependent pathways. Although most current melanoma therapies target mitochondrial dysregulation, there is increasing evidence that endoplasmic reticulum (ER) stress-



ways to both apoptosis and autophagy: significance for melanoma treatment



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2014年2月24日 - Using tumor biopsies from BRAF<sup>V600E</sup> melanoma patients treated either with ... therapy and concurrently with cell death pathways such as apoptosis, ... and that targeting multiple components of the ER stress–autophagy pathway ... demonstrated persistently elevated levels of autophagy in both patients.

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2013年1月29日 - Vemurafenib-treated melanoma cells showed increased cytosolic ... The UPR pathway is triggered through three sensors: activating ... Both BRAF inhibitors and ER stress increase the abundance of the proapoptotic protein BIM (16, 18). .... sensitizes melanoma cells to ER stress-mediated apoptosis (33).

## Oncogenic RAS/RAF Signaling in Melanoma Impairs the





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