

# Targeting the unfolded protein response for disease intervention

Por: [Rivas, A](#) (Rivas, Alexis)<sup>[1,2]</sup>; [Vidal, RL](#) (Vidal, Rene Luis)<sup>[1,3]</sup>; [Hetz, C](#) (Hetz, Claudio)<sup>[1,2,4]</sup>

## EXPERT OPINION ON THERAPEUTIC TARGETS

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## Resumen

**Introduction:** The accumulation of misfolded proteins in the endoplasmic reticulum (ER) generates a stress condition that engages the unfolded protein response (UPR). The UPR is an adaptive reaction that aims to reestablish ER proteostasis by recovering the folding capacity of the cell. However, chronic ER stress results in apoptosis.

**Areas covered:** This review focuses on discussing the emerging role of the UPR as a driver of several human pathologies including diabetes, neurodegenerative diseases and cancer. The involvement of specific UPR signaling components on different diseases is highlighted based on preclinical models and pharmacological and genetic manipulation of the pathway.

**Expert opinion:** Therapeutic strategies directed to regulate the activity of different UPR signaling arms may reduce stress levels with a therapeutic gain. Recent drug discovery efforts have identified small molecules that target specific UPR components, providing protection on various disease models. However, important side effects are predicted in the chronic administration due to the fundamental role of the UPR in highly secretory organs such as liver and pancreas. To overcome these problems, we propose the use of combinatorial treatments of selected drugs with natural compounds that are known to modulate the ER proteostasis network.

## Palabras clave

**Palabras clave de autor:** [endoplasmic reticulum stress signaling](#); [pharmacological modulator](#); [protein misfolding disorders](#); [unfolded protein response](#)


## Información del autor

**Dirección para petición de copias:** Hetz, C (autor para petición de copias)

 Univ Chile, Cellular & Mol Biol Program, Inst Biomed Sci, Santiago 1027, Chile.

## Direcciones:

 [ 1 ] Univ Chile, Biomed Neurosci Inst, Fac Med, Santiago 1027, Chile

 [ 2 ] Univ Chile, Program Cellular & Mol Biol, Inst Biomed Sci, Ctr Mol Studies Cell, Santiago 1027, Chile

[ 3 ] CENPAR, Neurounion Biomed Fdn, Santiago, Chile

+ [ 4 ] Harvard Univ, Sch Publ Hlth, Dept Immunol & Infect Dis, Boston, MA 02115 USA

**Direcciones de correo electrónico:** [chetz@med.uchile.cl](mailto:chetz@med.uchile.cl)

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