# Deciphering post-transcriptional regulation mechanism mediated by p53 during the unfolded protein response (UPR).

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The tumor suppressor protein p53 is a central factor that contributes to cell homeostasis as it regulates expression of many genes associated with normal cellular processes such as cell cycle, proliferation, apoptosis, senescence, autophagy and metabolism, among others. Most of the known regulation exerted by p53 occurs at the transcription level, which is supported by its well characterized DNA-binding and trans-activation domains that are altered by many cancer-associated p53 mutations. In addition, p53 is involved in cellular responses to various types of stress, among which DNA damage, oncogene activation and ribosomal stress are the most studied. However, recent studies have proposed that p53 also plays a role in coordinating post-transcriptional regulatory mechanisms during unfolded protein response (UPR). The UPR is activated when misfolded or unfolded proteins accumulate in the lumen of the endoplasmic reticulum (ER), and although its main purpose is to restore the proteostasis of normal cells that produce large amounts of proteins, it has been found altered in pathologies such as cancer, diabetes, and neurodegenerative diseases. In order to elucidate the possible regulatory mechanisms mediated by p53, we have analyzed the transcriptome and proteome of p53-null human H1299 cells under ER stress conditions both in presence and absence of p53. The results show that p53 activity is required to elicit a fully operational UPR and that, unlike what occurs in other conditions, it promotes a marked inhibition of gene expression, both at the mRNA and protein levels. Moreover, many proteins down-regulated during the UPR in a p53-dependent manner show no difference in mRNA abundance suggesting that post-transcriptional mechanisms are particularly relevant during the UPR and are the current focus of our work.