Multidrug resistance revisited: A new mechanism and a possible solution

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**Chemotherapy triggers endoplasmic reticulum (ER) stress.**

**Drug-resistant cells are also resistant to ER stress-triggered cell death.**

**Conclusions and significance:**

Chemoresistant cells. However, LIP was rapidly degraded by proteasomal and lysosomal proteases in the MDR tumor (B16 melanoma, inducibly over-expressing LAP or LIP). Meir, O., et al, 2010)

Inducible over-expression of LIP reversed the resistance to ER stress (HT29 subclone ½, 3, and 6). The same results were obtained with: A549-A549/MDR lung carcinoma cells, Constitutively chemoresistant Caco-2 colorectal carcinoma cells, Constitutively chemoresistant Caco-2 colorectal carcinoma cells (late UPR)

The expression of LAP or inhibition of its degradation attenuates ER stress and renders many tumor types sensitive to chemotherapy. C/EBPβ is over-expressed in many tumor types. LIP is regulated post-translationally by proteasomal and lysosomal degradation (HT29 cells).