

Supplemental Methods

Antibodies

Antibodies used for western blot or immunoprecipitation were:

Actin (ICN clone C4), ATF4/CREB2 (Santa Cruz, sc-200), Bax (Santa Cruz, SC-493), Bak (Upstate, clone NT), Bcl-2 (Becton, 550847), Bcl-xL (Cell Signaling, 2764), Bim (BD, Pharmingen, 559685), Caspase-8 (MBL, 5F7), eIF2-alpha (Santa Cruz, sc-11386), phospho-eIF2-alpha (Cell signaling, 3597), FOXO1a (Cell Signaling, 2880), GRP58 (Acris antibodies SP5391), GRP78 (Santa Cruz, sc-1050), GRP 94 (Santa Cruz, sc-1794), HIF-1 α (RD, aF1935), Mcl-1 (Santa Cruz, sc-819), Noxa (Calbiochem, OP180), Puma (Abcam, ab9643), phospho-S6 (Cell Signalling, 2211), S6 (Upstate, 05-781R), alpha-tubulin (Abcam, ab28439), PARP (Cell Signaling, 9542).

HRP-conjugated secondary antibodies (Sigma) were detected with ECL reagent (Pierce).

siRNA

Previously published sense sequences of siRNA duplexes were:

- Bim: 5'-GCACCAUGAGUUGUGACA-3', Noxa: 5'-GGUGCACGUUUCAAAUU-3' (Sheridan, C., Brumatti, G., Elgendy, M., Brunet, M., and Martin, S. J. An ERK-dependent pathway to Noxa expression regulates apoptosis by platinum-based chemotherapeutic drugs. *Oncogene*, 2010.).
- Mcl-1: 5'-AAUAACACCAGUACGGACGGG (Lopez-Royuela, N., Perez-Galan, P., Galan-Malo, P., Yuste, V. J., Anel, A., Susin, S. A., Naval, J., and Marzo, I. Different contribution of BH3-only proteins and caspases to doxorubicin-induced apoptosis in p53-deficient leukemia cells. *Biochem Pharmacol*, 79: 1746-1758, 2010)
- Bcl-xL: 5'-ACAAGGAGAUGCAGGUAUUUU (Zhang, H., Guttikonda, S., Roberts, L., Uziel, T., Semizarov, D., Elmore, S. W., Levenson, J. D., and Lam, L. T. Mcl-1 is critical for survival in a subgroup of non-small-cell lung cancer cell lines. *Oncogene*, 30: 1963-1968, 2011)
- HIF-1 α : 5'-GCCACTTCGAAGTAGTGCT-3' and 5'-CCTATATCCCAATGGATGATG-3' (Fitsialos, G., Bourget, I., Augier, S., Ginouvès, A., Rezzonico, R., Odorisio, T., Cianfarani, F., Virolle, T., Pouysségur, J., Meneguzzi, G., Berra, E., Ponzio, G., and Buscà, R. HIF1 transcription factor regulates laminin-332 expression and keratinocyte migration. *Journal of Cell Science*, 121: 2992-3001, 2008)

ATF4 sequence was: 5'-GCCUAGGUCUCUUAGAUGA. As a control, an irrelevant siRNA oligonucleotide (pBlue, sense strain: 5-GUAAGACACGACUUAUCGC-3) was used. The same sequence coupled to a fluorochrome (pBlue-FITC) was used to measure transfection efficiency, which was around 80% in all cases.

Microscopy

For immunofluorescence, mouse IgG-FITC from Sigma was used as a secondary antibody. Cells were visualized in an Olympus BX-60 microscope.

Phase-contrast microscope pictures were taken with an Olympus (Center Valley, PA, USA) IX70 inverted microscope with a 20x objective and an Olympus C-5060 camera. One tenth of the whole field is shown.

Statistical analysis

Paired, two-tailed T-student test was used. One asterisk denotes $p < 0.05$ when compared to the control condition; two asterisks, $p < 0.01$.