Endoplasmic reticulum (ER) stress triggers a cellular response termed unfolded protein response (UPR) which initially promotes pro-survival signaling, protecting transformed cells. Activation of the UPR affects tumour growth and causes resistance of cancer cells to chemotherapeutic agents. ERp29 is an ER luminal protein that was found to be overexpressed in some primary tumors and under the conditions of genotoxic stress in cancer cells \textit{in vitro}. In the present study we explored the role of ERp29 during chemotherapy. We found that ERp29 is upregulated after administration of the anticancer agent doxorubicin in lung cancer cells. \textit{In vitro} experiments in p53-null cells and \textit{in vivo} studies using p53-deficient mice revealed that doxorubicin effect on ERp29 is p53-dependent. We also found that ERp29 interacts physically with the ER stress-activated eukaryotic translation initiation factor 2-alpha kinase 3 (PERK), increases its levels, and confers resistance to DOX. These findings provide a direct link between the cellular response against genotoxic stress and the execution of UPR, identifying PERK as a nodal point between ER and genotoxic stress induction. Subsequently we investigated if UPR is involved in the communication between cancer cells and fibroblasts. \textit{In vitro}, paracrine activity related assays indicate that induction of ER stress by tunicamycin and overexpression of the transcription factor XBP1 leads to paracrine stimulation of fibroblasts proliferation, forming a permissive environment for tumor progression.