



Key Effects of Hsp27

Some of the known key effects of Hsp27 – here restricted to similar effects which have been observed in our own experiments with cancer cells or in RP101 treated cancer patients – are:

Chemoresistance: Hsp27 is expressed in response to anticancer chemotherapy, Hsp27 is thought to participate in oncogenesis and in resistance to chemotherapy.

e.g. Increased Hsp27 expression is related to higher rates of gemcitabine resistance in patients with pancreatic cancer.

Multi drug resistance: Hsp27 is linked to multi drug resistance (MDR) in human hepatic cancer cells.

Influence on oncogenes: In prostate cancer Hsp27 interacts with the oncogene Stat3.

Stat3 levels correlated directly with Hsp27 levels. Hsp27 was identified as a modulator of Stat3-regulated apoptosis. These findings have identified Hsp27 as a potential therapeutic target in advanced prostate cancer.

DNA-repair: Enzymes of DNA base excision repair (BER) are associated with Hsp27. The association of Hsp27 with BER enzymes was confirmed by hydroxyl radical protein-protein footprinting and immunoaffinity tests. HSPs may have functional roles in BER.

Genetic recombination: DNA topoisomerases are involved in several aspects of DNA metabolism, in particular genetic recombination. The relative levels of both topo II alpha and beta were higher in the controls than the Hsp27-overexpressing clones, suggesting that the apoptotic protective effect of Hsp27 overexpression is associated with altered topo II expression.

Gene amplification: Abnormal amplification/expression of HER-2/neu oncogene has been causally linked with tumorigenesis and metastasis in breast cancer. A significant correlation between phosphorylated Hsp27, HER-2/neu status and lymph node positivity in breast cancer has recently been described.

Apoptosis: Hsp27 inhibits cytochrome c induced apoptosis and binding of caspase-3 prodomain to Hsp27 also regulates apoptosis.

Immune response: Infiltrations of natural killer (NK) cells may have internal correlation with the expression of Hsp27. Moreover, Hsp27 protects cells from monocyte cytotoxicity.

Metastasis: In cancer patients high levels of hsp27 are associated with metastatic tissues compared to non metastatic tissues suggesting that it plays a key role in metastases formation.

In addition to the known effects of Hsp27, it is important to recognize that Hsp27 over expression has been detected in a wide range of different tumors, reinforcing it as an important target in tumor biology.



**Leukemias,
bladder, sarcomas,
malignant melanomas,
pancreas,
breast,
ovary,
liver,

gastric,
lung,
colon,
endometrial, and
prostate cancers.**