Heat Shock Protein 27 (HSP27) and Anti-Apoptosis Activity in Cancer Cells

A molecular chaperone, heat shock protein 27 (HSP27, heat-shock 27-KD protein 1, HSPB1) is one of the small heat shock protein family. It modulates the ability of cells to respond to several types of injury, heat shock, oxidative stress and other stresses. HSP27 is expressed in almost all organisms from prokaryotes to mammals. It interacts with many proteins and can prevent a wide variety of apoptotic agents from causing cell death. HSP27 regulates apoptosis by interacting with key components of the apoptotic signaling pathway [1]. It was reported that HSP27 inhibited cytochrome c and dATP triggered activation of procaspase-9 and prevented etoposide-induced apoptosis [2], and HSP27 altered the expression of topoisomerase II and inhibited doxorubicin-induced apoptosis [3]. Furthermore, it was reported that over-expression of HSP27 in prostate cancer cells rendered cells resistant to etoposide-, diethylmaleate-, cycloheximide- or radiation-induced apoptosis, which may be mediated by the production of survival factors [4]. From our recent studies, up-regulation of HSP27 in pancreatic cancer cells has been clarified to be linked to the resistance to gemcitabine (GEM), and the down-regulation of HSP27 by using HSP27 inhibitors; siRNA for HSP27, interferon γ and KNK437 in Gem-resistant cells showed the increasing sensitivity for GEM [5-8]. They showed that the up-regulation of anti-apoptotic pathways induced by HSP27 enhanced the resistance of cancer cells to apoptosis. Enhanced resistance to apoptosis in cancer cells induced by HSP27 may be caused by many factors. HSP27 protects the cells from apoptosis by concerning with DAXX, Bid, cytochrome c, IKK, caspase-3 and etc. [9,10]. For the chemotherapies which aim at the induction of apoptosis in cancer cells, it is very important to control such factors concerning with HSP27 or itself.

HSP27 and Cancers

In these days many reports about the up-regulation of HSP27 in cancer tissues of stomach, head and neck, renal, prostate and etc. have been published [11-14]. Why is HSP27 up-regulated in cancer cells? Song et al. [15] showed that constitutively activated signal transducer and activator of transcription 3 (STAT 3) up-regulated HSP27 in breast cancer cells. What does up-regulated HSP27 do in cancer cells? We should clarify the roles of HSP27 in cancer cells. As described above, increased HSP27 prevents the induction of apoptosis by anti-cancer drugs, oxidative stress, irradiation or etc in cancer cells. Over-expressed HSP27 helps cancer cells to survive. Does HSP27 play a role as an outside player? Increased levels of HSP27 were observed in metastatic HCC tissues compared with non metastatic tissues [16]. Furthermore, in vitro studies have shown that over-expression of HSP27 increased the metastatic capacity on several factors in human melanoma and prostate cancer cells [17,18], and HSP27 depletion induced apoptosis and inhibited tumor progression in prostate cancer cells [19]. These suggest that HSP27 plays a key role in metastasis formation as an offensive player, too.

Furthermore, in these days some groups reported up-regulation of HSP27 in cancer stem cells. Wei et al. [20] showed increased expression and phosphorylation of HSP27 in breast cancer stem cells, and knockdown of HSP27 in breast cancer stem cells decreased characters of them. They concluded that HSP27 regulated the epithelial-mesenchymal transition process to contribute the maintenance of breast cancer stem cells. Hsu et al. [21] demonstrate that lung cancer stem cells have elevated levels of activated HSP27 upon treatment with superoxide and traditional chemotherapy.

Therefore, it seems to be the most important to control HSP27 in cancer cells to conquer the cancers.

References

Heat shock proteins 27, 60 and 70 as prognostic markers of prostate cancer. APMIS 116: 888-895.


