Hsp27 knockdown

Hsp27 knockdown using nucleotide-based therapies inhibit tumor growth and enhance chemotherapy in human bladder cancer cells

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Abstract
Heat shock protein 27 (Hsp27) is a cytoprotective chaperone that is phosphoactivated during cell stress that prevents aggregation and/or regulate activity and degradation of certain client proteins. Recent evidence suggests that Hsp27 may be involved in tumor progression and the development of treatment resistance in various tumors, including bladder cancer. The purpose of this study was to examine, both in vitro and in vivo, the effects of overexpression of Hsp27 and, correspondingly, the down-regulation of Hsp27 using small interfering (si) RNA and OGX-427, a second-generation antisense oligonucleotide targeting Hsp27. Hsp27 overexpression increased UMUC-3 cell growth and resistance to paclitaxel. Both OGX-427 and Hsp27 siRNA decreased Hsp27 protein and mRNA levels by >90% in a dose- and sequence-specific manner in human bladder cancer UMUC-3 cells. OGX-427 or Hsp27 siRNA treatment induced apoptosis and enhanced sensitivity to paclitaxel in UMUC-3 cells. In vivo, OGX-427 significantly inhibited tumor growth in mice, enhanced sensitivity to paclitaxel, and induced significantly higher levels of apoptosis compared with xenografts treated with control oligonucleotides. Collectively, these findings suggest that Hsp27 knockdown with OGX-427 and combined therapy with paclitaxel could be a novel strategy to inhibit the progression of bladder cancer. [Mol Cancer Ther 2007;6(1):299-308]

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