Ciocca DR, Calderwood SK.

Abstract
Heat shock proteins (Hsps) are overexpressed in a wide range of human cancers and are implicated in tumor cell proliferation, differentiation, invasion, metastasis, death, and recognition by the immune system. We review the current status of the role of Hsp expression in cancer with special emphasis on the clinical setting. Although Hsp levels are not informative at the diagnostic level, they are useful biomarkers for carcinogenesis in some tissues and signal the degree of differentiation and the aggressiveness of some cancers. In addition, the circulating levels of Hsp and anti-Hsp antibodies in cancer patients may be useful in tumor diagnosis. Furthermore, several Hsp are implicated with the prognosis of specific cancers, most notably Hsp27, whose expression is associated with poor prognosis in gastric, liver, and prostate carcinoma, and osteosarcomas, and Hsp70, which is correlated with poor prognosis in breast, endometrial, uterine cervical, and bladder carcinomas. Increased Hsp expression may also predict the response to some anticancer treatments. For example, Hsp27 and Hsp70 are implicated in resistance to chemotherapy in breast cancer, Hsp27 predicts a poor response to chemotherapy in leukemia patients, whereas Hsp70 expression predicts a better response to chemotherapy in osteosarcomas. Implication of Hsp in tumor progression and response to therapy has led to its successful targeting in therapy by 2 main strategies, including: (1) pharmacological modification of Hsp expression or molecular chaperone activity and (2) use of Hsps in anticancer vaccines, exploiting their ability to act as immunological adjuvants. In conclusion, the present times are of importance for the field of Hsps in cancer, with great contributions to both basic and clinical cancer research.

Targeting heat shock proteins in cancer.
Jego G, Hazoumé A, Seigneuric R, Garrido C.

Abstract
Heat shock proteins (HSPs) HSP27, HSP70 and HSP90 are powerful chaperones. Their expression is induced in response to a wide variety of physiological and environmental insults including anti-cancer chemotherapy, thus allowing the cell to survive to lethal conditions. Different functions of HSPs have been described to account for their cytoprotective function, including their role as molecular chaperones as they play a central role in the correct folding of misfolded proteins, but also their anti-apoptotic properties. HSPs are often overexpressed in cancer cells and this constitutive expression is necessary for cancer cells’ survival. HSPs may have oncogene-like functions and likewise mediate "non-oncogene addiction" of stressed tumor cells that must adapt to a hostile microenvironment, thereby becoming dependent for their survival on HSPs. HSP-targeting drugs have therefore emerged as potential anti-cancer agents. This review describes the different molecules and approaches being used or proposed in cancer therapy based on the in inhibition of HSP90, HSP70 and HSP27.
Heat shock proteins in obesity: links to cardiovascular disease.
Habich C, Sell H.

Abstract
Adipose tissue expansion is associated with adipocyte dysfunction and increased inflammatory processes. In the obese state, adipose tissue is characterized by an impaired intracellular stress defense system and dysbalanced heat shock response. Several members of the heat shock protein (HSP) family have been identified as novel adipokines released upon cellular stress, which might be a molecular link from adipose tissue inflammation to the cardiovascular system. Therefore, this review aims at summarizing and discussing our recent knowledge on HSPs in relation to obesity and their potential links to cardiovascular disease. Of particular importance/interest are two members of the HSP family, HSP60 and heme oxygenase 1 (HO-1), which have been well described as adipokines, and studied in the context of obesity and cardiovascular disease. HSP60 is regarded as a novel molecular link between adipose tissue inflammation and obesity-associated insulin resistance. The role of HO-1 induction in the obese state is well-documented, but a causal relationship between increased HO-1 levels and obesity-associated metabolic diseases is still controversial. Both HSP60 and HO-1 are also forthcoming targets for the treatment of cardiovascular disease, and the current knowledge will also be discussed in this review.

The small heat shock proteins and their role in human disease.
Sun Y, MacRae TH.

Abstract
Small heat shock proteins (sHSPs) function as molecular chaperones, preventing stress induced aggregation of partially denatured proteins and promoting their return to native conformations when favorable conditions pertain. Sequence similarity between sHSPs resides predominately in an internal stretch of residues termed the alpha-crystallin domain, a region usually flanked by two extensions. The poorly conserved N-terminal extension influences oligomer construction and chaperone activity, whereas the flexible C-terminal extension stabilizes quaternary structure and enhances protein/substrate complex solubility. sHSP polypeptides assemble into dynamic oligomers which undergo subunit exchange and they bind a wide range of cellular substrates. As molecular chaperones, the sHSPs protect protein structure and activity, thereby preventing disease, but they may contribute to cell malfunction when perturbed. For example, sHSPs prevent cataract in the mammalian lens and guard against ischemic and reperfusion injury due to heart attack and stroke. On the other hand, mutated sHSPs are implicated in diseases such as desmin-related myopathy and they have an uncertain relationship to neurological disorders including Parkinson's and Alzheimer's disease. This review explores the involvement of sHSPs in disease and their potential for therapeutic intervention.