Heat shock protein expression analysis in canine osteosarcoma reveals HSP60 as a potentially relevant therapeutic target

Abstract

Heat shock proteins (HSP) are highly conserved across eukaryotic and prokaryotic species. These proteins play a role in response to cellular stressors, protecting cells from damage and facilitating recovery. In tumor cells, HSPs can have cytoprotective effects and interfere with apoptotic cascades. This study was performed to assess the prognostic and predictive values of the gene expression of HSP family members in canine osteosarcoma (OS) and their potential for targeted therapy. Gene expressions for HSP were assessed using quantitative PCR (qPCR) on 58 snap-frozen primary canine OS tumors and related to clinic-pathological parameters. A significant increased expression of HSP60 was found in relation to shorter overall survival and an osteoblastic phenotype. Therefore, the function of HSP60 was investigated in more detail. Immunohistochemical analysis revealed heterogeneous staining for HSP60 in tumors. The highest immunoreactivity was found in tumors of short surviving dogs. Next HSP expression was shown in a variety of canine and human OS cell lines by qPCR and Western blot. In two highly metastatic cell lines HSP60 expression was silenced using siRNA resulting in decreased cell proliferation and induction of apoptosis in both cell lines. It is concluded that overexpression of HSP60 is associated with a poor prognosis of OS and should be evaluated as a new target for therapy.

Keyword: Heat shock proteins (HSP); Osteosarcoma; Dog; Canine; Bone cancer.