
Abstract:
A high percentage of oesophageal adenocarcinomas show an aggressive clinical behaviour with a significant resistance to chemotherapy. Heat-shock proteins (HSPs) and glucose-regulated proteins (GRPs) are molecular chaperones that play an important role in tumour biology. Recently, novel therapeutic approaches targeting HSP90/GRP94 have been introduced for treating cancer. We performed a comprehensive investigation of HSP and GRP expression including HSP27, phosphorylated (p)-HSP27((Ser15)), p-HSP27((Ser78)), p-HSP27((Ser82)), HSP60, HSP70, HSP90, GRP78 and GRP94 in 92 primary resected oesophageal adenocarcinomas by using reverse phase protein arrays (RPPA), immunohistochemistry (IHC) and real-time quantitative RT-PCR (qPCR). Results were correlated with pathologic features and survival. HSP/GRP protein and mRNA expression was detected in all tumours at various levels. Unsupervised hierarchical clustering showed two distinct groups of tumours with specific protein expression patterns: The hallmark of the first group was a high expression of p-HSP27((Ser15, Ser78, Ser82)) and low expression of GRP78, GRP94 and HSP60. The second group showed...
the inverse pattern with low p-HSP27 and high GRP78, GRP94 and HSP60 expression. The clinical outcome for patients from the first group was significantly improved compared to patients from the second group, both in univariate analysis (p = 0.015) and multivariate analysis (p = 0.029). Interestingly, these two groups could not be distinguished by immunohistochemistry or qPCR analysis. In summary, two distinct and prognostic relevant HSP/GRP protein expression patterns in adenocarcinomas of the oesophagus were detected by RPPA. Our approach may be helpful for identifying candidates for specific HSP/GRP-targeted therapies.