A specific expression profile of heat-shock proteins and glucose-regulated proteins is associated with response to neoadjuvant chemotherapy in oesophageal adenocarcinomas.

Abstract:

Background: Oesophageal adenocarcinomas often show resistances to chemotherapy (CTX), therefore, it would be of high interest to better understand the mechanisms of resistance. We examined the expression of heat-shock proteins (HSPs) and glucose-regulated proteins (GRPs) in pretherapeutic biopsies of oesophageal adenocarcinomas to assess their potential role in CTX response.

Methods: Ninety biopsies of locally advanced adenocarcinomas before platin/5-fluorouracil (FU)-based CTX were investigated by reverse phase protein arrays (RPPAs), immunohistochemistry (IHC) and quantitative RT-PCR.

Results: CTX response strongly correlated with survival (P=0.001). Two groups of tumours with specific protein expression patterns were identified by RPPA: Group A was characterised by low expression of HSP90, HSP27 and p-HSP27((Ser15, Ser78, Ser82)) and high expression of GRP78, GRP94, HSP70 and HSP60; Group B exhibited the inverse pattern. Tumours of Group A were more likely to respond to CTX, resulting in histopathological tumour regression (P=0.041) and post-therapeutic down-categorisation from cT3 to ypT0-T2 (P=0.040). High HSP60 protein (IHC) and mRNA
expression were also associated with tumour down-categorisation (P=0.016 and 
P=0.004). Conclusion: Our findings may enhance the understanding of CTX response mechanisms, 
might be helpful to predict CTX response and might have translational relevance as they highlight the 
role of potentially targetable cellular stress proteins in the context of CTX response.

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