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New insights on molecular signature of drug resistance in human cancers

Stefania Staibano
University Federico II of Naples, Italy

Abstract

Hypoxic markers have been found hyper-expressed at the invasive border of several solid human cancers and corresponding metastases. Tumor carbonic anhydrase 9 (CAIX) is a key hypoxia regulated gene which is currently considered a reliable tissue marker of tumor hypoxia.

The up-regulation of endogenous markers of different Hypoxia Response Pathways has been recently associated with tumor aggressiveness and resistance to therapy.

CAIX is overexpressed in most of malignant metastasizing and/or radio/chemoresistant human tumors. However, it is still unclear if its location (cellular/extracellular, or membrane/cytosolic or nuclear) could have a role in determining the biological behaviour of tumors.

For this reason, we analyzed the immunohistochemical expression pattern of CAIX in a series of malignant tumors with different histogenesis, with the aim to give further insights on the correlation between the site of expression of the protein and the prognostic and predictive value of CA IX in solid human cancers.

The results of our study favour the hypothesis that the overexpression of CAIX per se is not sufficient as a marker of biological aggressiveness of solid tumours, whereas it reaches prognostic relevance when compared with the involved tissue compartment.