Abstract title: CA IX and Inflammatory Cytokines in Pancreatic Cancer – a functional cross-talk

Authors:

Strapcová, S. [1], Sedláková, O. [1], Lukačíková, Ľ. [1], Bartošová, M. [1], Csáderová, L. [1], Bizík, J. [2], Smolková, B. [2], Švastová, E [1].

[1] Biomedical Research Center, Department of Cancer Biology, Slovak Academy of Sciences, Bratislava, Slovakia
[2] Biomedical Research Center, Department of Molecular Oncology, Slovak Academy of Sciences, Bratislava, Slovakia

Abstract body text:

Carbonic anhydrase IX (CA IX), a transmembrane zinc metalloenzyme, is expressed in a variety of solid tumours via the HIF pathway. Through its involvement in the pH regulating apparatus and the metastatic cascade, CA IX drives the formation of an acidic tumor microenvironment, mediates cell survival, migration and metastatic lesion formation. Thus, CA IX serves as a marker of bad prognosis, a diagnostic marker, and a promising therapeutic target in different carcinomas. While CA IX is poorly expressed in the healthy pancreas, CA IX expression in pancreatic cancer favours malignant progression and correlates with poor patient survival. Since CA IX expression *in vivo* was shown to be controlled via additional hypoxia-unrelated mechanisms of the tumour micorenvironment, and pancreatitis remains the leading risk factor for PDAC development, we explore the functional cross-talk between CA IX and inflammatory molecules. In pancreatic cancer lines, we show that inflammatory cytokines up-regulate *CA9* transcription even in normoxia and that inflammatory cytokines promote the aggressive tumour phenotype by up-regulating mesenchymal markers, cell-stemmnes markers, and ECM-degrading metalloproteinases. We assume that CA IX plays a principal role in this type of malignancy, particularly in combination with inflammation, by proving that protein inhibition *in vitro* negatively affects cancer cell migration and adhesion on collagen I – a matrix excessively overexpressed in pancreatic cancer patients.

Acknowledgement: This work was supported by APVV 14-0816, VEGA 2/0105/19, VEGA 2/0052/18 and by the H2020 project VISION grant agreement No 857381.

Online conference Preveda - https://www.preveda.sk/conference/.