ABSTRACT: In the last fifteen years, our research group has been studying pancreatic adenocarcinoma (PDAC) cell lines derived from different origins (primary tumours, liver and lymph node metastasis, ascites) and with different genetic profiles. On these cells we have mainly investigated: i) the molecular effects of different chemotherapeutic drugs; ii) the metabolic regulations and the redox mechanisms responsible for the antitumoral action of gemcitabine (GEM) in combination with various compounds or drugs, such as pyrrolidine dithiocarbamate, disulfiram and cannabinoids; iii) the effect, both in vitro and in vivo, of hyaluronic acid-coated liposomes containing a lipophilic derivative of GEM on PDAC cells expressing high levels of CD44, a typical cancer stem cell (CSC) marker. More recently, we have focused on the study of the biological role of CSCs in PDAC and we have obtained CSCs from several PDAC cell lines. We showed that these cells are differentially resistant to various anticancer agents and possess higher tumorigenic and metastatic activity compared to parental cells. Furthermore, on the PDAC cell line Panc1 and Panc1 CSCs we have performed an iTRAQ-based analysis to compare the proteome and secretome and now we are testing the effect of new disulfiram nanoparticle and GEM pro-drug formulations. In addition, our group has focused on the in vitro amplification, characterization and metabolic analysis of CSCs derived from PDAC patient tissues.

TWO MAIN REFERENCES: