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Different uptake of Ukrain can explain the selective effect against pancreatic adenocarcinoma cell cultures *in vitro*

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Introduction: Current therapy for PDAC is surgery followed by adjuvant chemotherapy for early-stage and palliative chemotherapy for advanced disease. Gemcitabine is the standard drug in both adjuvant and palliative treatment. The mixture of Alkaloids (NSC-631570) in combination with gemcitabine significantly increased the median survival of advanced PDAC patients with respect to gemcitabine alone (10.4 vs 5.2 months; $p<0.001$). Furthermore, preclinical studies showed that this mixture had selective citotoxic effects in cancer cell lines derived from different tumor types, but not in normal cell lines.

Aim: To evaluate the citotoxic effects of NSC-631570 in 2 Primary Pancreatic Cancer Cell Lines (PPTCCs), fibroblasts derived from PDAC specimens (F-PDAC) and an immortalized epithelial ductal pancreatic cell line (HNPE).

Materials & Methods: Cytotoxicity was assessed by the CellTiter 96 kit (Promega) based on the cellular metabolism of the tetrazolium compound XTT, which is reduced by living cells to yield a soluble formazan product in the presence of the electron coupling agent phenazine methosulfate, while the modulation of Ukrain uptake in the medium was studied using the fluorescence property of NSC-631570 with the AlphaDigiDoc software by UV light excitation (ULA-DC test).

Results: Citotoxic effects of Ukrain in PPTCCs were significantly higher than those observed in F-PDAC and HPNE cells (20% vs. 80% alive cells, at 10 μM [drug]). Furthermore, the ULA-DC test revealed that PPTCCs cells consumed more drug than F-PDAC and HPNE cells (paired Student's test, $n=4$, $p<0.001$).

Conclusion: These data demonstrated the selective effect of NSC-631570 in PPTCCs, which may be related to a different transport system or higher metabolism of the drug in PDAC. Indeed, the two differents up-take of alkaloids discovered in cancer and non cancer pancreatic cells seem to suggest an higher expression of multi drug resistant systems (MDR) in F-PDAC and HPNE cells and warrant further investigations in order to support the possible role of Ukrain in PDAC treatment.

Biography

Niccola Funel received his first graduation in Bio-Molecular Science (2000) from Pisa University, Italy, where he acquired both PhD graduation in "Experimental and Molecular Oncology" (2006) and Specialization in "Clinical Pathology" (2008). Since 2002 he have been working in Surgical Pathology division (Department of Surgery, University of Pisa) where he involved in different projects focused on Pancreatic Ductal Adenocarcinoma (PDAC). In 2010 he become PI of his project regarding "News therapeutic strategies against PDAC". In 2011 he became council member of Italian Society for Pancreas Study (AISP) for three years. He is also EPC member (European Pancreatic Club) and PC member (Pancreatic Club) since 2009. He awarded six time from AISP at the annual meeting as " young investigator". He received a grant as "Young Investigator 2013" from "Fondazione Veronesi", Milan, Italy. Dr. Funel is author and co-author of 60 papers, more than 130 abstracts presented at national, International and world-wide congresses. Field of expertize: PDAC, Oncology, Biomarkers, TMA, Laser Microdissection and Primary Cell Cultures.

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