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Different uptake of Ukraine 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% live 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 different up-takes of alkaloids discovered in cancer and no pancreatic cancer cells seem to suggest a 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 Ukraine 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 has been working in Surgical Pathology division (Department of Surgery, University of Pisa) where he is involved in different projects focused on Pancreatic Ductal AdenoCarcinoma (PDAC). In 2010 he becomes PI of his project regarding "News therapeutic strategies against PDAC. He awarded six times from AISP at the annual meeting as "young investigator". He received a grant as "Young Investigator 2013" from "Fondazione Veronesi", Milan, Italy. He published 65 full papers and more that 150 abstracts presented in international congresses. His field of expertise includes PDAC, Oncology, Biomarkers, TMA, Laser Micro-dissection and Primary cell Cultures.

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