Treatment of cancer cells based on Circulating Tumor Cell's expression profile using off-label drugs

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Background: Circulating tumor cells (CTCs) constitute a cell subpopulation with great prognostic value in oncology. They detach from the primary tumor, and through the blood stream can initiate metastatic spread to other organs. Their gene and protein expression profile, provides useful information about their resistance to specific therapeutic agents, including chemotherapeutic drugs, targeted therapies (monoclonal antibodies (MoAbs) or small molecular weight molecules (SMW)), or their sensitivity to other treatment options, such as hyperthermia or radiation. The present study aimed to identify whether the expression profile could contribute to success treatment using off-label drugs.

Conclusion: In this study, we demonstrated that CTCs' expression profile, could be an indicator of treatment response, using off-label drugs. It is noteworthy that efficient data were also observed in refractory cases, representing different types of cancer. Drug repositioning might be beneficial for cancer patients, and it should be taken into consideration, mainly in cases where no other options are available.

Methods: Blood samples were collected from more than 500 patients, suffering from different types of cancer. CTCs detected and isolated with Fluorescence Activated Cell Sorting (FACS), evaluated with specific biomarkers for each cancer type, and then used for gene and protein expression assays, with qPCR and Flow Cytometry respectively. In parallel, literature research was performed for these proteins, and the approved drugs against them. Based on the expression profile, off-label drugs for the specific targets were used, and viability/chemosensitivity assays on patients' isolated CTCs were performed.

Results: Expression profile of CTCs revealed overexpression in a wide variety of biomarkers, for whom there are already approved drugs, but only in specific types of cancer. The highest percentages observed for ALOX5, DHFR, DPYD, KIT, PDGFA, RET and others. The use of approved drugs against these targets, such us Zileuton, Pemetrexed, Capecitabine, Dasatinib, Imatinib and Cabozantinib respectively, led to decrease in CTCs' viability independent the type of cancer up in approximately 25% of the cases. Among them, there were also included refractory cases (5%).

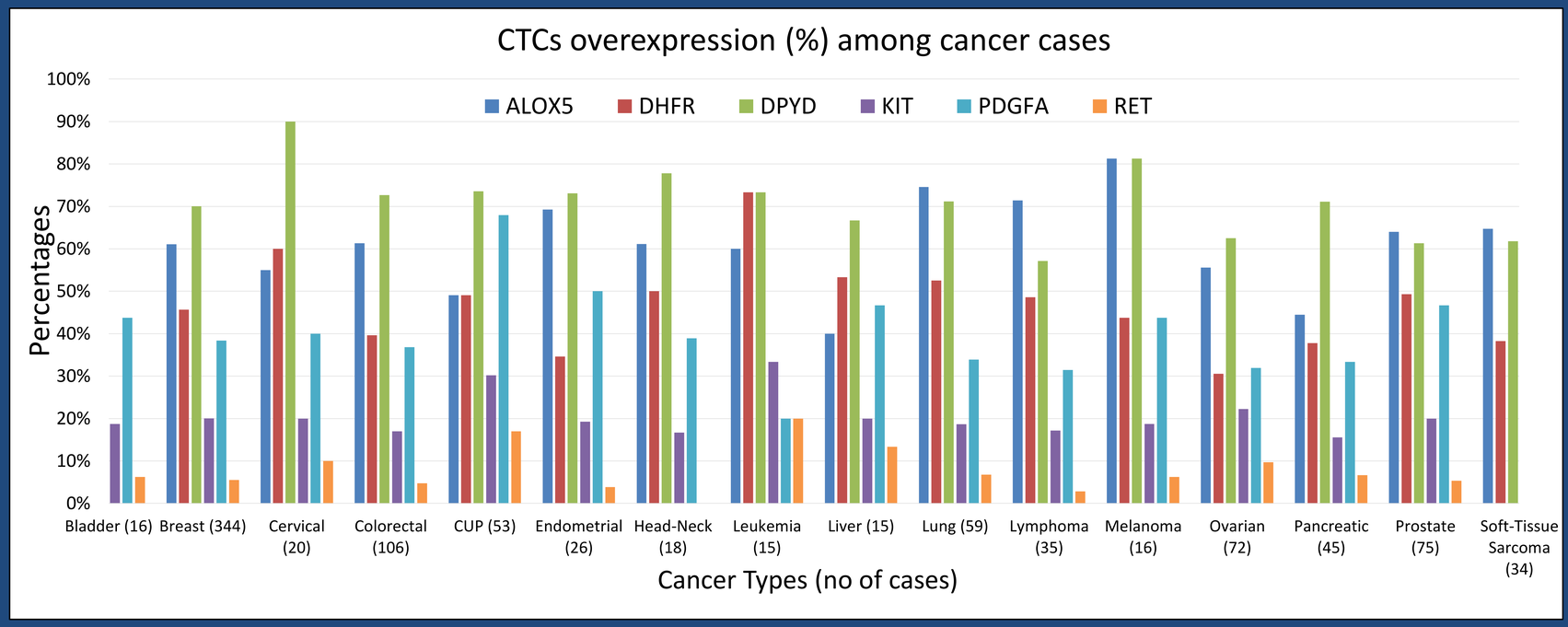

Table 1 . Gene expression profile of CTCs for specific types of cancer and genes

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Disclosure of Potential Conflicts of Interest

None of the authors of the above study has declared any conflict of interest

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