

Topics **CTCs / CECs (circulating tumor cells/ circulating epithelial cells)**

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Title. Early cancer detection with primitive localization through cytopathology evaluation of short-term blood-derived cultures

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Summary

Introduction Recent advances in medical diagnosis, tissue biopsy remains the gold standard for cancer detection and diagnosis. Nevertheless, while efficacious in many practical instances, biopsy is an invasive, non-quantitative technique of analysis, and does not achieve early detection of cancers. Despite the consolidate use of the circulating molecular biomarkers to monitor patient's disease, they fail as diagnostic biomarker for the high rate of false positive/negative.

Goals: Isolation, characterization and cytological evaluation of the Circulating cellular biomarkers with primitive site localization

Hypothesis: the Circulating Tumour cells could be eligible for a cytological evaluation if they were not a rare population to isolate and characterize We applying an optimized protocol, previously described (1,2,3,4,5), enables to prevalently collect non-haematological cells subset through a short-term in vitro-expansion (≤ 14 dys) highlight the cells able to proliferate making them numerically ready for further molecular characterization.

Materials and Methods We conducted an observational prospective CHARACTEX project in patients with a cancer diagnosis and healthy subjects. Within 4 hours from blood sampling collection, the cells were isolated through a gradient passage and seeded in chamber slide useful to obtain cytological

preparations. The pellet of cultivated cells were also included in paraffin to obtain cell blocks preparations in the same patient.

Ethical aspects Prospective project CHARACTERIZATION of Circulating Tumor cells and EXpansion (CHARACTEX) was approved by Regional Institutional Research Ethical Committee with the number 2013.34.

Results Cytological evaluation on short-time expanded blood-derived cells, distinguished with a high accuracy and specificity in healthy and cancer patients. The diagnostic correlation between cytological specimens blood-derived with the histopathology in the same patients was very high with low value of rate of false positive and false negative cases calculated in function of the combination of recognition of atypical cells and S-phase percentage. These values were efficacy reduced by ancillary techniques such as immunocytochemistry and mutational analysis.

Discussion the results of this study highlighted that it is possible, from blood derived cultures, to unmask the population of proliferating cells circulating in peripheral blood derived from tissues subjected to a high cell turnover.

Conclusions and recommendations The use of short time expanded blood-derived cells protocol is at least not inferior to traditional tissue biopsy, as no invasive procedure, to screen the general population. Further studies on machine learning in microscopy could be useful to standardize the individuation of atypical cells increasing the power of this methodology in field of personalized prevention medicine.

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