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Detection and characterization of *via*ble circulating tumor cells as liquid biopsy for cancer

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The enumeration and characterization of circulating tumor cells (CTCs) in the peripheral blood and disseminated tumor cells (DTCs) in bone marrow may provide important prognostic information and might help to monitor efficacy of therapy. Since current assays cannot distinguish between apoptotic and *via*ble DTCs/CTCs, it is now possible to apply a novel ELISPOT assay (designated 'EPISPOT') that detects proteins secreted/released/shed from single epithelial cancer cells. Cells are cultured for a short time on a membrane coated with antibodies that capture the secreted/released/shed proteins that are subsequently detected by secondary antibodies labeled with fluorochromes. In breast cancer, the release of cytokeratin-19 (CK19) and mucin-1 (MUC1) were measured and demonstrated that many cancer patients harbored viable DTCs in their bone marrow, even in patients with apparently localized tumors (stage M0: 54%). Preliminary clinical data (n=57) showed that patients with DTC-releasing CK19 have an unfavorable outcome. We also studied CTCs or CK19-releasing cells (CK19-RC) in the peripheral blood of 194 M1 breast cancer patients and showed that patients with CK19-RC had a worse clinical outcome. In prostate cancer patients (n=48), prostate-specific antigen (PSA) secretion as marker to detect PSA-secreting cells were used and observed that 83% and 42% of M1& M0 cancer patients, respectively, had CTCs with a difference in the CTC median (29 for M1& 9 for M0) and found that a significant fraction of CTCs also secreted fibroblast growth factor-2 (FGF-2), a known stem cell growth factor. More recently, in colon cancer, a considerable portion of viable CTCs detectable by the Epispot assay is trapped in the liver as the first filter organ in colon cancer patients. The enumeration of CK19-RC by the CK19-Epispot assay in 75 colorectal cancer patients revealed viable CTCs in 65.9% and 55.4% (p=0.04) patients in mesenteric and peripheral blood, respectively, whereas CellSearch detected CTCs in 55.9% and 29.0% (p=0.0046) patients. In mesenteric blood, the number of CTC was significantly higher than in the peripheral blood. Our clinical data showed that localized colon cancer patients with a high level of CTCs have an unfavorable outcome (n=60). In conclusion, the EPISPOT assay offers a new opportunity to detect and characterize viable DTCs/CTCs in cancer patients and it can be extended to a multi-parameter analysis revealing a CTC/DTC protein fingerprint.z

Biography

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