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Absorption of Circulating Tumor Cells by Hemoperfusion

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Introduction

Cancer related mortality is highly related to organ-metastases, like those of liver, lung and brain. Therefore, early identification or clearance of cells disseminating from the primary cancer site (circulating tumor cells, CTC) could be of great importance. Currently CTC are especially recognized as: **(i) liquid biopsy, (ii) method to identify novel therapeutic targets** and **(iii) way to measure treatment response.** It has previously been shown that CTC can efficiently bind to certain heparane sulfates. Therefore, we asked whether CTC can also bind to heparin and if isolation of CTC from heparin-coated beads is possible.

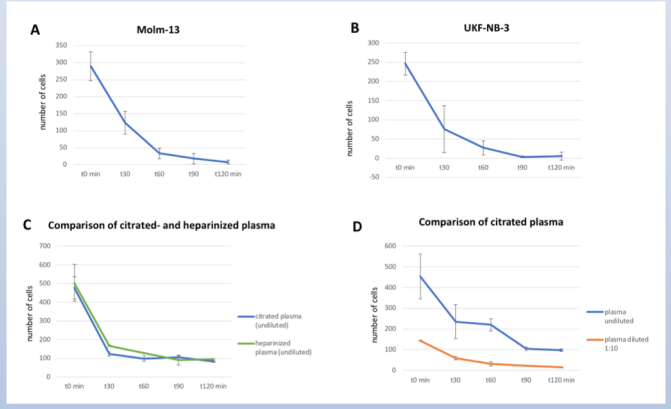

Fig.1: Cell amount reduction by Seraph mini-cartridges. **A):** Reduction of cell number for Molm-13 (n=3). **B)** Reduction of cell number for UKF-NB-3 (n=3). **C)** Comparison of reduction of cell number in undiluted citrated- or heparinized plasma (UKF-NB3 pc-scr) **D)** Comparison of reduction of cell number in undiluted and diluted citrated plasma (UKF-NB3 pc-scr).

Results

The experiments with the Seraph mini-cartridges show a time-dependent CTC reduction in the flow cytometry analysis **(Fig. 1).**

Furthermore, CTC from Molm-13, DU145 and UKF-NB-3 could be regrown in cell culture from Seraph resin (shown for UKF-NB-3, **Fig. 2**).

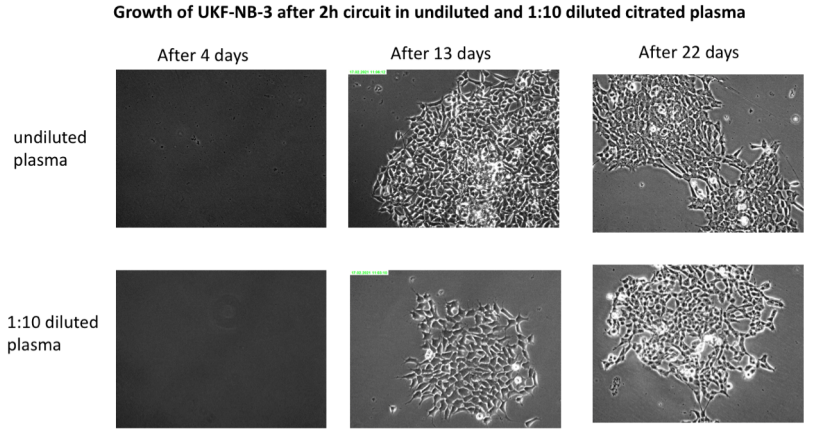

Fig.2: CTC cellular out-growth from Seraph mini-cartridges.

Conclusions

Our experiments show a time-dependent absorption of CTC-like cells by heparinized beads as well as cellular proliferation from the resin. These findings could be of clinical importance for (dialysis) patients with cancer or as a diagnostic device, but need further exploration, e.g. by analysis of cancer patient blood samples.

Methods

Resin was provided in 2.5 ml mini-cartridges by the manufacturer (ExThera Medical, Martinez, CA, USA). The resin is made of ultrahigh molecular weight polyethylene beads with covalently end-point-attached heparin. Cells from prostate cancer (DU145), neuroblastoma (UKF-NB-3) as well as leukemia cells (Molm-13) were cultured according to standard procedures, counted and checked for vitality. 5000 cells/ml were spiked into complete medium (IMDM with 10% FCS, Pen/Strep and glutamine, Sigma Aldrich, Taufkirchen, Germany) as well as citrated- and heparinized plasma. Undiluted plasma was compared to diluted plasma (1:10 in isotonic saline solution). Cartridges were equilibrated and integrated into a small extracorporeal circuit made of MicroPerpex tubing (i.d. 1.3 mm, o.d. 3.4 mm, silicone, GE Healthcare, Freiburg, Germany) and a LKB 2232 Microperpex peristaltic pump (LKB, Bromma, Sweden). The pump was set at a rate of 1 ml/min and samples taken every 30 minutes for 120 min. The amount of cells was detected in each sample (in duplicates) by flow cytometry (FACS Canto II, Becton-Dickinson, Heidelberg, Germany). Next, the mini-cartridges were slowly rinsed with 20 ml PBS, then heparinized beads were removed from the mini-cartridges under sterile conditions and cultured in complete medium to check if cells would grow again after detachment from the beads.

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