

Cancer and tumor markers

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**A SUBPOPULATION AMONG CIRCULATING EPITHELIAL TUMOR CELLS IN PATIENTS WITH SOLID CANCER IS CAPABLE OF SPHERE FORMATION AND CARRIES CANCER STEM CELL PROPERTIES**P. Monika<sup>1</sup>, Z. Dorothea<sup>1</sup>, P. Ulrich<sup>1</sup>, P. Katharina<sup>1</sup><sup>1</sup>Transfusion Center

**BACKGROUND:** A subpopulation of tumor cells with stem-like properties is responsible for tumor initiation, invasive growth and metastasis formation. This population is termed cancer stem cells (CSCs). Several approaches to identify cancer stem cells from the primary tumor including isolation by CSC-specific cell surface marker expression, assessment of their ability to grow as floating spheres, and aldehyde dehydrogenase (ALDH) activity assay are available. We have developed an approach (maintrac®) to detect and monitor the epithelial tumor cells circulating in blood. However, the question arises whether among them there are cells that have the potential to grow into metastases.

**METHODS:** Using a non-dissipative approach with only one enrichment step of red blood cell lysis, the cells from the pellet, containing the white blood cells with at least 1000/ml putative tumor cells were cultured together under conditions favoring the growth of epithelial cells. At days 7, 14 and 21 the cultured spheroids were stained with anti-EpCAM antibody and typical cancer stem cell markers. Cell viability and surface marker expression was evaluated by a fluorescence scanning microscope.

**RESULTS:** Tumor sphere formation was observed in 79% of breast cancer patients, 77% of colon cancer patients, 73% of prostate cancer patients and 75% of lung cancer patients ranging from 5-60/100 µl blood. The size of spheres increased from day 7 to day 21. The spheres were low or negative for CD24 and positive for CD44 in breast cancer patients and expressed a high level of ALDH1. Cells in colorectal tumor spheres had a typical phenotype for colorectal cancer stem cells and expressed high levels of EpCAM and CD 133. The tumor spheres cultured from CETCs by prostate cancer patients showed positive staining for CD 44 and CD 133. In lung cancer tumor spheres were positive for EpCAM and CD133. As a control 20 healthy donors were enrolled into the study and no sphere formation was observed.

**CONCLUSIONS:** This study demonstrates that tumor stem cells are present in peripheral blood from metastatic and non-metastatic tumor patients. They represent a small subpopulation of circulating epithelial tumor cells with the ability to growth as tumor spheres and might be the progenitors of metastasis.