

Tumor spheres growing from peripherally circulating tumor cells exhibit stem cell features

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Background: Among the cells that are disseminated from a malignant tumor some are capable of resettling in distant organs and growing into life-threatening metastases. Therefore, the question arises how and whether such cells which have the potential to grow into metastases can be detected.

Materials and Methods: Using a nondissipative approach with only one enrichment step of red blood cell lysis, cells were cultured under conditions favoring the growth of epithelial cells. At 7, 14 and 21 days the cell cultures were inspected for the appearance of spheroids staining with anti-EpCAM, anti-CD24 and anti-CD44 antibody and expressing ALDH1.

Results: Tumorspheres from peripherally circulating cells from patients with malignant tumors in different stages of disease could so far be grown from 79% of 100 patients in whom more than 1000 epithelial tumor suspect cells per ml were detected. Numbers of tumorspheres correlated with the aggressiveness of the tumor and were highest in patients after surgery who had not yet received any systemic therapy. The size of the spheres increased from day 7 to day 21. They were negative for CD24 and positive for CD44. They highly express ALDH1 and thus exhibit typical features of stem cells.

Conclusion: Here, we demonstrate that the circulating tumor cells, detected in our approach contain a subpopulation with stem cell-like properties capable of growing into tumorspheres. The frequency in peripheral blood of cells capable of forming tumor spheres seems to be dependent on the aggressiveness of the primary tumor.