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

Abstract

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

Materials and Methods: Using a noninvasive approach with only one enrichment step of red blood cell lysis, cells were isolated 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-CD44 and anti-CD24 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 received any systemic therapy. The size of the spheres increased from day 7 to day 21. They were negative for CD24 yet positive for CD44. They highly express ALDH1 and thus could so far be grown from 79% of 100 patients in whom more than 1000 epithelial tumor-suspect cells per ml were detected. Among the peripherally circulating tumor cells a variable fraction is able to express stem cell and adhesion properties and can be grown into tumor spheres, a property ascribed to cells capable of initiating tumors and metastases.

Conclusion: Tumor spheres growing from peripherally circulating tumor cells exhibit typical features of stem cells. ALDH1 positive cells could initially not be detected among the circulating tumor-suspect cells, however, all tumor spheres analyzed were highly positive for ALDH1. CD24 coexpression was low or lacking on the cells of the tumor spheres. In contrast, CD44 was highly coexpressed and growing into life-threatening metastases. Therefore, the circulating tumor-suspect cells represent a subpopulation with properties of growing into tumorspheres.