The side population of ovarian cancer cells defines a heterogeneous compartment exhibiting stem cell characteristics


Cancer stem cells (CSC) are believed to be involved in tumor evasion of classical antitumor therapies and have thus become an attractive target for further improvement of anticancer strategies. However, the existence and identity of CSC are still a matter of controversy. In a systematic screen of 13 ovarian cancer cell lines we show that cells with stem cell properties are reliably detectable as a minor population, characterized by ABC transporter expression resulting in the side population (SP) phenotype. In different cell lines, either ABCG2 or ABCB1 was found to be responsible for this effect. Purified SP cells featured virtually all characteristics of bona fide CSC, including clonogenicity, asymmetric division and high tumorigenicity in vivo. Using in-depth phenotyping by multicolor flow cytometry, we found that among the investigated ovarian cancer cell lines the SP compartment exhibits tremendous heterogeneity and is composed of multiple phenotypically distinct subpopulations. Thus, our study confirms previous results showing that CSC are contained within the SP. However, the exact identity of the CSC is still disguised by the high complexity of the CSC-containing compartment. Further functional studies are needed to determine whether a single cellular subset can unambiguously be defined as CSC or whether multiple stem cell-like cells with different properties coexist. Moreover, the observed heterogeneity may reflect a high level of plasticity and likely influences tumor progression, escape from immune-surveillance and development of resistance to anticancer therapies and should therefore be considered in the development of new treatment strategies.

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