Murine breast-cancer-cell/mesenchymal-stem-cell hybrids exhibit enhanced drug resistance to different cytostatic drugs
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Several data of the past 15 years suggest that cell fusion is not only a process of normal development and tissue homeostasis, it is also assumed to participate in cancer progression. Because of the high fusogenic capacity of cancer cells cell fusion may promote diversity in cancer cell populations. Therefore fusion of a cancer cell with another cancer cell, an immunocompetent cells or even an adult stem cell can give rise to hybrid cells with new properties.

Question: What is the role of cell fusion in cancer progression?

Methods: Characterisation of hybrid cells derived from spontaneous fusion of murine 67NR-Hyg breast cancer with puromycin resistant bone marrow derived MSCs, from Tg(GFPU)5Nagy/J mice in vitro, by Realtime PCR Arrays for analysing breast cancer and multi drug resistance associated genes, measurement of proliferation rate under influence of chemotherapeutic agents Doxorubicin, 17-DMAG, Etoposide, Paclitaxel and 5-FU over a period of 3 days, FACS analysis of Rhodamine 123 efflux and Western Blot analysis.

Results: Realtime PCR Arrays for analysing breast cancer and multi drug resistance associated genes revealed an increased expression of drug resistance proteins, in particular ABC-transporters. These findings correlated with high ABC-transporter mediated Rhodamine 123 efflux of hybrid cells in comparison to parental cell lines detected by FACS analysis. XTT-proliferation-assay after culturing cells over a period of 3 days among different concentrations of chemotherapeutic agents mentioned above showed an increased drug resistance of hybrid cells compared to parental cells for Doxorubicin, 17-DMAG, Etoposide and Paclitaxel. Hybrid cells exhibited an altered morphology under influence of chemotherapeutic agents, especially Doxorubicin and 17-DMAG, but even survived at concentrations of 10µM. Drug resistance of hybrid cells may be reversed by addition of 50µM Verapamil in some cases of tested chemotherapeutic agents.

Conclusions: We conclude that cell fusion between breast cancer cells and MSCs can give rise to hybrid cells with altered properties that direct enhanced ABC-transporter mediated drug resistance and therefore may promote cancer cell survival during chemotherapy.