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ORAL PRESENTATION

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The sialyl-glycolipid SSEA4 marks a subpopulation of chemotherapy resistant breast cancer cells with mesenchymal features

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Triple negative breast cancer (TNBC) is an aggressive breast cancer subtype associated with high risk of early relapse and metastasis [1]. At the moment chemotherapy remains the main option for systemic therapy of TNBC patients but complete remission occurs only in 20% of the patients [2]. In order to identify biomarker for chemotherapy-resistant TNBC cells, we performed a cell surface marker screen in 4 TNBC patient-derived xenograft (PDX) models that respond well to adriamycin/cyclophosphamide-based (A/C) chemotherapy but fail to reach complete pathological response. We used multi-parameter flow cytometry to screen the expression of 45 cell surface markers during the course of chemotherapy.

We identified the sialyl-glycolipid SSEA4 as a marker of chemotherapy-resistant cancer cells in all four models. In addition, 3 out of 4 TNBC PDXs showed higher percentage of SSEA4-positive cells compared to all A/C-sensitive TNBC PDXs analysed. Gene expression comparison between SSEA4-positive and SSEA4-negative tumor cells from 3 TNBC PDXs highlighted an overexpression of mesenchymal-associated genes and a deregulation of drug resistance pathway-associated genes and miRNAs in SSEA4+ breast cancer cells. In addition, high expression of ST3 beta-galactoside alpha-2,3-sialyltransferase 2 (ST3Gal2), the enzyme catalyzing the last step of SSEA4 synthesis, was found associated with poor outcome in ER-, PR- breast cancer patients treated with chemotherapy ($p < 0.01$, HR 3.08).

Thus, we propose SSEA4 as a novel marker of mesenchymal and chemoresistant breast cancer cells,

and ST3GAL2 expression as a predictive marker for chemoresistance associated with poor outcome in breast cancer patients.

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