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Background: Hypothesis: Non-stem (differentiated and progenitor) cancer cells can form metastases by performing a reverse transition to cancer stem cells (CSC) in organs under the influence of cytokines (SST - Somatic-Stem Transition). The ability to SST is acquired in the course of evolution and is ensured by ectopic expression of several stemness genes (such as SOX2, OCT3/4, MYC, KLF4, NOTCH1, NANOG ...), due to amplifications in chromosomal regions of their localization (3q, 5p, 6p, 7q, 8q, 13q, 9p, 9q, 10p, 10q21.1, 16p, 18chr, 19p). If there are no amplifications in the tumor, it is not capable of SST and will not metastasize.

Methods: Breast cancer cells of two patients were used to induce a SST. One patient had amplifications of 3q, 6q, 8q, 9q, 10q22.1 in the tumor, in which the SOX2, MYC, KLF4, NOTCH1, NODAL genes were localized. The other patient had no amplifications of stemness genes in the tumor. Magnetic separation was used to extract populations of EpCAM+CD44 tumor cells of both patients. SST was IL6-induced. Following this, the content of EpCAM+CD44+CD24- CSC was evaluated via flow cytometry, the increase in the number of cells after 3 passages, and the induction of mammospheres were measured.

Results: Under the influence of IL6, CSC emerged in the population of EpCAM+CD44 tumor cells with amplifications, the number of cells after 3 passages increased by a factor of 33, and mammospheres of 7-15 cells were induced. While SST was not induced in the population of EpCAM+CD44+ tumor cells taken from the patient with no amplifications, the number of cells after 3 passages was increased only by a factor of 5 and no mammospheres were formed. Prospective trials: in 11 breast cancer patients with stemness genes amplifications in the tumor, neoadjuvant chemotherapy (NAC) eliminated the clones with amplifications. All patients have a metastatic-free survival. 11 patients had no amplifications and they did not undergo NAC. All patients had 100% survival. 9 patients had no amplifications of their stemness genes before the treatment, and NAC induced their occurrence, 90% of the patients developed metastases.

Conclusions: We showed an SST in EpCam+CD44+ tumor cells, the importance of amplifications of stemness genes loci for its induction, and the importance of amplifications of stemness genes for metastasis.

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