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Profiling of suppressive immune subsets in metastasis negative and positive sentinel lymph nodes from patients with HER2- breast cancer

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Background

Since it is the site of initial immune activation and priming of antigen-specific T cells, as well as the first location to which tumor cells metastasize, our research focuses on understanding the immune status and tumor-induced suppression within breast cancer (BrCa)-draining sentinel lymph nodes (SLN).

Methods

Suppressive immune subsets were profiled by multi-color flow cytometry in two different BrCa SLN cohorts. In the first cohort, collected at the Providence Cancer Center (08/11-07/13), we looked at frequencies of HLA-DR- CD14+ myeloid cells and their expression of co-stimulatory and inhibitory receptors. Four metastasis+ SLN and 11 metastasis- SLN were assessed in this cohort. SLN in the second cohort were collected at the VUmc in Amsterdam and Kennemer Gasthuis in Haarlem (10/13-06/14) and contained 2 metastasis+ and 7 metastasis- SLN. In this cohort the frequencies of HLA-DR- CD14+ cells as well as CD25_hi FoxP3+ T regulatory cells (Treg) were analyzed. Since all tumors corresponding to the metastasis + SLN turned out to be HER2 negative, only metastasis- SLN from HER2- tumors were included. Apart from 2 tumors in the Providence cohort, all tumors did express progesterone and/or estrogen receptors.

Results

Elevated frequencies of HLA-DR- CD14+ immature myeloid cells could be detected in the metastasis+ SLN in both cohorts. This difference was statistically significant for the Providence cohort ($p < 0.0001$) (3.8 fold increase). No differences were observed for expression levels of the co-stimulatory molecules CD80 and CD86 or the inhibitory molecules PD-L1 and B7H4 on HLA-DR- CD14+ cells between positive or negative SLN and expression was low for all these markers. Due to the small number of metastasis+ SLN in the Dutch cohort statistics could not yet be performed, but a 2.3 fold increase in HLA-DR- CD14+ cells was seen. In this cohort, frequencies of Treg were found to be 4-fold higher in the metastasis+ SLN compared to metastasis- SLN (0.31 ± 0.22 vs. 1.22 ± 0.24 Treg of CD4 T cells). Moreover, a significant correlation was observed between the frequencies of HLA-DR- CD14+ immature myeloid cells and the frequencies of Treg in these BrCa SLN ($r = 0.718$, $p < 0.01$).

Conclusion

Our data suggest that tumor-derived factors negatively influence both the myeloid and the lymphoid compartments within SLN draining HER2 negative breast cancers.

Consent

Written informed consent was obtained from the patient for publication of this abstract and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

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