Annals of Oncology 25 (Supplement 1): i17–i18, 2014
doi:10.1093/annonc/mdu067.2

Breast cancer host immune and stromal biology

50P LYMPHOCYTES INFILTRATING BREAST CANCER : DENSITY, COMPOSITION AND ORGANIZATION

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The clinical relevance of tumor infiltrating lymphocytes (TIL) in breast cancer (BC) is controversial due to variation in the subpopulations of immune cells detected in tumors, with the balance of key players potentially explaining the protective immunity observed in some patients. To gain insight, we performed comprehensive immunophenotyping of T and B-TIL in early stage BC. This prospective analysis used flow cytometry to examine TIL in fresh tumor homogenates (n = 121). TIL were compared to lymphocytes in nonadjacent non-tumor breast tissue (NANT, n = 116) and normal tissue from mammary reductions (n = 28). TIL organization and spatial distribution was analyzed by immunohistochemistry and immunofluorescence on paraffin sections from a subset of patients (n = 78). The fresh tissue analyses revealed that tumors have a higher TIL density compared to normal tissue and NANT, the latter two being remarkably similar and thus used to establish a cutoff for TIL positive tumors. Using this threshold, 65% of the tumors were TIL positive. TIL density was correlated with proliferation (Ki-67 & histological grade) and inversely correlated with hormone receptor expression. Tumors have higher frequencies of lymphocytes compared with normal tissue, with associated increases in CD4+ T cells and CD19+ B cells. The frequency of CD4+ T cells is higher in TIL positive tumors with a median CD4/CD8 ratio > 1 compared to < 1 in TIL negative tumors and NANT. In all tissues, T cells are predominantly CD45RO+ memory cells, with a significant proportion expressing PD-1. The B cell population was more heterogeneous with higher numbers of naïve relative to memory B cells detected in both normal and tumor tissues. The distribution pattern of TILs (CD4 +, CD8+ & B cells) in infiltrated tumors was dispersed in the tumor bed and lymphocyte aggregates were principally in the peritumoral regions. Closer examination of these lymphoid aggregates shows they are tertiary lymphoid structures containing a T cell zone and a B cell follicle with an active germinal center. These data suggest that establishment of organized immune microenvironment in or adjacent to the tumor bed could be an effective mechanism for generating anti-tumor memory T and B cell responses.

Disclosure: All authors have declared no conflicts of interest.