Abstract citation ID: bvac150.1812

Tumor Biology

ODP559

The prognostic role of IL-17A-neutrophils crosstalk in triple-negative breast cancer

Freeha Khalid, PhD, Kiyoshi Takagi, PhD, Fouzia Guestini, PhD, Yasuhiro Miki, PhD, Minoru Miyashita, MD, PhD, Hisashi Hirakawa, MD, PhD, Yasuyo Ohi, MD, PhD, Yoshiaki Rai, MD, Phd, Yasuaki Sagara, Phd., M.D., M.P.H., Takashi Suzuki, MD, PhD, and Hironobu Sasano, M.D., Ph.D., D.A.B.P

Triple-negative breast cancer (TNBC) is an aggressive subtype of breast cancer that is characterized by extensive intratumoral heterogeneity. At this juncture, TNBCs are treated with conventional chemotherapy and have few targeted therapies. Due to the presence of increased tumor-infiltrating lymphocytes and immune-checkpoint molecules, TNBCs are considered highly immunogenic. This provides an opportunity to explore various immunotherapeutic options. The immune cells such as Th17 cells or neutrophils (tumor-associated neutrophils; TANs) can secrete a pro-inflammatory cytokine called IL-17A, which is known to be associated with poor outcomes in several cancers. TANs are related to tumor progression and are influenced by certain chemokines. Meanwhile, IL-17A can also regulate chemokine (C-X-C motif) ligand 1 (CXCL1), which is a strong chemoattractant for TANs and can lead to the growth of tumors in breast cancer. However, the significance of IL-17A and its interaction with TANs and CXCL1 has yet not been clearly understood in TNBC. For this purpose, formalin-fixed paraffin-embedded biopsy tissue specimens of 109 Japanese TNBC patients were included in this study. Immunohistochemistry was performed to assess the status of IL-17A, CXCL1, and CD66b (a neutrophil marker) and to understand their correlation among each other, with clinical parameters, and with the outcomes of patients. Also, in vitro studies were performed to evaluate the effect of recombinant IL-17A on TNBC cell lines proliferation, migration, and CXCL1 expression. Clinical results revealed that IL-17A was significantly correlated with CXCL1 and CD66b, which suggested potential crosstalk between them. On the other hand, CXCL1 significantly and CD66b tended to be correlated with tumor size. Also, CD66b was significantly correlated with the Ki-67 labeling index, showing that TANs may have a role in tumor cell proliferation. Kaplan-Meier survival curves showed that high IL-17A was significantly associated with poor disease-free and overall survival, indicating the poor outcome of the TNBC patients. To our great interest, in vitro results revealed that no difference was observed for proliferation or migration of TNBC cell lines (was only observed in the MDA-MB-231 cell line) after treatment with recombinant IL-17A. However, CXCL1 was highly up-regulated in a dose and time-dependent manner after exposure to IL-17A, indicating that IL-17A might be involved in the recruitment of neutrophils through up-regulation of CXCL1. Therefore, we concluded that IL-17A was a poor prognostic factor for TNBC patients, enhancing the chemokine-neutrophil recruitment to the tumor site, leading to tumor progression and aggression. In the future, we intend to explore different pathways for understanding the mechanism of CXCL1 up-regulation by IL-17A.

Presentation: No date and time listed