Atif S M I et al., J Clin Cell Immunol 2015, 6:5
http://dx.doi.org/10.4172/2155-9899.C1.025

OMICS International
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4th International Conference and Exhibition on
Immunology
September 28-30, 2015 Crowne Plaza Houston River Oaks, Houston, TX, USA

γδ T cells expansion and function stimulated with IL-18: Role of NK cells

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Introduction: Human γδ T cells display potent cytotoxicity against various tumor cells pretreated with zoledronic acid (Zol). Zol has shown benefits when added to adjuvant endocrine therapy for patients with early-stage breast cancer or to standard chemotherapy for patients with multiple myeloma. Although γδ T cells may contribute to this additive effect, the responsiveness of γδ T cells from early-stage breast cancer patients has not been fully investigated.

Objective: In this study, we determined the number, frequency and responsiveness of Vγ2Vδ2 T cells from early- and late-stage breast cancer patients and examined the effect of IL-18 on their *ex vivo* expansion.

Methods: Breast cancer patients (n=80) were enrolled after institutional review board approval and with written informed consent. Peripheral blood mononuclear cells (PBMC) were purified and stimulated with Zol/IL-2 or Zol/IL-2/IL-18 for 2 to 10 days. The expanded cells were assessed on flow cytometry and the production of IFN-γ and TNF-α measured through ELISA.

Results: The responsiveness of Vγ2Vδ2 T cells from patients with low frequencies of Vγ2Vδ2 T cells was significantly diminished. IL-18, however, enhanced ex vivo proliferative responses of Vγ2Vδ2T cells and helper NK cells (CD3-CD56 bright CD11c+CD14-CD16+NKGD2+NKp44 low) from patients with either low or high frequencies of Vγ2Vδ2 T cells. Cell-to-cell contact between γδ T and helper NK cells appeared to promote expansion of γδ T cells. Exogenous IL-18 markedly enhanced IFN-γ and TNF-α production from PBMC stimulated by Zol/IL-2, whereas the addition of an anti-IL-18Rα mAb reduced cytokine production.

Conclusion: These results demonstrated that Zol elicits immunological responses by γδ T cells from early-stage breast cancer patients and IL-18 enhances proliferative responses and effector functions of γδ T cells in the context of helper NK cells.

Biography

Atif SM Idrees has completed his PhD from Kyoto University School of Medicine, Kyoto, Japan. He is now the coordinator of educational media development at the Faculty of Science and Technology, Alneelain University, Khartoum, Sudan. He has been involved in many research activities beside serving as an advisor for undergraduate and postgraduate research projects. He is also available internationally through his collaboration with research institutes in more than country. His main research interest is in the field of Immunology, especially Cancer Immunology and Immunotherapy.

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