Journal for ImmunoTherapy of Cancer

POSTER PRESENTATION Open Access

Evidence for a coordinate role of CD14+ antigen-presenting cells and regulatory T cells in conditioning the microenvironment of metastatic lymph nodes from patients with cervical cancer

Marijne Heeren[1*], Bas Koster[2], Sanne Samuels[3], Debbie Ferns[1], Dafni Chondronasiou[2], Gemma Kenter[1], Ekaterina S Jordanova[1], Tanja D de Gruijl[2]

From Society for Immunotherapy of Cancer 29th Annual Meeting
National Harbor, MD, USA. 6-9 November 2014

A better understanding of the microenvironment in relation to lymph node metastasis is essential for the development of effective immunotherapeutic strategies against cervical cancer.

In the present study, we investigated the microenvironment of tumor-draining lymph nodes of cervical cancer patients, by comprehensive flow cytometry-based phenotyping and enumeration of immune-cell subsets in tumor-negative (LN-, n = 20) versus tumor-positive lymph nodes (LN+, n = 8), and by the study of cytokine release profiles (n = 4 for both LN- and LN+).

We found significantly lower $CD4^+$ and higher $CD8^+$ T-cell frequencies in LN+ samples, accompanied by increased surface levels of activation (HLA-DR and ICOS) and inhibitory markers (PD-1 and CTLA-4). Furthermore, in LN+ we found increased rates of a potentially regulatory antigen-presenting cell (APC) subset ($CD11c^{hi}CD14^+PD\text{-}L1^+$) and of myeloid-derived suppressor cell (MDSC) subsets, which in the case of the former correlated significantly with elevated frequencies of $FoxP3^+$ Tregs. After *in vitro* stimulation with different TLR ligands (PGN; Poly-IC; R848), we observed higher production levels of IL-6, IL-10 and TNFα but lower levels of IFNγ in LN+.

We conclude that, despite increased T-cell differentiation and activation, a striking switch to a profound immune suppressive microenvironment in LN+ of cervical cancer patients will enable immune escape. Our data point to the $CD14^+PD\text{-}L1^+$ APC/Treg axis as a particularly attractive and relevant therapeutic target to specifically tackle microenvironmental immune suppression and thus enhance the efficacy of immunotherapy in patients with metastasized cervical cancer.

Authors' details
[1]Obstetrics & Gynecology, VU University Medical Center, Amsterdam, The Netherlands. [2]Medical Oncology, VU University Medical Center, Amsterdam, The Netherlands. [3]Gynecology, The Netherlands Cancer Institute, Amsterdam, The Netherlands.

Published: 6 November 2014

doi:10.1186/2051-1426-2-S3-P211
Cite this article as: Heeren *et al.*: Evidence for a coordinate role of CD14 + antigen-presenting cells and regulatory T cells in conditioning the microenvironment of metastatic lymph nodes from patients with cervical cancer. *Journal for ImmunoTherapy of Cancer* 2014 **2**(Suppl 3):P211.

[1]Obstetrics & Gynecology, VU University Medical Center, Amsterdam, The Netherlands
Full list of author information is available at the end of the article