ImmunoTools *special* Award 2015

Marijne Heeren, PhD-student

Supervisor(s): Prof. Dr. Tanja D. de Gruijl
Prof. Dr. Gemma G. Kenter

Department of Obstetrics & Gynaecology, VU University medical Center/CCA, CCA 2 – 48, De Boelelaan 1117, 1081 HV Amsterdam, The Netherlands

Translating immune characteristics of metastatic tumour cells into therapeutic targets for cervix carcinoma.

Cervical cancer is the fourth most common cancer in women worldwide and is caused by a persistent infection with high-risk human papilloma virus (HPV) types, in particular HPV16 and HPV18 which account for approximately 70% of all cervical carcinomas. The most important prognostic factor in early stage cervical cancer is the presence of metastatic tumor cells in the pelvic lymph nodes, found in 27% of the cases. Due to its viral origin, this type of cancer is highly immunogenic and particularly suitable for immunotherapy. Therefore, a better understanding of the microenvironment in primary tumor and in tumor-draining lymph nodes is essential for the development of effective immunotherapeutic strategies against cervical cancer.

In a recent study, we have investigated the microenvironment of cervical tumor-draining lymph nodes by comprehensive flowcytometry-based phenotyping and enumeration of several immune-cell subsets and by the study of cytokine profiles. We found major differences in the microenvironment between metastasis-free lymph nodes compared to metastatic lymph nodes, in which metastatic lymph nodes had a more immunosuppressive state with i.e. more myeloid-derived suppressor cells (MDSC), high and interrelated levels of $CD25^{+}FoxP3^{+}$ regulatory T cells and $CD14^{+}$ macrophage-like cell subset expressing the inhibitory programmed death-ligand 1 (PD-L1), and high levels of IL-6 and IL-10 (Heeren, 2014).

This study was an interesting immune monitoring study, but we want to delineate this immunosuppressive microenvironent in patients with cervical cancer in more detail by studying more markers and conducting functional assays. The

ImmunoTools antibodies and growth factors would be of great help in distinguish between metastatic tumor cells and immune cells (CD45) and analyzing more markers on these tumor cells (like HLA-ABC), immune cells (CD21, and CD35) and soluble factors produced by these cells (e.g. IL-6 and IL-10) following stimulation and/or blocking of immune checkpoint molecules. Additionaly, we want to investigate what happens with the frequencies and activation of the previously identified immune cells like dendritic cells (DCs) (CD14, CD11c, CD1a, CD80 and CD86) and T cells (CD3, CD8 and CD4, HLA-DR) to be present in the cervical tumor-draining lymph nodes after these functional assays. The products from ImmunoTools might bring us a step closer in unravelling the microenvironment in primary and metastatic cervical cancer and help to find ways to interrupt the immunosuppressive cycle and induce effective antitumor immunity in the fight against (advanced) cervical cancer.

Reference:
Heeren,A.M., Koster,B.D., Samuels,S., Ferns,D.M., Chondronasiou,D., Kenter,G.G., Jordanova,E.S. and de Gruijl,T.D., 2014. High and Interrelated Rates of PD-L1^{+}CD14^{+} Antigen-presenting Cells and Regulatory T cells mark the Microenvironment of Metastatic Lymph Nodes from Patients with Cervical Cancer. Cancer Immunol. Res.

ImmunoTools *special* AWARD for **Marijne Heeren** includes 21 reagents

FITC - conjugated anti-human CD4, CD35, CD80, CD86, HLA-ABC, HLA-DR, Control-IgG1, Control-IgG2a,

PE - conjugated anti-human CD8, CD45,

PerCP - conjugated anti-human CD3, CD14,

APC - conjugated anti-human CD11c, CD21, Control-IgG1,

human ELISA-set for 96 wells, human IL-6, human IL-10 (each 3 reagents)

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