Quantitative Pathology

Improving Cancer Vaccine Efficacy: Study of a Cell Population Suspected of Counteracting Dendritic Cell Vaccinations using Multiplex and Multispectral Analyses

A recent study of a melanoma patient cohort treated with a BDCA1+ dendritic cell (DC) vaccine indicated links between reduced immune response and a previously uncharacterized cell population within that vaccine. Varying levels of a previously unknown suppressive myeloid cell subset - identified by co-expression of the DC marker BDCA1 and the monocytic marker CD14 - form part of the cellular content of this vaccine that is produced on the basis of the patients’ own dendritic cells.

Tumors have been shown to evade the immune system with the help of a number of cell types within their microenvironment; these cell types display immune-evasive properties or actively recruit cells that confer immunosuppressive properties. In a bid to improve tumor vaccine efficacy, this study characterizes the blood-borne BDCA1+CD14+ myeloid cell population within blood and tissue of healthy individuals versus cancer patients, and their negative effect on T-cell proliferation.

To assess whether BDCA1+CD14+ myeloid cells were present in the tissue (as well as in the blood), samples of metastatic melanoma within the skin, colon and draining lymph nodes were fluorescently stained using Opal™ multiplex reagents. A multiplexed Opal staining panel was optimized for detecting CD14, BCDA1, HLA-DR and melanoma cells using a cocktail of SOX-10, Tyrosinase, HMB-45 and Mart-1. The metastatic lesions were clearly highlighted through the use of this melanoma cocktail. Multispectral images of the samples were acquired with the Vectra® automated multispectral imaging system (Figure 1).
inForm® software was subsequently used to unmix images for quantitative batch image analysis (Figure 2). Image analysis involved segmenting images into areas of tumor versus stromal tissue, and detecting individual cells and their cellular compartments. The signal levels of the four markers and their localization within specific cellular compartments were then used to classify the cells into seven different cell types, using inForm’s phenotyping function (Figure 2). Five of the cell types were immune cells, exemplified in Figure 2 (inset).

The study concluded that metastatic melanoma patients with elevated levels of BDCA1+CD14+ myeloid cells in the blood can also exhibit elevated levels in their metastatic lesions. As such cells exhibit antigen-specific immunosuppressive properties, taking steps to eliminate these cells from DC vaccine preparations might increase the efficacy of the anti-tumor vaccine.
Reference

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The mission of the Radboud Institute for Molecular Life Sciences (RIMLS) is to achieve a greater understanding of the molecular mechanisms of disease. By integrating fundamental and clinical research, the institute obtains multifaceted knowledge of (patho) physiological processes. To have a significant impact on healthcare, these findings are translated into diagnostics, therapeutics and personalized treatment strategies.

The RIMLS accommodates research groups from the Radboud university medical center (Radboudumc) and the Faculty of Science of the Radboud University Nijmegen. RIMLS aims to advance innovation in translational research, based on integrating diverse areas of scientific expertise within the molecular and medical sciences. In line with the Radboudumc’s strategic vision to “have a significant impact on healthcare”, research is bundled into clinically-orientated research themes from molecule-to-man (M-2-M) plus a “mechanism-based” theme focusing on chemical biology and nanomedicine. RIMLS works closely with the Radboud Institute for Health Sciences (RIHS), thereby extending many of the research themes from ‘man’ to ‘population’ studies.

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