

POSTER PRESENTATION

Open Access

Generation of tumor antigen-specific CD4⁺ and CD8⁺ T cells by simultaneous MHC-I and -II epitope presentation *in vitro* and *in vivo*

Carina Wehner^{1*}, Christian Ellinger¹, Silke Raffegger¹, Susanne Wilde¹, Barbara Mosetter², Judith Eckl¹, Bernhard Frankenberger², Manon Weis¹, Giulia Longinotti¹, Nadja Sailer¹, Dolores J Schendel¹, Slavoljub Milosevic¹

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

In recent years, activation of the patient's immune system to defend against tumors was demonstrated to be a promising alternative strategy to classical cancer treatments. Dendritic cells (DCs) can present antigens on MHC-II and -I leading to the activation of CD4⁺ or CD8⁺ T cells, respectively. Stimulated CD4⁺ T cells act as helper cells for cytotoxic CD8⁺ T cells to kill tumor cells by mediating strong proliferation and licensing DCs, increasing their presentation capacity. Tumors bearing MHC-II molecules can also be directly destroyed by cytotoxic CD4⁺ T cells. As an efficient anti-tumor response strongly depends on the interplay of DCs, CD4⁺ and CD8⁺ T cells, these three cell types are considered to be essential for successful immunotherapy design.

In clinical trials, DCs were either endogenously or exogenously loaded with tumor antigens for the presentation on MHC-I rather MHC-II. As the antigen presentation pathways differ, a simultaneous loading of MHC-I and -II was suboptimal. To overcome this obstacle, we used a signaling sequence (CrossTAG) to force MHC-II cross-presentation of tumor-associated antigens (TAAs) encoded by *in vitro* transcribed (*ivt*) RNA. Subsequently, peripheral blood lymphocytes were primed by DCs expressing TAAs on MHC-I and -II enabling activation and interaction of CD4⁺ and CD8⁺ T cells. By this approach, we were able to induce and identify TAA-specific CD4⁺ and CD8⁺ T cells in the same experiment.

In addition, superior induction efficiency of DCs loaded with CrossTAG-TAA-*ivt*RNA compared to conventional TAA-*ivt*RNA was shown in the humanized NOD/scid IL2Rgnull (NSG) mouse model. NSG mice

were engrafted with human peripheral blood mononuclear cells (PBMC) and vaccinated twice with DCs either transfected with CrossTAG-TAA-*ivt*RNA or conventional TAA-*ivt*RNA. Reisolated PBMC of mice vaccinated with CrossTAG-TAA-*ivt*RNA transfected DCs showed higher numbers of antigen-specific CD8⁺ T cells and stronger activation/cytotoxic activity against tumor cells.

These *in vitro* and *in vivo* data illustrate the benefits of loading DCs with CrossTAG-linked target antigens as CD8⁺ and CD4⁺ T cells can be induced side by side allowing interactions and T cell help.

Authors' details

¹Trianta Immunotherapies GmbH - a subsidiary of Medigene AG, Germany.

²Institute of Molecular Immunology/Helmholtz Center Munich, Germany.

Published: 6 November 2014

doi:10.1186/2051-1426-2-S3-P65

Cite this article as: Wehner et al.: Generation of tumor antigen-specific CD4⁺ and CD8⁺ T cells by simultaneous MHC-I and -II epitope presentation *in vitro* and *in vivo*. *Journal for ImmunoTherapy of Cancer* 2014 **2**(Suppl 3):P65.

¹Trianta Immunotherapies GmbH - a subsidiary of Medigene AG, Germany
Full list of author information is available at the end of the article