brought to you by CORE

Obermajer et al. Journal for ImmunoTherapy of Cancer 2013, 1(Suppl 1):P146 http://www.immunotherapyofcancer.org/content/1/S1/P146



ImmunoTherapy of Cancer

POSTER PRESENTATION



Development and stability of Th17 cells in ovarian cancer requires nitric oxide and endogenous NOS2 activity in cancer-associated CD4+ T cells

Natasa Obermajer^{1*}, Jeffrey L Wong¹, Robert P Edwards^{4,5,6}, Kong Chen⁷, Melanie Scott¹, Shabaana Khader⁷, Jay K Kolls⁷, Kunle Odunsi⁸, Timothy R Billiar¹, Pawel Kalinski^{1,2,3}

From Society for Immunotherapy of Cancer 28th Annual Meeting National Harbor, MD, USA. 8-10 November 2013

Th17 cells play reciprocal roles in different forms and at different stages of cancer. We report that the presence of Th17 cells in ovarian cancer ascites correlates with local expression of nitric oxide synthase-2 (NOS2). Furthermore, the development of RORyt+IL-23R+IL-17+ Th17 cells from human naive-, memory- or tumorinfiltrating CD4+ T cells critically depends on NO and endogenous NOS2 induced in CD4+ T cells by Th17inducing cytokines (IL-1\beta/IL-6/IL-23) or by cancerassociated IL-1B/IL-6/IL-23/NO-producing MDSCs. Inhibition of NOS2 or its downstream cGMP/cGK signaling pathway abolishes de novo induction of Th17 cells. Moreover, even short-term blockade of NOS/cGMP suppresses the IL-17 production by established Th17 cells isolated from ovarian cancer patients, demonstrating the novel key role of NOS/cGMP in Th17 cell physiology and providing for new therapeutic targets to manipulate Th17- and NOS/cGMP-associated immunity in precancerous lesions and advanced cancer.

Authors' details

¹Department of Surgery, University of Pittsburgh, Pittsburgh, PA, USA.
²Department of Immunology, University of Pittsburgh, Pittsburgh, PA, USA.
³Department of Infectious Diseases and Microbiology, University of
Pittsburgh, Pittsburgh, PA, USA. ⁴Magee-Womens Research Institute Ovarian Cancer Center of Excellence, Pittsburgh, PA, USA. ⁵Peritoneal/Ovarian Cancer Specialty Care Center, Pittsburgh, PA, USA. ⁶University of Pittsburgh Cancer Institute, University of Pittsburgh, PA, USA. ⁶University of Pittsburgh Cancer Institute, University of Pittsburgh, PA, USA. ⁶Department of Pediatrics, University of Pittsburgh School of Medicine, Pittsburgh, PA, USA.
⁸Departments of Gynecologic Oncology and Immunology, Roswell Park Cancer Institute, Buffalo, NY, USA.

¹Department of Surgery, University of Pittsburgh, Pittsburgh, PA, USA Full list of author information is available at the end of the article

Published: 7 November 2013

doi:10.1186/2051-1426-1-S1-P146 Cite this article as: Obermajer *et al.*: Development and stability of Th17 cells in ovarian cancer requires nitric oxide and endogenous NOS2 activity in cancer-associated CD4+ T cells. *Journal for ImmunoTherapy of Cancer* 2013 1(Suppl 1):P146.

Submit your next manuscript to BioMed Central and take full advantage of:

- Convenient online submission
- Thorough peer review
- No space constraints or color figure charges
- Immediate publication on acceptance
- Inclusion in PubMed, CAS, Scopus and Google Scholar
- Research which is freely available for redistribution

) BioMed Central

Submit your manuscript at www.biomedcentral.com/submit



© 2013 Obermajer et al; licensee BioMed Central Ltd. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/2.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.