**Ex-Th17 Foxp3+ T cells - a novel subset of Foxp3+ T cells induced in cancer**

Stephanie Downs-Canner1, Roshni Ravindranathan1, Robert P Edwards2, Pawel Kalinski1, Kunle Odunsi3, David L Bartlett1, Natasa Obermajer1*

From 30th Annual Meeting and Associated Programs of the Society for Immunotherapy of Cancer (SITC 2015)
National Harbor, MD, USA. 4-8 November 2015

Th17 and regulatory T (T_{reg}) cells are integral in maintaining immune homeostasis and Th17-T_{reg} misbalance associates with inflammation.

We demonstrate that in addition to natural (n)T_{reg} and induced (i)T_{reg} cells developed from naïve precursors, Th17 cells are a novel source of Foxp3+ cells by converting into ex-Th17 Foxp3+ cells, and this helps to reconcile the contradictory information about the relevance in particular of Th17 subset in immune surveillance.

We identified IL-17A+Foxp3+ double-positive and ex-IL-17-producing IL-17A-Foxp3+ T cells to be the underlying mechanism of immune regulation in mesenchymal stem cell-mediated prolonged allograft survival. Further, we identified accumulation of IL17A Foxp3+ and ex-Th17 Foxp3+ cells in tumor bearing mice, indicating progressive direct Th17-into-T_{reg} cell conversion as a novel phenomenon in cancer.

Moreover, we determined the importance of the Th17 cell plasticity for tumor induction and/or progression in ROR-g-/- mice. Our data indicate that RORgt is required not only for Th17 development, but also for effective T_{reg} cell induction. TGF-b1 induced Foxp3 expression was reduced in ROR-g-/- cells. Further, tumor bearing ROR-g-/- mice showed significantly less Foxp3+ T_{reg} cells, but higher IFNg+ Tcells compared to wild type animals.

Increased infiltration of IL17+ and FoxP3+ CD4+ T cells in the human ovarian cancer ascites, with the presence of a distinct IL17+FoxP3+ subset, and a significant correlation between tumor-associated Th17 and T_{reg} cells demonstrates the existence of Th17-Foxp3+ T cell inter-relationship in cancer patients.

Yin-yang of IL17+ and Foxp3+ is important principle for improved clinical approaches targeting responses against self, allo and/or neo-self.

Authors’ details
1University of Pittsburgh, Pittsburgh, PA, USA. 2Magee-Womens Research Institute Ovarian Cancer Center of Excellence, Pittsburgh, PA, USA. 3Roswell Park Cancer Institute, Buffalo, NY, USA.

Published: 4 November 2015

doi:10.1186/2051-1426-3-S2-P273