



POSTER PRESENTATION

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

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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- b_1 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.

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