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SIgN Immunology Seminar



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Intratumoral immune landscape: From immunogenicity to tolerogenicity

Host
Prof Laurent Renia
Singapore Immunology Network, A*Star

Date
Thursday
4 February 2016

Time
11am – 12pm

Venue
SIgN Seminar Room
Immunos Building
Level 4
Biopolis

Immune system possesses distinct innate and adaptive branches which act in a collaborative way to eliminate neoplastic transformation. In spite of the presence of immune response, tumors develop spontaneously through different immune escape strategies. It has been demonstrated that dysfunction of the host's immune system is one of the major mechanisms by which immunogenic immune system becomes tolerogenic. This dysfunction includes but not limited to loss of effector-/memory-T cells, Th2 cell bias and T-regulatory (Treg) cell expansion. However, the molecules involved in these processes were not fully understood. We observed that tumor-shed various soluble factors play critical role in suppression of anti-tumor immunity. Adding to the knowledge of abundant T cell plasticity in terms of cytokine production our study identifies an IL10-producing FOXP3^{+} Treg cell population that contributes to IL10-dependent type-2 cytokine bias in breast cancer patients. The master transcription factor FOXP3 associates with multiple interatomic partners which include tolerance partners, epigenetic modifiers, and differentiation factors to execute Treg-mediated immunosuppression. Targeting FoxP3-interatomic partners by micro-RNA would be promising approach to prevent the Treg-mediated tumor immune evasion. In recent findings we have identified miR-325 that regulates Treg development and function by interfering 3'-UTR region of FOXP3 and FOXP3-associated interactome partners. Lentiviral-mediated miR-325 over-expression hindered Treg augmentation and substantially reduced tumor progression in tumor-bearing mice. Hence targeting miR-325 may boost anti-tumor immunity.