OMICS Group Conferences
Accelerating Scientific Discovery

2nd International Conference and Exhibition on
Pathology

August 05-06, 2013 Embassy Suites Las Vegas, NV, USA

B lymphocytes regulate a pro-inflammatory T cell balance in human type 2 diabetes

Jason DeFuria, Madhu Jagannathan-Bogdan, Ramya Kuchibhatla, Marie McDonnell, Caroline Apovian, Barbara Nikolajczyk and Gerald Denis
Boston University School of Medicine, USA

Lymphocytes play key roles in the chronic inflammation critical for T2D pathogenesis. We have shown T2D patients have an elevated ratio of pro- to anti-inflammatory T cells, and B cells that produce a pro-inflammatory cytokine profile. Thus lymphocytes promote T2D-associated inflammation. Although the pro-inflammatory $CD4^+$ T cell balance has been specifically implicated in T2D pathogenesis by numerous studies, mechanisms that underlie elevated CD4+ T cell inflammation are poorly understood. B cells have recently become appreciated as regulators of CD4+ T cell subset differentiation and function, but the possibility that the T2D-associated changes we identified in B cell function regulate T cell inflammation in T2D is untested. Our new data demonstrate that B cells control the T2D-associated increase in CD4+ Th17-mediated inflammation in both T2D patients and in obese/insulin resistant mice. Surprisingly, the disease-associated ability of B cells to regulate T cell function was contact-dependent, despite the demonstration that multiple cytokines hyper-secreted by B cells from T2D patients activate T cells. In contrast, elevated activation of CD4+ Th1 axis cytokines was B cell-independent. We conclude that both T cell-intrinsic and T cell-extrinsic changes regulate T cell-mediated inflammation in T2D. These data indicate that B cell depletion may partially curb T2D-associated T cell inflammation thus disease pathogenesis, but that combinatorial treatments may be required for favorable clinical outcomes. Thus our work suggests that the currently modest efficacy of anti-inflammatory drugs in T2D may be predictable, and that drug combinations will be required to leverage our understanding of T2D as an inflammatory disease into new treatments.