BIO ENGINEERING

SEMINAR

Joint MRDG-BE Seminar at 4:00 PM on February 11th, 2015
MRDG Seminar Hall, First Floor, Biological Sciences

Unique T-cells in autoimmune diabetes: What have we learnt from the NOD model

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Abstract: Type 1 diabetes (T1D) results from a progressive loss of the insulin producing beta cells due to immunologic assaults. In past several years, a lot of interest has been generated in the understanding of a/cellular etiologies, processing and presentation of diabetogenic auto antigens in the islets of Langerhans, and lack of an efficient thymic purging--all of which are important features in the T1D pathogenesis. Nearly every characterized autoantigen associated with T1D is a member of the secretory granules that elicit CD4 T cells and auto-antibodies. While trafficking of these granule antigens have not been well established for immunologic priming and more importantly how a granule membrane protein becomes available to the immune system remains a conundrum in the autoimmunity of T1D. We attempted to gain some mechanistic insight by study of a candidate granule-membrane protein (Zn transporter: Slc30a8 or ZnT8) in the spontaneous and induced diabetes of NOD mouse. Two notable observations were made from this study: 1) NOD mice lacked a deletional tolerance to ZnT8 as both protein and peptide reactive T cells were found in the periphery, 2) Adoptive transfer of T cells raised to a terminal cytosolic epitope (i.e. 345-359) transferred diabetes. Uniquely, ZnT8 T cell were diabetogenic in lightly irradiated recipients but not in intact recipients where irradiation stimulated radioadaptive changes including expression of intercellular adhesion molecules. By use of co-culture assays with beta-cells and insulinomas, we further demonstrated that immunologic transfer of granule antigens is contact dependent. Collectively, observations from this study indicate that passage of autoantigens to the immune system in T1D is reminiscent of granule capture by the presenting cells.

About the speaker:

Dr. Deepak Nayak is a Staff Scientist, Section of Transplantation at the Department of Surgery, Washington University School of Medicine, St. Louis, USA.