Applicant’s Name: Zuoxiang Xiao  Degree: PhD, MD

Applicant’s Division: Immunology

Faculty Preceptor: Abdel Hamad

Appointment Category: Research Fellow

Register for: Basic Research

Full Poster Title:* Survival of diabetogenic T cells in pancreatic islets is mediated by Fas ligand

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Author(s) (First & Last) Zuoxiang Xiao, Abdel Rahim A. Hamad

In-House Address: Room 659 Ross Building

Telephone: 410-614-3021  Beeper:_________________________

Fax: 410-614-3548  E-mail: zxiao5@jhmi.edu

**INCLUDE A ONE-PAGE ABSTRACT (including title and all authors) OF THE WORK YOU WILL BE PRESENTING**

E-mail COMPLETED Registration form and abstract to: Stacey Morgan (smorgan9@jhmi.edu) on or before Friday, March 14th, 2008

If you have questions or problems regarding your submission, please contact Stacey Morgan via e-mail (smorgan9@jhmi.edu)
Survival of diabetogenic T cells in pancreatic islets is mediated by Fas ligand

Zuoxiang Xiao, Abdiazziz S. Mohamood, Dongfeng Zheng, Jonathan P. Schneck and Abdel Rahim A. Hamad

Type 1 diabetes (T1D) is an important autoimmune disease that is becoming an increasing health problem. Diabetogenic T cells primed by islet derived autoantigens in pancreatic lymph nodes (PLN) migrate into pancreatic islets where they expand and cause destruction of insulin-producing beta cells. However, molecular mechanisms that regulate survival of autoreactive T cells in pancreas are poorly understood. Our previous data show that pharmacological blockade of FasL prevents diabetes in non-obese diabetic (NOD) mice, a wildly used model for T1D. Here we show that intact Fas pathway is essential for survival and accumulation of diabetogenic T cells in pancreas of diabetes in NOD mice. This is demonstrated using adoptive transfer of islet-reactive BDC2.5 TCR transgenic T cells and analysis of endogenous diabetogenic T cells in NOD mice bearing gld mutation of Fas ligand (FasL). Proliferation and differentiation of diabetogenic T cells in PLN is not affected by the gld mutation. However, unlike in wild type mice, diabetogenic T cells that enter the pancreas of gld mice fail to express CD44, CD40L and undergo apoptosis. Our data point to deficient CD40 expression on B cells in the pancreas but not PLN as an important factor in aborting the diabetogenic process in gld mice. Immunization of gld mice with agonist CD40 antibody restores CD40L and CD44 expression on T cells and inhibits their apoptosis. These date reveal that full expression of FasL is essential for survival of effector T cells in pancreas and promotion of autoimmune diabetes development by CD40/CD40L dependent pathway.