Loss of a Treg Population in Diabetes Prone NOD mice

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A population of $CD8^+CD122^+$ regulatory T cells has recently been identified in C57BL/6 (B6) mice (1,2). We hypothesized that this population might be absent in mice prone to autoimmune diseases. We examined NOD mice, which spontaneously develop autoimmune diabetes, along with a genetically similar control strain NOR for this population of T cells using 7 color flow cytometry. In B6 mice, the $CD8^+CD122^+$ cells are uniformly $CD44^{hi}$ and CD27 ^{hi}, a cell surface expression pattern that is consistent with central memory. In B6 mice, an average of 1.5 x 10^6 $CD8^+CD122^+CD44^{hi}$ cells was detected per spleen. In striking contrast, NOD and NOR mice have only 2.4 x 10^5 $CD8^+CD122^+CD44^{hi}$ cells per spleen or an 85% reduction of the number of these cells found in B6 mice. Interestingly, diabetic NOD mice have a large population of $CD8^+CD122^+CD44^{lo}$ cells in their pancreatic and peripheral lymph nodes that is absent in B6 mice. This population of T cells was also found in the pancreatic lymph nodes of all 5 week old NOD and NOR mice tested. Three month old non-diabetic NOD mice have essentially undetectable levels compared to the diabetic NOD or NOR mice, 1700 vs. 250,000 $CD8^+CD122^+CD44^{lo}$ cells, in their pancreatic lymph nodes. Currently, work is ongoing to determine whether reduced numbers of $CD8^+CD122^+CD44^{hi}$ cells contribute to autoimmune diabetes in NOD mice.

1. Rifa'i M, Kawamoto Y, Nakashima I, and Suzuki H 2004. Essential Roles of $CD8^+CD122^+$ Regulatory T Cells in the Maintenance of T Cell Homeostasis *J. Exp. Med.* 200(9): 1123–1134.

2. Endharti AT, Rifa'I M, Shi Z, Fukuoka Y, Nakahara Y, Kawamoto Y, Takeda K, Isobe K and Suzuki H 2005. $CD8^+CD122^+$ Regulatory T Cells Produce IL-10 to Suppress IFN-g Production and Proliferation of $CD8^+$ T Cells *J. of Immunology* 175(11): 7093-7097.