Natural history of type 1 diabetes in humanized mouse model

Ahmad Aldasouqi[1,2], Shafiya Imtiaz Rafiqi DVM, PhD[3,4], Shahnawaz Imam DVM, PhD[3,4*]

[1]College of Natural Sciences and Math, The University of Toledo, Toledo, OH 43614

[2]College of Medicine and Life Sciences, The University of Toledo, Toledo, OH 43614

[3]Division of Diabetes, Endocrinology, and Metabolism, Department of Medicine, The University of Toledo, Toledo, OH 43614

[4]Center for Diabetes and Endocrine Research (CeDER), University of Toledo, Toledo, OH 43614

*Corresponding author: Shahnawaz.imam@utoledo.edu

Keywords: T1D, Type 1 Diabetes, Humanized Mouse Model, T1D Pathophysiology

Published: 14 December 2023

Type 1 diabetes (T1D) is an autoimmune disease caused by an imbalance in T-regulatory and T-effector cells characterized by the destruction of insulin-producing beta cells by diabetogenic T-effector cells, leading to insulin deficiency and complexities like diabetic nephropathy, retinopathy, and neuropathy. Researchers at The University of Toledo have developed a humanized mice model that spontaneously develops T1D at 3-5 weeks and mimics human T1D. This study aims to monitor blood glucose levels before the onset of T1D (pre-weaned stage mice) and track the dynamics of immune cells using flow cytometry throughout the progression of the disease. Our results show that T-regulatory cells constitute 4.773% ± 0.81% cells at preweaning, which significantly ($p<0.05$) drops to 2.60± 0.35 (%) in males and 1.78 ± 0.58 (%) in females at the 10th week, while CD8+ T cells produce interferon-gamma (cytotoxic lymphocytes, CTLs) constitute 3.32 ± 0.60 (%) at preweaning, which increased significantly ($p<0.05$) to 27.625± 1.43 (%) in males and 21.13± 2.87 (%) in females as the disease progresses. This reduction in T-regulatory cells and enrichment of CD8s and CTLs leads to the destruction of beta cells, as seen in humans. Dysregulation of immune responses can be correlated with the progression of diabetes in terms of blood glucose levels, which increased from 147mg/dl (preweaning), which significantly ($p<0.05$) peaked at 373mg/dl in 5th week, and was observed in partial remission stage around the 8th week as observed in human T1D 'honeymoon period.' This study will help us to understand the immune dynamics in the progression of T1D as it helps us to present a better picture of the status of immune cells in a human-like immune system and provides benchmark data of the interplay of the immune system.

