COLLEGE OF SCIENCE
THE UNIVERSITY OF ALABAMA IN HUNTSVILLE

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Research Horizons Day

LEW.1WR1 rats have altered inflammation responses during Type 1 Diabetes Induction

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Abstract

Type 1 Diabetes(T1D) is a disorder characterized by the autoimmune destruction of beta cells, the cells that produce insulin. After the destruction of these cells, some patients go on to develop insulin resistance in response to subcutaneous insulin injections and become overweight.[1] This observation has led to a recent interest in understanding if there are underlying metabolic dysfunctions that could lead to increased T1D susceptibility. Our lab studies the LEW.1WR1 rat, an inducible T1D rat model.[2] We sought to analyze changes in the metabolic status of these animals at 6 days 7 hours into induction protocol to observe if there are significant shifts in metabolism and immune signaling at this time point that lead to increased susceptibility to T1D compared to resistant rodents. We chose this as an prior to insulitis but shortly after daily injection time point to observe relevant cytokine and chemokine changes. Lipid metabolism is also going to alternate with T1D induction.

Key Findings

1. At 6 days into the protocol the rats were not showing signs of T1D.

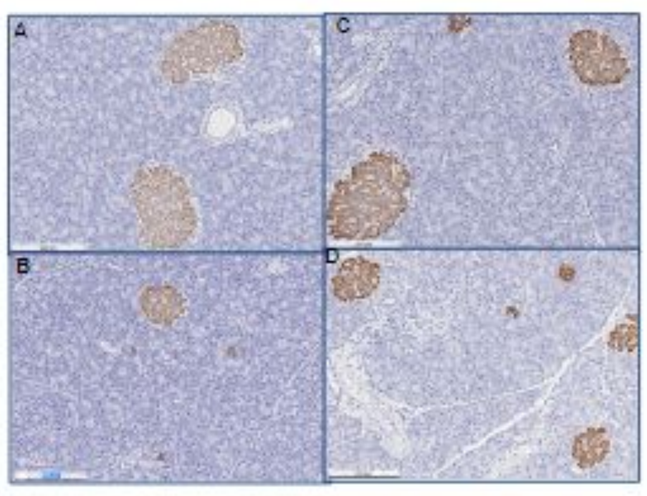


Figure 1. Representative Micrograph of Insulin stained pancreas. (A)LEW.W1R1-Control, (B)LEW.W1R1-Treated, (C)LEW/SsNHsd-Control, (D)LEW/SsNHsd-Treated. Red stained clusters of cells are islets

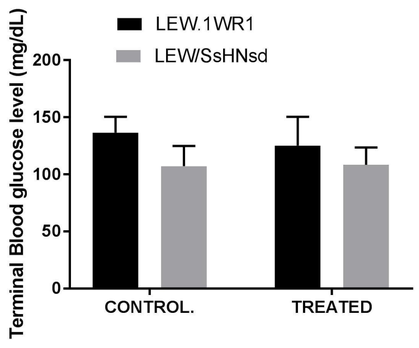
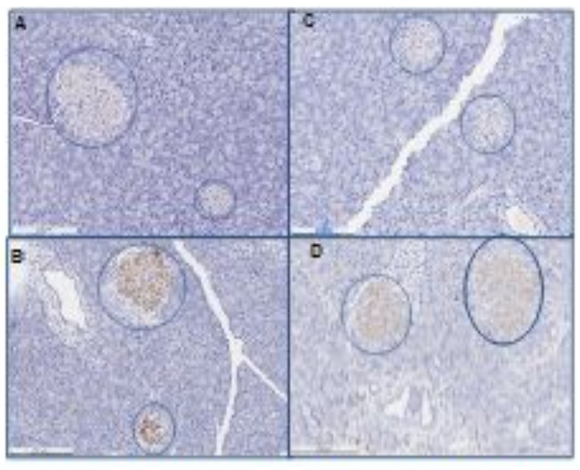


Figure 2. *Terminal Fasting Blood Glucose*. The Terminal Blood Glucose levels of rats from both groups. Rats were fasted for 6 hours prior to collection. Error bars represent an SD of n=8.

2. Poly IC injections are triggering increased pancreatic immune cells in both models.



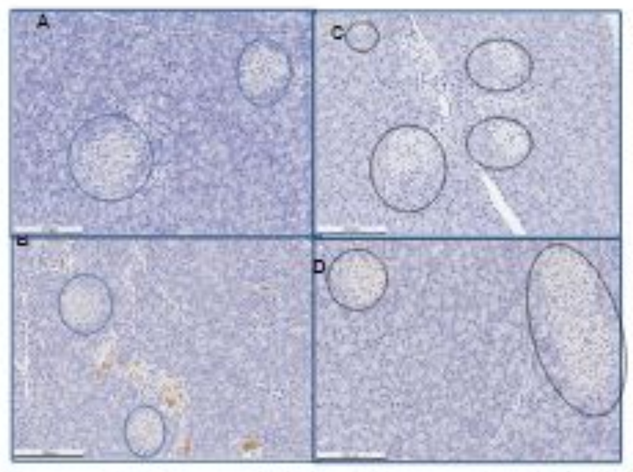


Figure 3. *Representative Micrographs of CD3 stained pancreas.* **(A)**LEW.W1R1-Control, **(B)**LEW.W1R1-Treated, **(C)**LEW/SsNHsd-Control, **(D)**LEW/SsNHsd-Treated. Islets are circled.

Figure 4. *Representative Micrograph of CD68 stained pancreas.* **(A)**LEW.W1R1-Control, **(B)**LEW.W1R1-Treated, **(C)**LEW/SsNHsd-Control, **(D)**LEW/SsNHsd-Treated. Islets are circled.

3. Poly IC injected animals have increased serum chemokine and cytokine proteins. In inflammatory signals like Eotaxin,IL-18,IL-17 The SsNHsd rats have a more robust response than the 1WR1 rats.

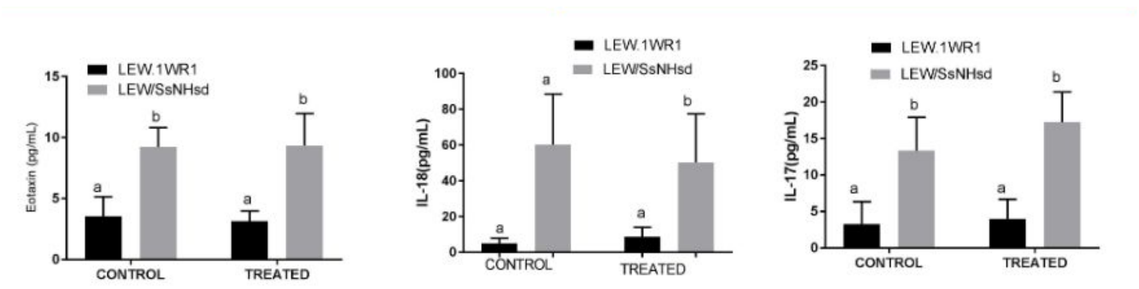


Figure 5a. *Terminal Serum Cytokine/Chemokine Multiplex Data.* This data represents cytokine and chemokine data which showed significant differences p>0.05. Error bars are SD of n=8 samples.

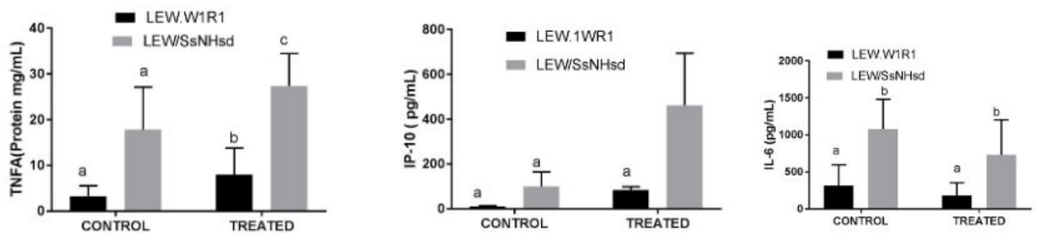


Figure 5b. *Terminal Serum Cytokine/Chemokine Multiplex Data(continued).* This data represents cytokine and chemokine data which showed significant differences p>0.05. Error bars are SD of n=8 samples.

4. We also observed differences in plasma metabolic hormones of the 1WR1 rats. The animals had more GIP and Ghrelin while having less PP and Leptin

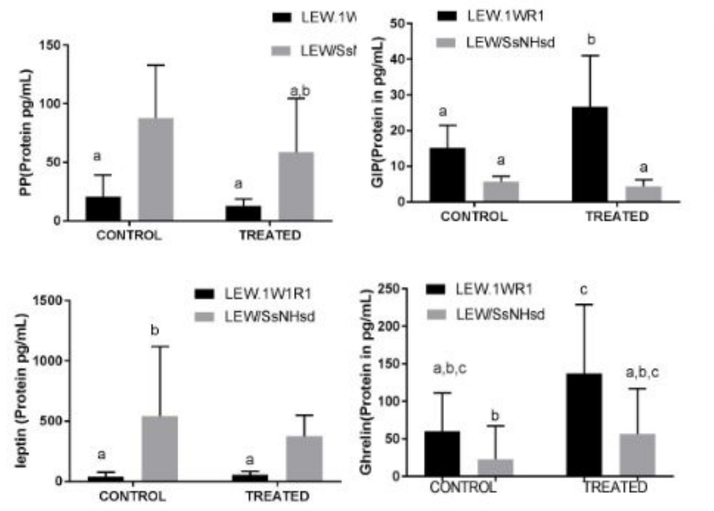


Figure 6. *Terminal Serum Metabolic hormone data.* This data represents selected proteins from the metabolic array which were significantly different. Difference is defined at p>0.05 with different letters representing difference. Error bars are SD of n=8.

5. We also observed differences in cholesterol levels and triglycerides level

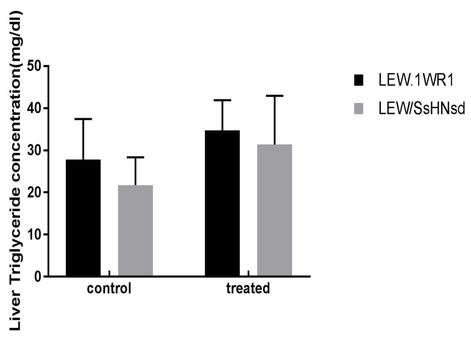


Fig-10-Liver Triglyceride concentration.This data represents rat liver triglyceride concentration using the Cayman Chemicals Colorimetric Triglyceride assay. There were no significant differences between groups. p<0.05

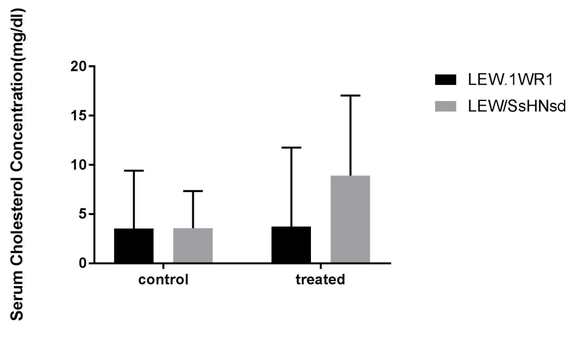


Fig-7-Serum Cholesterol concentration.This data represents serum Cholesterol level using Cayman chemical Cholesterol assay(p<0.05)

Future Works

- Identifying gene expression and protein level differences in the muscle liver and splenocytes in these animals
- Quantifying metabolite differences related to glucose processing in urine and plasma
- Quantifying islet size to determine if there are differences between strains

Acknowledgements

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