

IL-1RA Gene Knockout has no Effect on Development of Type 1 Diabetes in Non Obese Diabetic Mice

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INTRODUCTION

Type 1 diabetes is an autoimmune disease that attacks the islet cells in the pancreas that make the insulin. The pancreas has two functional components: the exocrine and the endocrine. The exocrine part produces enzymes to help with the breaking down of proteins, lipids, carbohydrates and nucleic acids in food. While the endocrine component secretes insulin for glucose regulation. IL-1RA an anti-inflammatory mediator, is a part of the interleukin 1 cytokine family. Previously, it has been shown that IL-1RA has a negative impact on type 1 diabetes and patients are more likely to go into remission. Here, we viewed role of IL-1RA on destruction of pancreatic islet cells in non-obese diabetic (NOD) mice. The IL1RN gene was knocked out of the NOD mouse. Three different types of mice were used: the wild type (IL-1RA +/+, WT), the knock out (IL-1RA -/-), and the heterozygous (IL-1RA +/-). The mice were then monitored for development of diabetes and insulinitis in the pancreas. There were no differences in mice in terms of body weight. Our results suggest that removal of IL1RN gene in NOD mouse has no significant effect in terms of development of diabetes in NOD mouse.

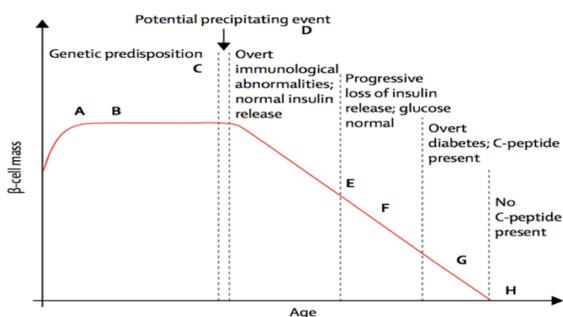


Figure 1. Eisenbarth model of the history of type 1 diabetes

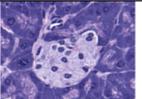
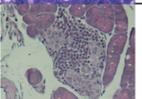
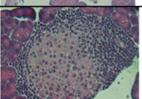
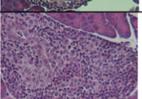
METHODS

Murine models:

1. Wild type: have the IL-1RA gene
 2. Knock out mice: did not have the IL-1RA gene
 3. Heterozygous mice: carriers of the IL-1RA gene. The mice were bred by crossing two heterozygous mice at the Jackson laboratory.
- All models are on a genetic background non-obese diabetic mice crossed with C57BL/6 mice.

Insulinitis scoring system:

Used tissue from the pancreas from three different types of mice. Stained the tissue with hematoxylin (blue color) and eosin (red). Scored each section of the pancreas from 1 to 4.

Scoring Number	Image	Description
1		There is some infiltration in the islet, but it is very little.
2		Half of the islet is infiltrated
3		More than half of the islet is infiltrated but not all of it.
4		The whole islet is infiltrated.

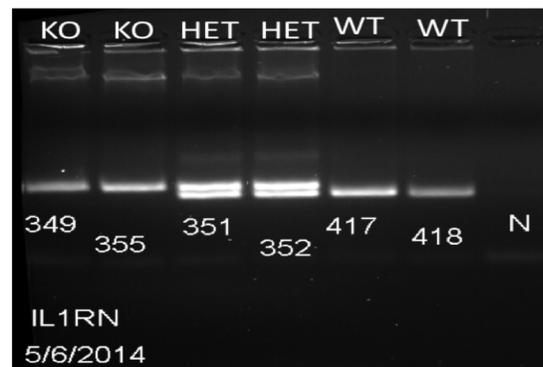
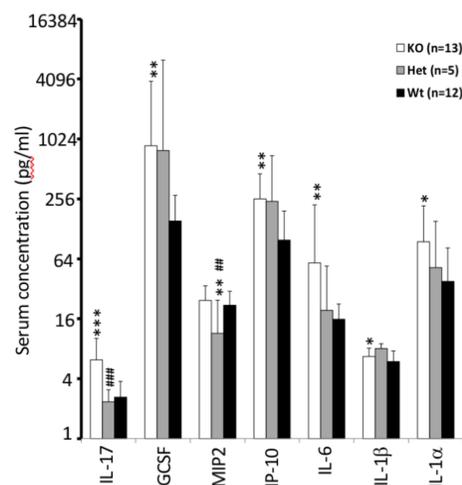


Figure 2. Shows the genotypes in the mice that were used



***P<0.001, **P<0.01, *P<0.05 compared with the wild type mice
###P<0.001, ##P<0.01, #P<0.05 compared with the Knockout mice
Figure 4. Comparison of serum concentration in different types of mice

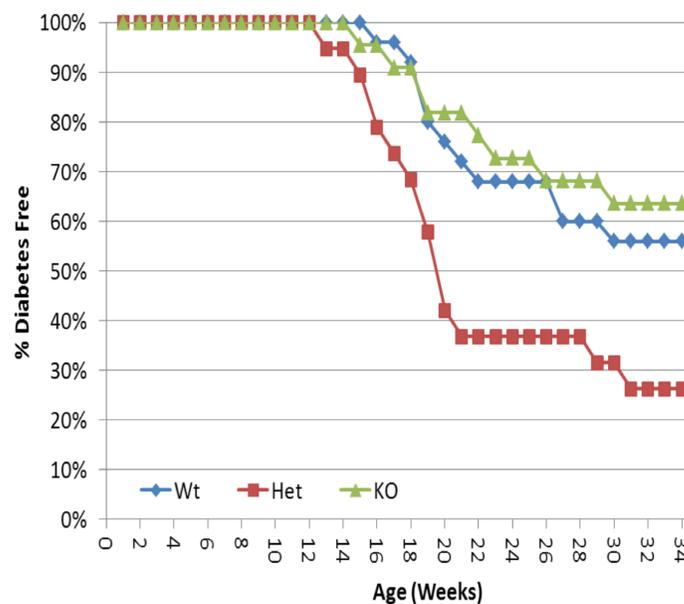


Figure 6. Compares the three types of mice over weeks to see how long it takes the mice to start showing symptoms of diabetes

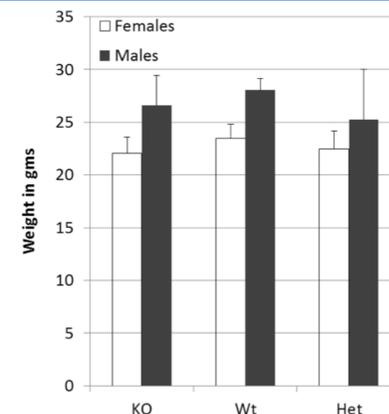


Figure 3. A comparison of the average weights of female and male according to their genotypes

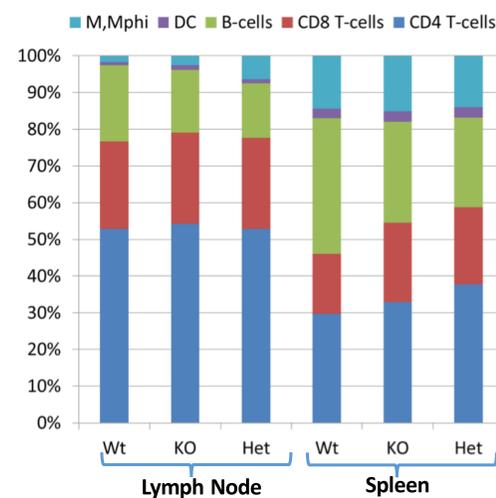


Figure 5. Explains the differences of the amount of different types of cells while comparing them in wild type, knock out and heterozygous mice in the lymph node and spleen

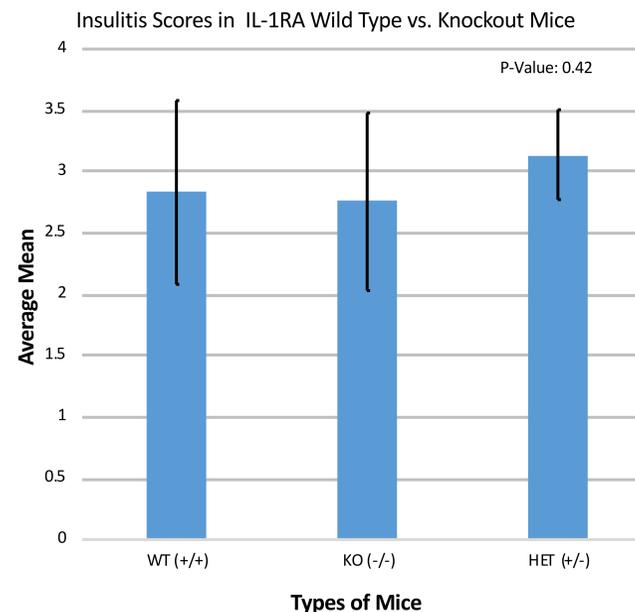


Figure 7. Compares the average insulinitis score in the three types of mice. The p-value is 0.42 which shows that it is not significant.

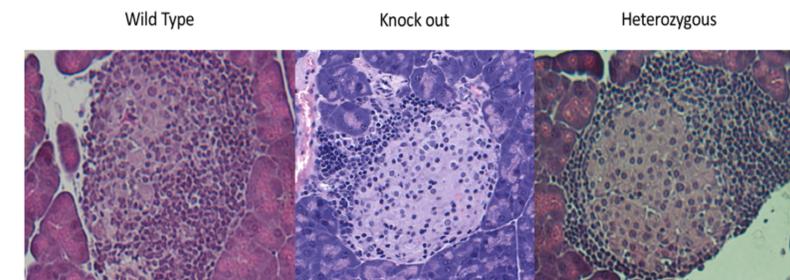


Figure 8. Image of an islet from each mice

DISCUSSION and Future Direction

In this study, we found that the IL-1RA gene expression has no effect on the development of Type 1 diabetes in NOD mice. In figure 2, the PCR shows that there were three different NOD mice used to study the development. Phenotypically, these mice were very similar. The figure 3 shows that there was no significant difference in the weight of the different mice between male and female. Figure 4 shows how the serum concentration also showed no significant difference except for IL-17. There is also no difference in the number of different cells in the lymph node and spleen of the three types of mice. So overall, there was no significant phenotypic difference between the three different genotypes of mice.

The results showed how the heterozygous mice had more infiltration and the mice were also showing symptoms of type 1 diabetes faster. However, there was not a significant difference because the p-value of figure 7 is 0.42 which is greater than 0.05, but there was intra-group variability which could explain why the histologic insulinitis score for the heterozygous mice may be higher. In the future, we plan to continue this project to understand what the IL-1Ra affects and how it can be changed. It can also be tested whether a different gene plays a role in the development of type 1 diabetes and the destruction of islets.

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