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 breakdown 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 reviewed the 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 knockout (IL-1RA -/-), and the heterozygous (IL-1RA +/). The mice were then monitored for development of diabetes and insulitis 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.

METHODS

Murine models:
1. Wild type: have the IL-1RA gene
2. Knockout mice: does 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.

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

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. 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 insulitis score for the heterozygous mouse 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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