



IL-17 is expressed in insulin-containing islets of donors with type 1 and type 2 diabetes

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PURPOSE

IL-17 is a pro-inflammatory cytokine, important in shaping host immune responses against pathogens. IL-17 is also attributed to cause tissue damage and chronic inflammation in autoimmune diseases such as psoriasis, rheumatoid arthritis and multiple sclerosis. An increase in IL-17 secreting CD4+ T cells and Th17 cells were observed in pancreatic lymph nodes and peripheral blood of subjects with type 1 diabetes (T1D). However, it is not known whether IL-17 is expressed in human pancreata in health and during T1D or T2D pathogenesis. Here, we report that IL-17 is expressed in the islet cells of donors with type 1 and type 2 diabetes.

METHODS

IL-17 antibody was first optimized in human tonsils. We then stained human pancreatic FFPE tissues sections from non-diabetic (n=3), autoantibody positive (n=3), T1D (n=4) and T2D (n=3) donors for IL-17, Insulin and Glucagon. Whole tissue imaging was performed using axio scanner. 30-40 islets were randomly cropped across the pancreatic tissue and percentage of IL-17 positive area was quantified through Image pro software. Results were cross-verified by acquiring high resolution images of at least 10 islets per case by confocal LSM780 followed by subsequent analysis in Zen.

SUMMARY OF RESULTS

In all non-diabetic and auto-antibody positive cases, IL-17 staining was very weak or punctate and sparse in pattern, accounting for less than 5% of total islet area. In donors with T1D, insulin containing islets had a clear and markedly stronger cytoplasmic expression of IL-17 in islet cells, accounting to an average of 8.6% of total islet area. IL-17 expression was almost completely lost in insulin-deficient islets of all T1D donors. IL-17 expression was even more increased in islets of donors with T2D, constituting to an average of 26.26% of islet area. Most of the IL-17 production was accounted by either beta or alpha cells, while in many cases beta cells were the major source.

CONCLUSIONS

According to literature, expression of IL-17 is usually restricted to Th17, $\gamma\delta$ T cells and some cell types of innate immune system. Our finding that IL-17 can be expressed in islet cells of T1D or T2D is quite intriguing. Further functional studies in islet organoid models are required to determine if a metabolic stress or immune stress can induce IL-17 expression in human islets.