INTERNATIONAL SUMMIT ON DIABETES, ENDOCRINOLOGY, AND METABOLIC DISORDERS

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Immunomodulatory Nanodrugs Targeting TCL1A in Naïve B Cells to treat Type 1 Diabetes

Abstract:

Type 1 diabetes (T1D) arises from autoimmune destruction of pancreatic β-cells, with B cells contributing through antigen presentation and autoantibody production. However, the role of B cell subsets in early disease remains unclear. We performed scRNA-seq and flow cytometry on PBMCs from newly- diagnosed T1D patients, their relatives, and healthy controls. scRNA-seq analysis showed that naïve B cells were expanded in early T1D and exhibited upregulated TCL1A, an AKT coactivator. TCL1A knockdown suppressed AKT2 phosphorylation, reducing B cell proliferation and survival. NOD mice mirrored these findings, with elevated naïve B cells and Tcl1a linked to glucose intolerance. We developed a Tcl1a-targeted siRNA nanodrugs, which could reduce Tcl1a expression and naïve B cell number, protected β-cell mass, and restored glucose tolerance in NOD mice. Our work suggests that TCL1A in naïve B cells plays a key role in T1D pathogenesis and demonstrates the therapeutic potential of precision nanodrugs for early intervention.

Keywords: Type 1 diabetes, Single-cell RNA-sequencing, B cell, TCL1A, Nanodrugs

Biography:

Dr. Zhou completed his doctoral studies at the Graduate University for Advanced Studies (SOKENDAI) and National Institute for Physiological Sciences in Japan. He then did his postdoctoral training at Harvard Medical School Brigham and Women's Hospital and the Broad Institute, where he was appointed as instructor. Dr. Zhou established his independent laboratory at Sun Yat-sen Memorial Hospital, Sun Yat-sen University in China. Dr. Zhou's research focuses on autoimmune disorders and the development of novel therapeutic interventions. He has published over 30 papers in high-impact scientific journals.

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