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INPLASY

Emerging Role of Gene Therapy in Immune Modulation and Beta Cell Preservation in Type 1 Diabetes

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ADMINISTRATIVE INFORMATION

Support - Not Applicable.

Review Stage at time of this submission - The review has not yet started.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202520108

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 24 February 2025 and was last updated on 24 February 2025.

INTRODUCTION

Review question / Objective How effective is gene therapy in modulating immune responses and preserving beta-cell function in preclinical models of Type 1 Diabetes (T1D)?

Condition being studied Type 1 Diabetes (T1D).

METHODS

Search strategy PubMed, EMBASE, Scopus, and Web of Science.

Participant or population This systematic review focuses on preclinical studies evaluating the potential of gene therapy for immune modulation and beta-cell preservation in Type 1 Diabetes (T1D). The studies included in this review primarily utilized animal models of T1D, such as non-obese diabetic (NOD) mice, streptozotocin (STZ)-induced diabetic models, and genetically modified models. These models closely mimic the autoimmune destruction of insulin-producing β-cells observed in human T1D, providing a relevant platform for assessing gene therapy interventions.The included studies investigated gene therapy strategies targeting immune pathways (e.g., regulatory T-cell enhancement, cytokine modulation, immune checkpoint expression) and beta-cell survival (e.g., β-cell regeneration, apoptosis prevention, alternative insulin-producing cells). By analyzing these preclinical models, this review synthesizes existing evidence on gene therapy's efficacy, delivery methods, and potential for translation into human clinical applications.

Intervention Gene therapy.

Comparator Untreated animals.

Study designs to be included Preclinical Animal Model Studies.

Eligibility criteria This systematic review included preclinical animal studies investigating gene therapy interventions for Type 1 Diabetes (T1D). Eligible studies utilized established T1D animal models, such as non-obese diabetic (NOD) mice, streptozotocin (STZ)-induced diabetic models, or genetically modified models, and employed gene therapy approaches, including viral or non-viral vector-based delivery systems, gene-editing technologies like CRISPR-Cas9, or RNA-based strategies targeting immune pathways or beta-cell survival. Studies were required to report measurable outcomes related to immune modulation, such as reduced autoimmunity or increased regulatory T-cell activation, or beta-cell preservation, including improved survival, insulin production, and glucose regulation. Only peer-reviewed, full-text articles published in English between 2014 and 2024 were considered. Excluded studies included those unrelated to gene therapy, lacking relevant immune or beta-cell outcomes, review articles, conference abstracts, unpublished data, and those focusing solely on Type 2 Diabetes or non-relevant animal models.

Information sources The systematic review will retrieve literature from key databases, including PubMed, EMBASE, Scopus, and Web of Science.

Main outcome(s) The evaluation of gene therapy outcomes in preclinical models of Type 1 Diabetes (T1D) will include parameters assessing beta-cell function, glycemic control, immune modulation, and long-term therapeutic effects. Key measures will encompass insulin production, beta-cell mass, glucose levels, and glucose tolerance, along with immune markers such as regulatory T cells, cytokine profiles, and insulitis severity. Beta-cell protection will be analyzed through apoptosis markers and oxidative stress indicators, while gene delivery efficiency will be assessed by vector transduction rates and gene expression stability. Alternative insulin production will be evaluated based on the ability of engineered cells to secrete insulin in response to glucose. Additionally, the duration of normoglycemia, safety assessments, and potential off-target effects will be considered to determine the feasibility and clinical potential of gene therapy for T1D.

Quality assessment / Risk of bias analysis The quality assessment and risk of bias analysis of the preclinical animal studies will be conducted using the SYRCLE (Systematic Review Centre for Laboratory Animal Experimentation) risk-of-bias tool.

Strategy of data synthesis The data synthesis strategy for this systematic review will involve a structured approach to consolidating findings from preclinical animal models of Type 1 Diabetes (T1D) treated with gene therapy interventions. Extracted data will be categorized based on the type of gene therapy used, including viral and non-viral vector-based delivery systems, gene editing technologies such as CRISPR-Cas, and RNA-based approaches. Studies utilizing established T1D animal models, such as non-obese diabetic (NOD) mice, streptozotocin-induced models, and genetically modified models, will be systematically reviewed to assess immune modulation and beta-cell preservation outcomes. Data synthesis will emphasize key therapeutic mechanisms, including regulatory T-cell modulation, cytokine expression changes, and beta-cell survival enhancement. Narrative synthesis will be employed to summarize findings, while a risk-of-bias assessment using the SYRCLE tool will be performed to evaluate study quality and reliability.

Subgroup analysis Not applicable.

Sensitivity analysis Not applicable.

Country(ies) involved United States.

Keywords Type 1 Diabetes; Gene Therapy; Beta-Cell Regeneration; Immune Modulation; CRISPR/Cas9.

Dissemination plans A paper will be published in the leading journal.

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