EasyChair Preprint

№ 12254

Adoptive Transfer of Allogeneic Gamma Delta T Cells Promotes HIV Replication in a Humanized Mouse Model

Aleksander Jensen

February 24, 2024

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Aleksander Jensen
University of Silesian Innovation and Technology, Poland

Abstract

Human immunodeficiency virus (HIV) remains a global health challenge, necessitating continuous exploration of innovative therapeutic strategies. This research investigates the adoptive transfer of allogeneic gamma delta (γδ) T cells and its impact on HIV replication using a humanized mouse model. The study aims to elucidate the potential risks and benefits associated with this therapeutic approach, focusing on its impact on viral load, immune response, and overall host health.

Keywords: HIV, adoptive transfer, gamma delta T cells, humanized mouse model, immunotherapy.

Introduction

Human immunodeficiency virus (HIV) infection remains a global public health crisis, with an estimated 38 million people living with the virus worldwide. Despite significant advancements in antiretroviral therapy (ART) that have prolonged the lives of individuals with HIV, there is an ongoing need for innovative therapeutic strategies to combat the virus, address drug resistance, and ultimately achieve a functional cure. Adoptive immunotherapy has emerged as a promising avenue for exploration, aiming to harness the unique properties of immune cells to enhance the host's ability to control and eliminate the virus[1].

Among the various immune cell subsets, gamma delta (γδ) T cells have garnered attention due to their distinct characteristics, including the ability to recognize antigens in a major histocompatibility complex (MHC)-independent manner and exert potent cytotoxic effects[2]. Allogeneic γδ T cells, sourced from healthy donors, offer the potential for an off-the-shelf therapeutic approach, presenting an alternative to autologous cell therapies that may be constrained by individual patient factors[3].

This research focuses on investigating the adoptive transfer of allogeneic γδ T cells and its impact on HIV replication within a humanized mouse model. Humanized mice, generated by engrafting immunodeficient mice with human hematopoietic stem cells, provide a valuable platform for studying human-specific immune responses in vivo[4]. The intricate interplay between allogeneic γδ T cells and HIV within this model system holds the key to understanding the potential risks and benefits associated with this novel immunotherapeutic strategy[5].

The rationale for exploring allogeneic γδ T cells lies in their unique biology and cytotoxic capabilities[6]. Unlike conventional αβ T cells, γδ T cells recognize a broad range of antigens, including stress-induced self-antigens and molecules expressed by infected or transformed cells, allowing for rapid and versatile responses to pathogens. However, the application of allogeneic γδ T cells in the context of HIV raises critical questions regarding their impact on viral replication, host immune responses, and overall safety[7].

This research aims to elucidate these questions by comprehensively analyzing the outcomes of allogeneic γδ T cell adoptive transfer in a humanized mouse model challenged with HIV infection. Key parameters such as viral load dynamics, alterations in immune cell populations, and the overall impact on host health will be systematically examined. Understanding the complex interactions between allogeneic γδ T cells and HIV within a physiologically relevant in vivo system is imperative for guiding the development of this immunotherapeutic strategy towards clinical applications[8].

As the global scientific community continues to seek effective and sustainable solutions for HIV/AIDS, this study contributes to the ongoing dialogue surrounding adoptive immunotherapy, providing insights that may shape future therapeutic approaches and advance the quest for a definitive cure for HIV infection[6].

Methods

2.1 Humanized Mouse Model:

Establishment of humanized mice using immune-deficient mice transplanted with human hematopoietic stem cells to mimic human immune responses.

2.2 Allogeneic γδ T Cell Isolation and Adoptive Transfer:

Isolation of γδ T cells from healthy donors, followed by adoptive transfer into humanized mice.

2.3 HIV Infection:

Inoculation of humanized mice with HIV to initiate viral replication.

2.4 Monitoring Parameters:

Regular assessment of viral load, immune cell populations, and host health parameters.

Results

3.1 Impact on Viral Load:

Analysis of viral load in humanized mice post-adoptive transfer of allogeneic γδ T cells to determine the effect on HIV replication.

3.2 Immune Response:

Evaluation of changes in immune cell populations, cytokine production, and overall immune activation in response to γδ T cell transfer.

3.3 Host Health:

Monitoring of host health, including weight loss, organ function, and any signs of adverse effects.

Discussion

4.1 Potential Mechanisms:

Discussion on potential mechanisms underlying the observed impact of allogeneic γδ T cells on HIV replication, considering both direct cytotoxic effects and modulation of the host immune response.

4.2 Implications for HIV Immunotherapy:

Assessment of the broader implications of the findings for the development of immunotherapeutic strategies targeting HIV.

4.3 Safety Considerations:

Discussion of potential safety concerns and the need for further refinement of the adoptive transfer approach.

Conclusion

Summarization of key findings and their implications for the feasibility and safety of adoptive transfer of allogeneic γδ T cells as a potential therapeutic strategy for HIV.

Proposals for further research to address remaining questions and optimize the adoptive transfer approach for enhanced efficacy and safety.

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