Universal, MHC-E restricted killer T cell responses: Identification of a novel immune response against HIV

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1. Introduction

The Human Immunodeficiency Virus (HIV) has devastated millions of lives, with 35 million infected individuals and over 2 million new cases each year. After infection, many develop the Acquired Immunodeficiency Syndrome (AIDS), which ultimately leads to CD4+ T cell depletion, opportunistic infections, and often death.

Since the late 1980s, anti-retroviral therapy (ART) has been the paradigm for treatment and has been shown to lengthen the life expectancy of many infected individuals.

However, significant cost barriers, availability issues, and lifestyle changes make ART a reasonable treatment option for only a small subset of infected individuals. Additionally, ART has numerous side effects.

Multiple vaccine trials have failed against HIV largely due to genomic sequence diversity and oligoclonal surface proteins (see Box 2). As a result, an unconventional, prophylactic HIV vaccine is necessary.

2. Methods: Overview & Transfectant Design

Overview of Methodology

There were four major steps in this study:

1. B lymphoblastoid cell lines (BLCL) with single MHC-E allele expression were generated when Rhesus macaques were stimulated with pCEP4 (Invitrogen).

2. The BLCLs were used to focus on cell population of interest: CD3+; CD4-, CD8+; Quadrant Gating on flow cytometry (BD Biosciences).

3. B-LCL transfectants were used to focus on cell populations of interest: CD3+; CD4-, CD8+; Quadrant Gating on flow cytometry (BD Biosciences).

4. The BLCL transfectants were used to focus on cell populations of interest: CD3+; CD4-, CD8+; Quadrant Gating on flow cytometry (BD Biosciences).

Transfectant Design

Transfecting that express single class I alleles was critical to successfully generating transfectants. The MHC-E restricted killer T cell responses

3. Results

A. Single MHC-E class I transfectants are able to clear HIV.

B. In vitro HIV infection.

C. HIV infection in vitro.

4. Discussion

The responses characterized in this study support that there are universal, classical and non-classical MHC restricted CD8+ T cell responses induced by the RhCMV vaccine that can be directed to the Gag120 peptide.

5. Conclusions & Outlook

HIV is still a devastating virus today despite numerous treatment options. Multiple vaccine trials have failed, so a novel vaccine modality is needed.

6. Literature Cited

7. Figure Credits

8. Acknowledgements

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