KDDF
Korea Drug Development Fund

Asset #23
Dana-Farber Cancer Institute

LMP1 Based Approach to Producing Multi-specific CD4+ CTLs for Cancer Immunotherapy

Therapeutic Area	Oncology	**Indications**	Cancer
Modality	Cell Therapy	**Development Stage**	Pre-clinical

Overview

Background

- Epstein-Barr virus (EBV) establishes latent infection in B cells, occasionally expanding during immunosuppression. Latent membrane protein 1 (LMP1) has a dual role: driving B cell transformation and triggering immune responses against EBV-infected cells.
- A novel cancer immunotherapy leverages LMP1's immunostimulatory function to efficiently generate polyclonal CD4 cytotoxic T lymphocytes (CD4 CTLs) targeting multiple tumor antigens. This approach holds promise for treating diverse cancers, complementing CD8-mediated killing and allowing combination with immune checkpoint blockade therapies.

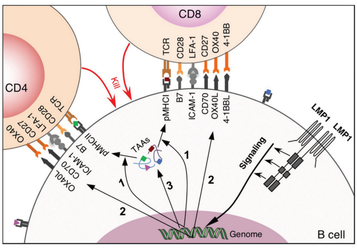
Technology Advantages

- Dana-Farber's approach generates CD4 CTLs targeting multiple tumor antigens in a speedy way
- This approach can be used as an ACT for multiple cancers
- CD4 CTLs are superior at in vivo persistence providing long-lasting antitumor immunity

Key Data

Schematic view of how LMP1 signaling in B cells induces cytotoxic CD4 and CD8 T cell responses to TAAs

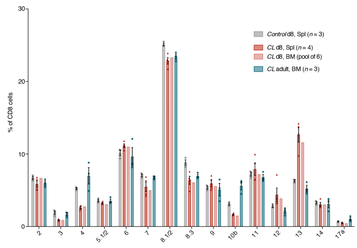
A



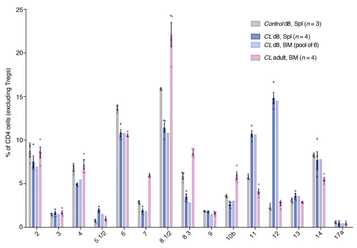
LMP1 signaling in B cells induces massive cellular gene expression. This leads to (1) upregulation of cellular machinery involved in antigen processing and presentation, (2) upregulation of costimulatory ligands (CD70, OX40L and others), and (3) overexpression of many cellular antigens known as TAAs. Presentation of the LMP1-induced cellular antigens/TAAs and simultaneous costimulation through CD70 and OX40L drive cytotoxic CD4 and CD8 T cell responses

CD4 and CD8 cells mount a polyclonal response to LMP1+ B cells

B



C



Analysis of TCR Vβ repertoire on CD8 cells (B) and CD4 cells (excluding Foxp3+ Tregs) (C) from spleen (Spl) or bone marrow (BM) of control or CL mice, using a panel of monoclonal antibodies for the indicated Vβ chains. These antibodies collectively detected 85–95% of TCRs in all the samples. The majority of CD4 and CD8 cells in the spleen and BM of 8-day-old CL mice and BM of adult CL mice were CD44+CD62L– effector/memory cells6,9. Control d8, 8-day-old CD19-cre/+ mice; CL adult, 6–12-week-old CL mice

IP Status & Publication(s)

Intellectual Property

Patent Number
US 11369635 B2 (2022.06.28)

Patent Family
PCT, US, EP, CN, CA, AU

Publication(s)

- Choi at al. (2020). Mechanism of EBV inducing anti-tumour immunity and its therapeutic use. Nature