Enabling the Rapid Generation of Allogeneic Artificial Antigen Presenting Cell (aAPC) Red Cell Therapeutics with a Loadable MHC System

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INTRODUCTION
Current peptide-based vaccine approaches are promising, but do not adequately stimulate and expand patient T cells to the levels required to achieve robust efficacy.

Rubius Therapeutics has developed allogeneic artificial antigen-presenting cells (aAPCs), which express the required antigenic peptides in a partially or fully HLA-compatible manner, in a stimulatory ligand and in a cytokine. To allow the aAPCs to be used for personalized vaccines, Rubius Therapeutics has developed a loadable MHC system that enables the rapid generation of aAPCs.

RESULTS AND METHODS
Figure 1. Rubius Therapeutics is Developing an aAPC Platform to Be Used With Personalized Peptides

- Antigen-specific TCR

Figure 2. RTX-aAPC Is a Cellular Therapy That drives Antigen-Specific

- MHC = major histocompatibility complex; RTX-aAPC = artificial antigen-presenting cell; TCR = T-cell receptor

Figure 3. Rubius Therapeutics Is Developing an aAPC Platform to Be Used

- Allogeneic, Off-the-shelf Cellular Therapies

OBJECTIVES
- To engineer loadable MHC class I and class II to achieve robust expression on the cell surface
- To determine whether any MHC can be loaded with exogenous peptides
- To determine if TCRs expressing loadable MHC can activate TCRs in a peptide-dependent manner

RESULTS AND METHODS
Figure 4. Empty Loadable MHC Constructs Can Be Stably Expressed at High Levels on the Cell Surface of an RBC

- An aAPC approach using loadable forms of the 5 most prevalent human leucocyte antigen (HLA) class I alleles in the U.S. population can cover approximately 70% of patients

Figure 5. A Peptide Can Be Loaded Onto Engineered Empty MHCs

- Disulfide engineering slightly improves expression compared to wild-type HLA-A2

Figure 6. Loadable MHC Constructs Are Stable, Independent of Peptide Pulping

- Peptides synthesized for individual patient populations presenting multiple antigenic peptides

Figure 7. Peptide-Loadable MHC Constructs Can Functionally Engage the TCR

- Loadable MHC constructs demonstrate functional TCR engagement directly after peptide pulsing

Figure 8. RCTs With Peptide-Loaded MHC Constructs Achieve Robust Expansion of Primary CMV-Specific T Cells

- RCT with peptide-pulsed HLA-A2 (wild-type and disulfide engineered, wt and ds, respectively), was assessed for CMV-specific TCR activity and CMV tetramer+ cell counts

Figure 9. Loadable MHC Platform Can Be Extended to MHC class II

- The loadable aAPC platform can be developed to utilize signaling mediated by MHC class II

CONCLUSIONS
- Loadable MHC class I and class II molecules can be robustly expressed on the RBC cell surface
- In the presence of a single polyclonal RCT TCR, RCTs loaded with MHC can significantly expand antigen-specific T cells in a peptide-dependent manner
- Rubius Therapeutic’s loadable aAPC system can be applied to produce aAPC populations presenting multiple antigenic peptides
- Further development of loadable aAPC system may enable effective personalized antigen therapies

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DISCLOSURES
All authors: Employment with and equity ownership in Rubius Therapeutics

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