Combination Immunotherapy with NY-ESO-1 Specific CAR T cells and T-Cell Vaccine Improves Anti-Myeloma Effect

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MAIN CONCLUSION

WE DEMONSTRATE THE FEASIBILITY OF GENERATING T-APC THAT PROPAGATE NY-ESO-1-SPECIFIC CAR T CELLS, INCREASE T-CELL PERSISTENCE IN VIVO, AND IMPROVE ANTI-MYELOMA EFFECT.

INTRODUCTION

- Multiple Myeloma
  - Systemic plasma cell malignancy
  - NY-ESO-1, a tumor-associated antigen (TAA)
  - Expressed by majority of patients with high risk or relapsed multiple myeloma
  - Absent expression on healthy cells/tissues
  - Prognostic
  - Overall survival less than 2 years concordant with high risk disease
  - Incrable in standard risk and high risk disease despite combination of novel therapies including Bortezomib/IMiDs/lenalidomide and autologous transplant with lenalidomide maintenance

- T cells expressing chimeric antigen receptor (CAR)
  - Early clinical trials in myeloma patients have shown promise
  - High risk patients with myeloma in urgent need of effective novel therapies
  - CAR can recognize peptide processed from NY-ESO-1 in context of HLA A2

- T cells expressing T-cell receptor (TCR)
  - Clinical trials in synerial carcinoma and multiple myeloma demonstrate that T cells expressing NY-ESO-1-specific TCR have anti-tumor effects
  - Affinity-modified TCR can recognize peptide processed from NY-ESO-1 in context of HLA A2

- Cancer vaccine
  - T cells as antigen presenting cells (T-APC)
  - Generation and manipulation of clinical grade T-APC to present TAA has a path for clinical translation.

- Premise
  - Enforced expression of membrane-bound IL-15 (mIL-15) on the surface of NY-ESO-1-pulsing T-APC by non-viral gene transfer using Sleeping Beauty (SB) system improves persistence of T cells
  - Autologous T-APC expressing NY-ESO-1 can activate and neurologically expand antigen-specific effector T cells as effectively as our control activating and propagating cells (A/Pc) derived from genetically modified K-562 cells.
  - The NY-ESO-1 specific effector T cells will persist longer in vivo when infused with T-APC versus alone and will lead to improved myeloma control.

HYPOTHESIS

- To Improve Treatment Outcome
  - Adipotively transfer genetically modified T cells expressing CAR for T-cell receptor, TCR specific for NY-ESO-1 with autologous T-APC expressing NY-ESO-1 for improved persistence and anti-tumor effect
  - Combination of NY-ESO-1 CAR T cells with NY-ESO-1 T-APC vaccine

STUDY RATIONALE

RESULTS

Generation of NY-ESO-1-specific effector T cells

Characterization of T-APC

Generation of T-APC

CONCLUSIONS

- SB system can be used to generate NY-ESO-1 T-APC from peripheral blood mononuclear cells.
- NY-ESO-1 T-APC can propagate NY-ESO-1 specific CAR T cells.
- Propagated CAR T cells exhibit redirected specificity for NY-ESO-1 to multiple myeloma.
- Co-administration of NY-ESO-1 T-APC with NY-ESO-1 CAR T cells leads to improved persistence of effector T cells.

FUTURE DIRECTIONS

- Continue evaluation of CAR T cells in combination with T-APC vaccine in vivo.
- Consider clinical trial using the combination of CAR T cells and T-APC vaccine in high risk and/or relapsed refractory multiple myeloma patients.

REFERENCES


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CONFLICT OF INTEREST

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