Molecular Characterization of T Cell Receptor and HLA in T cell Derived iPSCs

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INTRODUCTION

As the immunotherapy market continues to grow, significant progress has been made in treating diseases and cancer by leveraging the potential of immune cells, particularly T cells. Autologous CAR T cell therapy has shown high levels of complete remission in treatment of blood-based cancers, but the personalized medicine is hard to scale. Off-the-shelf, allogeneic CAR T treatments derived from donor T cells are being explored as a potential to address issues with the autologous treatments. CAR T cell therapies could be advanced through the use of induced pluripotent stem cells (iPSC). iPSCs derived from T cells offer advantages over traditional solid cell iPSCs by conservation of T cell receptor (TCR) through reprogramming. Additionally, the ability to engineer chimeric antigen receptors (CAR) into iPSCs, which can then be expanded and differentiated back to T cells, provides a cost-effective method to generate large number of allogeneic CAR-T cells. The therapeutic success of such allogeneic T cell therapies can be further increased with high-resolution HLA typing to reduce the risk of any post-transplant complications.

RESULTS

The Oncomine TCR Beta-LR Assay uses a TCRβ primer panel to amplify the TCRβ rearrangements prior to Next Generation Sequencing (NGS). This assay was performed using gDNA isolated from iPSC colonies.

CONCLUSIONS

- Introducing T cell derived iPSCs offers solutions to many of the current issues of CAR T cell therapies, such as T cell exhaustion and low CAR transduction efficiencies. iPSCs also have the potential to create allogeneic therapies without the issues of lot-to-lot variation.
- TCR sequencing and HLA typing are necessary for autologous and allogeneic cell therapies. TCR sequencing requires method like NGS or other high-throughput sequencing methods. HLA typing may either be done by qPCR or NGS, however, qPCR is much faster and more cost-effective to perform.
- Immediately after T cell reprogramming, TCR sequencing should be the first method of characterization to confirm T cell lineage in iPSC colonies.

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TRADEMARKS/LICENSING

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