

Fote
THERAPEUTICS

*Better Cells For
Better Therapies™*

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RESULTS

A. **hiPSC (Day 0)** **Hemogenic Endothelium (Day 10)** **iMDS (Day 10+9)**

B.

	MDS
CD45 ⁺	95.15 ± 1.57
CD45 ⁺ CD33 ⁺	93.75 ± 1.77
Erythrocytes (CD45 ⁺ CD235 ⁺)	0.084 ± 0.05
Lymphoid (CD45 ⁺ CD7 ⁺)	0.015 ± 0.01
Granulocytes (CD45 ⁺ CD33 ⁺ CD66b ⁺)	3.833 ± 2.19
Monocytes (CD45 ⁺ CD33 ⁺ CD14 ⁺)	52.8 ± 8.93
PDL1 expression (CD45 ⁺ PDL1 ⁺)	56.66 ± 9.297

C.

D.

HSPC	
CD34	
CD90	
CD38	
CD49f	

Lymphoid	
CD2	
CD3	
CD19	
CD20	
CD56	
TCR γ/δ	
TCR Vβ13.2	
TCR Vβ23	
TCR Vβ8	
TCR Vβ9	
TCR Vβ2	
Vγ9	
TCR Va24-Jα18	
TCR Va7.2	
TCR α/β	

E.

MHC/co-stimulation	
CD40	
CD80	
CD83	
CD86	
ICOSL	
OX40L	
4-1BB Ligand	
HLA-A,B,C	
HLA-DR	

Immune-Regulation	
PDL1	
PDL2	
B7H3	
Galectin-9	
HLA-E	
HLA-G	
Tim-3	
Siglec-9	
CD200R	
CD112	
CD155	
HVEM	

% Expression

0 10 20 30 40 50 60 70 80 90 100

— Ctrl — iMDS

Figure 1. Scalable generation of immune-regulatory myeloid cells from human induced pluripotent stem cells under serum free and feeder-free conditions. A. Parental human induced pluripotent stem cells (hiPSCs) are differentiated through a 10 day multi-staged monolayer culture process to CD34⁺ hemogenic endothelium (HE, CD34⁺). Day 10 iCD34⁺ HE cells are isolated by FACS and cultured in myeloid promoting conditions resulting CD45⁺ cells emerging from the endothelial layer starting day 3 after plating and acquiring CD33 by day 9. B. The CD45⁺ cell population manufactured using this 19 day process is highly enriched for myeloid cells (>90%) and is free of granulocytes, erythrocytes, and lymphoid cells. C. This process enables the production of over 1,000 CD45⁺CD33⁺ cells for 1 iPSC. D-E. Immunophenotyping by LEGENDScreen™ demonstrates that day 19 CD45⁺CD33⁺ cells express predominantly early myeloid markers and several immune-regulatory surface proteins. In light of the similarities of this marker profile to that of MDSCs, day 19 CD45⁺CD33⁺ cells are termed iMDSCs.

A. NSG mouse irradiated with 2Gy, followed by intravenous (iv) injection of iMDSCs (2.5×10^6) and PBMCs (7.5×10^6). The experimental setup is designed to analyze weight, GVHD score, survival, and PB analysis.

B. GVHD Score over time (Days). Control (n=5, black circles) and iMDSC (n=5, blue circles) groups are compared. The iMDSC group shows significantly lower GVHD scores (P<0.0001).

C. Percent survival over time (Days). Control (n=5, black circles) and iMDSC (n=5, blue circles) groups are compared. The iMDSC group shows significantly higher survival (P=0.0753).

D. Bar graphs showing the percentage of human CD45⁺ cells in PBMCs alone and PBMCs + iMDSC. The iMDSC group shows a significant increase in CD45⁺ cells (***).

- Established scalable, feeder free manufacture of myeloid derived suppressor cells (iMDSCs) from human induced pluripotent stem cells
- iMDSCs potently suppressed T cell proliferation and effector function independently of HLA matching
- A single injection of iMDSCs attenuated disease and prolonged survival in a xenogenic mouse model of GvHD, and is associated with increased levels of Tregs