Transplantation of Hematopoietic Stem and Progenitor Cells from Cadaveric Organ Donors Leads to Long-Term Multilineage Engraftment in NSG Mice

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INTRODUCTION

Hematopoietic Stem and Progenitor Cells (HSPC) from cadaveric donors (CDs) have been used historically almost exclusively in the context of tolerance induction in combined bone marrow (BM) and solid organ transplantation. To date, no systematic study has addressed their functional long-term engraftment capacities. However, HSPC from banked CDs might be of high importance since they increase the still limited donor pool with on-demand availability as well as allow potential tolerance induction for patients undergoing combined transplantation.

AIM

With our study, we aim to investigate the capacity of CD bone marrow to achieve long-term multi-lineage engraftment and evaluate, whether cells from CDs maintain equal quality to those from living donors (LDs).

METHODS

Bone marrow was recovered from vertebral bodies of CDs and CD34⁺ selected.

Primary transplants: 5x10⁵ hCD34⁺ cells from 24 different CDs were transplanted i.v. in to NSG mice (n=5 per donor), following 1Gy total body irradiation (TBI). Blood was drawn every two weeks, starting week 4 and human CD45⁺ chimerism was analyzed via flow cytometry.

Secondary transplants: BM of 15 primary engrafted donors was harvested, hCD45⁺ cells were selected with immunobeads and transplanted into 1Gy irradiated NSG mice (n=2-4 per donor). Human chimerism was analyzed as in primary transplants.

Side by side comparison: 1 CD and 1 LD were transplanted side by side following the same procedures as primary transplants.

Competitive Assay: 2.5x10⁵ hCD34⁺ cells of CD **and** LD were transplanted simultaneously into NSG mice (n=5 per donor) after 1Gy TBI. 6 groups were transplanted in total, with 2 different LD being paired with 3 different CD each. Blood was drawn every two weeks, starting week 4 and analyzed via flow cytometry. CD and LD cells were distinguishable based on their HLA-A2 *status*, which was confirmed pre-transplant.

RESULTS

All **primary transplanted** CDs engrafted successfully and robust long-term multi-lineage PB engraftment >16 weeks was seen in 19 out of 24 donors.
All but one CD showed hCD45⁺ chimerism >1% upon takedown (between w14-22) with a mean chimerism of 40.27% +/-30.53%.

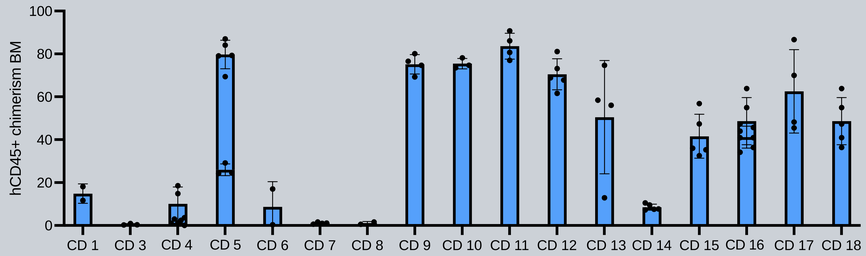

Figure A: hCD45⁺ BM engraftment of all transplanted donors upon takedown (w14-22)

Secondary transplants led to successful initial engraftment in PB in ? out of 19. BM data is so far only available for 8 donors: 7/8 CDs showed hCD45⁺ cells with a mean chimerism of 19.11% +/-22.49%.

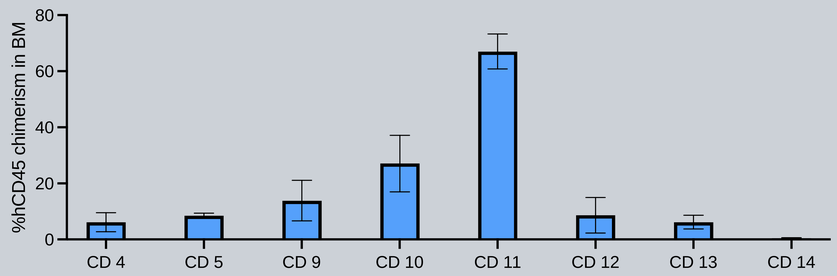

Figure B: hCD45⁺ BM engraftment for all available secondary donors upon takedown

Side by side transplantation of one CD and one LD led to equivalent PB and organ engraftment. The tissues showed a mean engraftment of hCD45⁺ cells of 87% +/- 9.6% vs. 71% +/- 9.5% in spleen and 76% +/- 5.3% vs. 78% +/- 4% (NS) in BM upon takedown 20 weeks post-transplant.

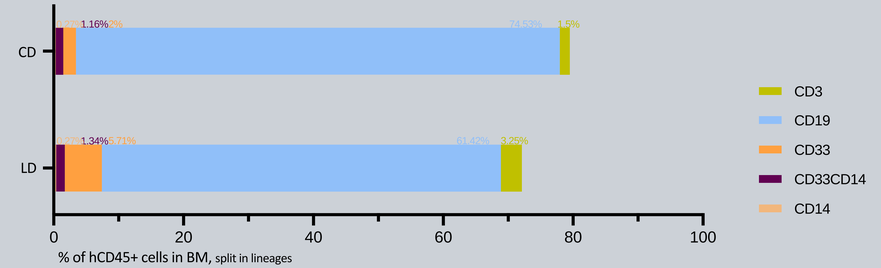

Figure C: hCD45⁺ BM engraftment, split into different lineages of side by side transplanted CD (n=1) and LD (n=1) cells upon takedown at week 20

In two separate **competitive assays,** 1/2 and 4/6 CDs were able to win over their LD counterpart to constitute the mayor fraction of hCD45⁺ cells.

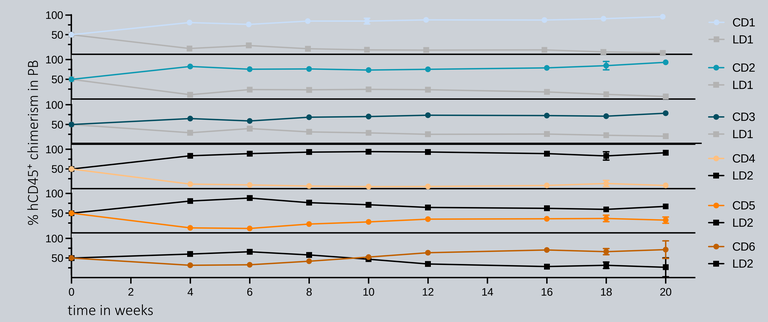

Figure D: hCD45⁺ chimerism in PB over time of competitively transplanted CD and LD cells

CONCLUSION

- CD34⁺ HSPC from CDs **retain** their **capacity for long-term multi-lineage engraftment** and can be **serially** transplanted.
- Cells from **cadaveric donors** seem to maintain at least **equipotent engraftment potential** as those from **living donors.**

ACKNOWLEDGMENTS

Mapara lab: Huihui Ma
CCTI flow core: Caisheng Lu
Sykes lab: Nichole Danzl
Snoeck lab: Corey Gary and Hans Snoeck

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