Expansion of phenotypically senescent CD57+ CD8 T cells is associated with impaired immunocompetence after allogeneic hematopoietic stem cell transplantation

Sarah Morin[1]*, Amandine Pradier[1,2]* Anne-Claire Mamez[1], Federica Giannotti[1], Diem-Lan Vu-Cantero[3,4], Marta Fabra Urdiola[1], Caroline Stephan[1], Chiara Bernardi[1], Astrid Melotti[1,2]Stavroula Masouridi-Levrat[1], Eddy Roosnek[1,4], Laurent Kaiser[3,4], Yves Chalandon[1,2], and Federico Simonetta[1,2]

*[1]Division of Hematology, [2]Translational Research Center for Oncohematology, [3]Division of Infectious Diseases , [4]Faculty of Medicine, Geneva University Hospitals and Geneva University, *Equal contribution*

INTRODUCTION

CD57 has been reported as a marker of human senescent CD8 T cells. Early studies have reported increased proportions of CD57-expressing CD8 T cells after autologous and allogeneic hematopoietic stem cell transplantation (HSCT).

OBJECTIVES

To determine whether the expansion of CD57+ CD8 T cells is associated with impaired immunocompetence after allogeneic HSCT.

METHODS

Peripheral blood mononuclear cells were collected from **healthy controls** (HC, n=21) and patients undergoing **allogeneic HSCT** (n=115) at Geneva University Hospitals.

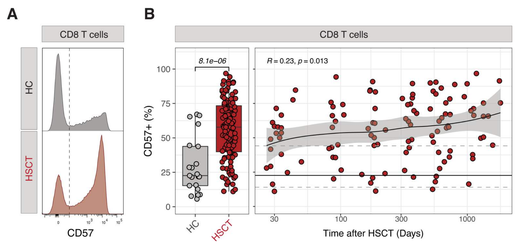
Proportions of CD57+ CD8 T cells as well as **phenotypic and functional characteristics** of CD57+ CD8 T cells were assessed by flow cytometry.

Virus-specific CD8 T cells were identified by flow cytometry based on IFNγ and/or TNFα intra-cytoplasmic expression after 6h in vitro stimulation with peptides derived from CMV, EBV, HHV6, BKV and Adenovirus.

Replication of Torque Teno Virus (TTV), a non-pathogenic anellovirus reported to reflect the quality of post-transplant immune reconstitution was quantified by quantitative PCR.

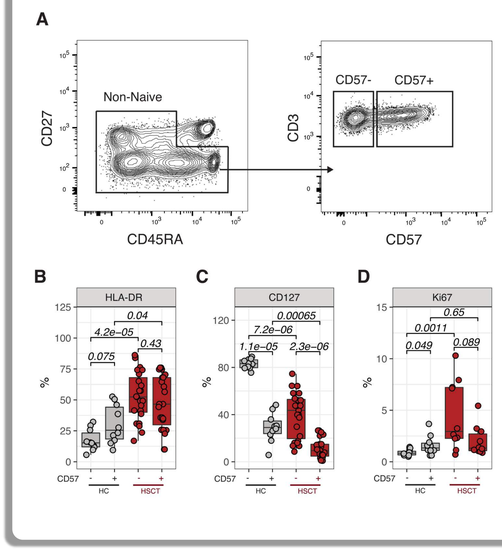
RESULTS

1. CD57+ CD8 T cells are expanded after allogeneic HSCT



A,B. Proportion of CD57+ cells among CD8 T cells on representative (A) and pooled (B) specimens from healthy controls (grey) and HSCT recipients (red)

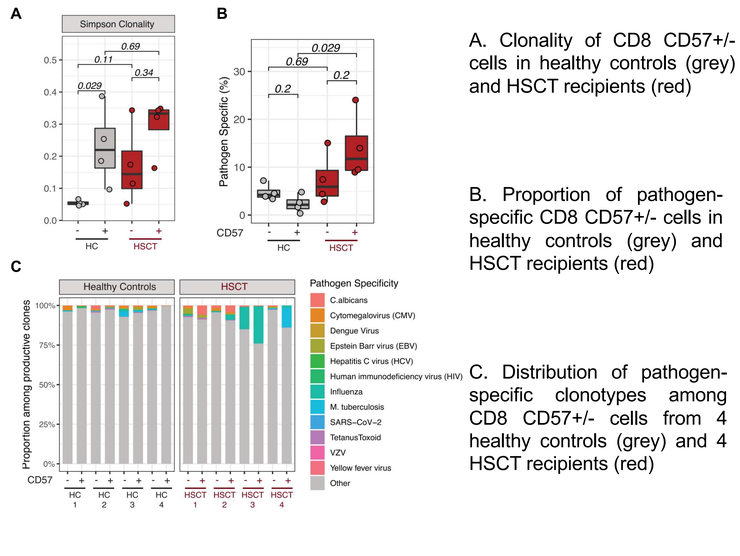
2. CD57+ CD8 T cells from allogeneic HSCT recipients display a senescent phenotype



A. CD8+ CD57+ Memory cells gating strategy

B, C, D. Proportion of HLA-DR (A), CD127 (B) and Ki-67+ (C) cells among CD8+ CD57+/- cells in healthy controls (grey) and HSCT recipients (red)

3. TCRβ-sequencing reveals high pathogen-specific clonotypes enrichment in CD57+ CD8 T cells from allogeneic HSCT recipients

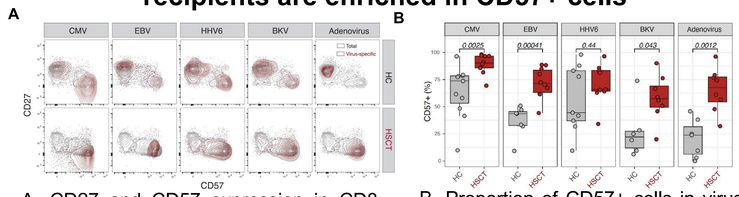


A. Clonality of CD8 CD57+/- cells in healthy controls (grey) and HSCT recipients (red)

B. Proportion of pathogen-specific CD8 CD57+/- cells in healthy controls (grey) and HSCT recipients (red)

C. Distribution of pathogen-specific clonotypes among CD8 CD57+/- cells from 4 healthy controls (grey) and 4 HSCT recipients (red)

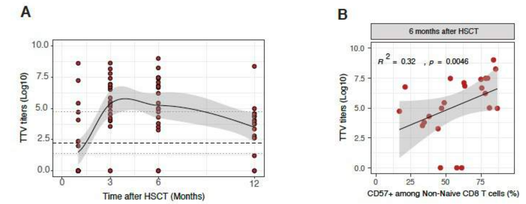
4. Virus-specific CD8 T cells from allogeneic HSCT recipients are enriched in CD57+ cells



A. CD27 and CD57 expression in CD8 non-naïve T cells from healthy controls (top) and HSCT recipients (bottom)

B. Proportion of CD57+ cells in virus-specific CD8 T cells in healthy controls (grey) and HSCT recipients (red)

5. Proportion of CD57-expressing cells among non-naive CD8 T cells positively correlates with TTV titers in allogeneic HSCT recipients



A. TTV titers evolution over time in HSCT recipients; B. Correlation between CD57+ among non-naïve CD8+ cells and TTV titers at 6 months after HSCT

CONCLUSIONS

Proportion of phenotypically senescent CD57+ CD8 T cells increases after allogeneic HSCT, in particular in virus-specific CD8 T cell clonotypes. CD57 expression at the surface of EM CD8 T cells, a highly enriched population in allogeneic HSCT recipients, correlated with higher replication of TTV, reflecting a status of impaired immunocompetence after allogeneic HSCT.

Studies are ongoing to determine the utility of CD57 expression on T cells as a biomarker to predict infectious complications after allogeneic HSCT.

DISCLOSURES

YC: Incyte, BMS, Pfizer, Abbie, MSD, Roche, Novartis, Gilead, Amgen, Jazz, AstraZeneca: Other: Travel Expenses; Incyte: Speakers Bureau; Incyte, BMS, Pfizer, Abbie, MSD, Roche, Novartis, Amgen: Other: Advisory Board. FS: consulting fees from BMS/Celgene, Incyte, Kite/Gilead; Travel Expenses from Kite/Gilead, BMS/Celgene, AstraZeneca; Research support from Kite/Gilead.