immunoSEQ®

TRANSPLANT/ INFECTIOUS DISEASE

CASE STUDY

CMV reactivation drives post-transplant T-cell reconstitution and results in defects in the underlying TCRB repertoire

Suessmuth Y, *et al.* (2015) *Blood* 125(25):3835-50
JUNE 2015

WHY IMMUNOSEQ?

The immunoSEQ Assay allowed investigators to monitor immune reconstitution post-transplant

Antigen-specific T cells could be tracked over time

The immunoSEQ Assay uncovered developmental defects within the $CD8^+$ T-cell compartment

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CASE STUDY: CMV reactivation drives post-transplant T cell reconstitution and results in defects in the underlying TCRB repertoire — Suessmuth Y, *et al.* (2015) *Blood* 125(25):3835-50

BACKGROUND

The impact of CMV reactivation in dysfunctional immune reconstitution after hematopoietic stem cell transplant (HSCT) is well established, but the causative molecular immunologic mechanisms remain unknown

AIM

To understand immunological phenomena underlying CMV-reactivation effects on immunologic reconstitution after unrelated-donor HSCT

METHODS

1. Peripheral blood samples were collected from 17 patients who underwent HSCT. Samples were also collected from healthy adult controls. CMV reactivation was determined by PCR.
2. PBMCs → **multiparametric flow cytometry**
   PBMCs → gDNA extraction → **immunoSEQ® (TCRB)**
3. cell sorting (naïve, T_{EM} and CMV-specific $CD8^+$ T cells) → **multiparametric flow cytometry**
   cell sorting (naïve, T_{EM} and CMV-specific $CD8^+$ T cells) → gDNA extraction → **immunoSEQ (TCRB)**

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RESULTS

Figure 1.

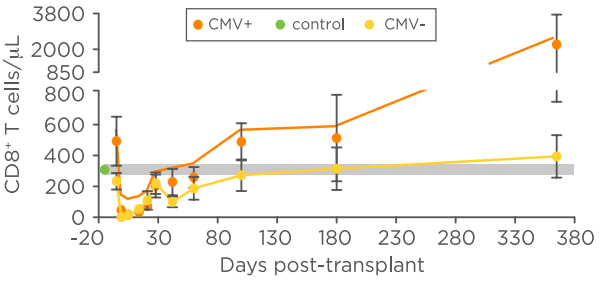

Figure 2.

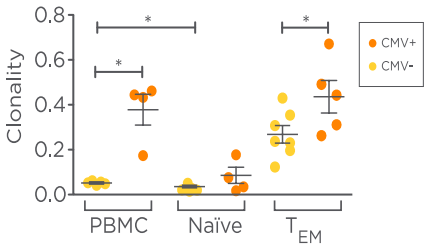

Figure 3.

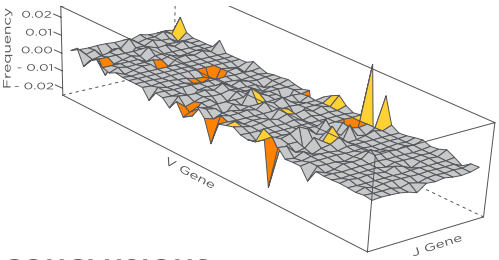

Figure 4.

Patient #	overlap between $CD8^+$ T_{EM}/ CMV-specific clones
001-001	67.8%
001-008	90.8%
001-009	14.4%
002-002	55.1%

Figure 1. CMV reactivation associated with an expansion of $CD8^+$ T cells, due both to the expansion of the $CD8^+$ T_{EM} comparment and the contraction of naïve $CD8^+$ T cells.

Figure 2. CMV reactivation resulted in increased clonality of the TCR repertoire, especially in the $CD8^+$ T_{EM} compartment.

Figure 3. CMV reactivation resulted in a compromised TCR repertoire as shown by the deficiencies in the use of some V and J genes in the $CD8^+$ T_{EM} compartment.

Figure 4. The high overlap between expanded $CD8^+$ T_{EM} clones and CMV-tetramer sorted clones suggests the clonal expansion is driven by CMV-specific $CD8^+$ T_{EM} cells.

CONCLUSIONS

- CMV reactivation resets post-transplant CD8 reconstitution, resulting in massive clonal expansion of CMV-specific $CD8^+$ T_{EM} cells
- CMV reactivation is associated with developmental defects in the underlying $CD8^+$ T_{EM} repertoire

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