immunoSEQ®

TRANSPLANT

CASE STUDY

Immune reconstitution/ immunocompetence in recipients of kidney plus hematopoietic stem cell transplants

Leventhal JR, *et al.* (2015) *Transplantation* 99(2):288-98
FEBRUARY 2015

WHY IMMUNOSEQ?

The immunoSEQ Assay enables the identification and tracking of TCRB sequences to evaluate chimerism

ImmunoSEQ quantitates immune repertoire diversity and clonality to evaluate immune reconstitution post-transplantation

amplify **discovery**™

CASE STUDY: Immune reconstitution/immunocompetence in recipients of kidney plus hematopoietic stem cell transplants — Leventhal JR, *et al.* (2015) *Transplantation* 99(2):288–98

BACKGROUND

- Solid organ transplant recipients require lifelong immunosuppressive therapy to avoid rejection
- This treatment can lead to renal dysfunction, metabolic abnormalities, susceptibility to opportunistic infections and malignancies
- Using a reduced-intensity conditioning before renal allograft, followed by infusion of stem cells (enriched for tolerogenic $CD8^+$/T-cell receptor [TCR]-facilitating cells and hematopoietic stem cells, and depleted of graft-versus-host disease [GVHD]-producing cells [FCRx]) can result in significant persistent chimerism in the recipient
- Persistently chimeric recipients can be removed from immunosuppressive therapies following mismatched related or unrelated transplants

AIMS

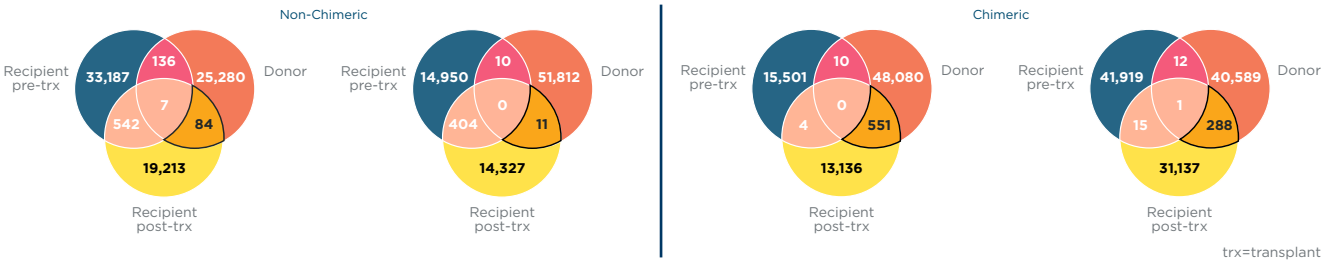
- Evaluate the immune reconstitution and immunocompetence in kidney plus FCRx transplant recipients
- Compare results between persistently chimeric, transiently chimeric and non-chimeric recipients

METHODS

1. Peripheral blood mononuclear cells (PBMCs) isolated → gDNA extraction → **immunoSEQ® (TCRB)**
2. **Transplant**
3. PBMC collection (2 years following transplantation) → gDNA extraction → **immunoSEQ (TCRB)**

RESULTS

Shifts in T-cell receptor beta (TCRB) repertoire in chimeric and non-chimeric patients (representative data from 4 subjects)



For both chimeric and non-chimeric patients:
- The TCRB repertoire is newly developed post-transplant
- Approximately 97% new clones

For reconstituted chimeric patients:
- The TCRB repertoire is more similar to the donor
- Chimerism induces tolerance to renal allografts

- Disease relapse was seen in the non-chimeric patients and in one of the four transiently chimeric patients, but in no chimeric persistent patients
- Chimeric patients were able to respond to vaccines and retained memory to vaccines post-transplant

CONCLUSIONS

- Achievement of chimerism induces tolerance to renal allografts and immunocompetence

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