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Human Antibody Repertoire and Allograft Rejection Among Kidney Transplant Recipients with HIV

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856

BACKGROUND

- Kidney transplantation (KT) between donors and recipients with HIV (D+/R+) is promising.
- However, allograft rejection risk among recipients with HIV (R+) is higher than recipients without HIV (R-).
- We compared the antibody repertoire between D+ vs D-, and evaluate the association between antibody targets from donors and recipients and KT allograft rejection.

METHODS

- The HOPE in Action Multicenter Kidney Trial performed KT in R+ between 2018-2021 from deceased donors and followed KT R+ for adverse events and survival.
- Targets of plasma antibody reactivity in donors and recipients were quantified using phage immuno-precipitation sequencing (PhIP-Seq), which is able to quantify all known peptides (~600,000) from human antibody libraries (e.g., virus, toxin, autoantibody).
- We used validated Viral Aggregate Reactivity score (VARscore) to integrate the intensity and breadth of response to all antibody peptides for each viral species.
- Moderated t-tests were used to evaluate the association between pre-KT antibody levels and rejection after KT.
- We used the false discovery rate (FDR) with threshold of 5% to correct multiple comparisons.

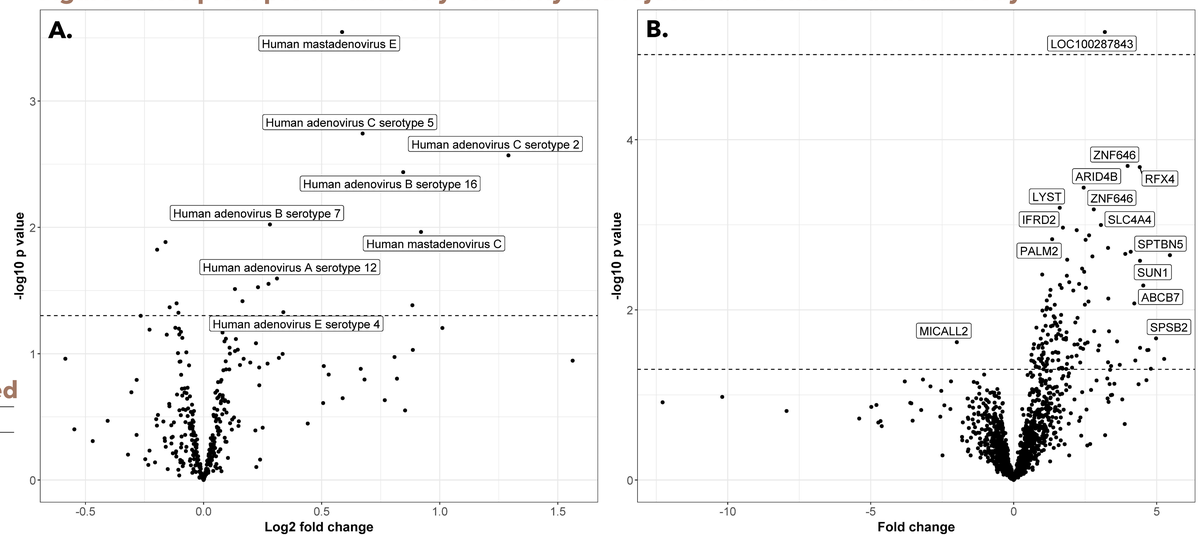
Table 1. Characteristics of donors and recipients included

Donors	D-, n = 41	D+, n =63
Age, years	36 (29-48)	36 (28-45)
Female sex	17 (41)	17 (27)
Black race	6 (15)	25 (40)
Brain death	33 (80)	53 (84)
Steroid administered	27(66)	38(60)
KDPI, score	44 (33-63)	37 (27-53)
Hypertension	9 (22)	10 (16)
Diabetes	3 (7)	2 (3)
Serum creatinine, mg/dL	1.10 (0.82-1.26)	0.96 (0.61-1.21)
Recipients	**R+/D-, n = 99**	**R+/D+, n = 99**
Age, years	57 (50-63)	53 (45-60)
Female sex	19 (19)	16 (16)
Black race	69 (70)	72 (73)
HIV RNA<200 copies/mL	98 (99)	98 (99)
CD4+ T cell, cells/μl	492 (382-686)	511 (375-652)
INSTI for ART	95 (96)	98 (99)
ATG immunosuppression	65 (66)	65 (66)
Causes of kidney failure		
HIV nephropathy	36 (36)	34 (34)
Diabetes	25 (25)	23 (23)
Hypertension	17 (17)	20 (20)

Note: Median (IQR) shown for continuous variables, n (%) for categorical variables.
Lower Kidney Donor Profile Index (KDPI) is associated with longer expected kidney function;
Antithymocyte Globulin (ATG) is a lymphocyte depletion induction immunosuppression.

Reactivity of donor HIV antibodies was not associated with rejection among recipients, adding the evidence of the safety of HIV kidney transplantation. However, pre-transplant adenoviruses infection and autoantibodies for both donors and recipients might require special attention.

Figure 3. Recipient pre-KT antibody reactivity and rejection. A: virus B: autoantibody



RESULTS

- D+ and D- had similar age and sex, while D+ were more likely to be black and had lower KDPI.
- The characteristics between recipients with D+ vs recipients with D- were similar.
- D+ had slightly higher total number of hits for human autoantibody targets, and also higher reactivity for CMV and EBV.
- While donor HIV antibodies had not association with rejection, donor adenovirus A 12 antibody was significantly associated with increased rejection risk among recipients (FDR<5%).
- Donor autoantibodies (e.g., BIRC6, SHANK3, ZNF646) and toxin (e.g., pneumoniae, albicans, influenzae) targets were associated with rejection, but not significant after correction for multiple comparisons.
- Recipients pre-KT adenovirus reactivity was also associated with rejection, though not statistically significant after accounting for multiple comparisons.
- Many recipient autoantibodies were positively associated with rejection, and a hypothetical protein LOC100287843 was statistically significant.

Figure 1. Donor total hits by donor HIV status

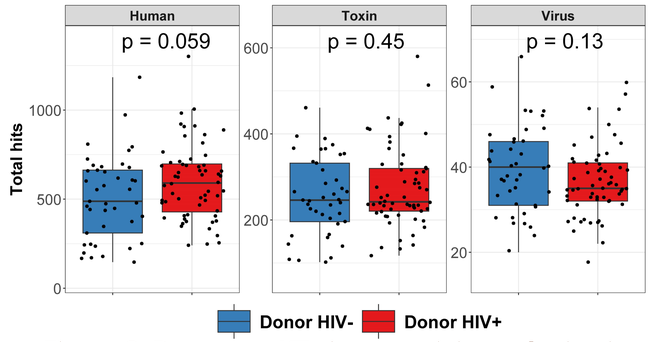
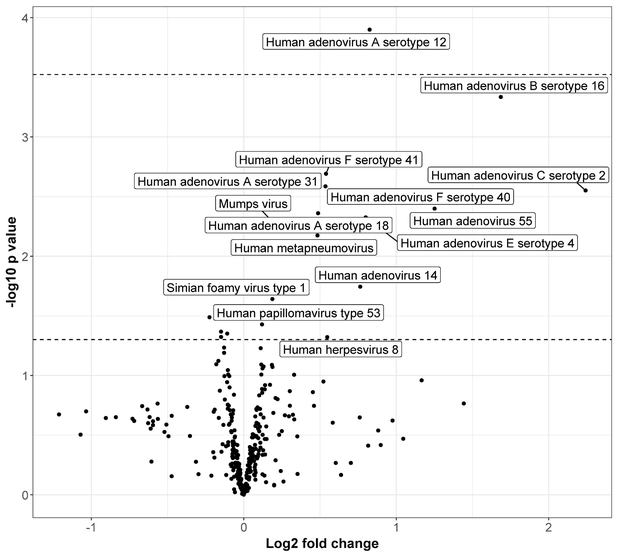


Figure 2. Donor pre-KT virus reactivity and rejection



CONCLUSIONS

- D+ had marginally more hits for autoantibodies and higher CMV and EBV antibody reactivity than D-, otherwise their antibody profile were similar.
- Autoantibodies may serve as a tool for screening recipients with high risk of rejection.
- Future studies are needed to evaluate the intervention against adenovirus infection for both donors and recipients before transplantation.

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