

HIGHLIGHTS
AMERICAN TRANSPLANT CONGRESS
ATC2023
JUNIO 3-7, 2023

En esta presentación puede haber mención a datos científicos que no están aprobados en el registro. Por favor, consulte la ficha técnica. Las opiniones expresadas en esta presentación corresponden únicamente a quienes las emiten y no representan necesariamente las opiniones de Chiesi España S.A.U.

HIGHLIGHTS
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Hospital Universitario
Puerta del Mar

Acceso al trasplante, donante vivo, donación y preservación del órgano, asignación del órgano, genética, pérdida no inmunológica del injerto, complicaciones cardiovasculares/metabólicas, inteligencia artificial, resultados del TR "alternativos" -PREMS, PROMS

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HOPE

IN ACTION →

Wait time advantage for transplant candidates with HIV who accept kidneys from donors with HIV under the HOPE Act

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HIV Organ Policy Equity (HOPE) Act

A goal of the HOPE Act, implemented in 2015, was to increase Access to KT to PLWH
HOPE Act allows for transplantation of organs from donors with HIV (D+) to recipients with HIV (R+) within research protocols

Donors	Recipients
 <ul style="list-style-type: none">• HIV D+ could not have active opportunistic infection or cancer.• No specific criteria for donors HIV RNA or CD4 count.• Organs from HCV-viremic donors were utilized for HCV-viremic recipients	 <ul style="list-style-type: none">• CD4 \geq 200 cells/μL within 16 weeks• Receiving ART with HIV RNA < 50 copies/mL

OBJECTIVES

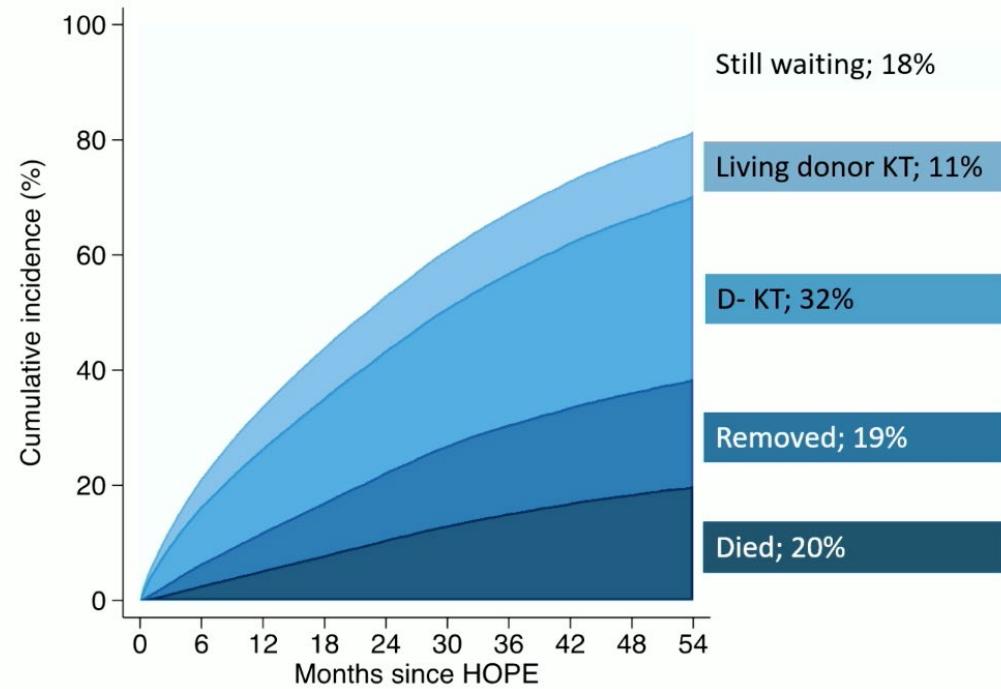
- To understand:
 - Outcomes of candidates following HOPE listing.
 - Compare time to KT to candidates not listed in HOPE.

METHODS: data source

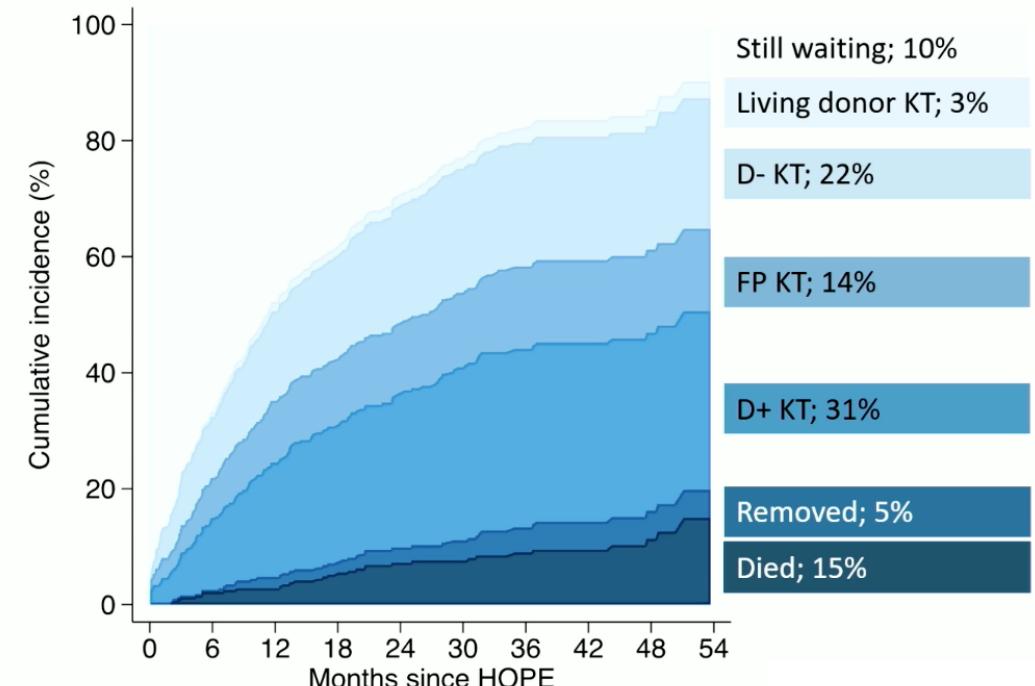
- HOPE in Action Multicenter Kidney U01 trial (NCT03500315)
 - All candidates enrolled provided written informed consent, and met standard center-specific clinical criteria for KT and HIV-specific inclusion criteria
 - HOPE candidates received organs from D+ or D- based on organ availability and standard allocation procedures
- Data linked to SRTR to identify KT candidates at the same centers who were not listed to accept D+ kidneys (non-HOPE)

- 324 HOPE and 47,501 non-HOPE candidates at 24 centers participating in the HOPE trial between April 26, 2018 and May 24, 2022
 - All candidates were adults (≥ 18 years), actively waitlisted for kidney-only transplant
- In SRTR, HIV status only available for KT recipients
 - Among non-HOPE candidates who eventually received KT, 98.9% did not have HIV

Waitlist outcomes of non-HOPE candidates

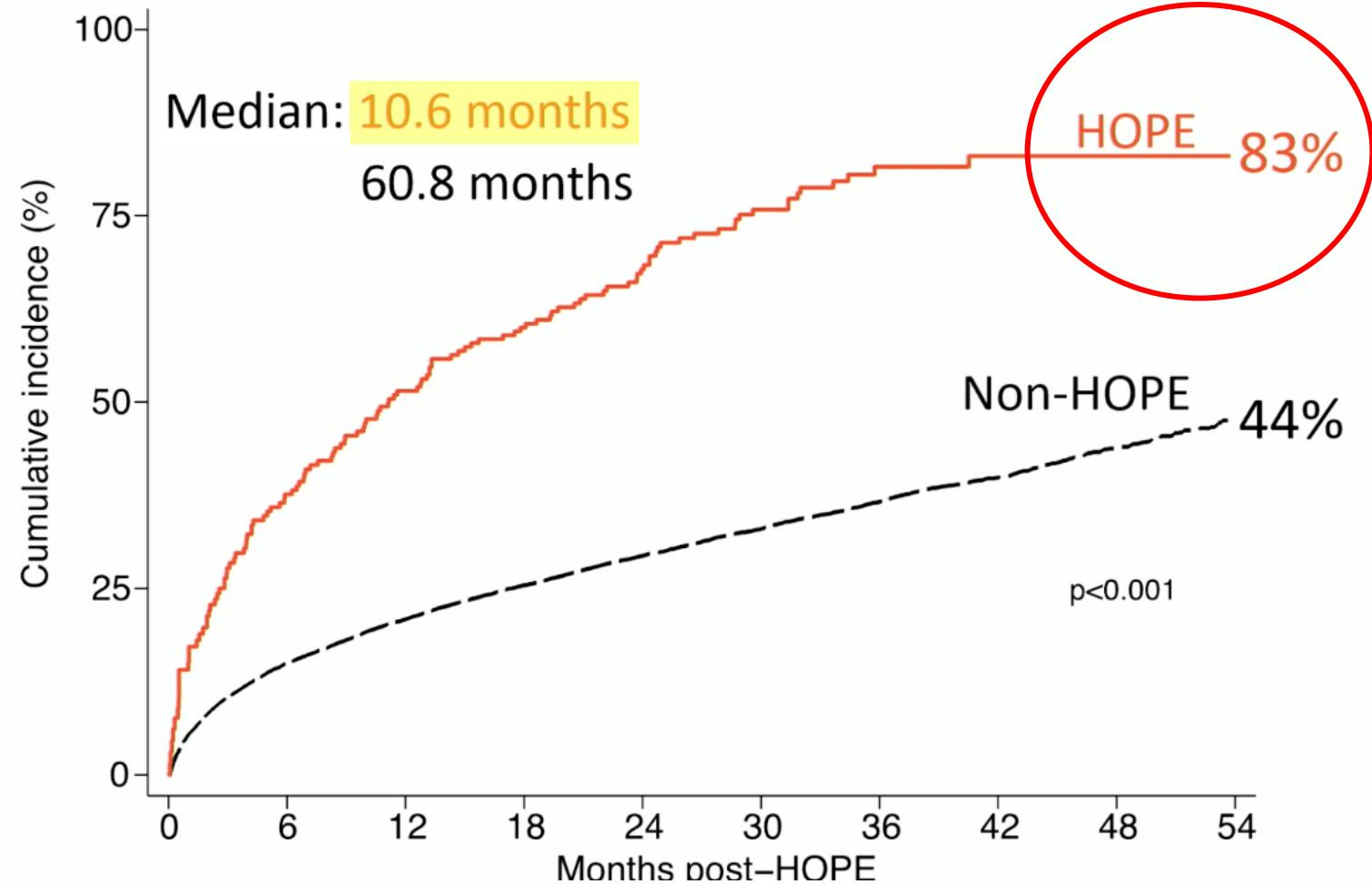


Waitlist outcomes of **HOPE** candidates



FP: donors with false-positive HIV test

Time to KT for HOPE candidates



CONCLUSIONS

- At 24 HOPE trial centers, 70% of HOPE candidates received a KT during the 54-month study period vs. 43% of non-HOPE candidates at the same center
- Candidates enrolled in the HOPE trial had shorter wait-times (median 10.6 vs. 60.8 months), and 3.2-fold higher rate of KT

Trend in utilization and transplant outcomes of COVID-positive deceased-donor kidneys

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Department of Medicine

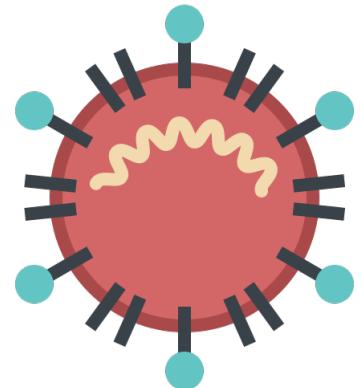
San Diego, June 6th, 2023

RESEARCH QUESTION

- To examine the national trend in utilization and medium-term outcomes of kidney transplantation (KT) from active or resolved COVID-19 positive donors remain unknown.

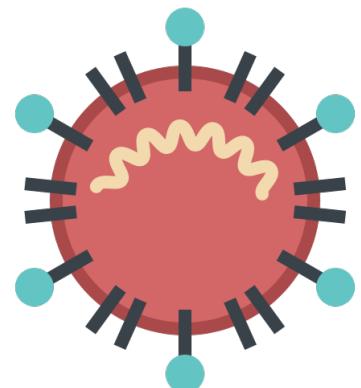
BACKGROUND

- Early in the pandemic, donors with COVID-19 **were not** considered eligible for transplantation.
- Concerns for using these organs:
 - Transmission of the virus to the recipients, causing COVID-19 infection
 - Worse kidney transplant outcomes
 - Patient's acceptability of these organs
- No cases of virus transmission with kidney transplantation causing COVID-19 infection



< 7 days

Active COVID-19



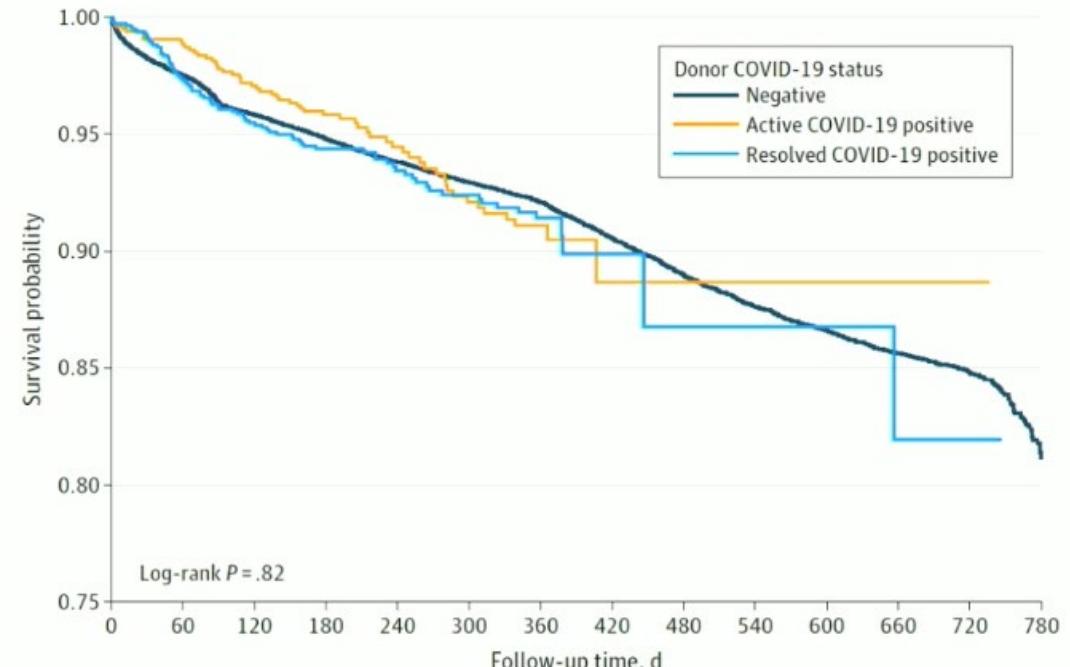
≥ 7 days

Resolved COVID-19



KIDNEY ALLOGRAFT OUTCOMES

Figure. Kaplan-Meier Curve for Graft Failure by Donor COVID-19 Status



No. at risk	Negative	40789	32463	31181	28572	24343	22810	18301	10050	9112	8823	8456	7723	5104	591
Active COVID-19 positive	1289	867	810	681	434	379	255	32	13	12	12	12	9	0	
Resolved COVID-19 positive	1435	1034	971	829	582	508	355	46	22	19	19	17	9	0	

RISK OF DISCARD

Table 2. Nonuse of Kidneys Recovered From Active and Resolved COVID-19-Positive Donors, Organ Procurement and Transplantation Network 2020-2023

	AOR (95% CI) ^a	2020 (March to December)	2021	2022	2023 (January to March)
COVID-19 status	Overall				
COVID-19 negative	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
Active COVID-19 positive	1.55 (1.38-1.76)	11.26 (2.29-55.38)	2.09 (1.58-2.79)	1.47 (1.28-1.70)	1.07 (0.75-1.63)
Resolved COVID-19 positive	1.31 (1.16-1.48)	3.87 (1.26-11.90)	1.94 (1.54-2.45)	1.09 (0.94-1.28)	1.18 (0.80-1.73)

Abbreviation: AOR, adjusted odds ratio.

^a Adjusted for donor characteristics, including age, sex, race and ethnicity, body mass index, presence of diabetes, presence of hypertension, kidney donor profile index

score, donation after cardiac death status, cause of death, serum creatinine level, and hepatitis C virus status.

SECONDARY OUTCOMES

- **Acute reject:** Kidneys was not associated with higher risk of acute rejection within 6 months post KT from donors with active COVID-19 (aOR, 0.99; 95%CI, 0.66-1.48) or resolved COVID-19 (aOR, 0.72; 95%CI, 0.47-1.09).
- **Delayed graft function:** Neither active donor COVID-19+ (aOR, 0.92; 95%CI, 0.79-1.05) or resolved donor COVID-19+ (aOR, 1.03; 95%CI, 0.91-1.17) were associated with risk of DGF.
- **Length of hospital stay:** Recipients of KT from donors with active COVID-19+ had 0.63 days (95%CI, 0.23-1.01, p=0.002) shorter LOS than recipients from COVID-19-negative donors.



Pre-Donation Hypertension and Post-Donation Kidney Function in Living Kidney Donors

**Ekamol Tantisattamo, MD, MPH^{1,2,3}; Sasithorn Kunupakan, MD^{1,4}; Chanokporn Puchongmart, MD⁵;
Piengpitch Naunsilp, MD⁶; Phuuwadith Wattanachayakul, MD⁷; Bima J. Hasjim, MD⁸; Natsuki Eguchi,
BS⁹; Antoney J. Ferrey, MD¹; Uttam G. Reddy, MD¹; Donald C. Dafoe, MD⁹; Hirohito Ichii, MD, PhD⁹**

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²*Nephrology Section, Department of Medicine, Tibor Rubin Veterans Affairs Medical Center, Veterans Affairs Long Beach Healthcare System, Long Beach, California, United States*

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⁹*Division of Kidney and Pancreas Transplantation, Department of Surgery, University of California Irvine School of Medicine, Orange, California, United States*

PURPOSE

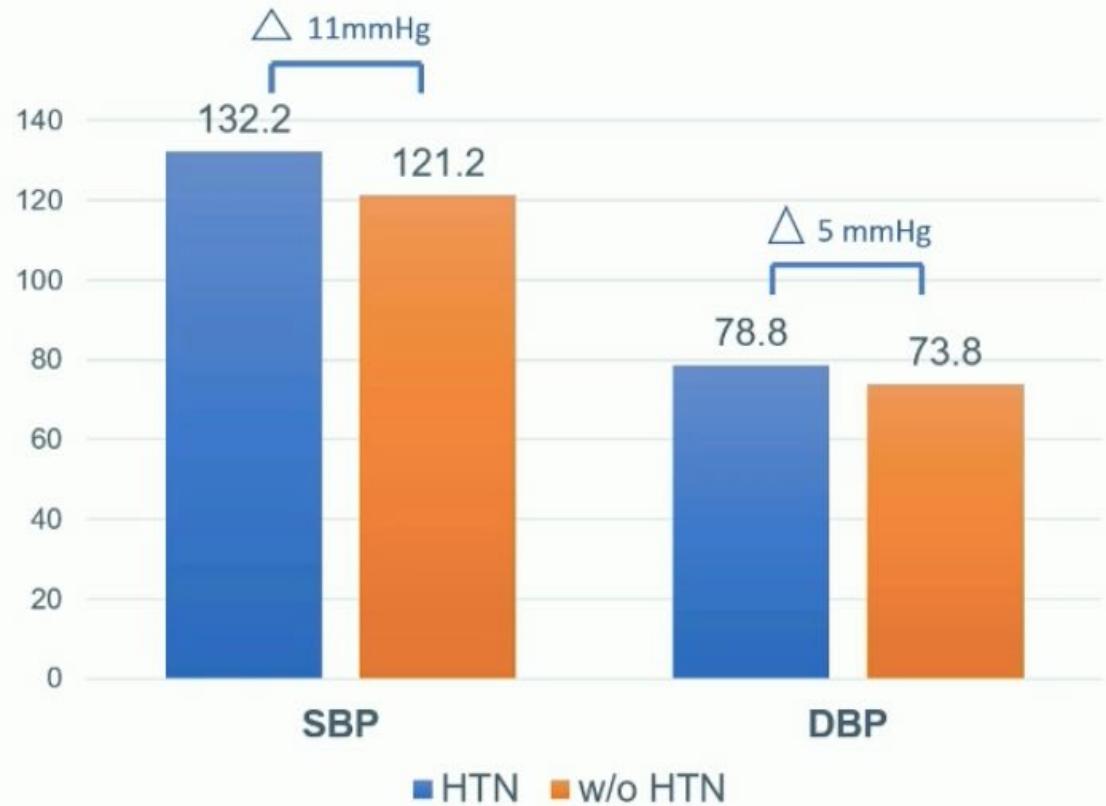
- To investigate the risk difference between LKD with and without hypertension for worsening kidney function after donation



RESULTS

- **38,062 LKD**

- **Age** : 44 ± 12 years
- **Sex** : female 65% (24,740)
- **Pre-donation HTN** : 5% (1,728)
- **Pre-donation SCr** : 0.85 vs 0.83 mg/dL
[with a mean difference of 0.02 mg/dL
(95%CI 0.01, 0.03).]
- **Follow-up time** : 6.5 months (IQR 5.8, 8.5)



	Hazard ratio	95%CI
Univariate	1.2	1.14, 1.26
Multivariate	1.12	1.05, 1.19



VS.



Adjusting

for:

Age (<65 vs ≥65 years)

- Gender
- Race/ethnicity
- Pre-donation BMI
- SBP and DBP
- Pre- and post-operative SCr



Inteligencia artificial

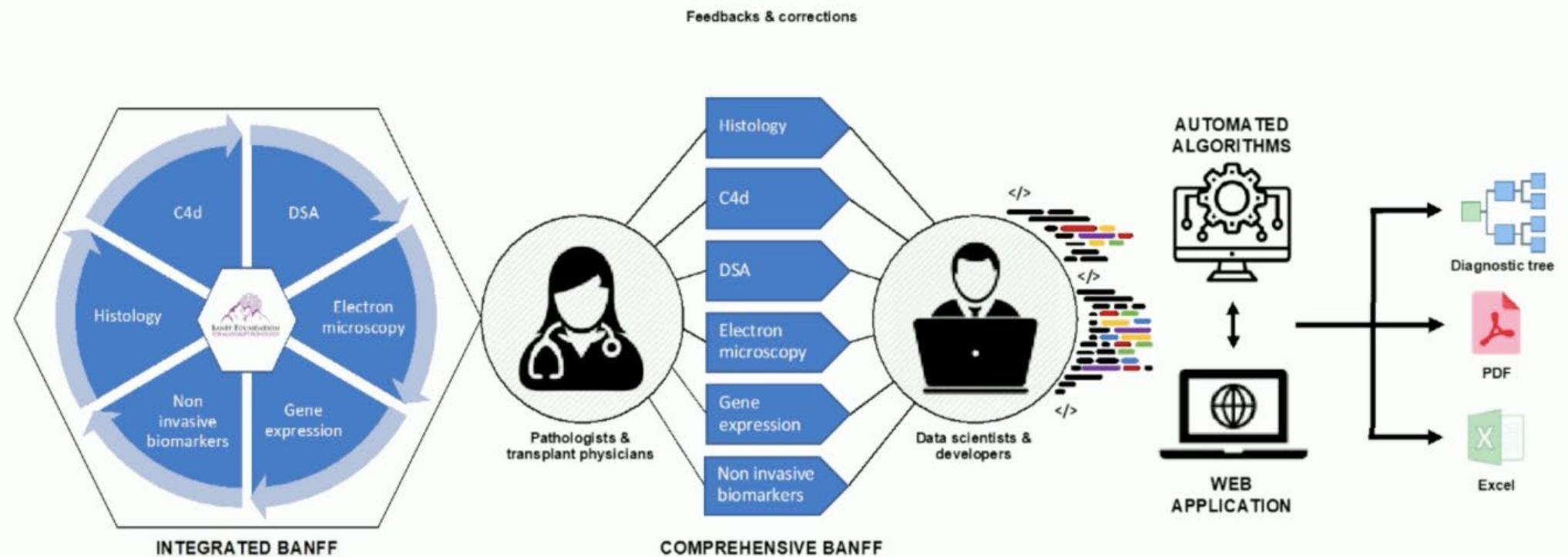


An automated histological classification system for precision diagnosis of kidney allografts

- 1) Integrate and decode all published Banff rules and develop a computer-based application which strictly follows the classification: the **Banff Automation System**.
- 2) Validate its ability to **reclassify and risk stratify** rejection diagnoses in **multicenter cohort studies** and **clinical trials**.

STUDY DESIGN

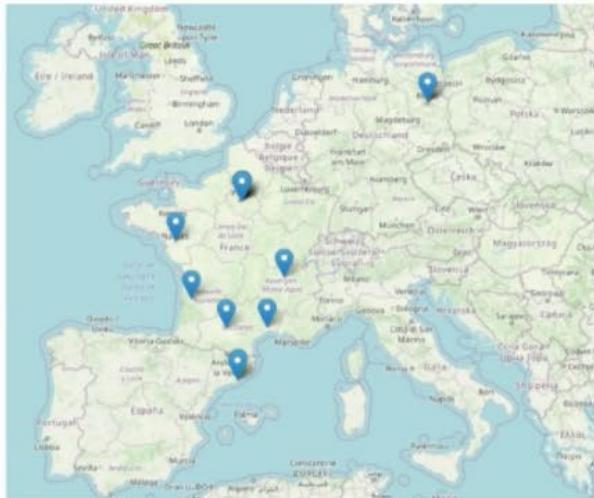
Development of the *Banff Automation System* for precision diagnostics of kidney allografts



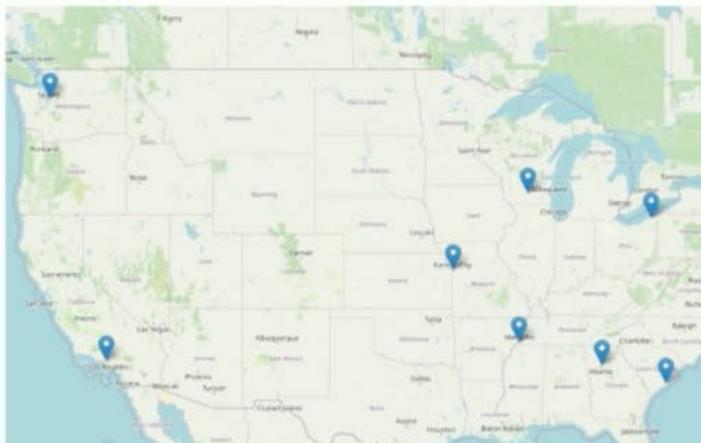
Validation in 3 multicenter cohorts and 2 clinical trials of adult and pediatric kidney transplant recipients

3,054 patients]
4,409 biopsies
 ➤ Adults (n = 3,895 biopsies)
 ➤ Pediatric (n = 514 biopsies)

Europe



United States



NIH U.S. National Library of Medicine
ClinicalTrials.gov

NCT05306795
Banff Automation System



Centres inclus:

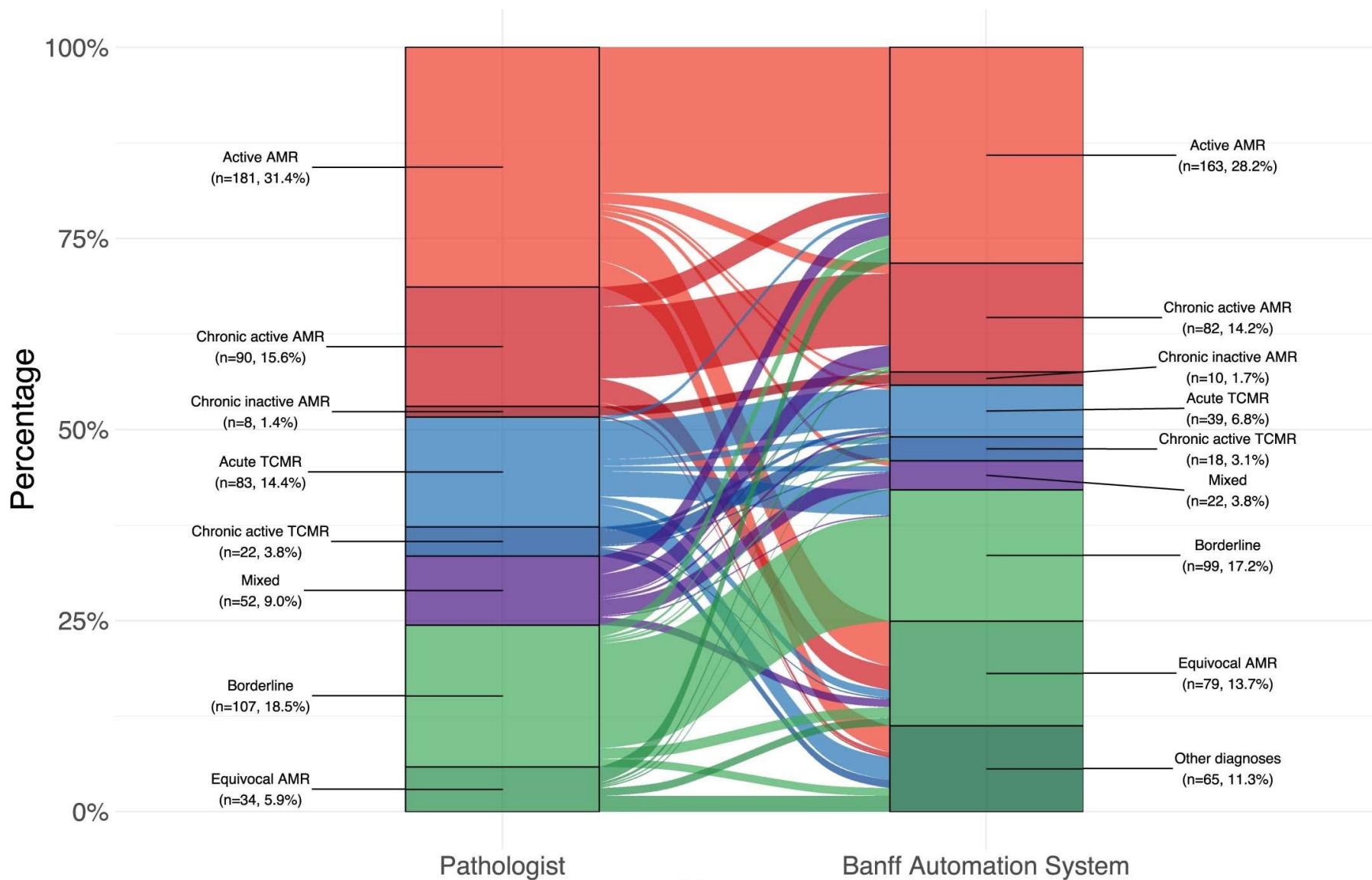
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4. Kremlin-Bicetre
5. CHU Bordeaux
6. CHU Nantes
7. CHU de Toulouse
8. Édouard Herriot University Hospital
9. CHU Montpellier
10. Bellvitge
11. Vall d'Hebron
12. Charité Virchow
13. Charité Mitte
14. Geneva University Hospitals
15. University of Wisconsin-Madison
16. Emory University
17. Children's Mercy
18. David Geffen School
19. Le Bonheur Children's hospital
20. Seattle Children's hospital

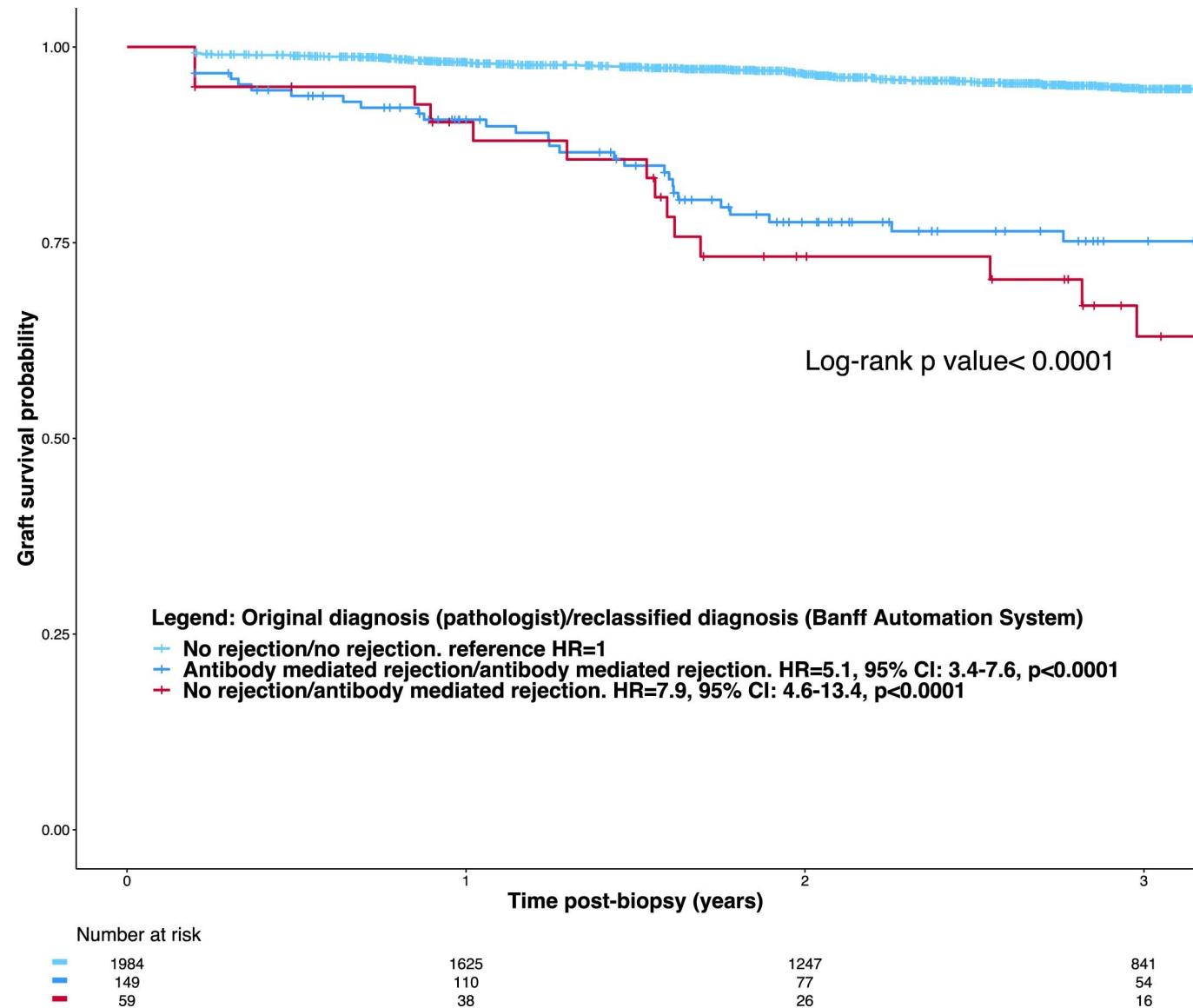
Banff Diagnosis Presubmission Accepted Report Available RETIREMENT

Banff individual lesions scores

Please click on every lesion that meets the Banff score.

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Genética



Changes In Endothelial and Proximal Tubule Cells In Focal Segmental Glomerulosclerosis: Single-Cell Resolution of Human Renal Allografts

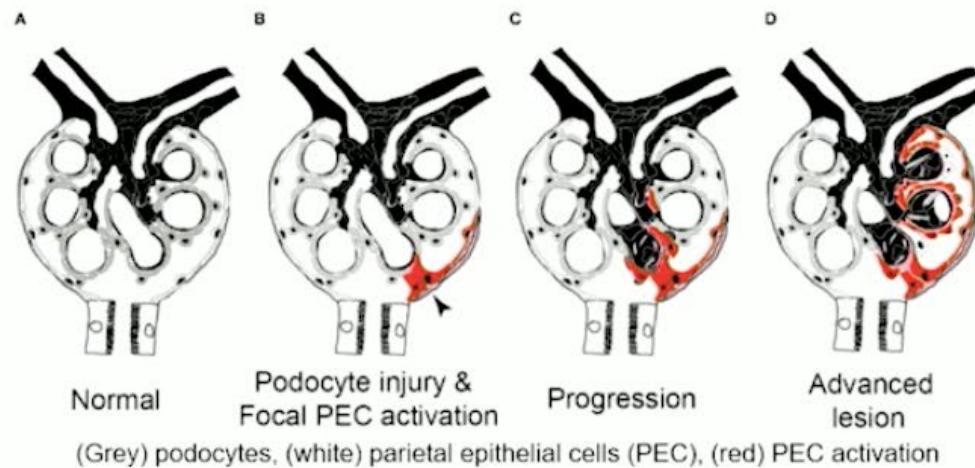
Contributors: L Gallon, H Zubair , AC Shetty, J McDaniels, T Rousselle, S Azim, C Kuscu, C Kuscu, J Eason, D Maluf, V Mas

Haseeb Zubair, Ph.D.

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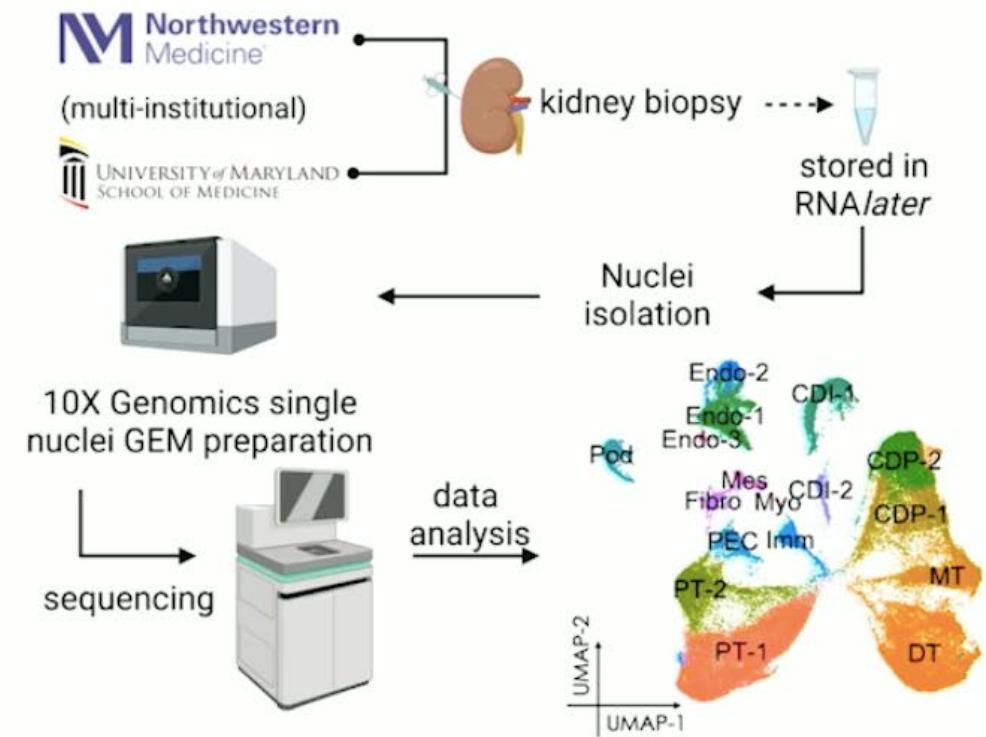
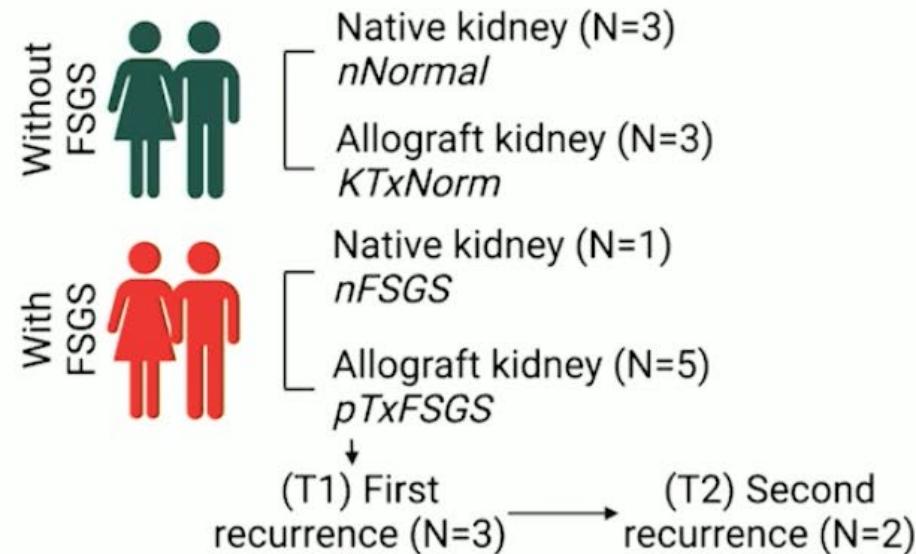


Disease recurrence post-kidney transplantation has been a major impediment in transplant outcomes

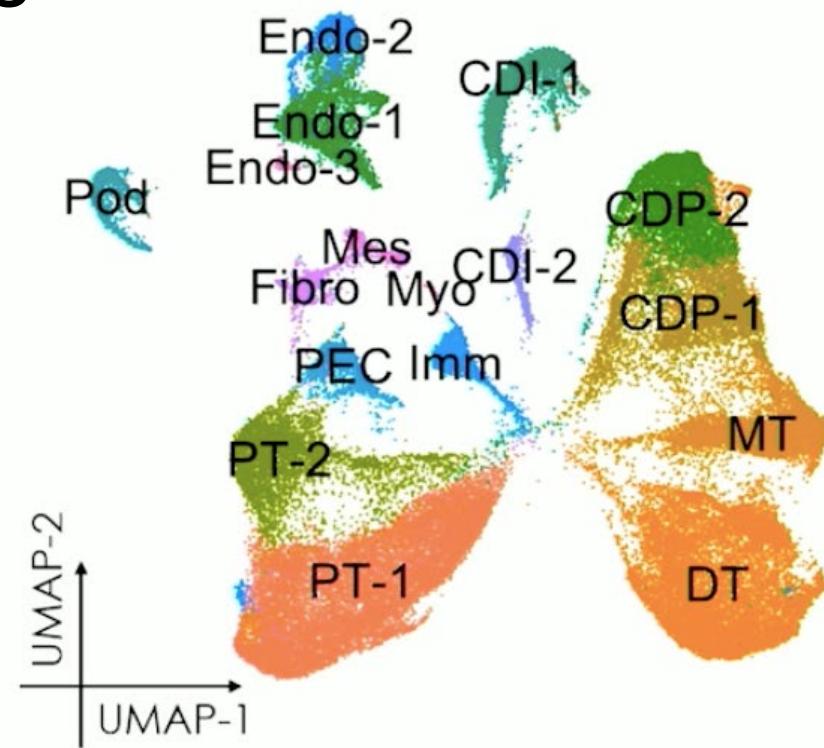


- Primary FSGS is one of the leading causes of end stage renal disease in the US and is a frequent recurrent disease in kidney transplant recipients.
- Characterized by the detachment (effacement) of podocytes from the glomerular basement membrane resulting in proteinuria, and ultimately complete renal failure.
- Etiology of primary FSGS is still unknown.
- Mechanisms, cells and cell-cell interactions that characterize disease initiation and injury have not been characterized in post-transplant recurrence.

STUDY OVERVIEW AND PATIENT POPULATION

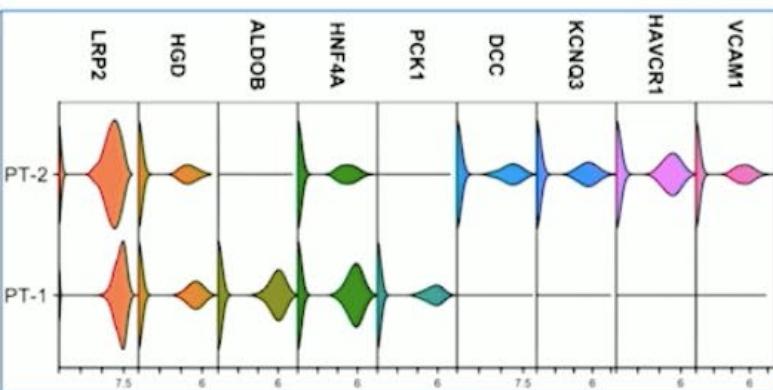
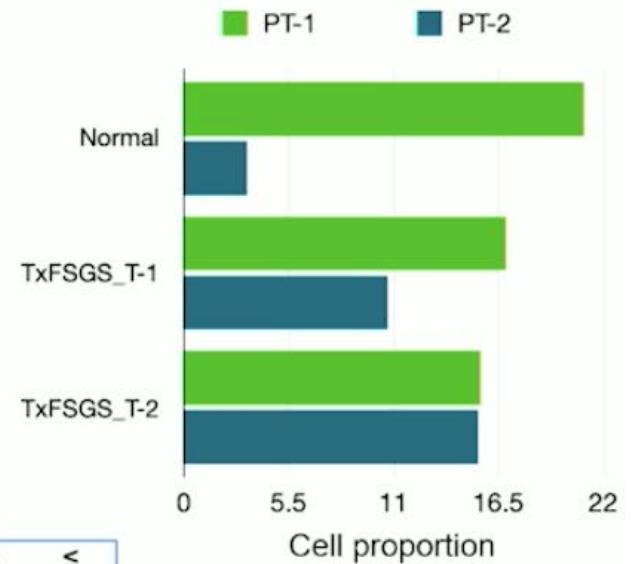
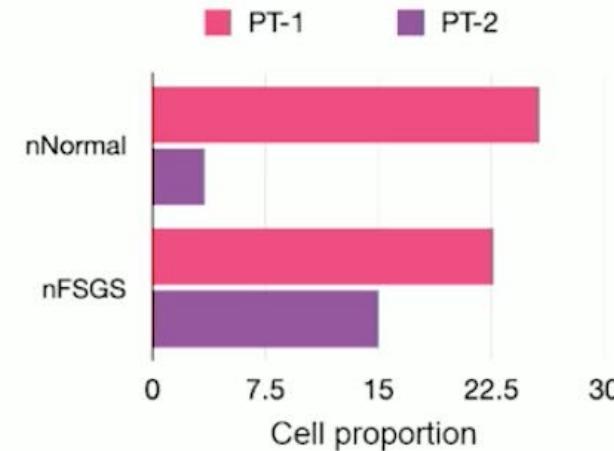
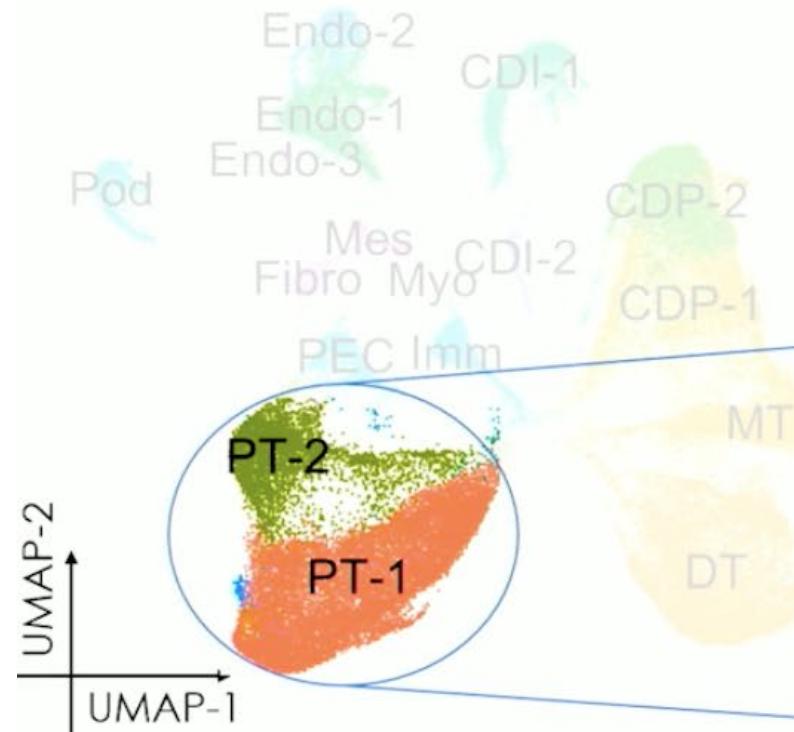


Uniform Manifold Approximation And Projection(UMAP) identified common kidney cell types



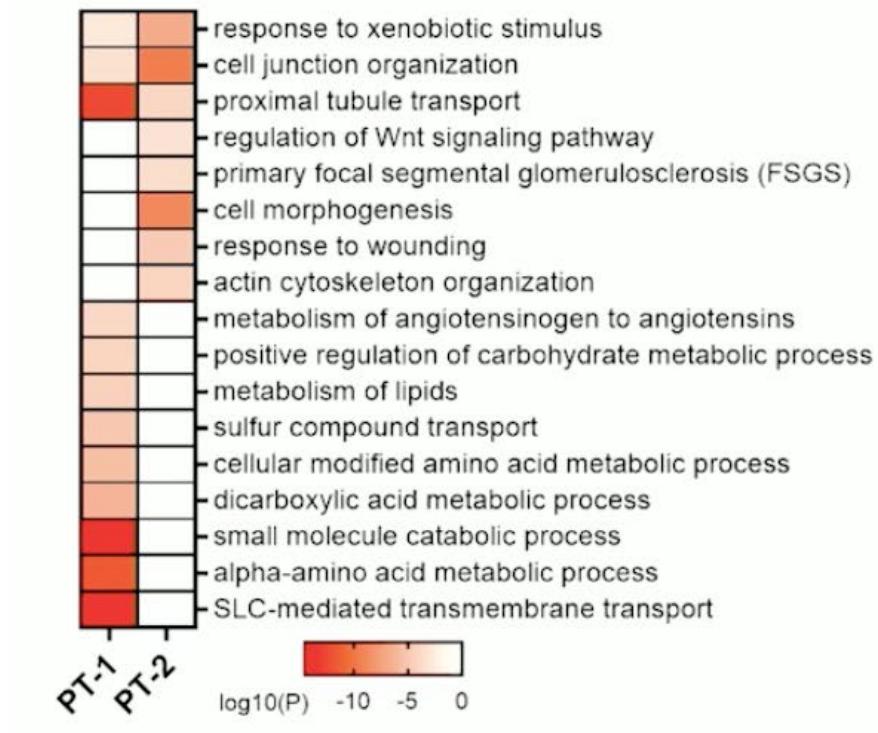
CDI-1: Collecting_duct_intercalated_1
CDI-2: Collecting_duct_intercalated_2
CDP-1: Collecting_duct_principal_1
CDP-2: Collecting_duct_principal_2
DT: Distal_tubule
Endo: Endothelial
Fibro: Fibroblast
Imm: Immune
Myo: Myocytes
Mes: Mesangial
MT: Mixed_tubule
PEC: Parietal_Epithelial_Cells
Pod: Podocyte
PT-2: Proximal_tubule_2
PT-1: Proximal_tubule_1

FSGS increases injured proximal tubule cells

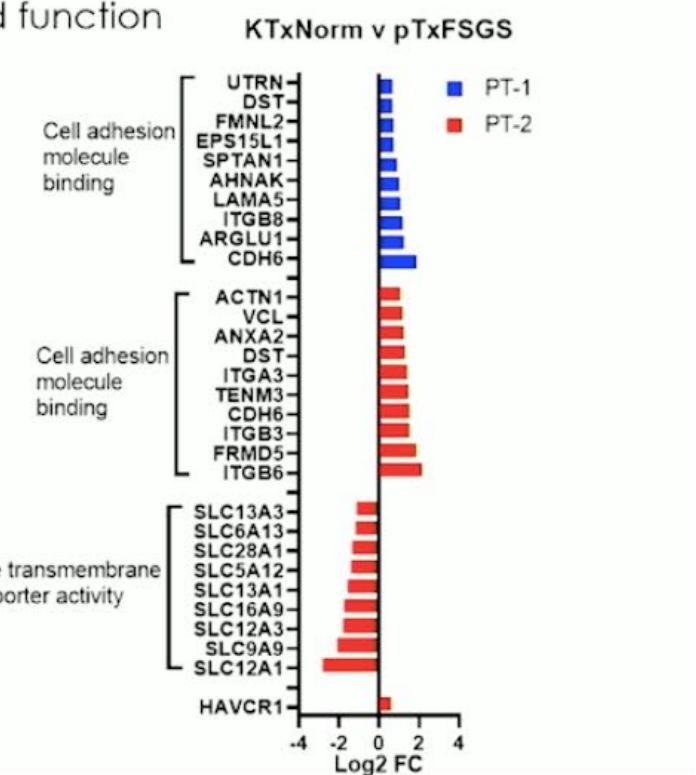


FSGS results in loss of activity and potential increase in immune cell adhesion by PT cells

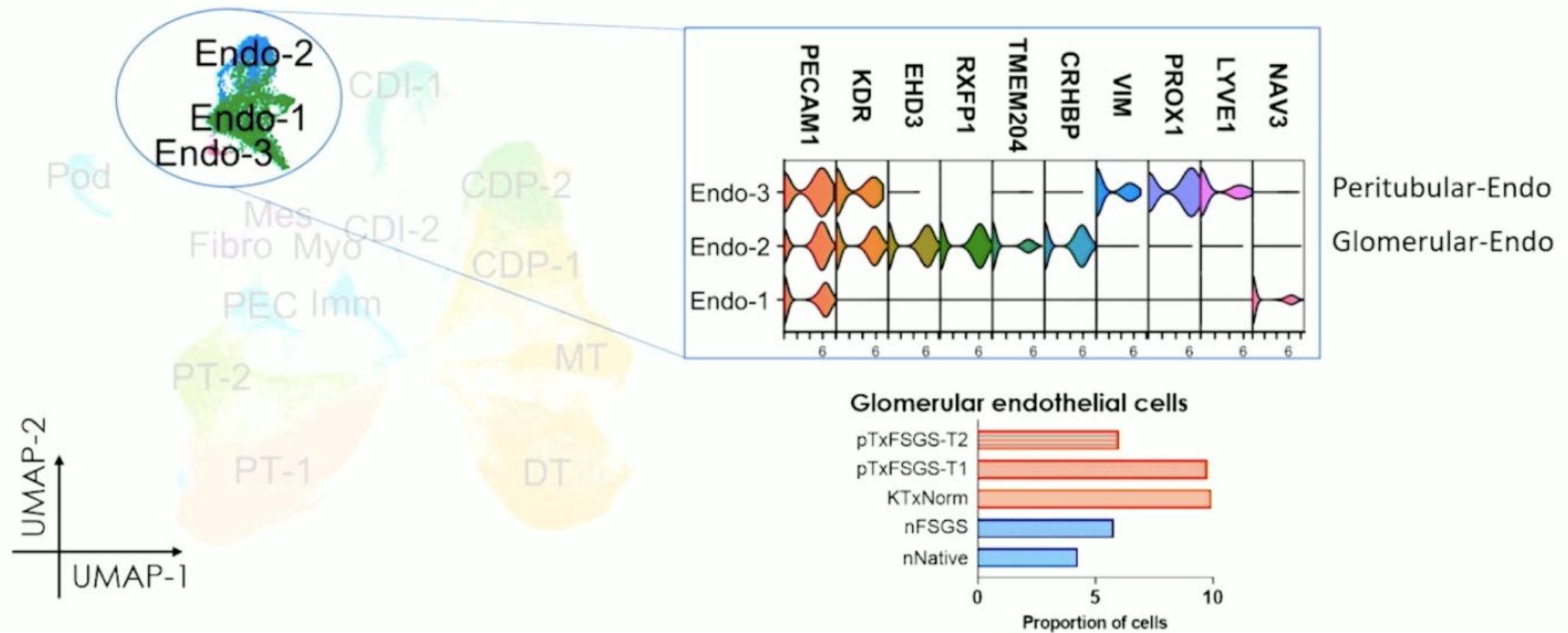
A. Molecular differences between PT-1 and PT-2 subcluster



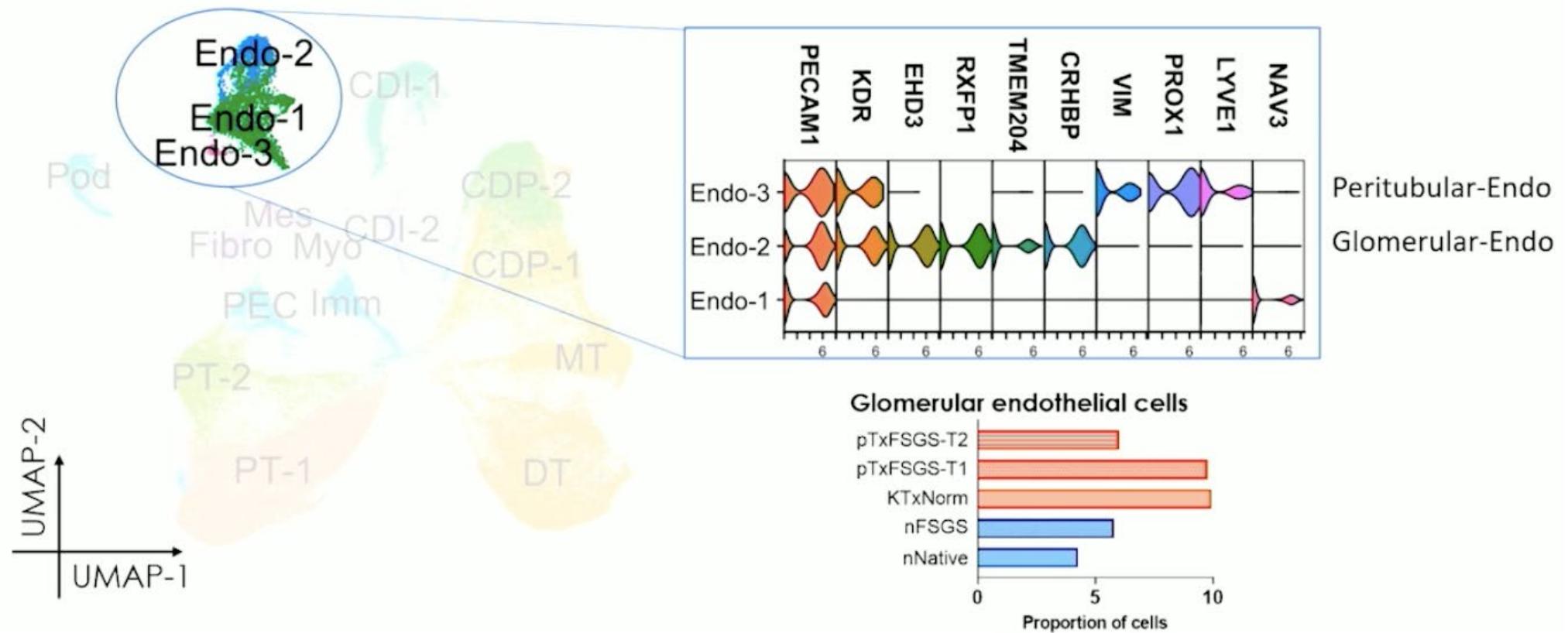
B. DEGs between re-FSGS and normal allograft and their associated function



Glomerular and Peritubular endothelial cells are clearly identified

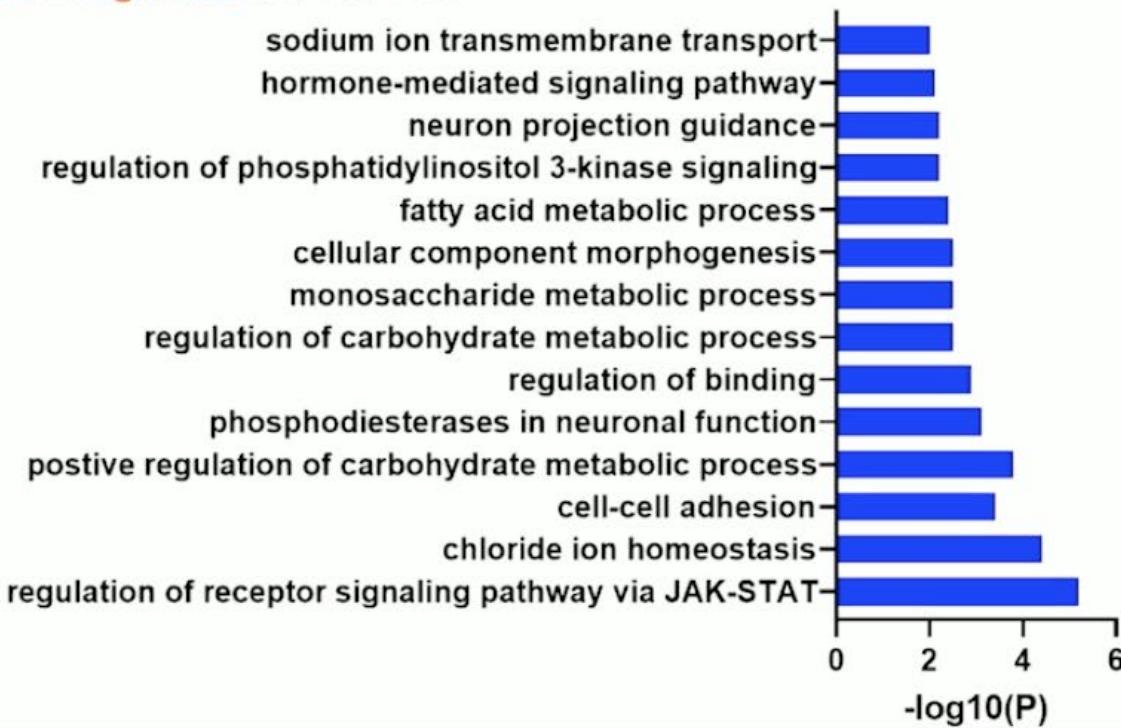


Glomerular and Peritubular endothelial cells are clearly identified

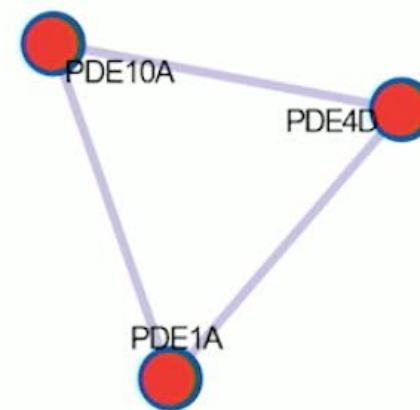


FSGS results in altered metabolism and disruption of normal processes in Endothelial cells and Proximal tubule

A. Gene set enrichment of molecular functions using genes **downregulated** in reTxFSGS



B. Protein-protein interactions using STRING of genes that were **downregulated**



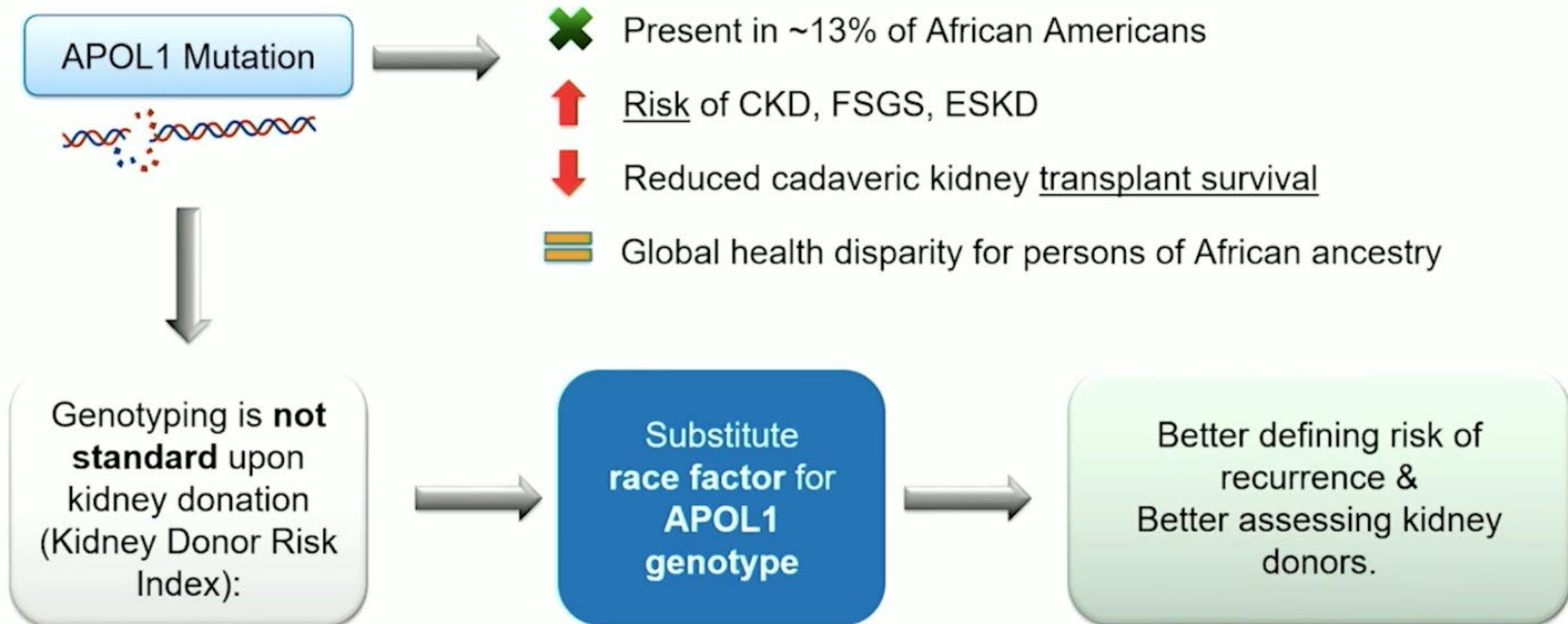


**CRISPR-Cas-Based Assay to Genotype
APOL1 High-Risk Variants**

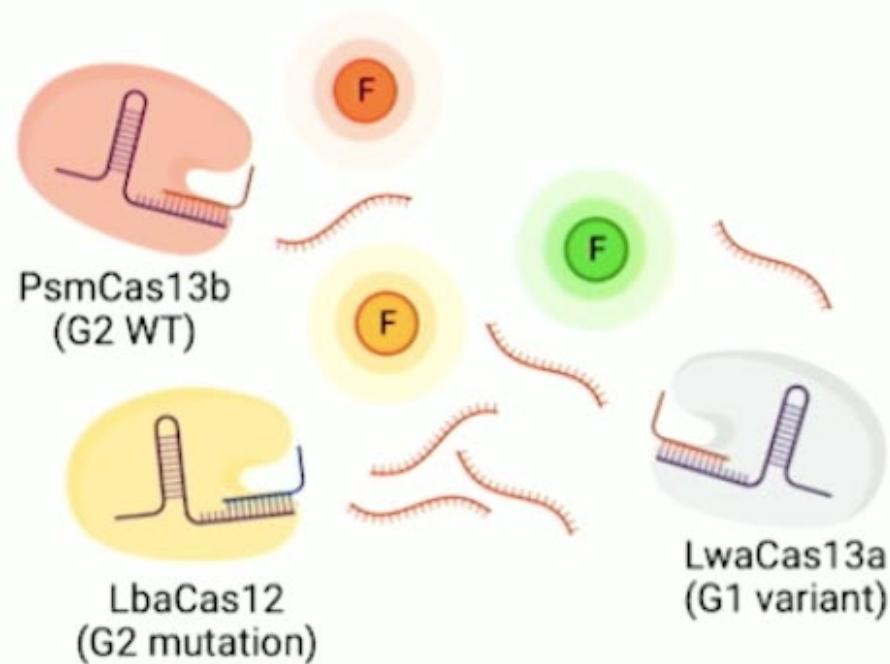
Isadora T Lape

June 5th, 2023

 MASSACHUSETTS
GENERAL HOSPITAL
TRANSPLANT CENTER



Multiplex CRISPR-based genotyping identifies APOL1 variants

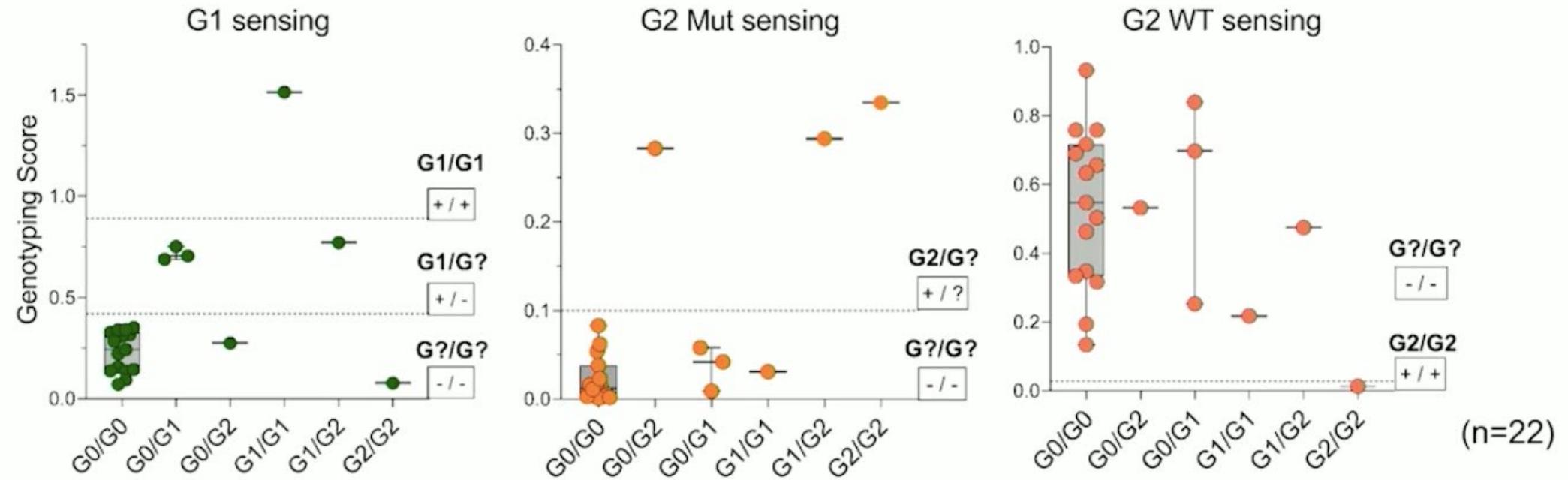


Assessment of kidney disease risk

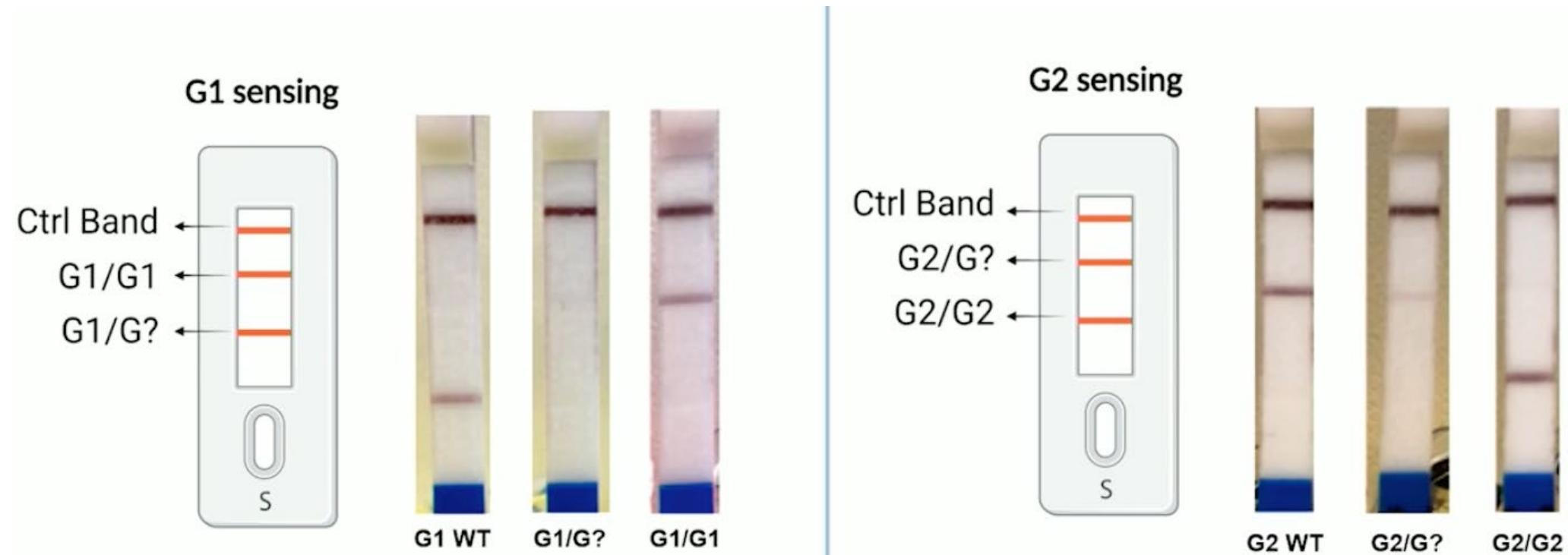


G0/G0	G1/G1
G0/G1	G1/G2
G0/G2	G2/G2

Low ↓ High ↑



- The genotyping score was significantly different between samples above and below the threshold, indicated by the horizontal lines.



GRACIAS