Organiza:

Chiesi

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.

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Chiesi

HIGHLIGHTS

AMERICAN TRANSPLANT CONGRESS

ATC2023

JUNIO 3-7, 2023

JUVEN

SENTRA

SENTRA

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

Tino Villanego Fernández

Nefrologo – Hospital Universitario Puerta del Mar (Cádiz)




HOPE IN ACTION

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

Jennifer D. Motter MHS, Sarah Hussain MBBS MSHI, Diane M. Brown MSN, Sander Florman MD, Meenakshi M. Rana MD, Rachel Friedman-Moraco MD, Alexander J. Gilbert MD, Peter Stock MD PhD, Shikha Mehta MD, Sapna A. Mehta MD, Valentina Stosor MD, Nahel Elias MD, Marcus R. Pereira MD MPH Ghady Haidar MD, Maricar Malinis MD, Michele I. Morris MD, Jonathan Hand MD, Saima Aslam MBBS MS Joanna M. Schaenman MD PhD, John Baddley MD, Catherine B. Small MD, David Wojciechowski DO, Carlos A. Q. Santos MD, Emily A. Blumberg MD, Jonah Odim MD PhD, Senu K. Apewokin MD, Emmanouil Giorgakis MD, Mary Grace Bowring MPH, William A. Werbel MD PhD, Niraj M. Desai MD, Aaron A. R. Tobian MD PhD, Dorry L. Segev MD PhD, Allan B. Massie PhD, Christine M. Durand MD

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
 • HIV D+ could not have active opportunistic infection or cancer. • TNo specific criteria for donors HIV RNA or CD4 count. • Organs from HCV-viremic donors were utilized for HCV-viremic recipients	 • CD4 ≥ 200 cells/µL within 16 weeks • Receiving ART with HIV RNA < 50 copies/mL

Durand CM, Zhang W, Brown DM, et al. A prospective multicenter pilot study of HIV-positive deceased donor to HIV-positive recipient kidney transplantation: HOPE in action. Am J Transplant. 2021 May;21(5):1754-1764. doi: 10.1111/ajt.16205.

OBJECTIVES

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

METHODS: data source

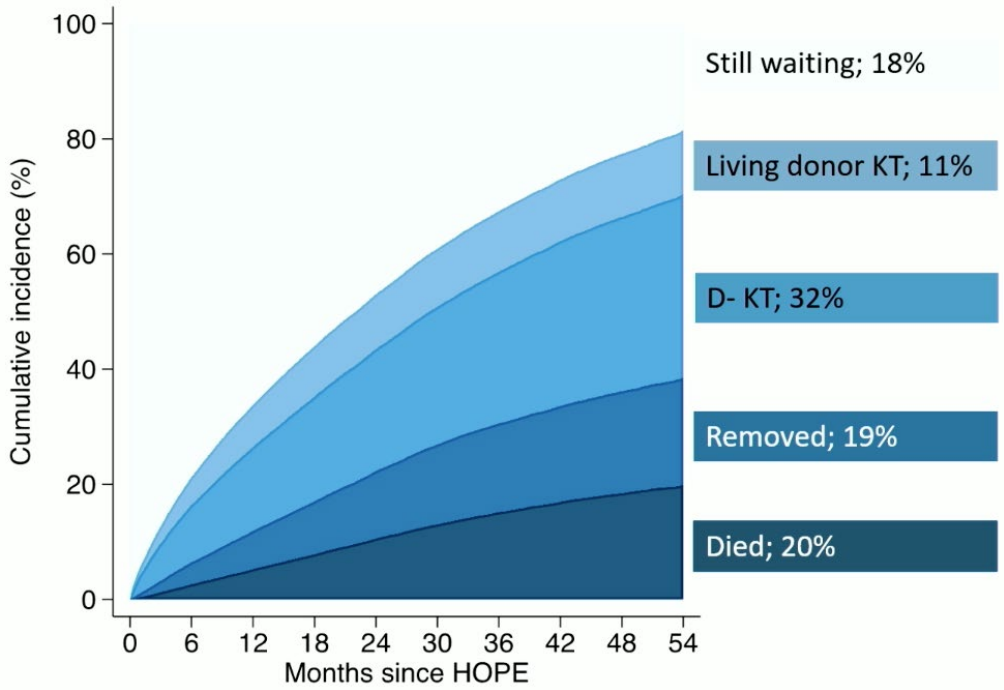
- HOPE in Action Multicenter Kidney U01 trial (NCT03500315)
  - All candidates enrolled provided written informed consent, and met standard center-specific clinical criteria for KT and HIV-specific inclusion criteria
  - HOPE candidates received organs from D+ or D- based on organ availability and standard allocation procedures

- Data linked to SRTR to identify KT candidates at the same centers who were not listed to accept D+ kidneys (non-HOPE)

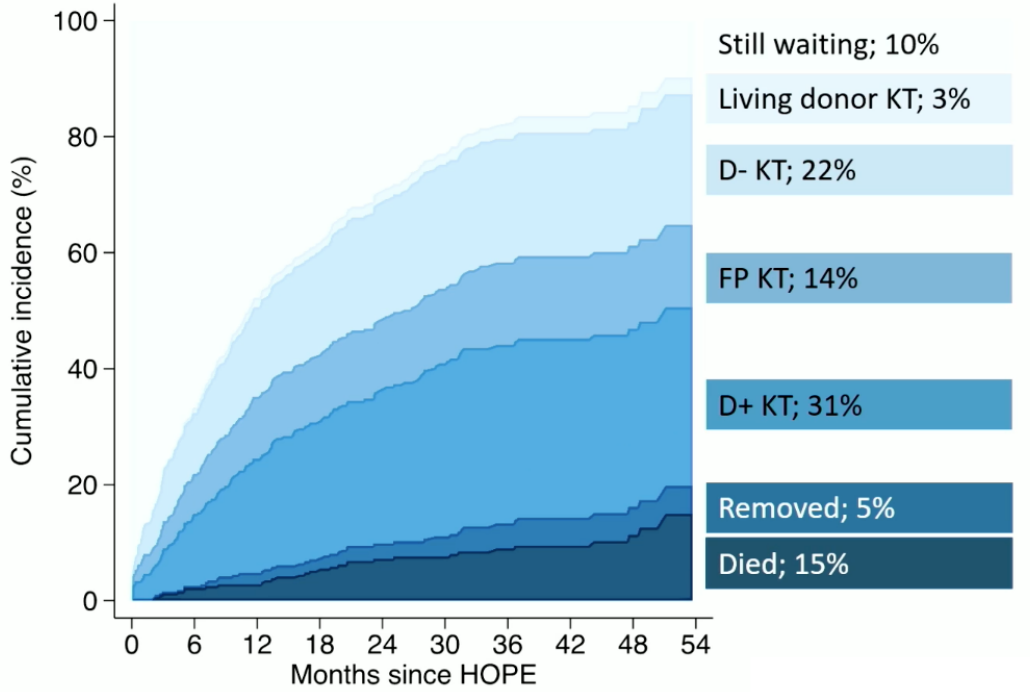
- 324 HOPE and 47,501 non-HOPE candidates at 24 centers participating in the HOPE trial between April 26, 2018 and May 24, 2022
  - All candidates were adults (≥18 years), actively waitlisted for kidney-only transplant

- 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

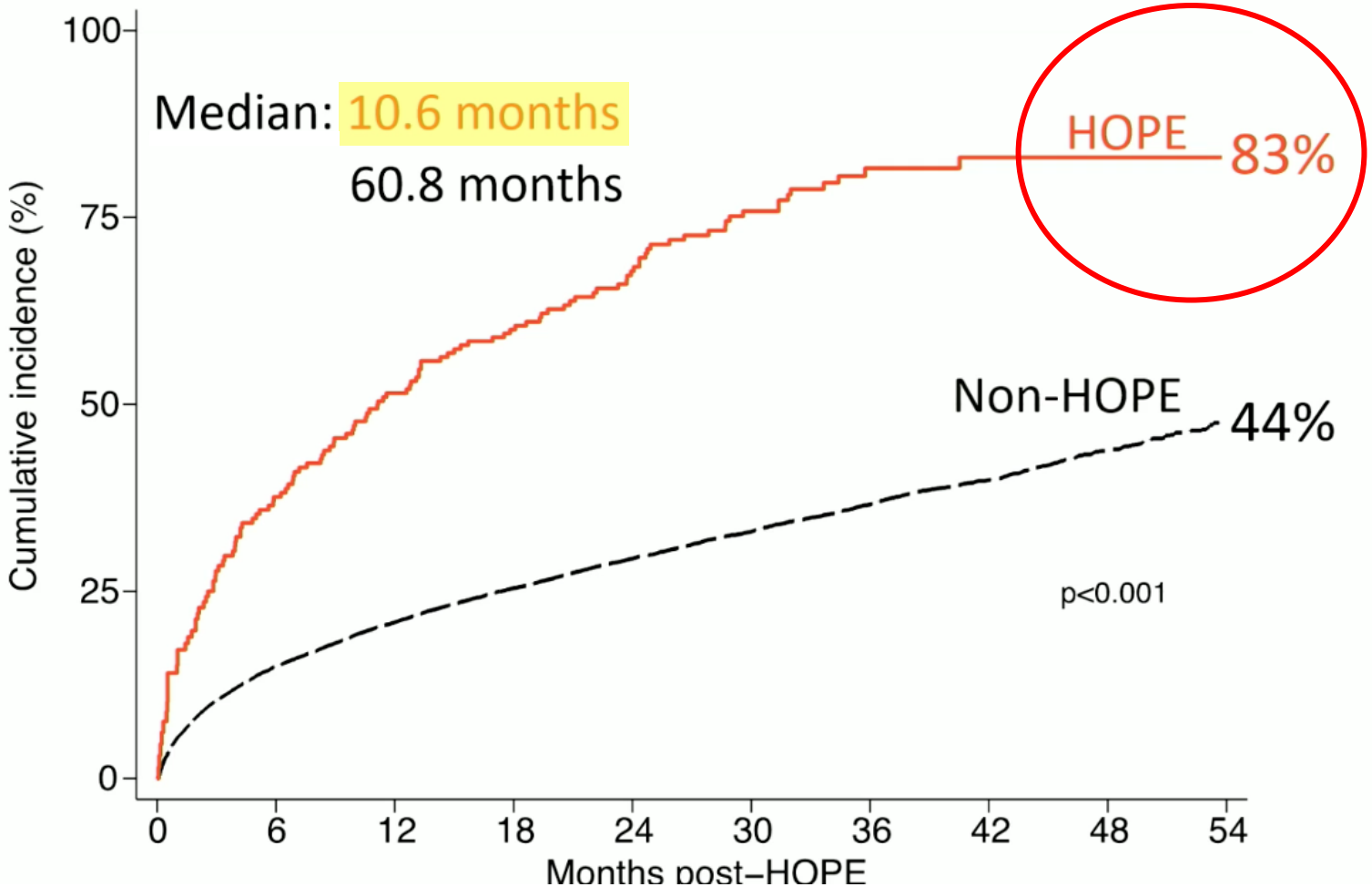


Waitlist outcomes of ***HOPE*** candidates



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 decease-donor kidneys

Massini Merzkani, MD

Assistant Professor of Medicine
Division of Nephrology
Department of Medicine

San Diego, June 6th, 2023

RESEARCH QUESTION

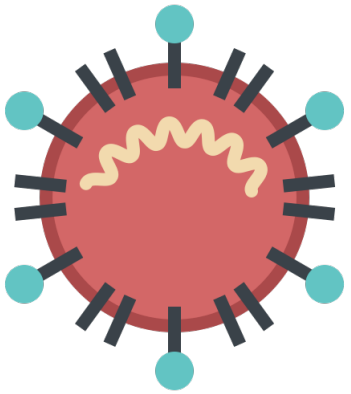
- To examine the national trend in utilization and medium-term outcomes of kidney transplantation (KT) from active or resolved COVID-19 positive donors remain unknown.

BACKGROUND

- Early in the pandemic, donors with COVID-19 were not considered eligible for transplantation.

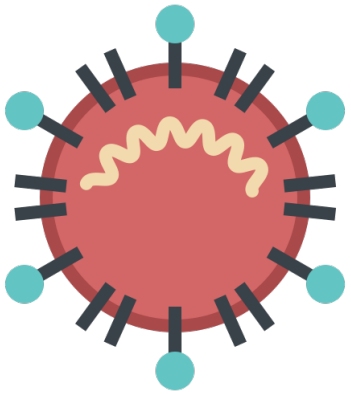
- Concerns for using these organs:
  - Transmission of the virus to the recipients, causing COVID-19 infection
  - Worse kidney transplant outcomes
  - Patient's acceptability of these organs

- No cases of virus transmission with kidney transplantation causing COVID-19 infection



< 7 days

Active COVID-19

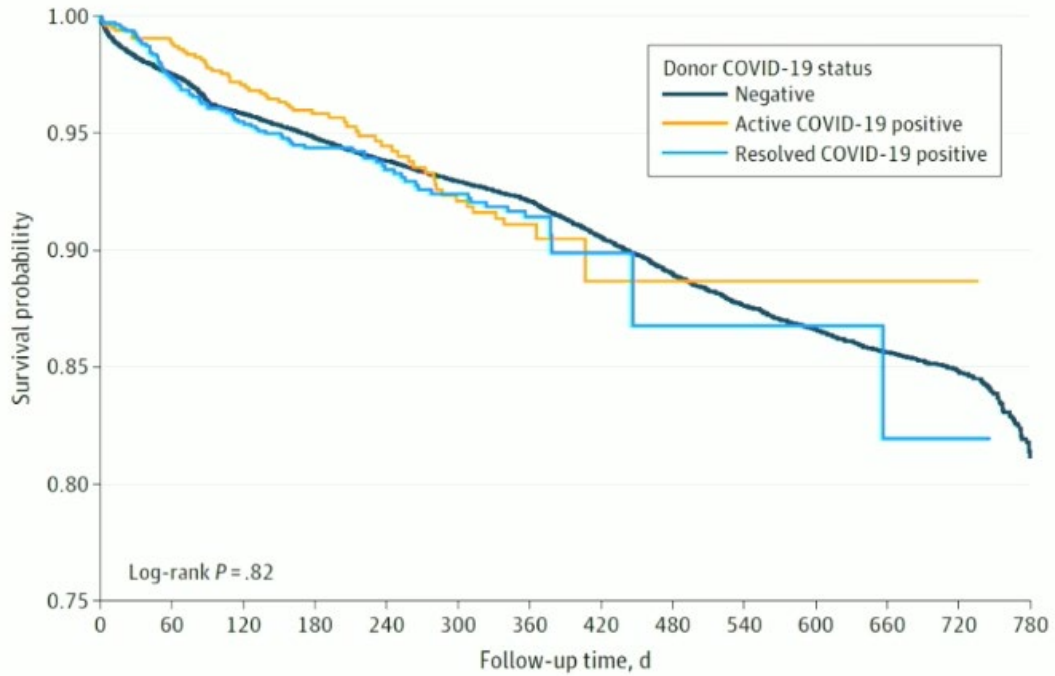


≥7 days

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

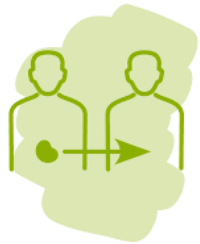
	AOR (95% CI)[a]				
COVID-19 status	Overall	2020 (March to December)	2021	2022	2023 (January to March)
COVID-19 negative	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
Active COVID-19 positive	1.55 (1.38-1.76)	11.26 (2.29-55.38)	2.09 (1.58-2.79)	1.47 (1.28-1.70)	1.07 (0.75-1.63)
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, MD[5]; Piengpitch Naunsilp, MD[6]; Phuuwadith Wattanachayakul, MD[7]; Bima J. Hasjim, MD[8]; Natsuki Eguchi, BS[9]; Antoney J. Ferrey, MD[1]; Uttam G. Reddy, MD[1]; Donald C. Dafoe, MD[9]; Hirohito Ichii, MD, PhD[9]

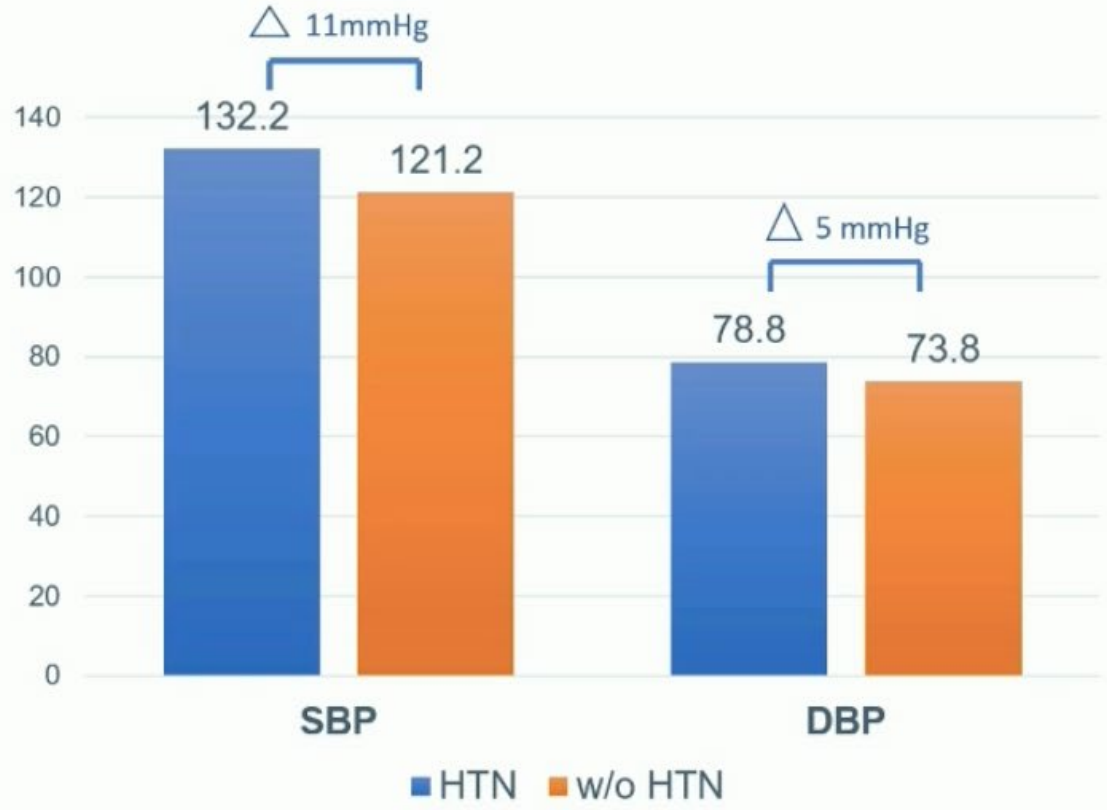
[1]Harold Simmons Center for Kidney Disease Research and Epidemiology, Division of Nephrology, Hypertension and Kidney Transplantation, Department of Medicine, University of California Irvine School of Medicine, Orange, California, United States
[2]Nephrology Section, Department of Medicine, Tibor Rubin Veterans Affairs Medical Center, Veterans Affairs Long Beach Healthcare System, Long Beach, California, United States
[3]Multi-Organ Transplant Center, Section of Nephrology, Department of Internal Medicine, William Beaumont Hospital, Oakland University William Beaumont School of Medicine, Royal Oak, Michigan, United States
[4]Ramathibodi Excellent Center for Organ Transplantation, Bangkok, Thailand
[5]Department of Emergency Medicine, Banpheao General Hospital, Samut Sakhon, Thailand
[6]Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand
[7]Department of Microbiology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand
[8]Department of Surgery, University of California Irvine School of Medicine, Orange, California
[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**

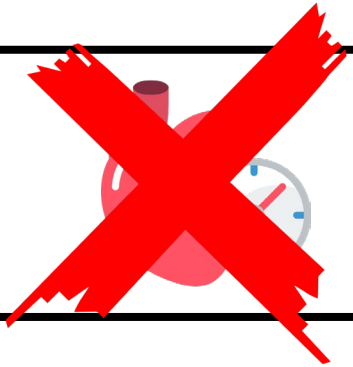
RESULTS

- **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

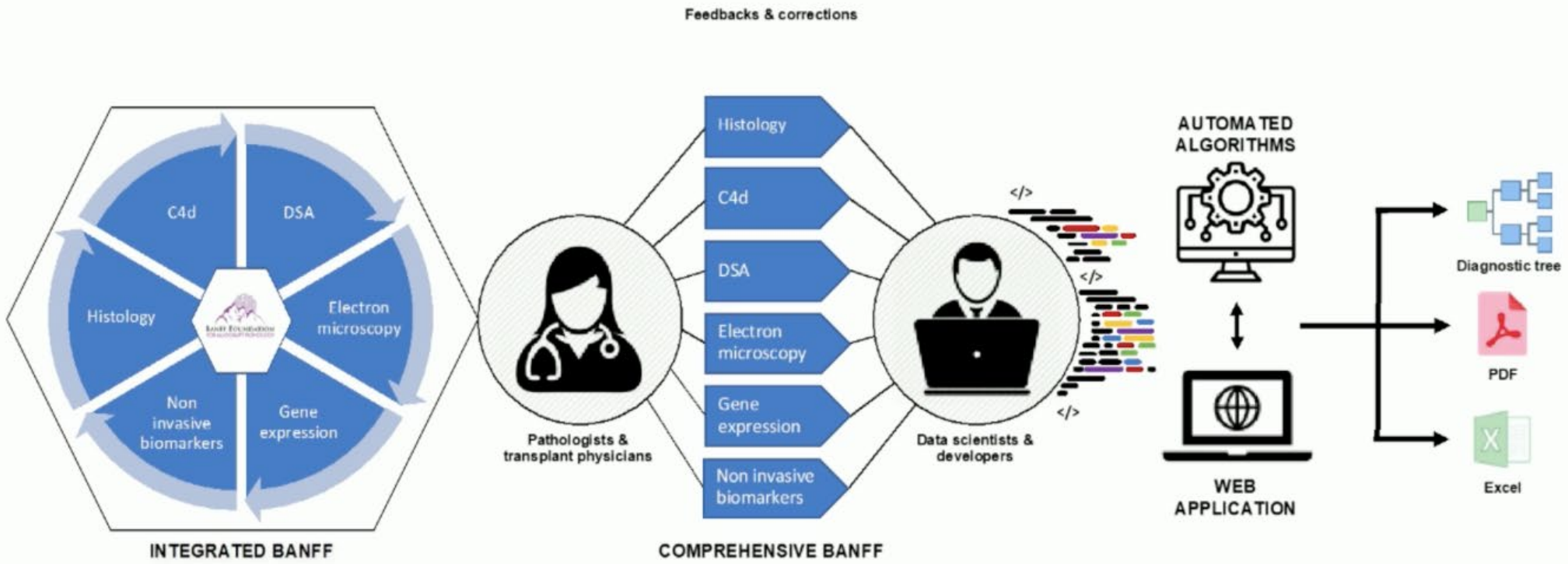
An automated histological classification system for precisión diagnosis of kidney allografts

1) Integrate and decode all published Banff rules and develop a computer-based application which stricly 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

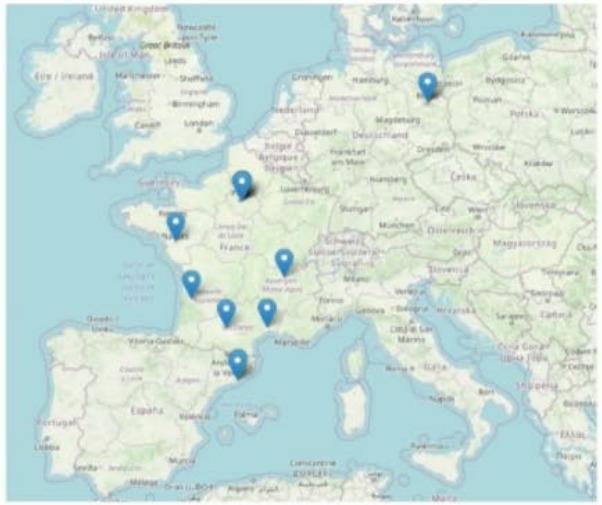
4,409 biopsies
- Adults (n = 3,895 biopsies)
- Pediatric (n = 514 biopsies)

U.S. National Library of Medicine
ClinicalTrials.gov

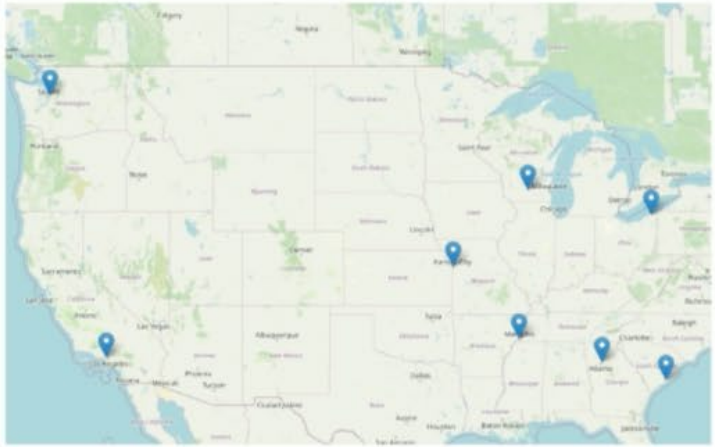
NCT05306795
Banff Automation System

KTDinnov eu train

Europe

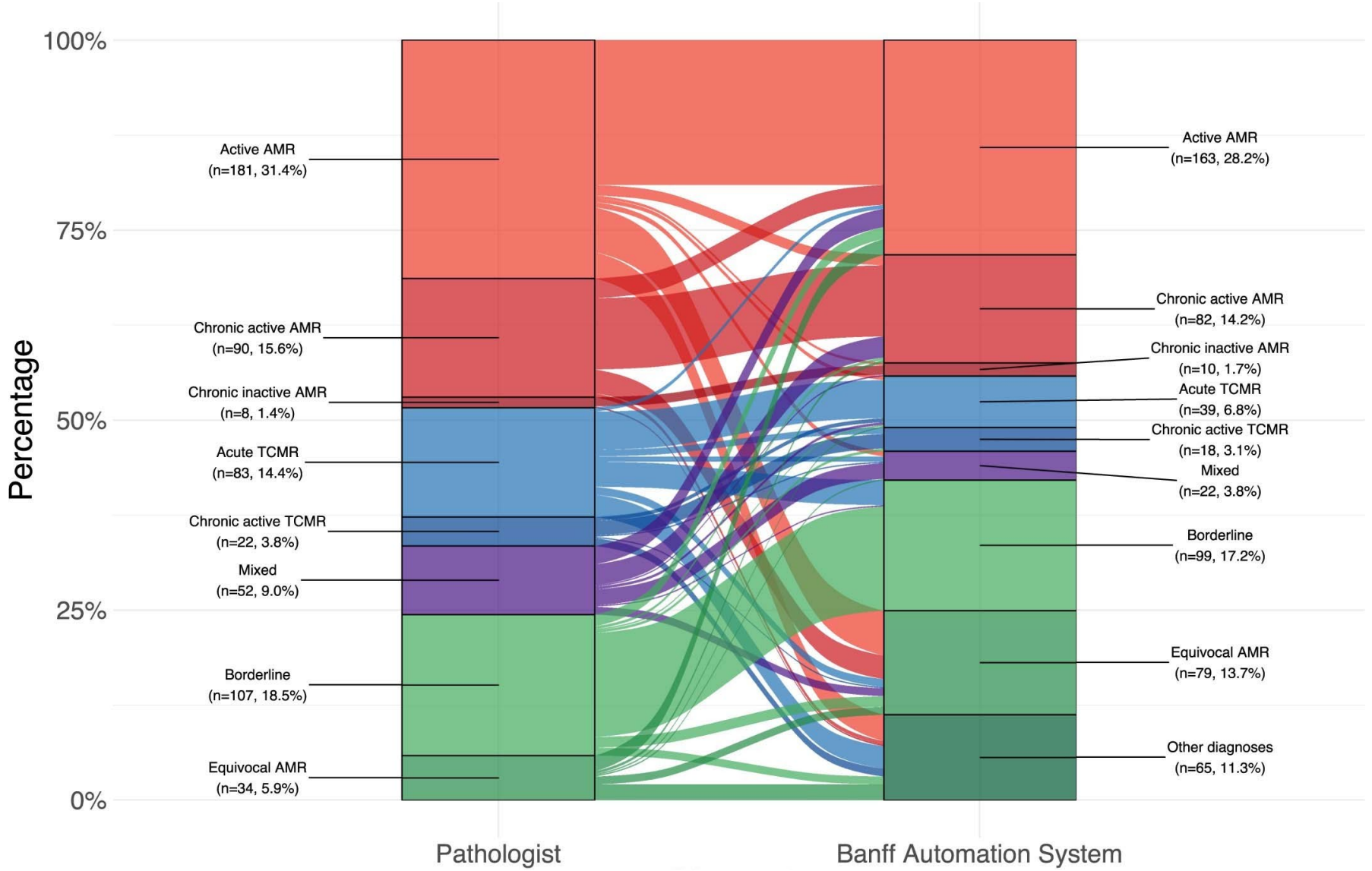


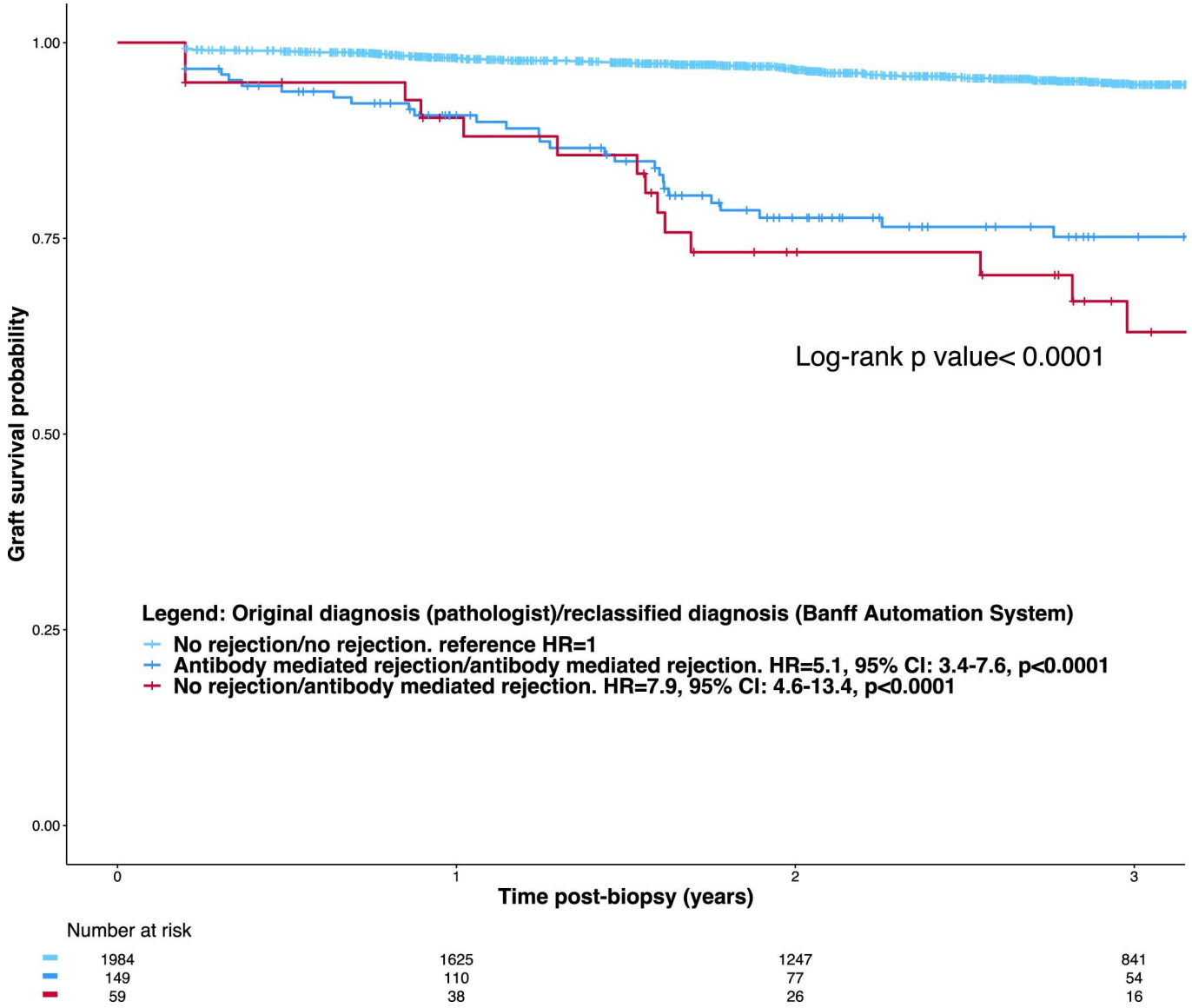
United States



Centres inclus:
1. Necker hospital
2. Robert-Debré Hospital
3. Saint-Louis
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
Banff individual lesions scores
Other diagnoses
SUBMIT


100%
75%
50%
25%
0%
Percentage
Active AMR
(n=181, 31.4%)
Chronic active AMR
(n=90, 15.6%)
Chronic inactive AMR
(n=8, 1.4%)
Acute TCMR
(n=83, 14.4%)
Chronic active TCMR
(n=22, 3.8%)
Mixed
(n=52, 9.0%)
Borderline
(n=107, 18.5%)
Equivocal AMR
(n=34, 5.9%)
Active AMR
(n=163, 28.2%)
Chronic active AMR
(n=82, 14.2%)
Chronic inactive AMR
(n=10, 1.7%)
Acute TCMR
(n=39, 6.8%)
Chronic active TCMR
(n=18, 3.1%)
Mixed
(n=22, 3.8%)
Borderline
(n=99, 17.2%)
Equivocal AMR
(n=79, 13.7%)
Other diagnoses
(n=65, 11.3%)
Pathologist
Banff Automation System


1.00
0.75
0.50
0.25
0.00
Graft survival probability
Log-rank p value< 0.0001
Legend: Original diagnosis (pathologist)/reclassified diagnosis (Banff Automation System)
No rejection/no rejection. reference HR=1
Antibody mediated rejection/antibody mediated rejection. HR=5.1, 95% CI: 3.4-7.6, p<0.0001
No rejection/antibody mediated rejection. HR=7.9, 95% CI: 4.6-13.4, p<0.0001
0
1
2
3
Time post-biopsy (years)
Number at risk
1984 1625 1247 841
149 110 77 54
59 38 26 16

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

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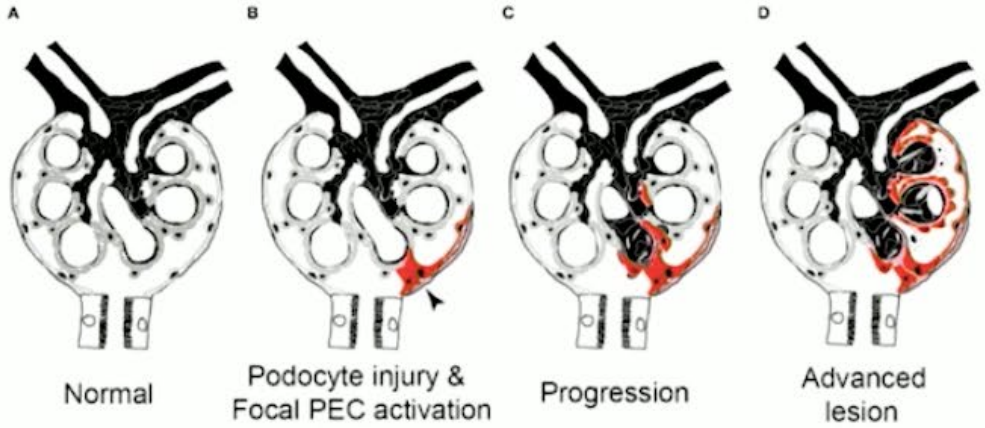
UNIVERSITY of MARYLAND
SCHOOL OF MEDICINE

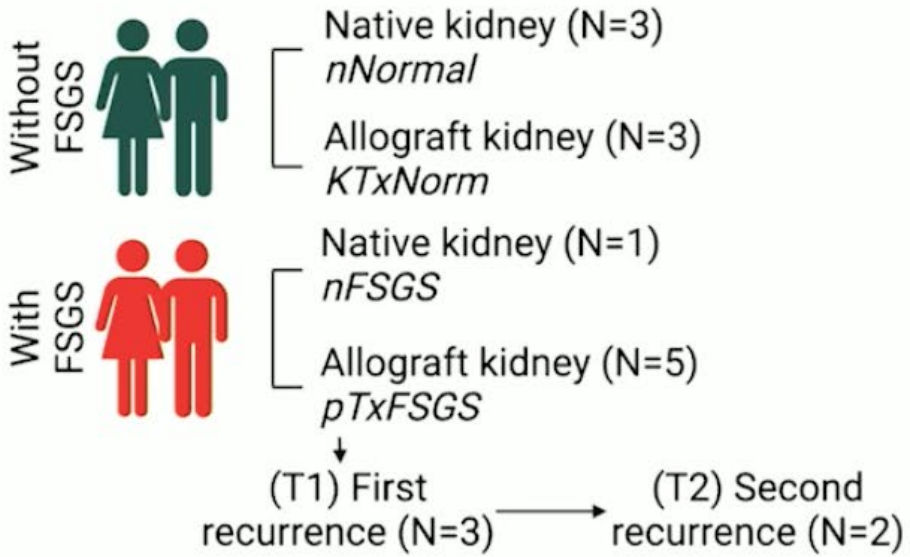
Disease recurrence post-kidney transplantation has been a major impediment in transplant outcomes

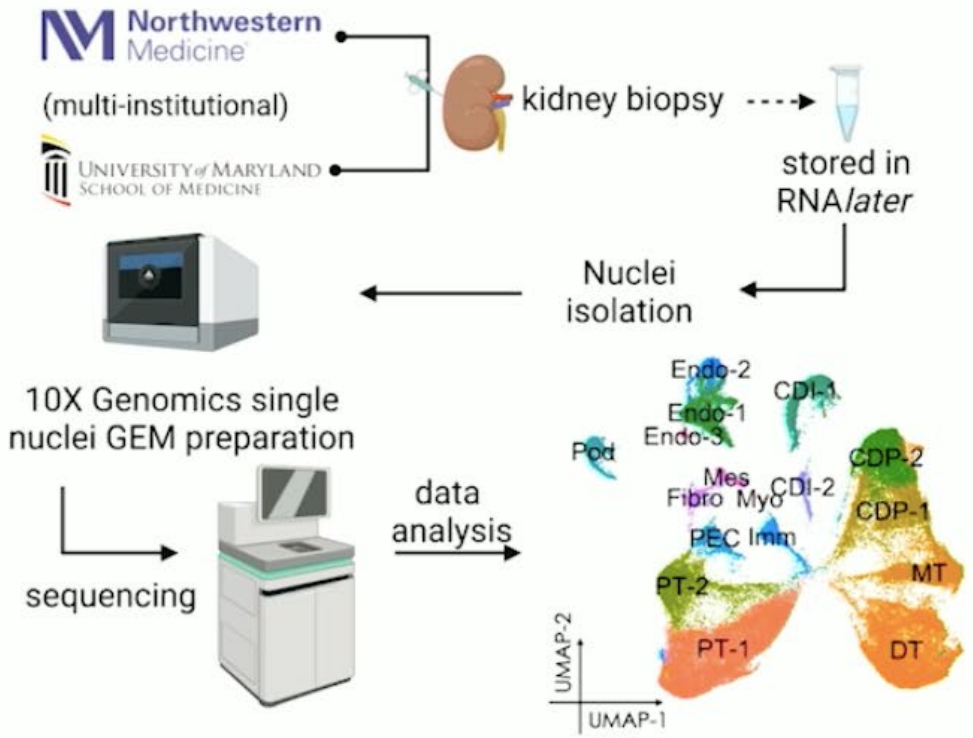


(Grey) podocytes, (white) parietal epithelial cells (PEC), (red) PEC activation

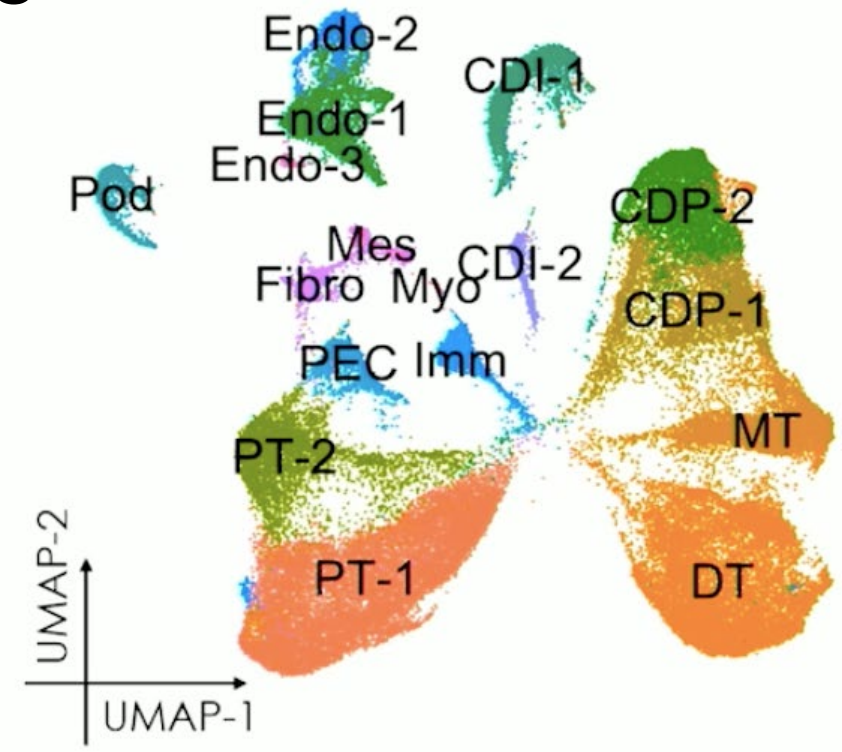
- Primary FSGS is one of the leading causes of end stage renal disease in the US and is a frequent recurrent disease in kidney transplant recipients.
- Characterized by the detachment (effacement) of podocytes from the glomerular basement membrane resulting in proteinuria, and ultimately complete renal 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



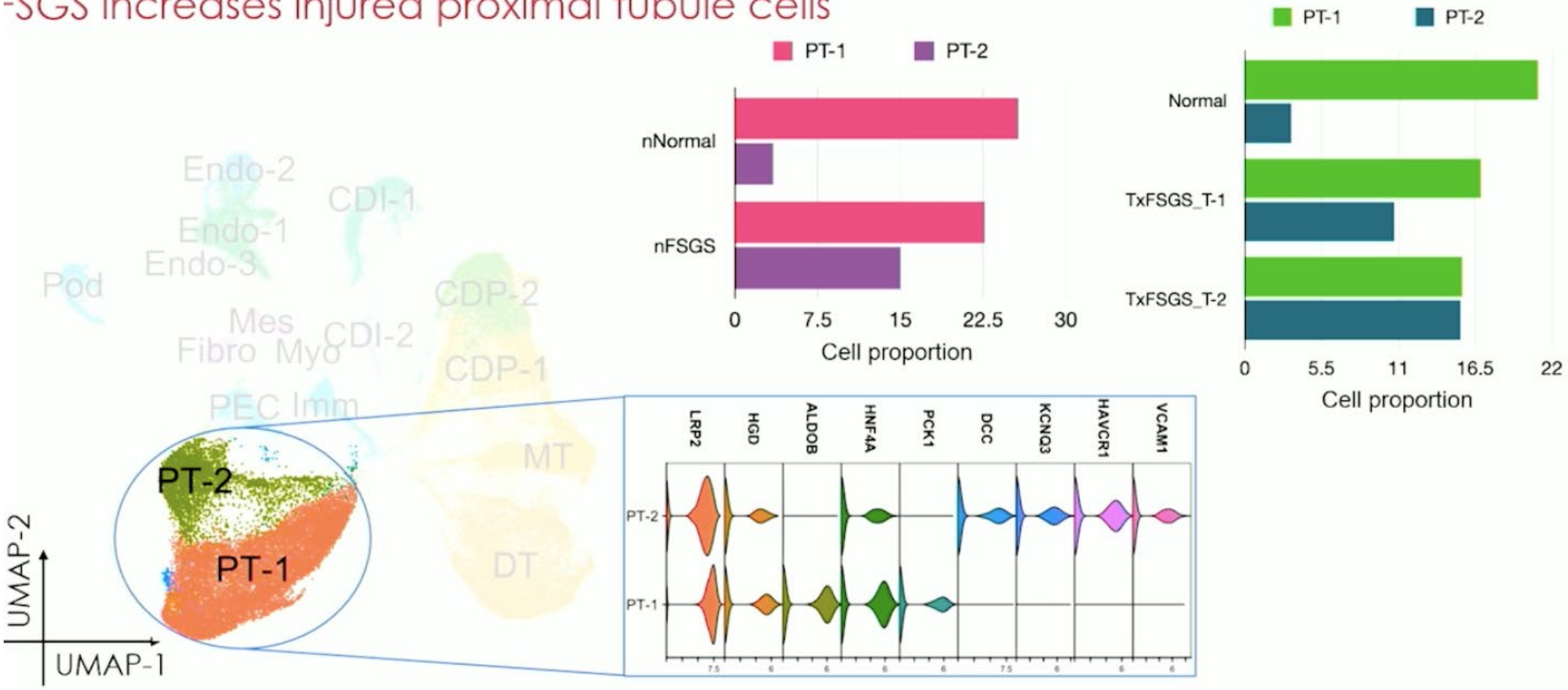


Uniform Manifold Approximation And Projection(UMAP) identified common kidney cell types



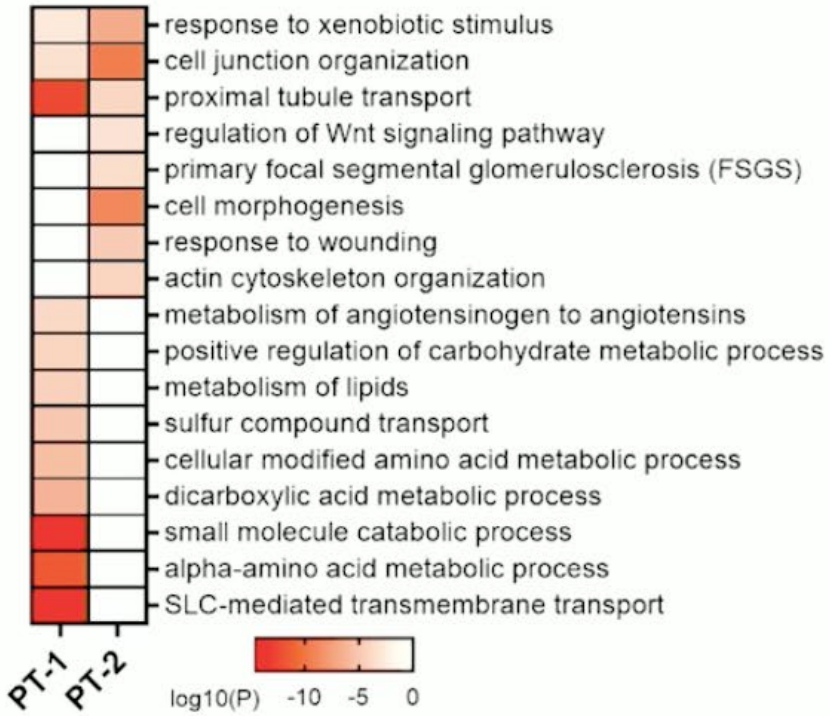
CDI-1: Collecting_duct_intercalated_1
CDI-2: Collecting_duct_intercalated_2
CDP-1: Collecting_duct_principal_1
CDP-2: Collecting_duct_principal_2
DT: Distal_tubule
Endo: Endothelial
Fibro: Fibroblast
Imm: Immune
Myo: Myocytes
Mes: Mesangial
MT: Mixed_tubule
PEC: Parietal Epithelial Cells
Pod: Podocyte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

FSGS increases injured proximal tubule cells

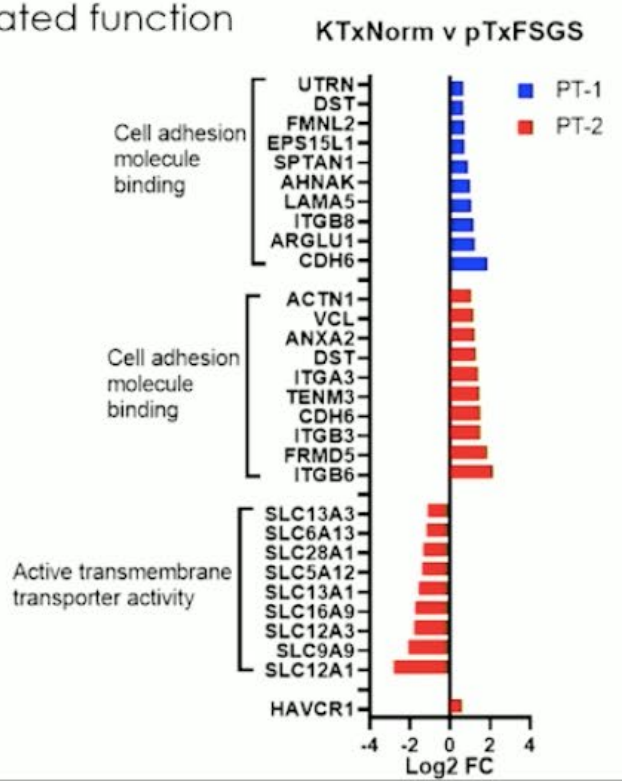


FSGS results in loss of activity and potential increase in immune cell adhesion by PT cells

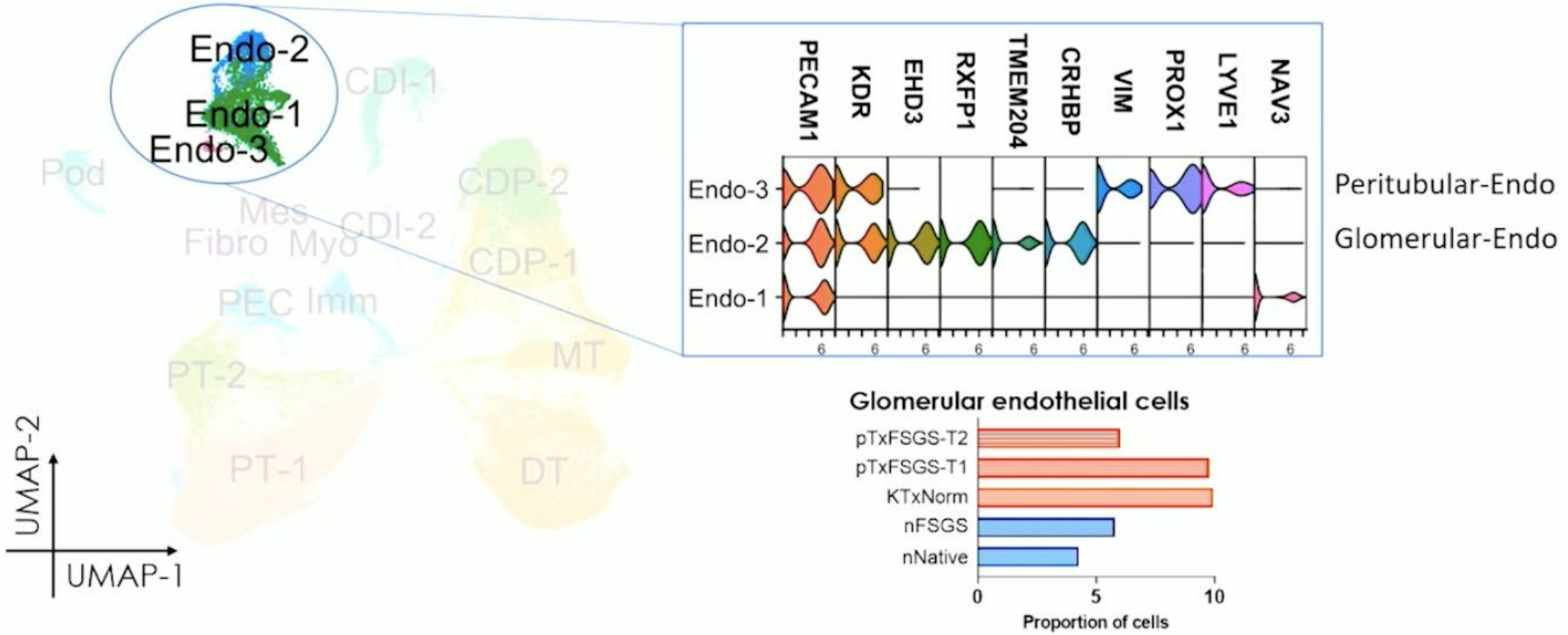
A. Molecular differences between PT-1 and PT-2 subcluster



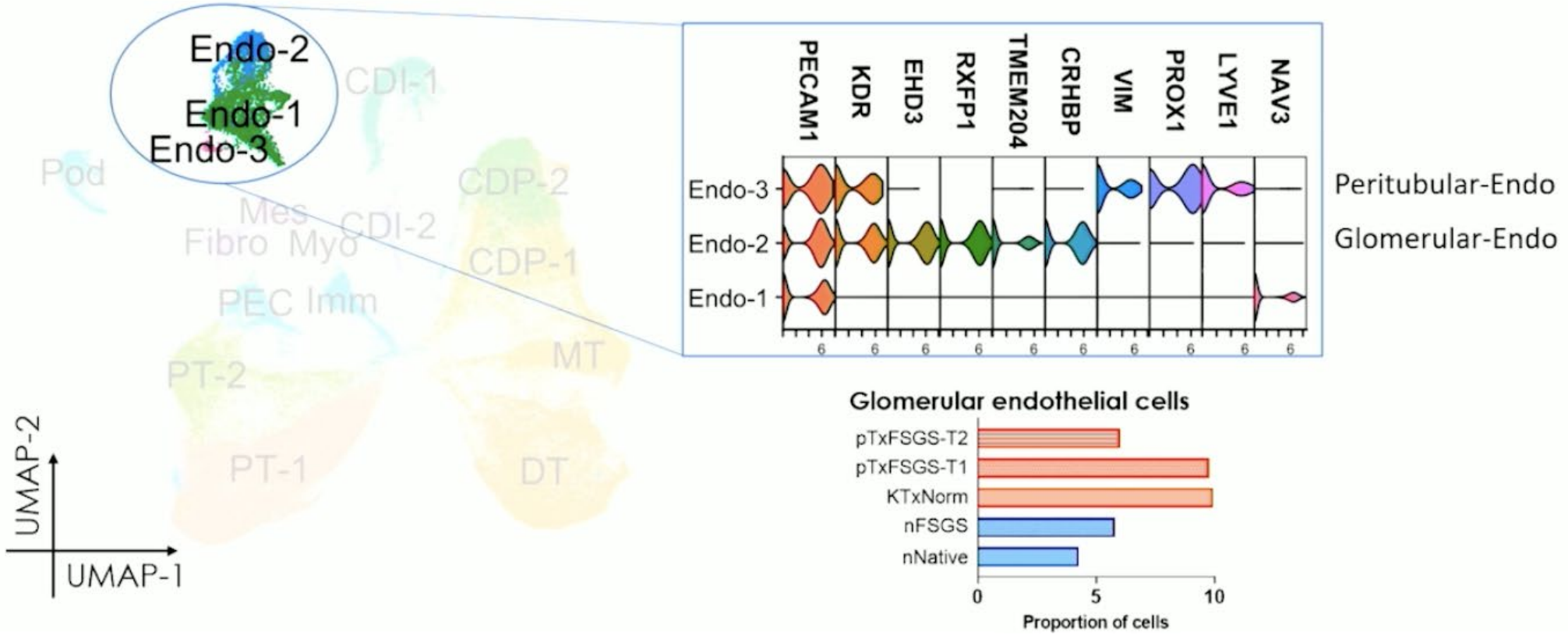
B. DEGs between re-FSGS and normal allograft and their associated function



Glomerular and Peritubular endothelial cells are clearly identified

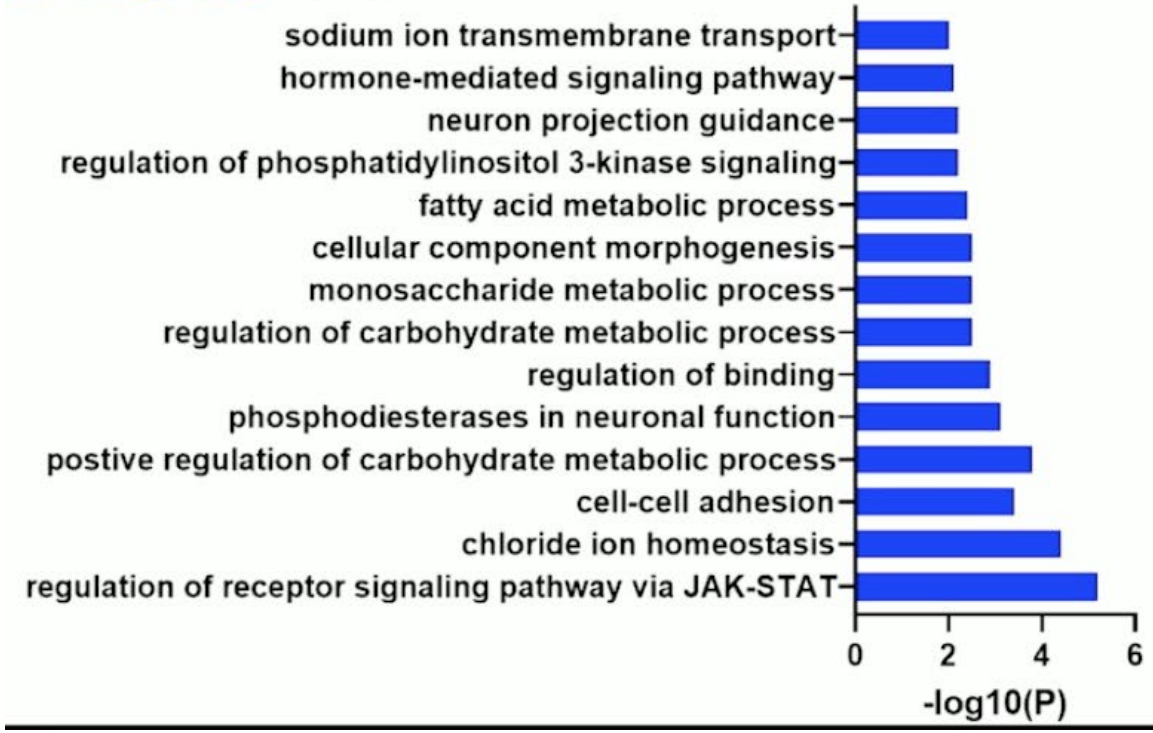


Glomerular and Peritubular endothelial cells are clearly identified

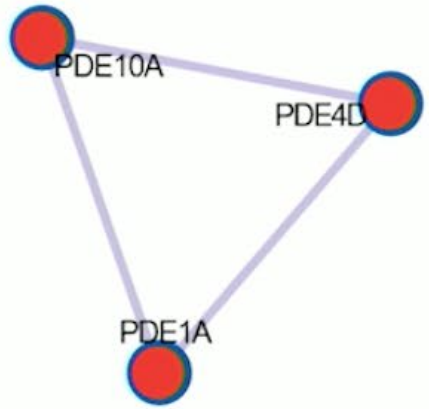


FSGS results in altered metabolism and disruption of normal processes in Endothelial cells and Proximal tubule

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

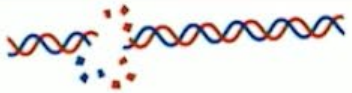


B. Protein-protein interactions using STRING of genes that were downregulated




CRISPR-Cas-Based Assay to Genotype APOL1 High-Risk Variants
Isadora T Lape
June 5th, 2023
MASSACHUSETTS GENERAL HOSPITAL
TRANSPLANT CENTER

APOL1 Mutation

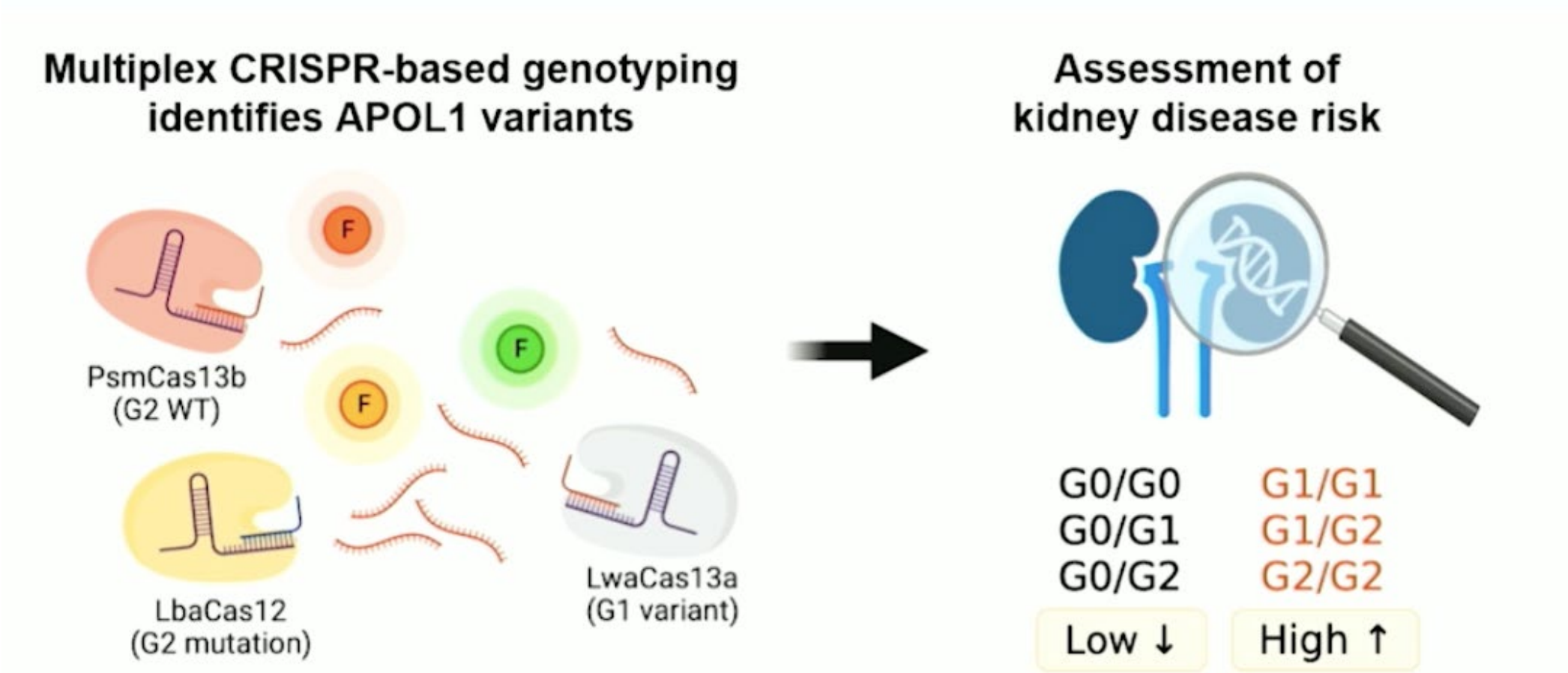


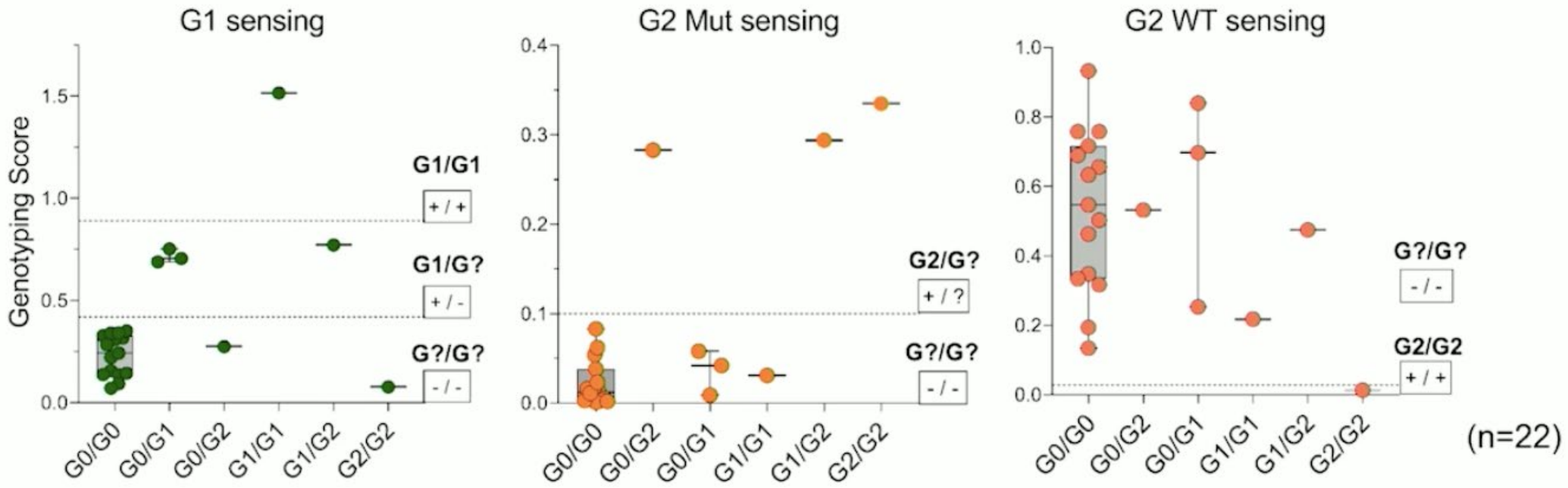
- Present in ~13% of African Americans
- Risk of CKD, FSGS, ESKD
- Reduced cadaveric kidney transplant survival
- Global health disparity for persons of African ancestry

Genotyping is **not standard** upon kidney donation (Kidney Donor Risk Index):

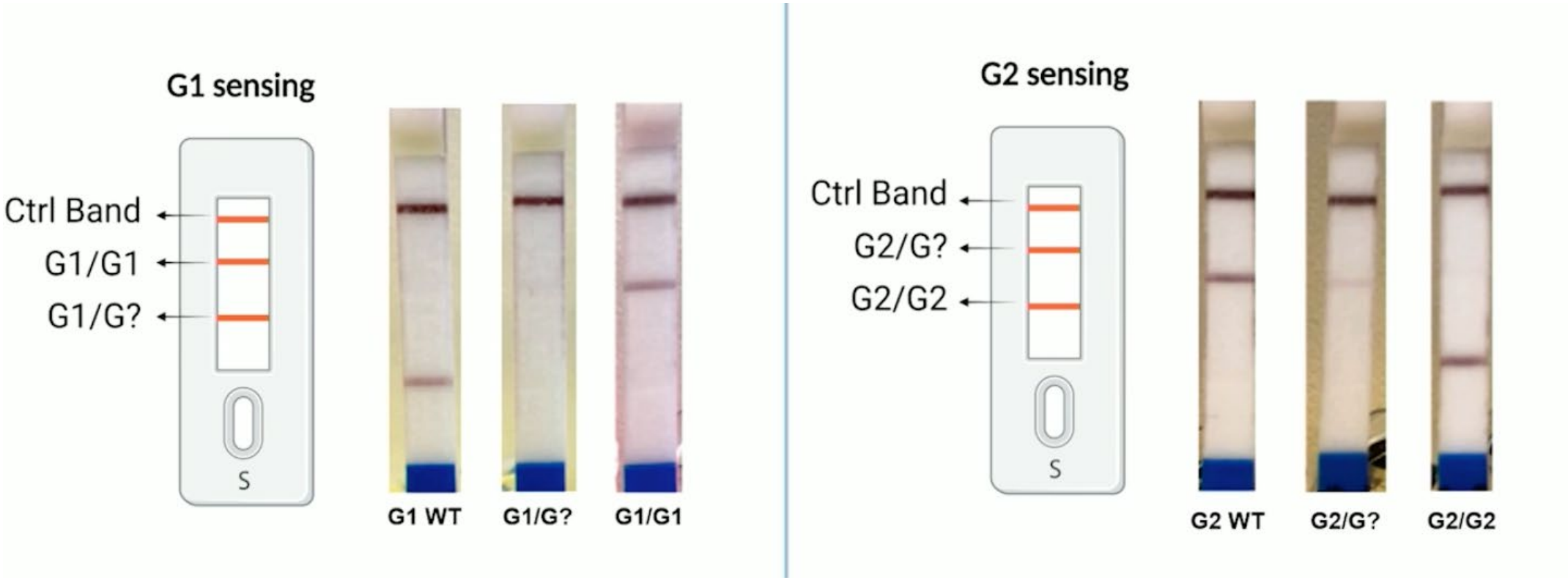
→ Substitute **race factor** for **APOL1 genotype**

→ Better defining risk of recurrence &
Better assessing kidney donors.


Multiplex CRISPR-based genotyping identifies APOL1 variants
F
F
F
PsmCas13b
(G2 WT)
LbaCas12
(G2 mutation)
LwaCas13a
(G1 variant)
Assessment of kidney disease risk
G0/G0
G0/G1
G0/G2
G1/G1
G1/G2
G2/G2
Low ↓
High ↑



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


G1 sensing
Ctrl Band
G1/G1
G1/G?
S
G1 WT
G1/G?
G1/G1
G2 sensing
Ctrl Band
G2/G?
G2/G2
S
G2 WT
G2/G?
G2/G2

GRACIAS