Rilparencel is associated with a graft-adjacent remodeling response & preserved vascular integrity in immunocompromised rodent CKD models

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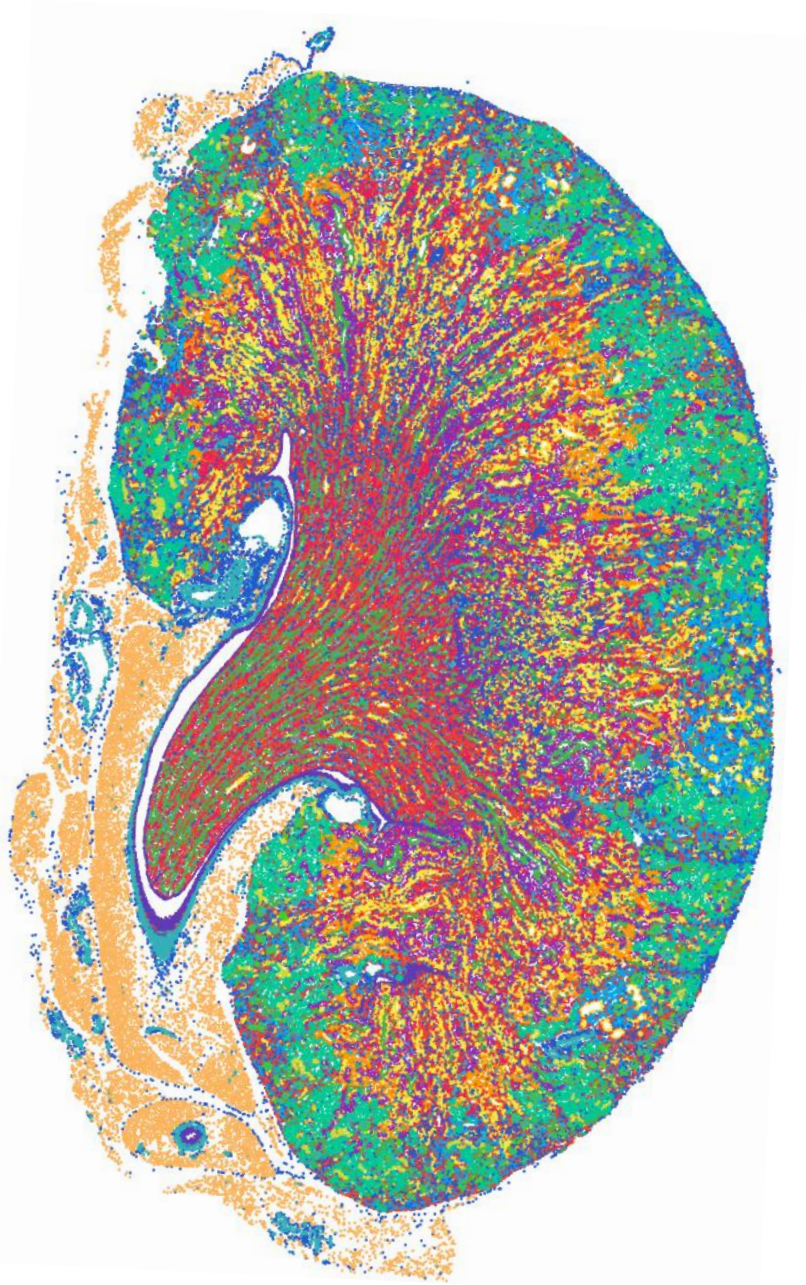
ProKidney, Research & Development

ASN 2026 Session: FR-OR044, Exciting Developments in CKD Research: From Diagnostics to Management & More [OR2202]

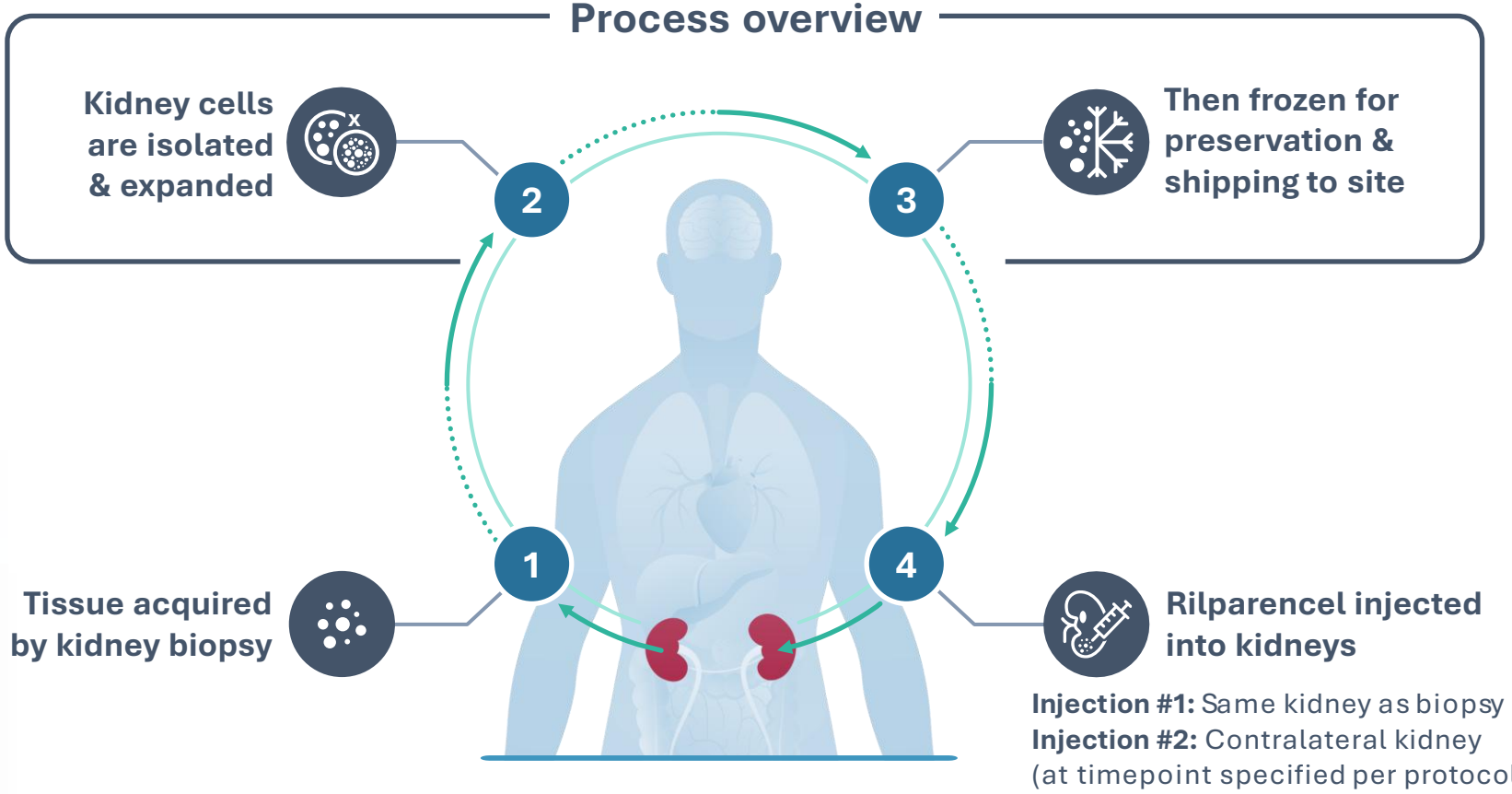
October 23, 2026



Rilparencel:
A patient's own cells – from biopsy to kidney therapy candidate

Rilparencel:

- Made from patient's own kidney cells
- No genetic modification
- No preconditioning
- No lifelong immunosuppression
- Well-tolerated in Phase 2 program[1]
- Associated with a **78% slower** annual eGFR decline in patients with advanced CKD & diabetes in cohort 1 of REGEN-007 Phase 2 study (n=24)[1]
- Currently in Phase 3 study (REGEN-006), topline readout expected Q2 2027



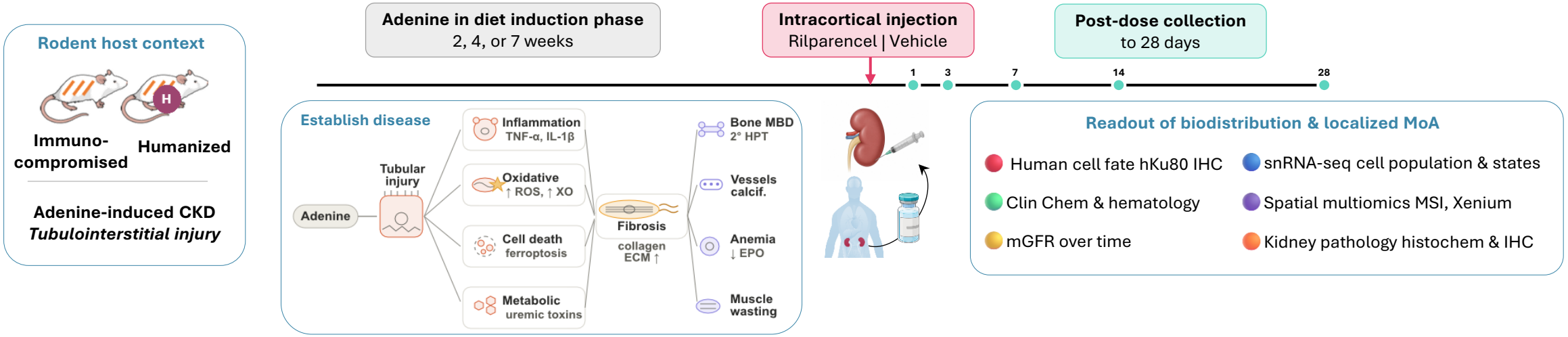
Characterizing responses in diseased kidney tissue will clarify the product's **mechanism of action (MoA)**

[1] Čižman *et al.* CJASN (2026)

Designing a multiomic approach to probe MoA in rodent CKD models

- **Preclinical proof-of-concept**: Intracortically administered syngeneic selected renal cells (SRC) extended survival & stabilized renal function (sCR, BUN) in rodent (Kelley *et al.*, 2010) & dog CKD models, improved survival & stabilized eGFR in a rodent model of diabetic kidney disease (Kelley *et al.*, 2013)
- **Human SRC**: Improved survival & stabilized renal function (sCr, BUN) in immunocompromised 5/6Nx rats (Guthrie *et al.*, ASN 2014)

Current study design (2026)

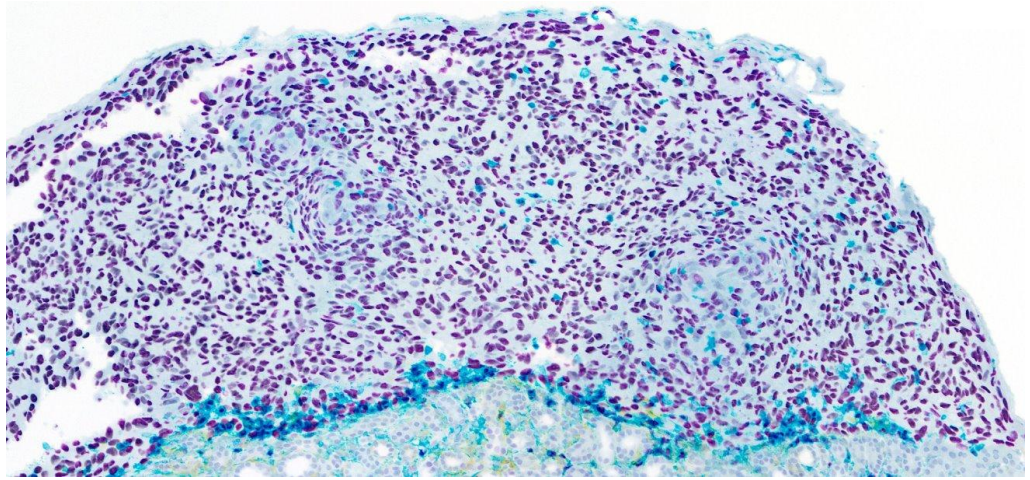


- Adenine feeding in immunocompromised / humanized rodent models demonstrated reliable kidney injury
  - **Rat models tested:** RNU, SRG; **Mouse models:** NSG-IL15 ± cord blood CD34^{+} humanization
- Vehicle controls were similarly injected intracortically with the excipient of rilparencel without any cells (SRC)

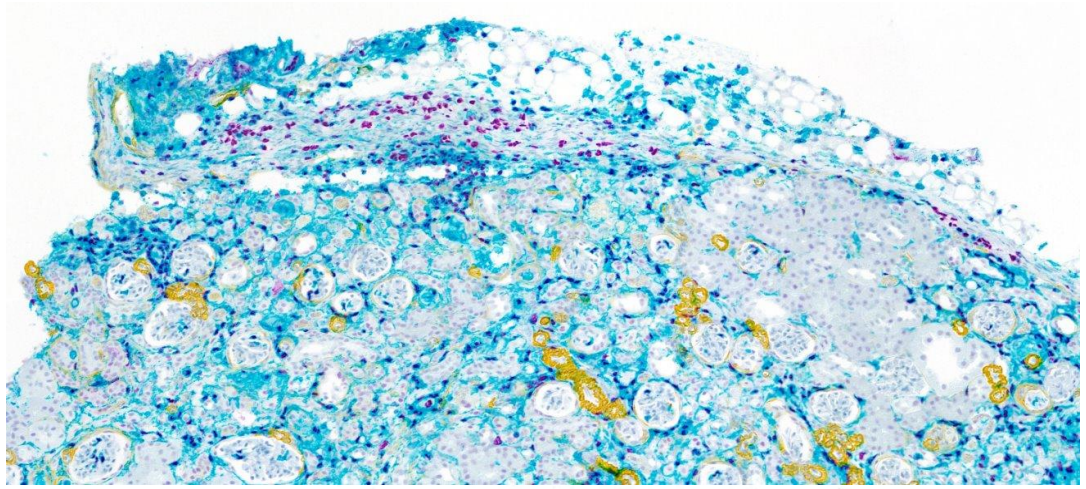
Rilparencel distributes to subcapsular & intraparenchymal renal compartments, persists through Day 28

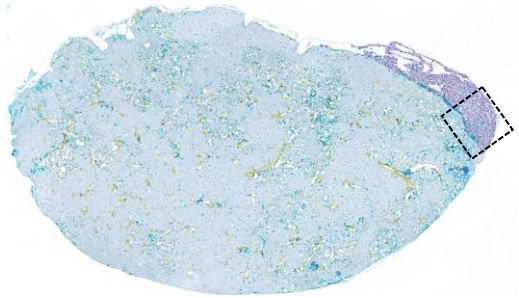
Humanized NSG-IL15 mice fed adenine

1-day post-dose

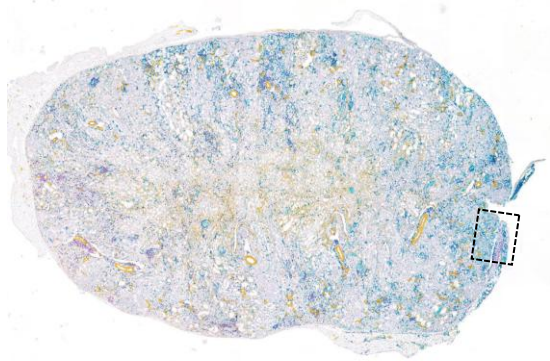


28 days post-dose

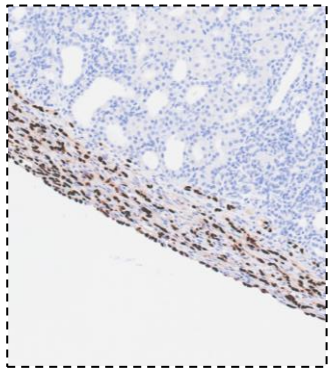




hKu80+ hmCD45- = **Rilparencel**
hKu80+ hmCD45+ = **Human immune cells**
hKu80- hmCD45+ = **Mouse immune cells**
Vascular smooth muscle cells / Myofibroblasts (αSMA)



Aligning multiomic analytical modalities after rilparencel injection



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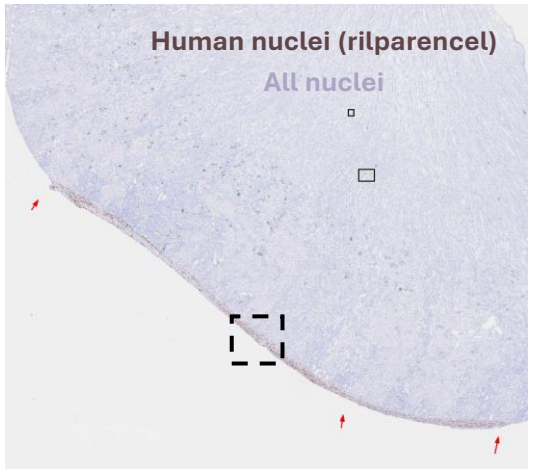
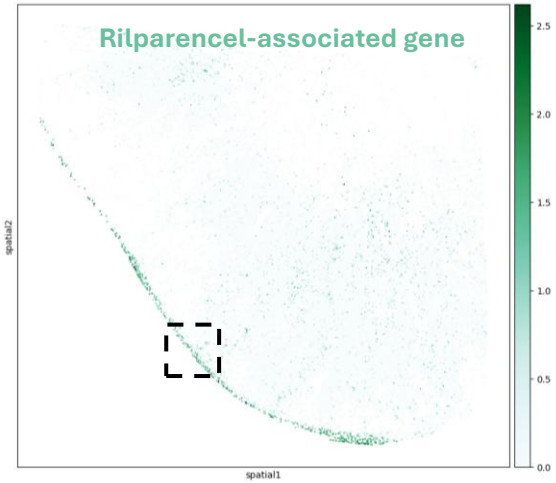


Spatial transcriptomics

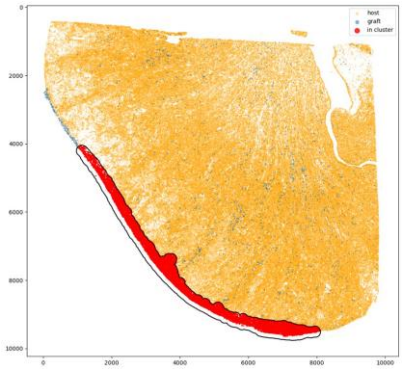


Single nuclei RNA-seq

Mass Spec Imaging (MSI)

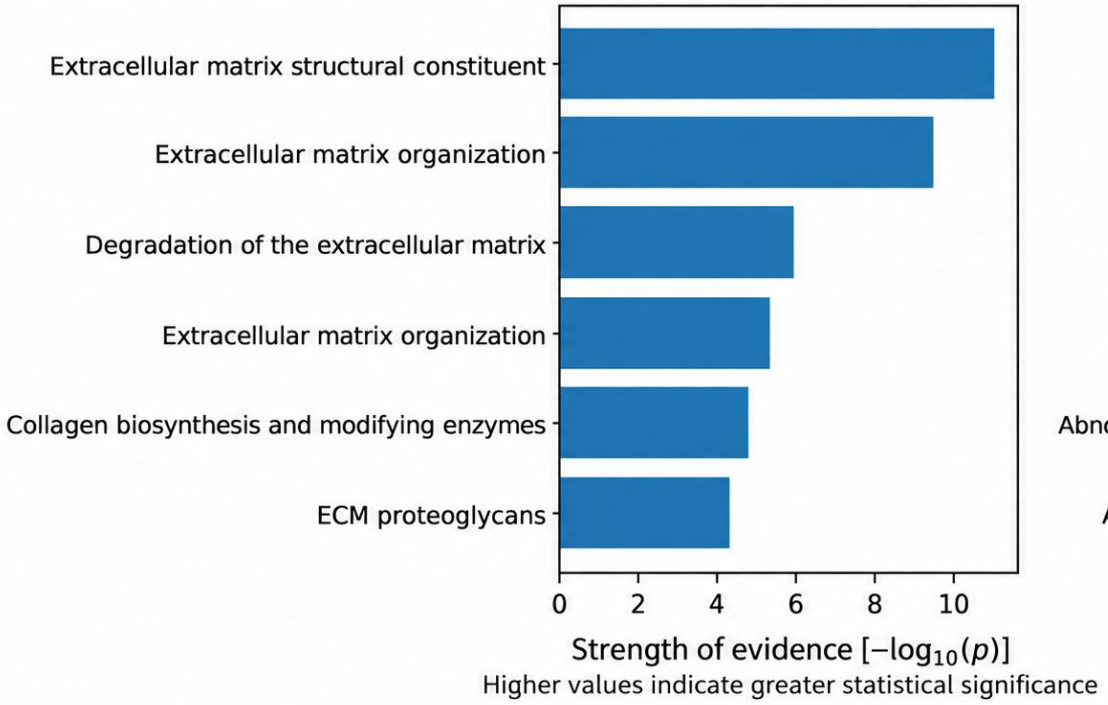
Graft-associated cells have a distinct transcriptional signature in injected rats

- Significantly upregulated genes in graft area cells **3 days post-rilparencel** are associated with **ECM remodeling & vascular development,** including matrix organization & turnover, collagen biosynthesis, & blood vessel morphogenesis

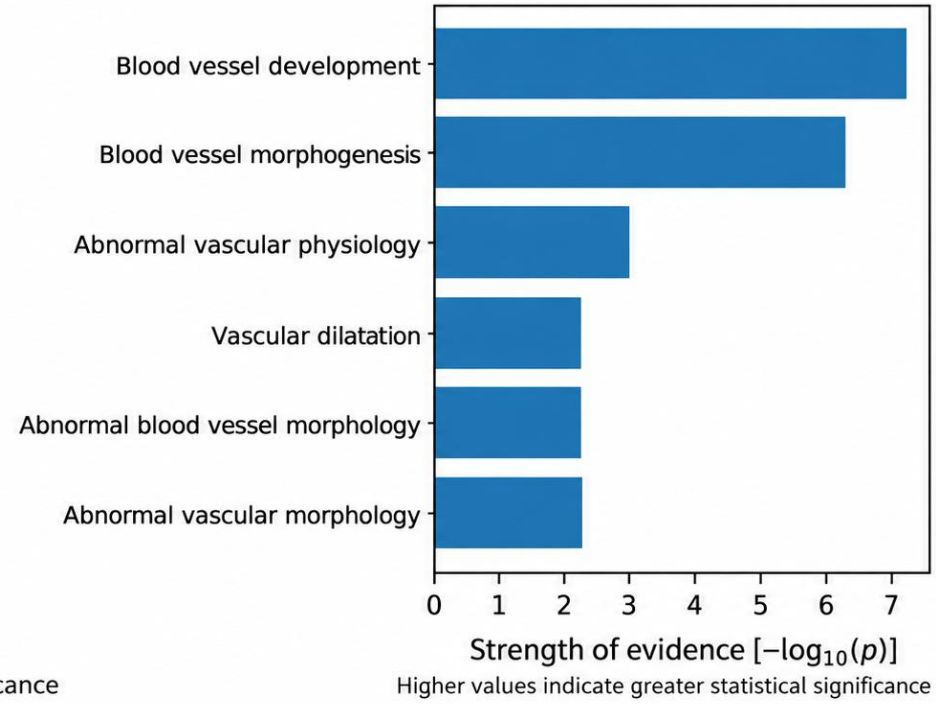


Rilparencel graft-associated gene signature

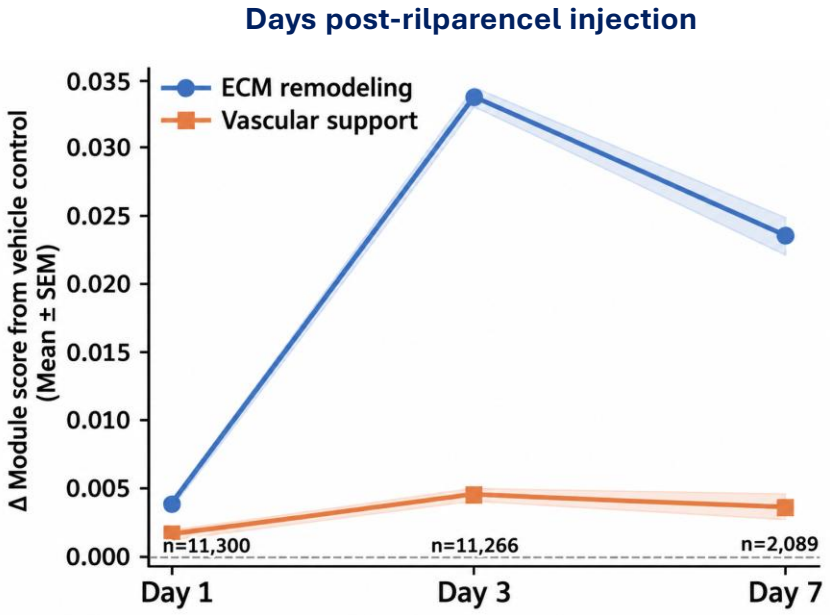
ECM remodeling



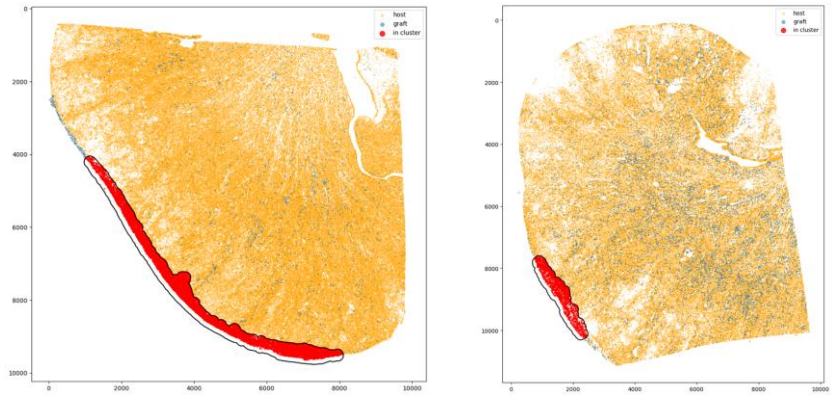
Vascular development & support



Transcriptional signature of graft-associated cells evolves over time

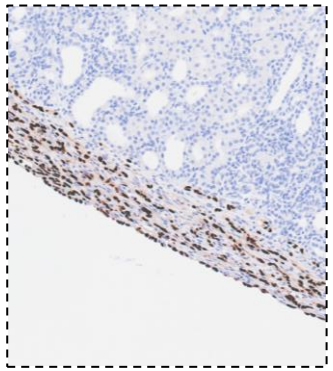


Rilparencel graft-associated gene signature



- The injured kidney's response to rilparencel is dynamic & evolves over time
- An initial higher upregulation in **ECM remodeling** gene expression drops over the first week after treatment but is maintained well above baseline
- Accompanying this matrix remodeling signal, population enrichment of **vascular support** gene expression occurs by day 3 at the site of rilparencel engraftment

Aligning multiomic analytical modalities after rilparencel injection



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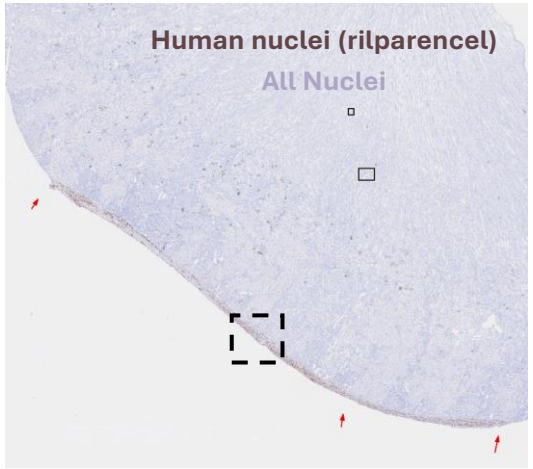
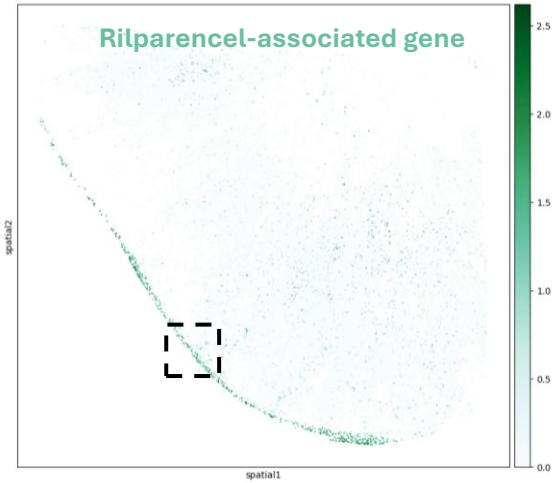
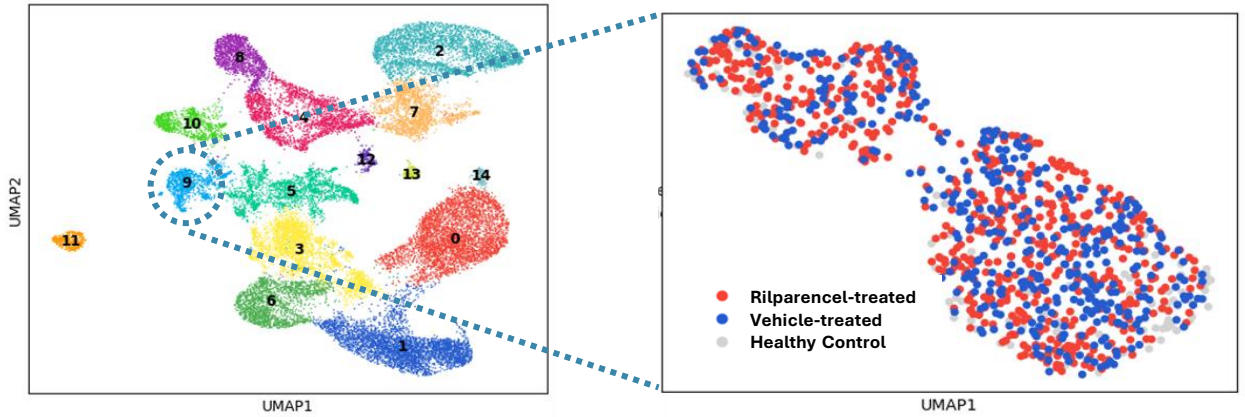


Spatial transcriptomics



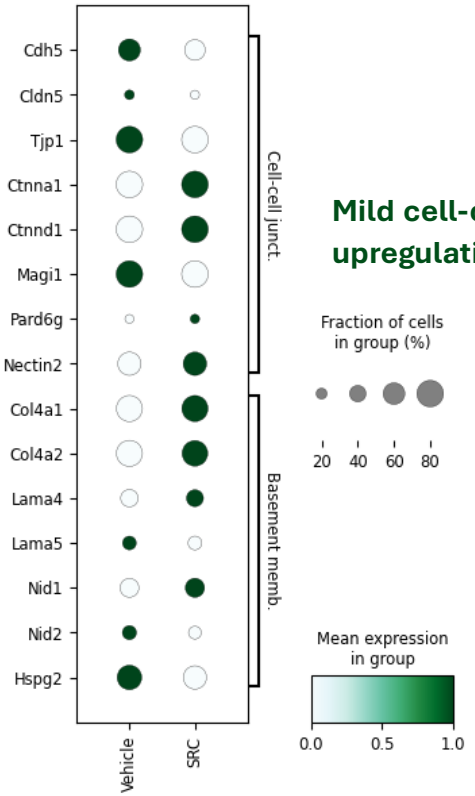
Single nuclei RNA-seq



Mass Spec Imaging (MSI)

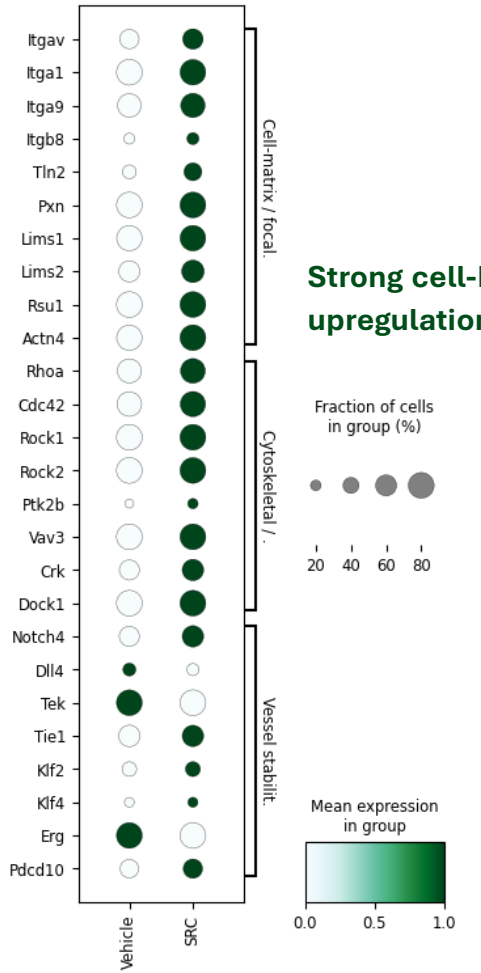
Vessel / ECM adhesion & signaling is upregulated in rat kidney endothelial cells

Endothelial junction & ECM programs



Mild cell-cell upregulation

Endothelial adhesion & stability programs

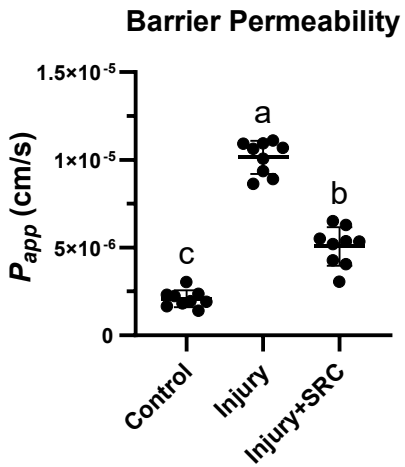


Strong cell-ECM upregulation

- Kidney snRNA-seq at **28 days post-dose** in RNU rats with adenine-induced CKD; endothelial nuclei identified using the KPMP kidney cell atlas as a reference
- There is a strong cell / ECM vascular program that is induced by rilparencel

In Vitro Endothelial Cell Injury Rescue Model

- P_{app} (apparent permeability coefficient) measures endothelial barrier function via FITC-dextran flux across a cell monolayer
- **Glomerular microvascular endothelial cell** monolayers were injured for 3 days (glucose, cytokine mix, lipid mix, uremic toxins), then ± SRC for 4 days
- SRC significantly reduced P_{app} vs. Injury alone, indicating improved barrier integrity



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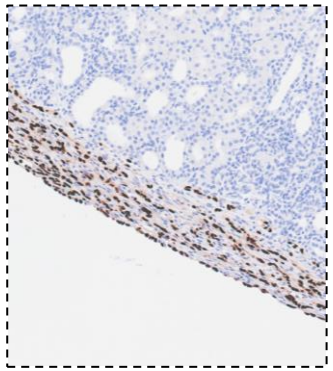

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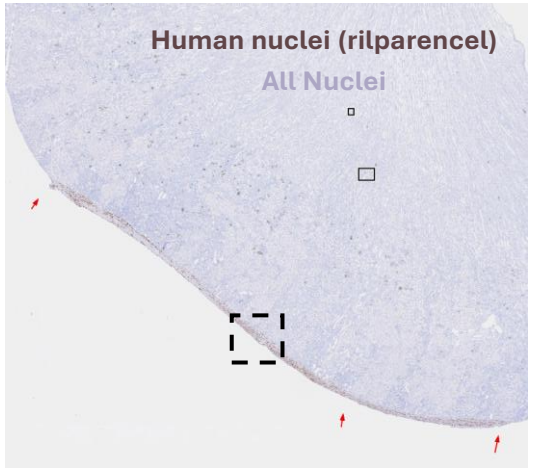

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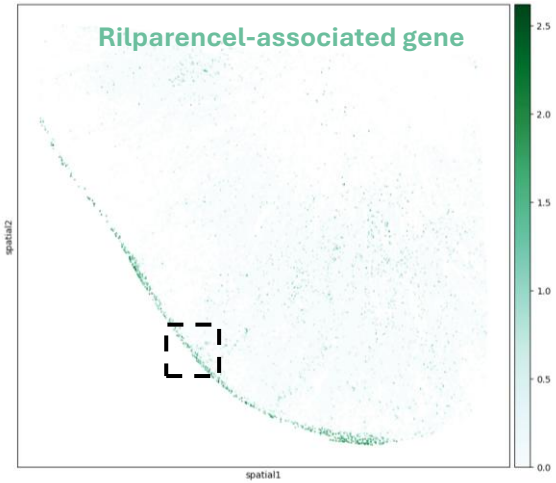

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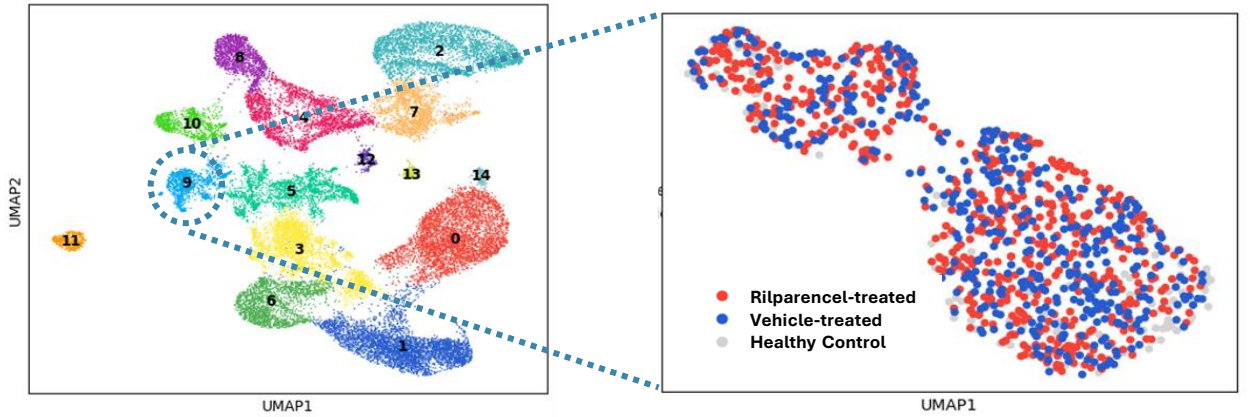
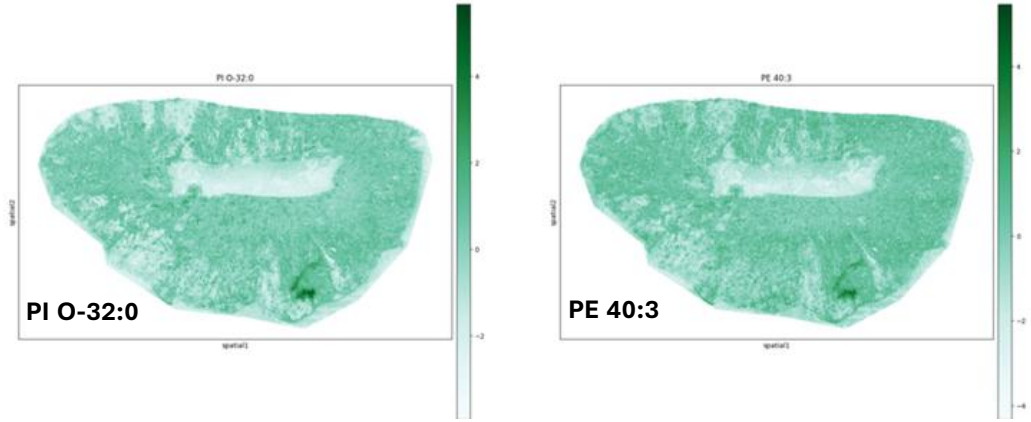


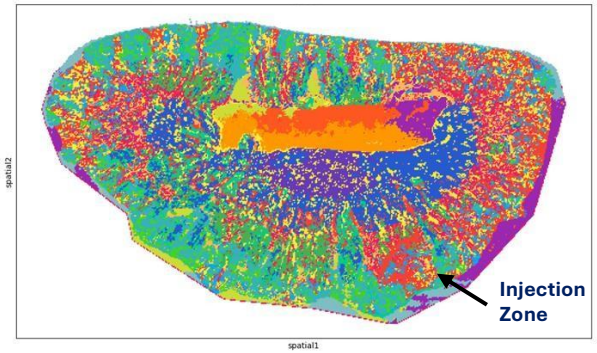
Mass spec imaging (MSI)



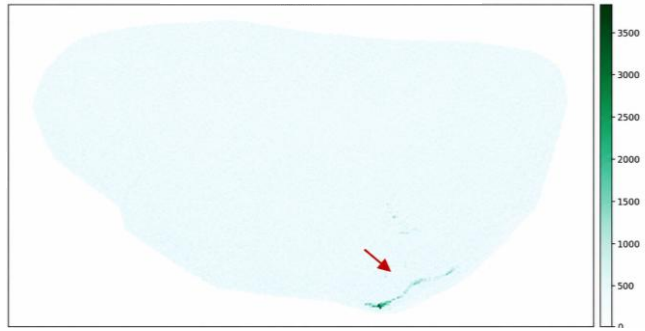
MSI reveals a distinct local protein & lipid tissue remodeling signature at the rilparencel injection site

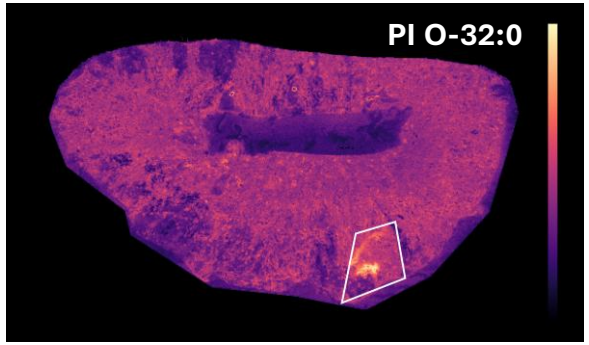
- MSI spatially resolved protein & lipid biomarkers within an injection-defined ROI encompassing the hKu80-associated rilparencel injection site at **day 3 post-injection**
- ROI showed enrichment of markers associated with immune responses, stromal / perivascular remodeling (↑ PDGFR-β, Vimentin), cell adhesion (↑ CD44), & autophagy (↑ LC3A)
- A distinct lipid profile within the ROI (↑ PI 38:4, PI O-34:4; ↓ LPC 22:5, LPI 18:2) suggests regional differences in membrane composition & lipid remodeling

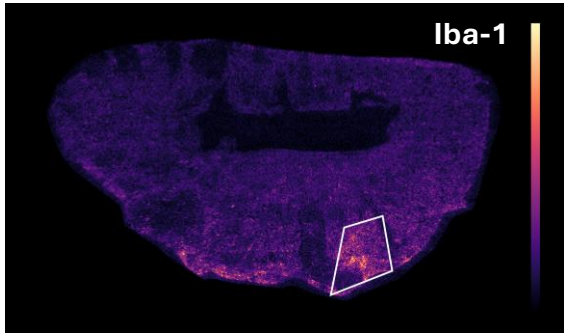
Signature domains



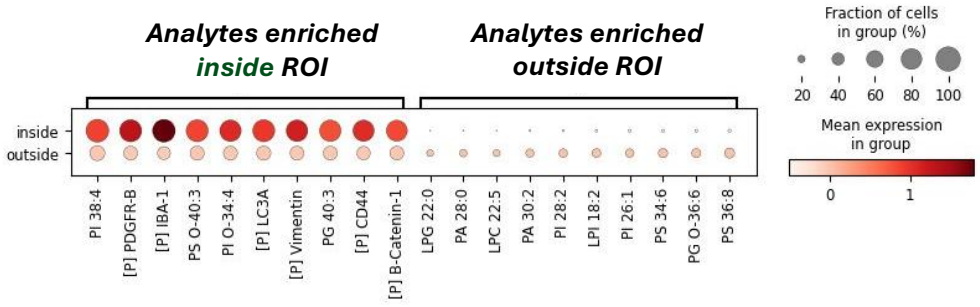
hKu80 (rilparencel)



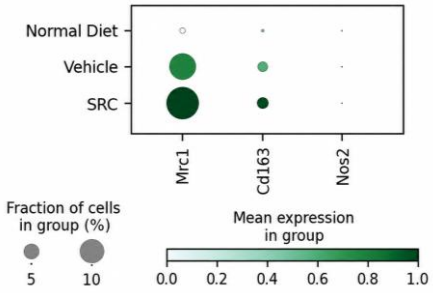




Differential lipid metabolite & protein enrichment
(MSI)



Scavenging & tissue-remodeling signature
(snRNA-seq)



Translational studies suggest multifactorial MoA for rilparencel

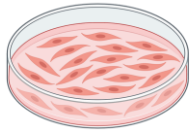
Rilparencel

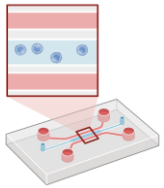
Transcriptomic analyses of REGEN-007 pre-formulation cell retains & patient biopsies, using the KPMP database (Poster SA-PO0014):

- **Cells of proximal & distal tubule origin exhibiting a reparative, plasticity-associated transcriptional signature with partial retention of native lineage identity**

In vitro

Primary kidney cells





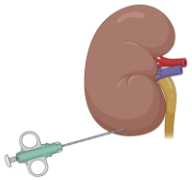
Kidney-on-chip

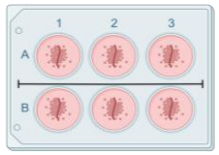
Human proximal tubule epithelial cell & glomerular vascular endothelial cell models of metabolic & inflammatory stress cultured with rilparencel showed (Poster TH-PO1128):

- **Regulated redox imbalance**
- **Improved mitochondrial fitness**
- **Reduced pro-inflammatory signaling**

Ex vivo

Kidney biopsy explant culture





Human CKD biopsy & rilparencel co-culture studies revealed (Poster TH-PO1129):

- **Treatment-based transcriptional changes in ferroptosis pathway** (also validated *in vitro*, see Poster *SA-PO0013*)

In vivo (rodent)

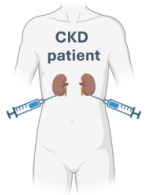
Rodent models of CKD

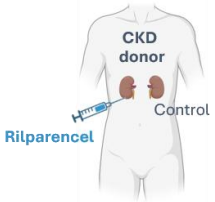
*Whole-kidney multi-omics following rilparencel injection show signatures of (**this talk**):*

- **Preserved vascular integrity, adhesion, ECM**
- **Improved lipid metabolism & redox balance**
- **Reduced pro-inflammatory transcriptional programs**

In vivo (human)

Clinic (Phase 2)





Decedent

Plasma & urine proteomic analysis from baseline & correlation studies show signatures of (unpublished):

- **Basement membrane remodeling & vascular preservation**

Human decedent study upcoming:

- **Longitudinal 39-day post-dose tissue, urine, & plasma multiomic analysis**

MoA Hypothesis

Rilparencel attenuates oxidative damage, metabolic dysregulation, & pro-inflammatory signaling to support cellular resilience, preserved vascular integrity & functional stabilization under chronic kidney disease-relevant conditions

Acknowledgements

Study Team

R&D team: Andrew Bruce, Caryn Cloer, Anthony Conway, Michael Czerwinski, Emily Manzon, Riann Shackett, & Carson Taylor

ProKidney team: Farah Ali, Borut Čižman, Ethan Holdaway, Alex Heintzelman, Michelle Holmes-Son, & Joseph Stavas

Collaborators

Research & analytical partners: AmberGen · Inotiv · OMAPiX · StageBio · Massachusetts General Hospital (Minxue Liao, Thiago De Jesus Borges)

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