ProKidney

American Society of Nephrology (ASN) Kidney Week Recap & Corporate Update

October 27, 2026



NASDAQ
PROK

Copyright © 2026 ProKidney Corp. All rights reserved.

Forward-looking Statements

This presentation includes “forward-looking statements” within the meaning of the “safe harbor” provisions of the Private Securities Litigation Reform Act of 1995. ProKidney’s actual results may differ from its expectations, estimates and projections and consequently, you should not rely on these forward-looking statements as predictions of future events. Words such as “expect,” “estimate,” “project,” “budget,” “forecast,” “anticipate,” “intend,” “plan,” “may,” “will,” “could,” “should,” “believes,” “predicts,” “potential,” “continue,” and similar expressions (or the negative versions of such words or expressions) are intended to identify such forward-looking statements. These forward-looking statements include, without limitation, the achievement and timing of the topline data readout of the Company’s PROACT 1 trial and other milestones provided, the Company’s beliefs that its Phase 3 REGEN-006 (PROACT 1) trial could be sufficient to support a potential BLA submission and full regulatory approval, eGFR slope can be used as a surrogate endpoint on an accelerated approval pathway for rilparencel, expectations with respect to financial results and expected cash runway, including the Company’s expectation that current cash will support operating plans into mid-2027, future performance, development and commercialization of products, if approved, the potential benefits and impact of the Company’s products, if approved, potential regulatory approvals, the size and potential growth of current or future markets for the Company’s products, if approved, the advancement of the Company’s development programs into and through the clinic and the expected timing for reporting data, the making of regulatory filings or achieving other milestones related to the Company’s product candidates, and the advancement and funding of the Company’s developmental programs, generally. Most of these factors are outside of the Company’s control and are difficult to predict. Factors that may cause such differences include, but are not limited to: disruptions to our business or that may otherwise materially harm our results of operations or financial condition as a result of our recent domestication to the United States; the inability to maintain the listing of the Company’s Class A common stock on Nasdaq; the inability of the Company’s Class A common stock to remain included in various indices and the potential negative impact on the trading price of the Class A common stock if excluded from such indices; the inability to implement business plans, forecasts, and other expectations or identify and realize additional opportunities, which may be affected by, among other things, competition and the ability of the Company to grow and manage growth profitably and retain its key employees; the risk of downturns and a changing regulatory landscape in the highly competitive biotechnology industry; the risk that results of the Company’s clinical trials may not support approval; the risk that the FDA could require additional studies before approving the Company’s drug candidates; the inability of the Company to raise financing in the future; the inability of the Company to obtain and maintain regulatory clearance or approval for its products, and any related restrictions and limitations of any cleared or approved product; the inability of the Company to identify, in-license or acquire additional technology; the inability of Company to compete with other companies currently marketing or engaged in the biologics market and in the area of treatment of kidney diseases; the size and growth potential of the markets for the Company’s products, if approved, and its ability to serve those markets, either alone or in partnership with others; the Company’s estimates regarding expenses, future revenue, capital requirements and needs for additional financing; the Company’s financial performance; the Company’s intellectual property rights; uncertainties inherent in cell therapy research and development, including the actual time it takes to initiate and complete clinical studies and the timing and content of decisions made by regulatory authorities; the fact that interim results from our clinical programs may not be indicative of future results; the impact of geo-political conflict on the Company’s business; and other risks and uncertainties included under the heading “Risk Factors” in the Company’s most recent Annual Report on Form 10-K, subsequent Quarterly Reports on Form 10-Q and other filings with the Securities and Exchange Commission. The Company cautions readers that the foregoing list of factors is not exclusive and cautions readers not to place undue reliance upon any forward-looking statements, which speak only as of the date made. The Company does not undertake or accept any obligation or undertaking to release publicly any updates or revisions to any forward-looking statements to reflect any change in its expectations or any change in events, conditions or circumstances on which any such statement is based.

Today's Agenda and Speakers



Bruce Culleton, MD, CEO

ProKidney



Anthony Conway, PhD, Head of R&D

ProKidney



Katherine Tuttle, MD, KOL

Providence | University of Washington

1. **Opening Remarks & Corporate Update**
2. **Rilparencel MoA Findings**
3. **The Quest to Save Kidneys, Hearts, and Lives: Mechanisms Matter**
4. **Q&A**

MoA = Mechanism of Action KOL = Key Opinion Leader



BRUCE CULLETON, MD, CEO

Opening Remarks & Corporate Update

ProKidney

Redefining What's Possible in the Treatment of CKD Through Innovation and Execution



Rilparencel

Potential first-in-class autologous cell therapy designed to preserve kidney function in patients with advanced CKD



Pivotal Phase 3 Study Ongoing

Phase 3 PROACT 1 trial in patients with Stage 3b/4 CKD and type 2 diabetes — ONGOING (Q2 2027 readout)

Three Phase 2 trials in Stage 3/4 CKD — ✓ COMPLETED



Large Untapped Market Opportunity

Over 1 million U.S. patients with Stage 3b/4 CKD and diabetes at high risk of progressing to kidney failure



Key Value Drivers

- ✓ Robust Clinical Data
- ✓ In-House Manufacturing
- ✓ RMAT Designation
- ✓ Cash Through Pivotal Data

Building a future where advanced CKD treatment means more options, time, and hope

RMAT = Regenerative Medicine Advanced Therapy

Anticipated Upcoming Milestones

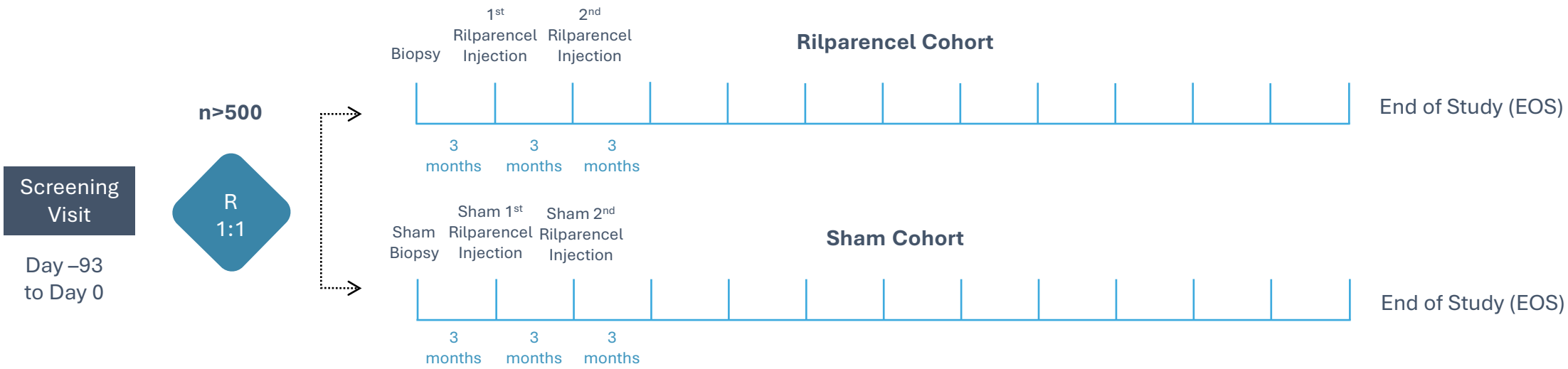
Timing	Milestones
Q1 2027	Complete full enrollment for the Phase 3 PROACT 1 study. Anticipate enrolling **over 500 patients** (up from 470) driven by an acceleration in patient recruitment in mid-2026.
Q2 2027	**Topline readout** for the Phase 3 PROACT 1 surrogate endpoint (eGFR slope) for accelerated approval. The efficacy analysis set is expected to include ~320 patients.
Q1 2028	BLA submission of rilparencel for accelerated approval.
1H 2029	BLA accelerated approval and commercial launch of rilparencel.
2H 2029	Topline readout for the Phase 3 PROACT 1 confirmatory endpoint (composite time-to-event) to support full approval of rilparencel.

BLA = Biologics License Application eGFR = Estimated Glomerular Filtration Rate

PHASE 3 REGEN-006 (PROACT 1)

Rilparencel Phase 3 Registrational Study Design

Topline results for the eGFR slope surrogate endpoint anticipated in Q2 2027



Key Entry Criteria

- Type 2 diabetes and CKD
- 30-80 years of age
- eGFR ≥20 and ≤35 mL/min/1.73m^2
- UACR 300-5,000 mg/g for eGFR 30-35
- HbA1c <9.5%

Surrogate Endpoint (Accelerated Approval Pathway)

- Annualized eGFR slope is the surrogate endpoint
- Efficacy analysis set is expected to contain approximately 320 patients and will include all patients with *at least* 6 months of follow-up after first injection
- Expected to have 80% power to detect an effect size in annualized eGFR slope of 1.5 mL/min/1.73m^2

Confirmatory Composite Time-to-Event Endpoint

- At least 40% reduction in eGFR;
- eGFR <15mL/min/1.73m^2 sustained for 30 days and/or chronic dialysis, and/or renal transplant; or
- Death from renal or cardiovascular causes

(The confirmatory analysis will be triggered when 122 participants have at least one event)



ANTHONY CONWAY, PhD, HEAD OF R&D

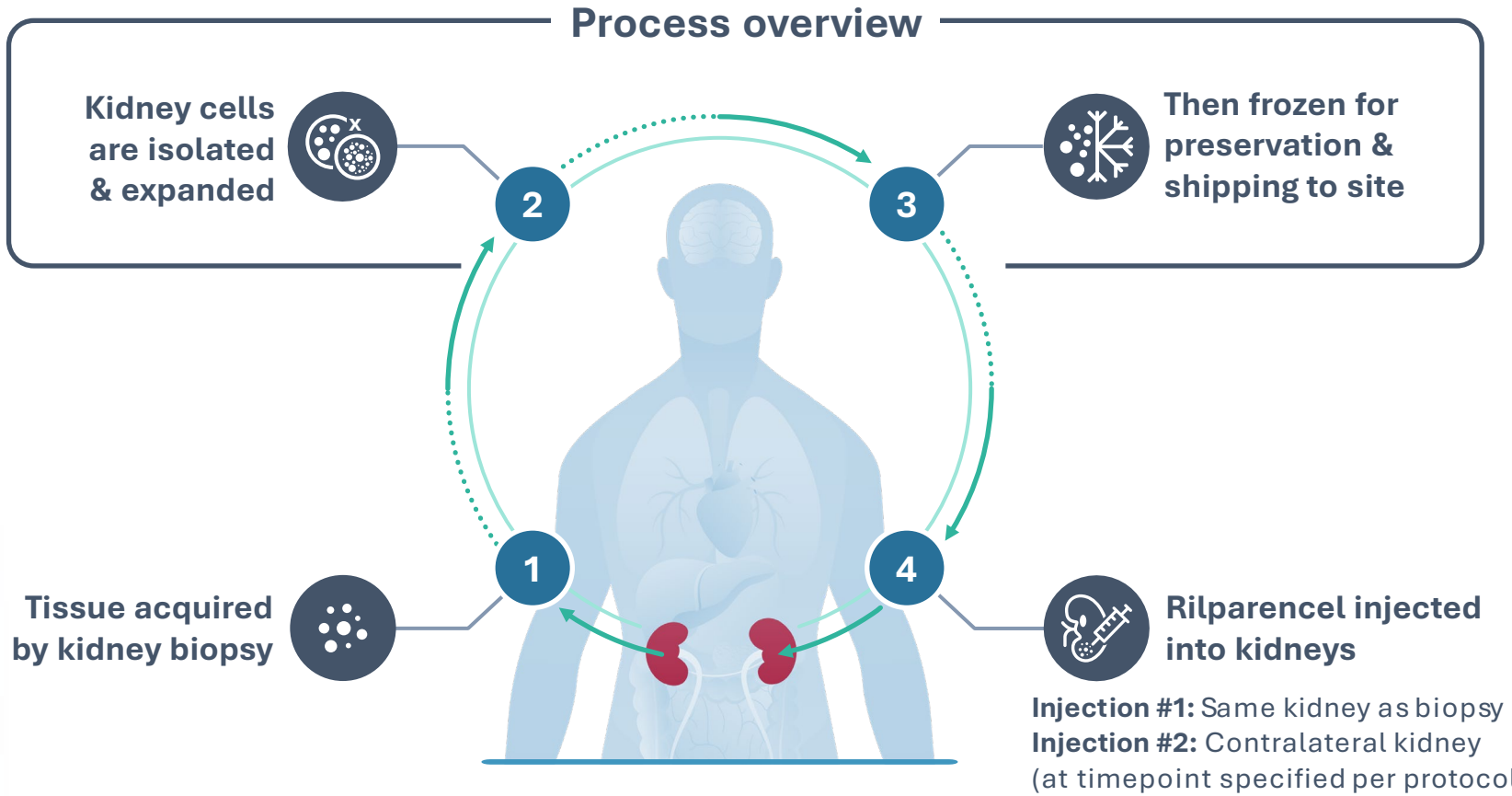
Rilparencel Mechanism of Action (MoA) Findings

ProKidney

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

Rilparencel:

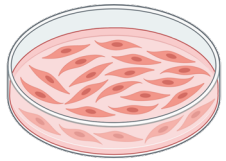
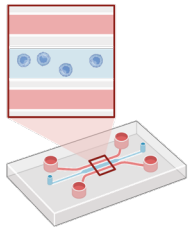
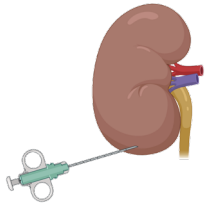
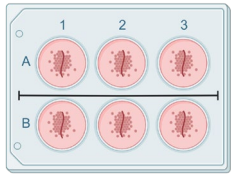
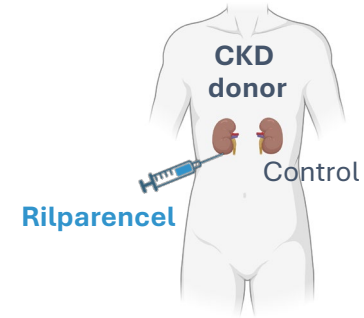
- Made from patient's own kidney cells
- No genetic modification
- No preconditioning
- No lifelong immunosuppression
- Outpatient procedures
- Well-tolerated in Phase 2 program[1]
- Associated with a **78% slower** annual eGFR decline in patients with advanced CKD & diabetes in cohort 1 of REGEN-007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



We need to uncover what's happening in diseased kidney tissue after our product is administered to understand its **mechanism of action (MoA)**

[1] Čižman *et al.* CJASN (2026)

Utilizing translational disease models to elucidate rilparencel MoA

In vitro	*Ex vivo*	*In vivo* (rodent)	*In vivo* (human decedent)
Primary kidney cells   Kidney-on-chip	Kidney biopsy explant culture  	Rodent models of CKD 	

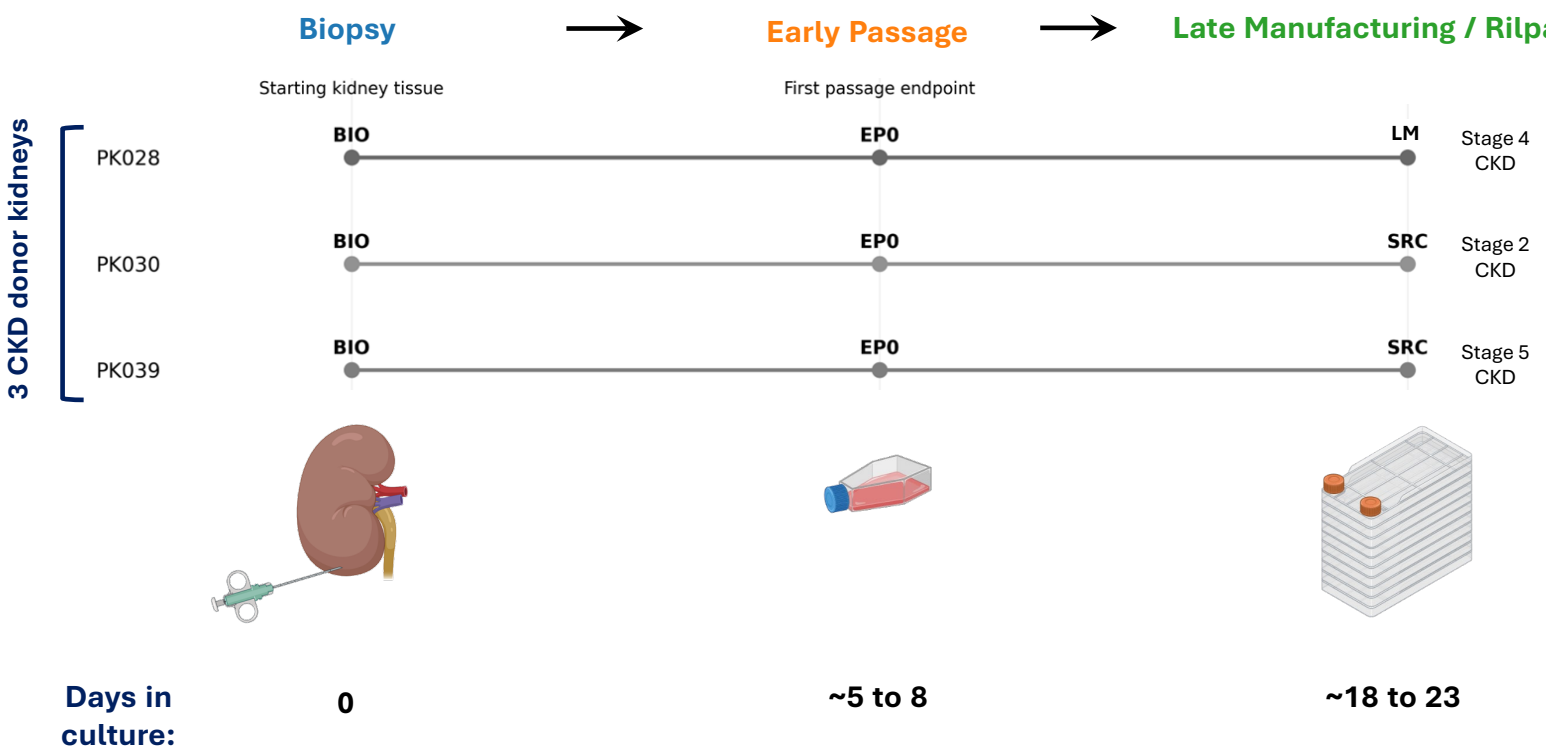
Advantages

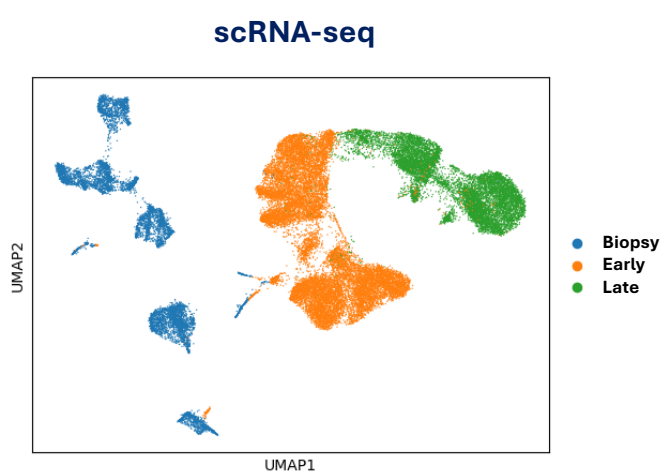
In vitro	*Ex vivo*	*In vivo* (rodent)	*In vivo* (human decedent)
• Quick: Fast design-test-learn cycles • High throughput: Simultaneously test multiple variables to deconvolute MoA • Cost-effective	• Native tissue structure & cell-cell interactions maintained • Fast design-test-learn cycles • Medium throughput	• Intact whole body physiology • Long-term post-treatment studies feasible	• Most representative of clinical setting • Serial biopsies & sampling possible to uncover temporal MoA

Anticipated Results

- Whole genome expression profile in diseased & normal kidney cells +/- rilparencel treatment
- Identification of key factors expressed by rilparencel, & the disease pathways they act upon, which are necessary & sufficient for its therapeutic effect
- Multi-omic gene expression, protein, & metabolite profiles in diseased kidney, urine, & blood +/- rilparencel treatment
- Single-cell & spatial datasets integrated with histopathological changes
- Association of molecular biomarker findings with clinically relevant measurements

Identifying the cellular origin of rilparencel from kidney biopsies





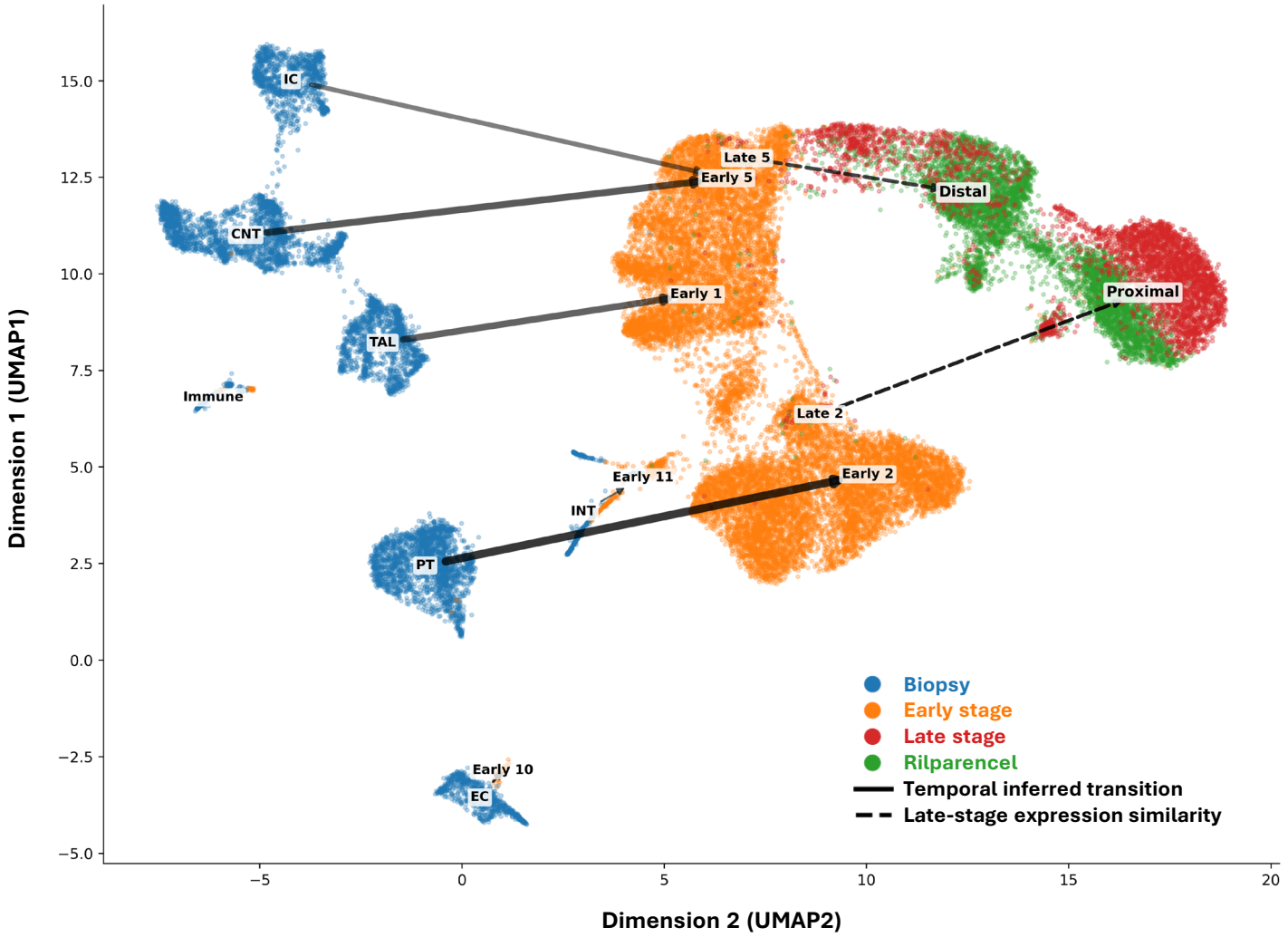
For the purpose of this presentation, rilparencel may refer to selected renal cells (SRC), which are **the cells formulated in rilparencel**, or may refer to SRC formulated as rilparencel

LM = late manufacturing

SRC = selected renal cells (rilparencel)

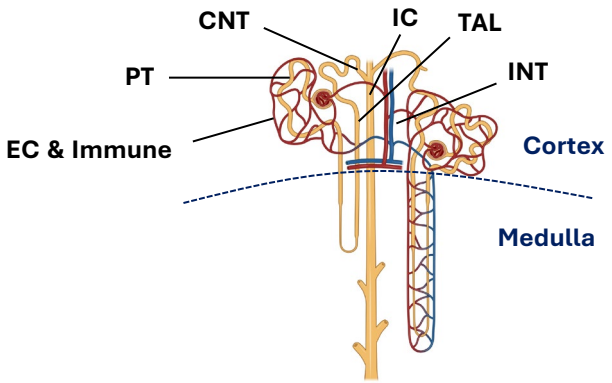
ProKidney

Cellular trajectory from biopsy to rilparencel

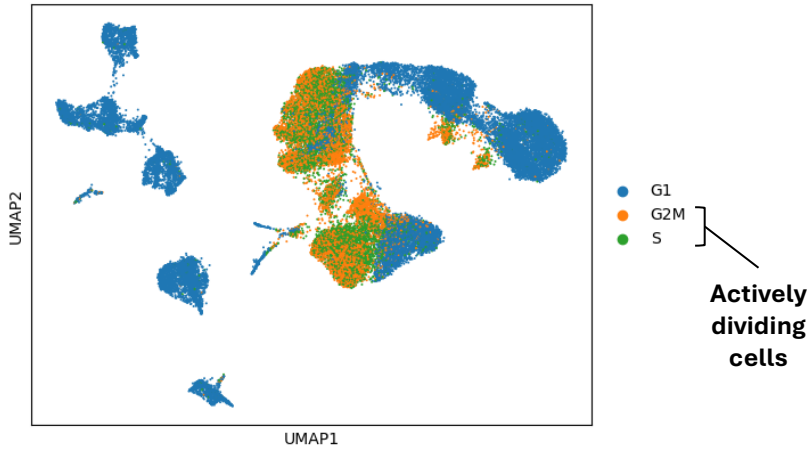


Nephron

(functional unit of kidney)



Cell cycle phase

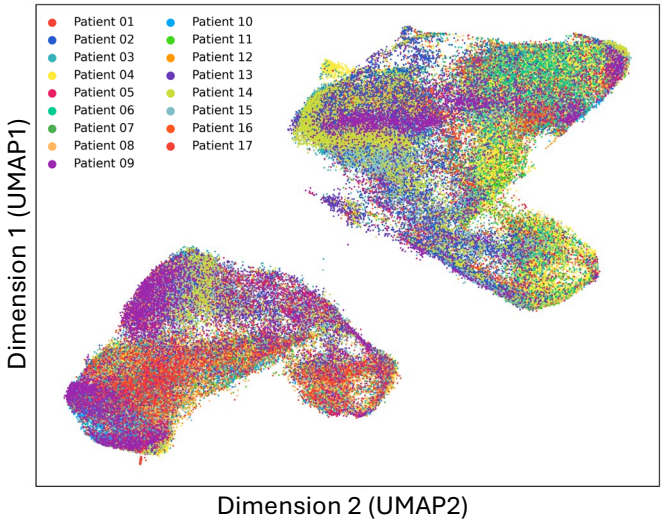


IC = Intercalated Cell **CNT** = Connecting Tubule **TAL** = Thick Ascending Limb **PT** = Proximal Tubule **EC** = Endothelial Cell **INT** = Interstitial Cell

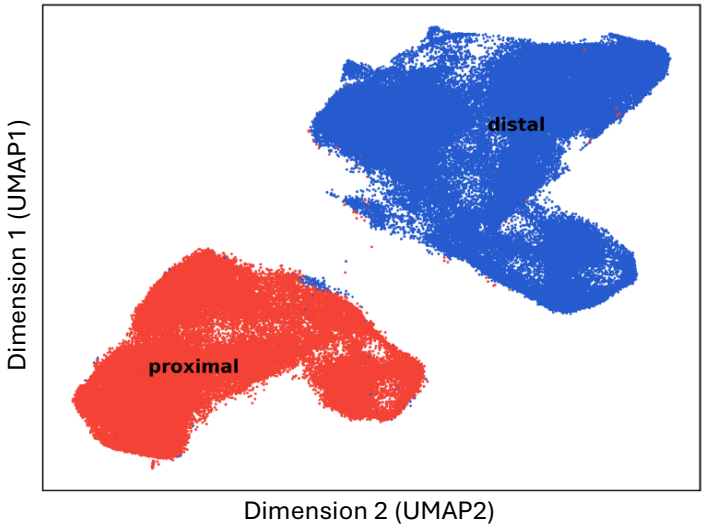
ProKidney

2 distinct lineage-associated populations in rilparencel present in 17 patient batches

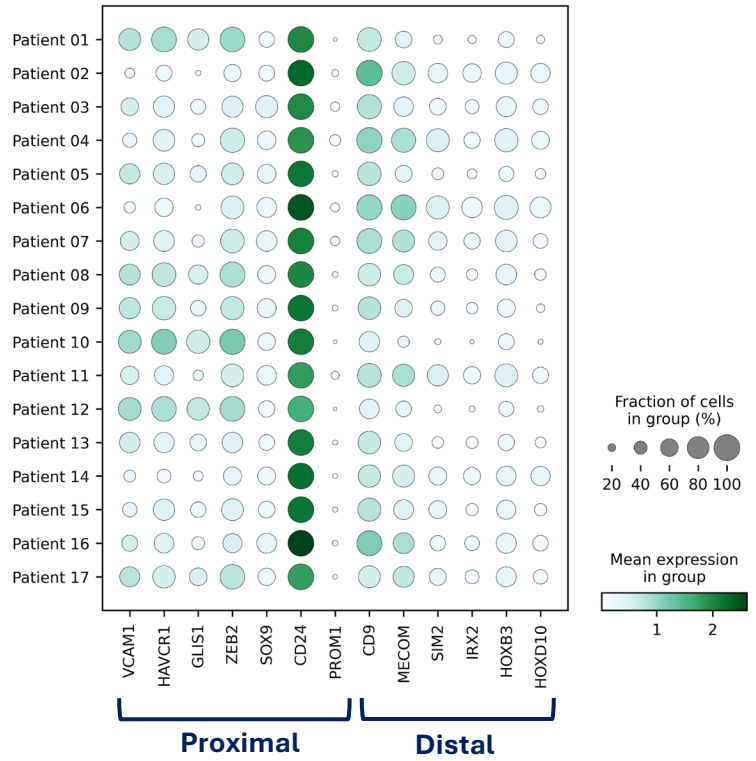
scRNA-Seq Unbiased Clustering



Proximal & Distal Population Clusters



Population Markers

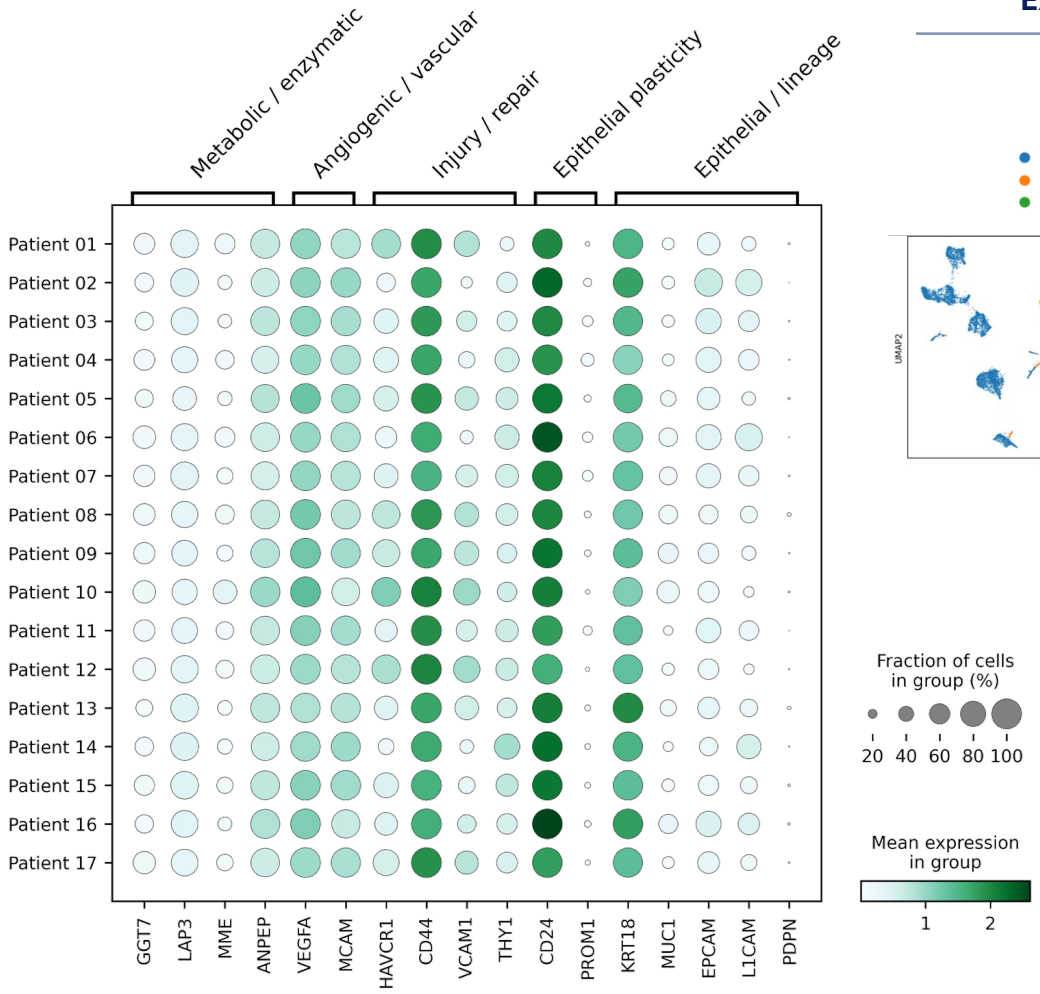


Lineage-associated rilparencel populations likely are derived from proximal & distal tubule epithelial cells from initial biopsies

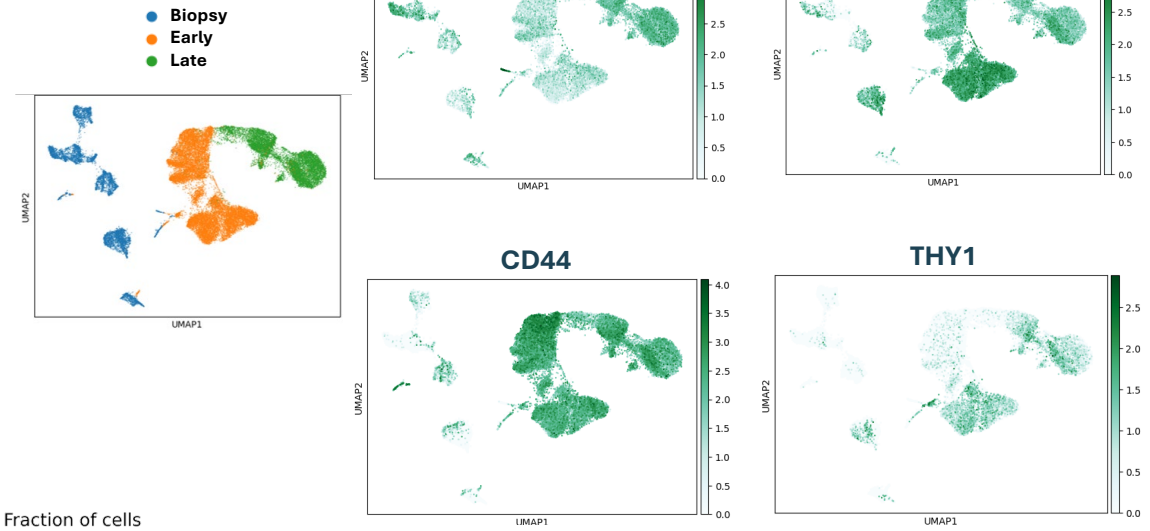
PROKIDNEY

Similar characterization marker expression across 17 rilparencel batches

Rilparencel Characterization Panel
(scRNA-Seq)



Examples of Expression Trajectory from Biopsy to Rilparencel





Rilparencel

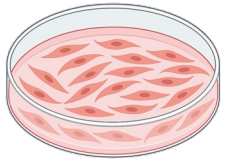
Cells of proximal & distal tubule origin exhibiting a reparative, plasticity-associated transcriptional signature with partial retention of native lineage identity

Remarkably consistent product characteristics across patients despite lineage & expression heterogeneity from starting biopsies

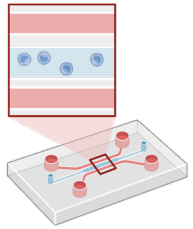
ProKidney

Utilizing *in vitro* CKD models to assess resolution of disease state by rilparencel

Primary kidney cells

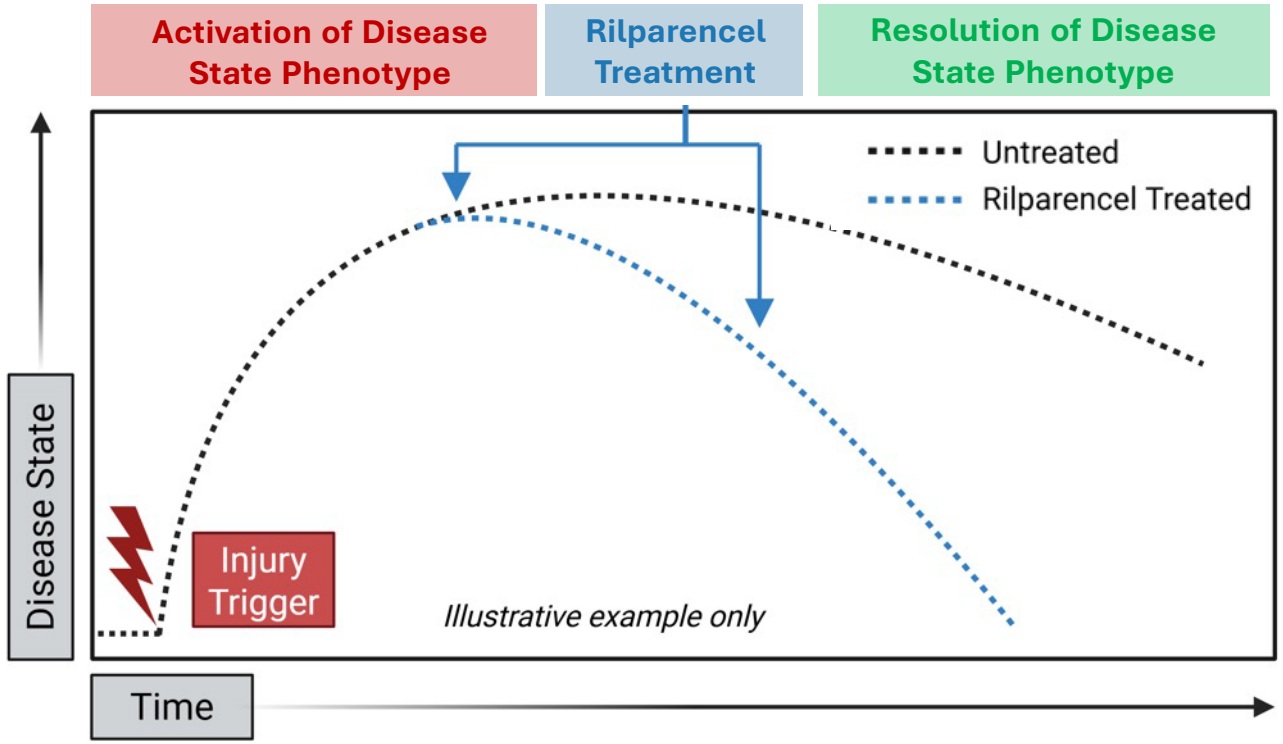


Kidney-on-chip



Workstream Goals

- Develop advanced, human-relevant *in vitro* disease models for rilparencel functional testing
- Identify & screen mechanism-aligned functional assays to elucidate the biological activity, timing, & durability of rilparencel treatment *in vitro*
- Support a defensible MoA hypothesis



Injury Mediators

- Hyperglycemia
- Hyperlipidemia
- Hypoxia
- Proinflammatory cytokines
- Uremic toxins
- ROS

Dosing Models

- Single, repeated
- Concentrated
- Isolated factors

Stabilization or Resolution

- Improved stabilization or resolution with treatment
- Pathway-specific attenuation

ProKidney

In vitro functional assays measure common CKD pathway-relevant readouts

CKD Inducers & Drivers

Hyperglycemia | Hyperlipidemia | Hypoxia

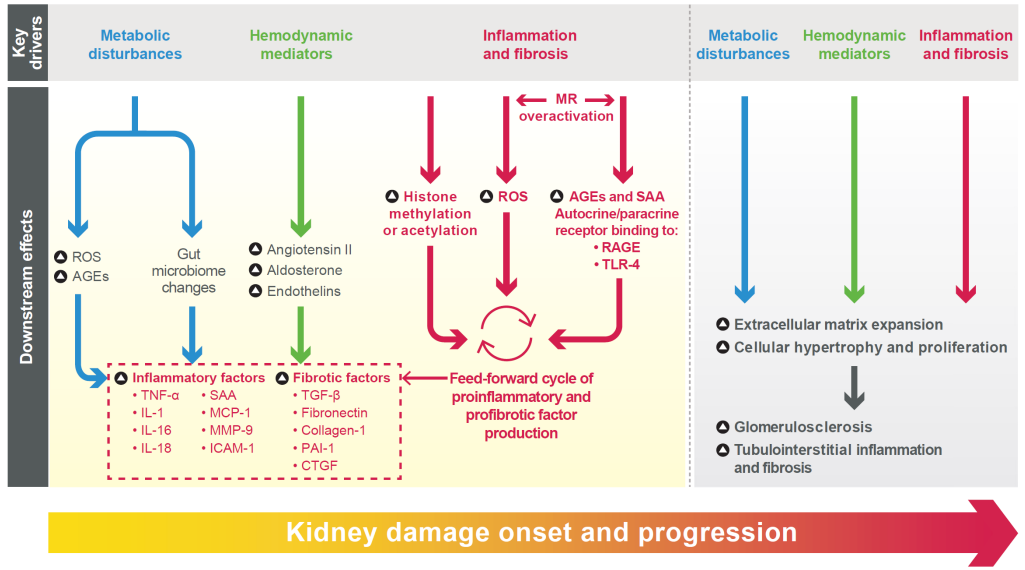
Common CKD Pathways

Oxidative stress | Metabolic dysregulation | Cell death

Inflammation | Fibrosis

Functional Assay Testing

Resolution of multiple orthogonal disease state-relevant assay readouts by rilparencel



Tuttle *et al.* Kidney International (2022)

Deconvolve how rilparencel may be able to preserve kidney function in patients with advanced CKD

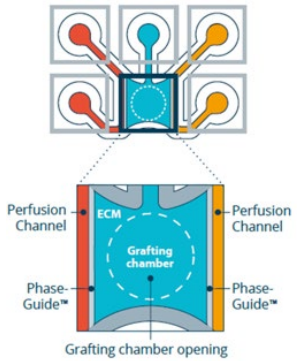
PROKIDNEY

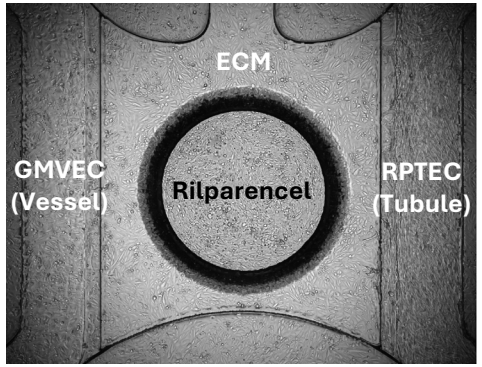
Rilparencel co-culture in injured kidney-on-chip experimental design

Key Considerations

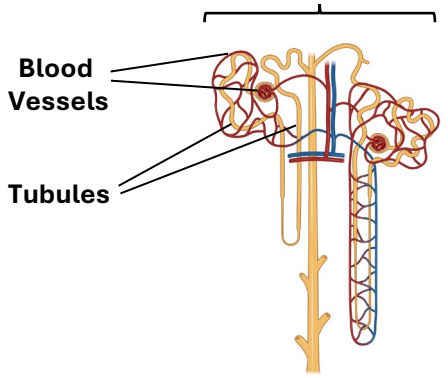
- Model captures endothelial : epithelial interface & crosstalk
- Rilparencel is administered directly on ECM in the grafting chamber
- Rilparencel is administered in continuous & ongoing **CKD-relevant injury** environment

Kidney-on-chip
(MIMETAS OrganoPlate)



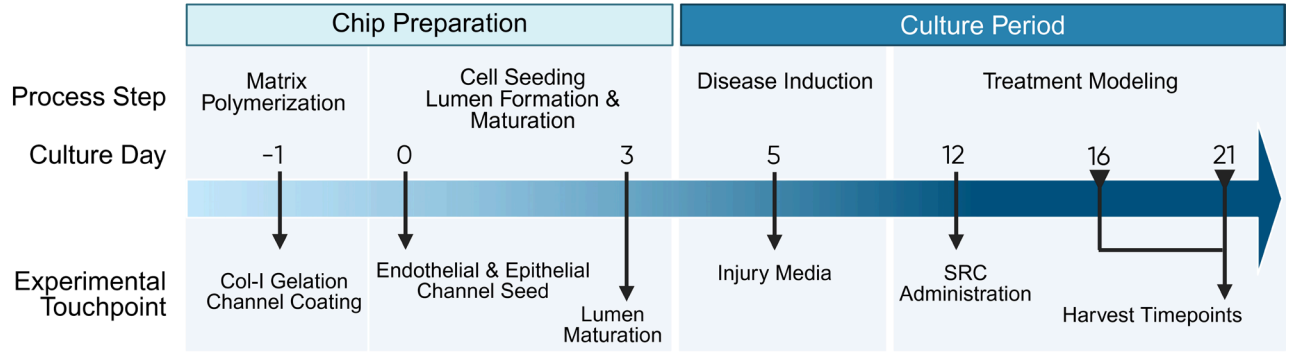


Nephron
(functional unit of kidney)



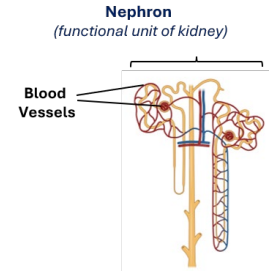
Injury media formulation (prepared in cell-specific basal media)

Injury Inducer	Components	Concentration
Glucose		4.5 g/L (25 mM)
CytoMix	IL-6, IL-1β, TNFα, MCP-1, CXCL8, TGF-β1	0.0325 - 2.5 ng/mL
LipidMix	arachidonic, linoleic, linolenic, myristic, oleic, palmitic, stearic acid, cholesterol	2 – 20 ng/mL
Uremic toxins	p-cresyl sulfate, indoxyl sulfate	10 µM

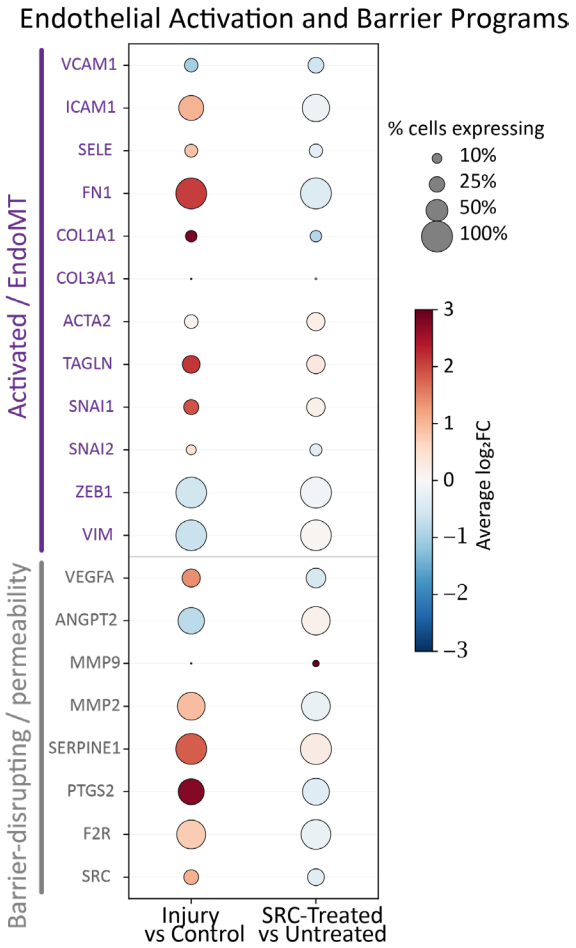


GMVEC = Glomerular Microvascular Endothelial Cells **ECM =** Extracellular Matrix **RPTEC =** Renal Proximal Tubule Epithelial Cells

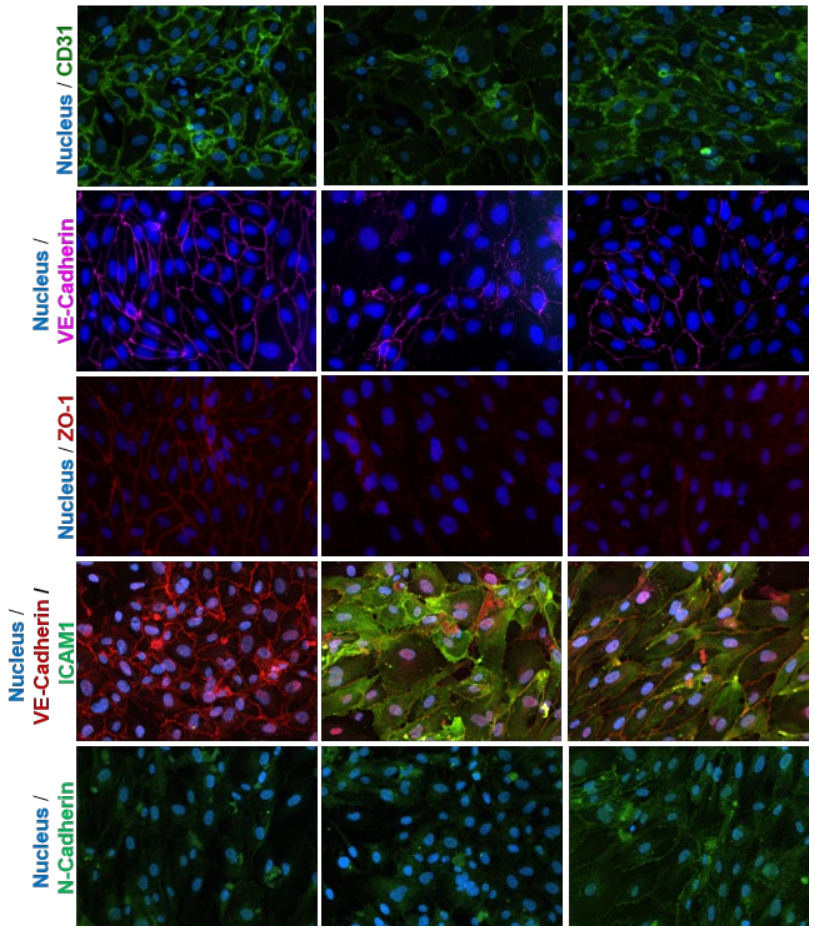
Rilparencel promotes endothelial junctional & barrier integrity

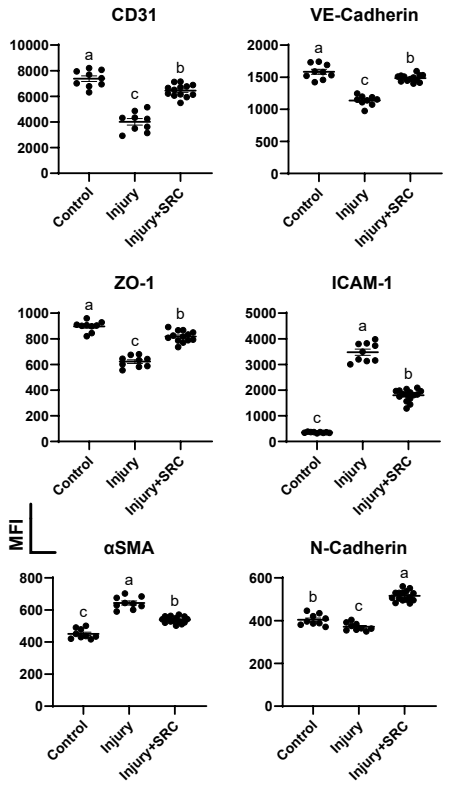


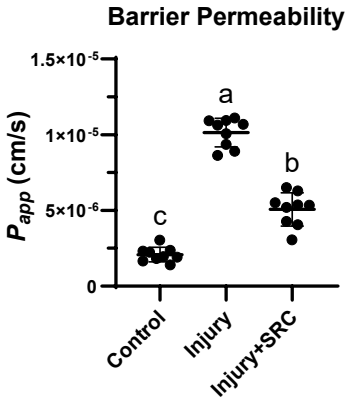
3D Mechanistic Discovery



3D & 2D Functional Validation







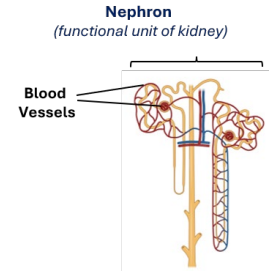
Dissimilar letters indicate $p<0.05$ via One-Way ANOVA
Mean ± SD; n=9 chips with n=3 donors

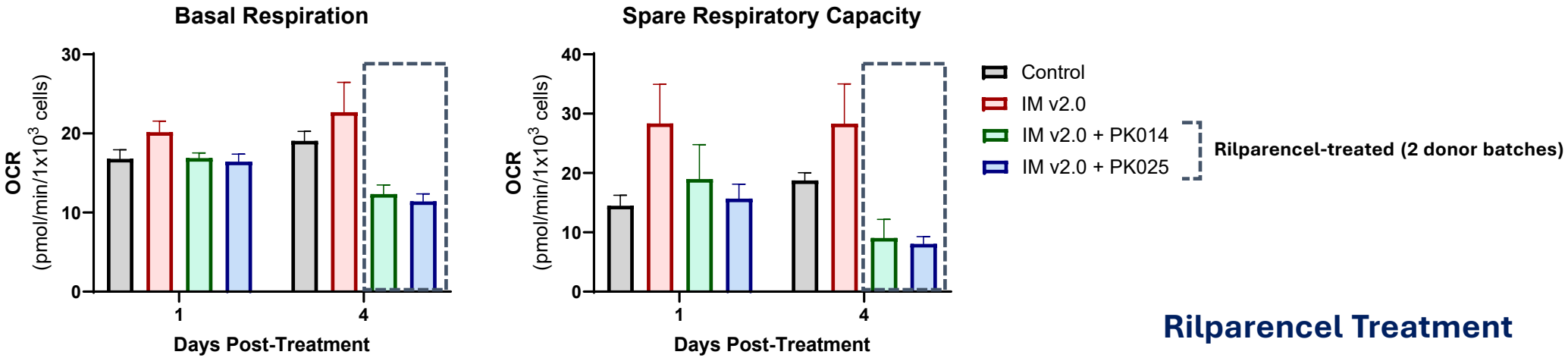
Key Findings

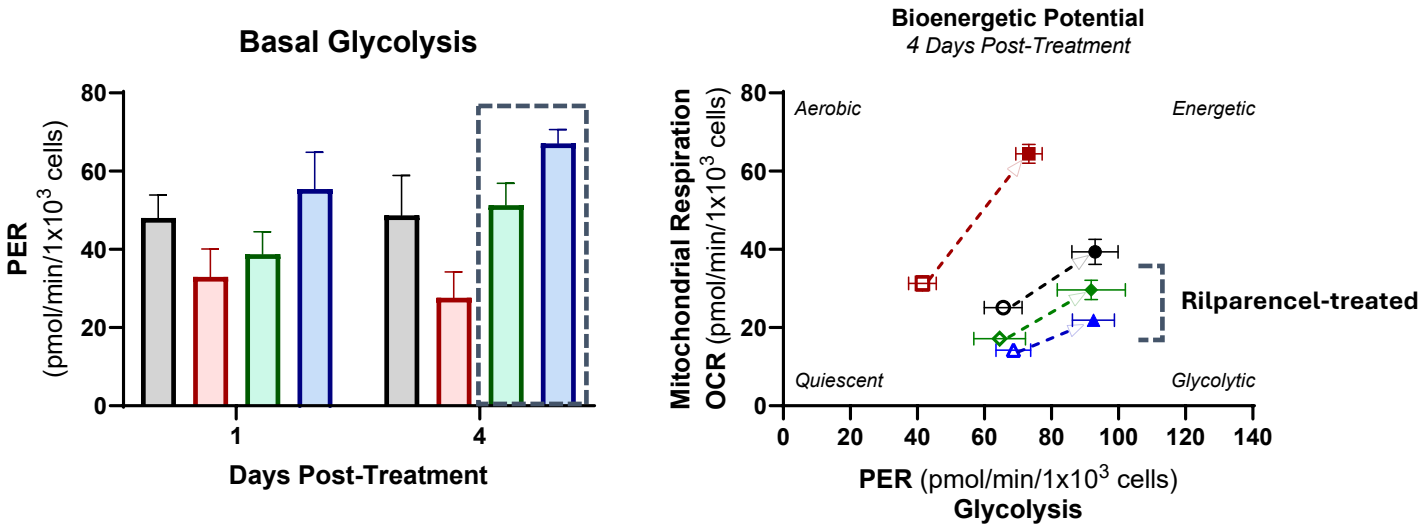
- Rilparencel improves injury-driven endothelial dysfunction at both the transcriptional & functional level

ProKidney

Rilparencel promotes native endothelial metabolic state







Rilparencel Treatment

- Promotes a more native endothelial metabolic state (quiescence) than control cells at later timepoints
- Strongly suggests pericyte-like endothelial cell metabolic reprogramming & stabilization

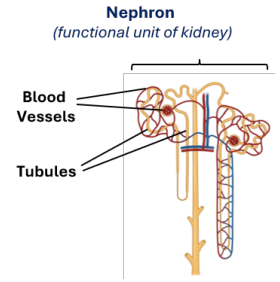
IM = Injury Media

OCR = Oxygen Consumption Rate

PER = Proton Efflux Rate

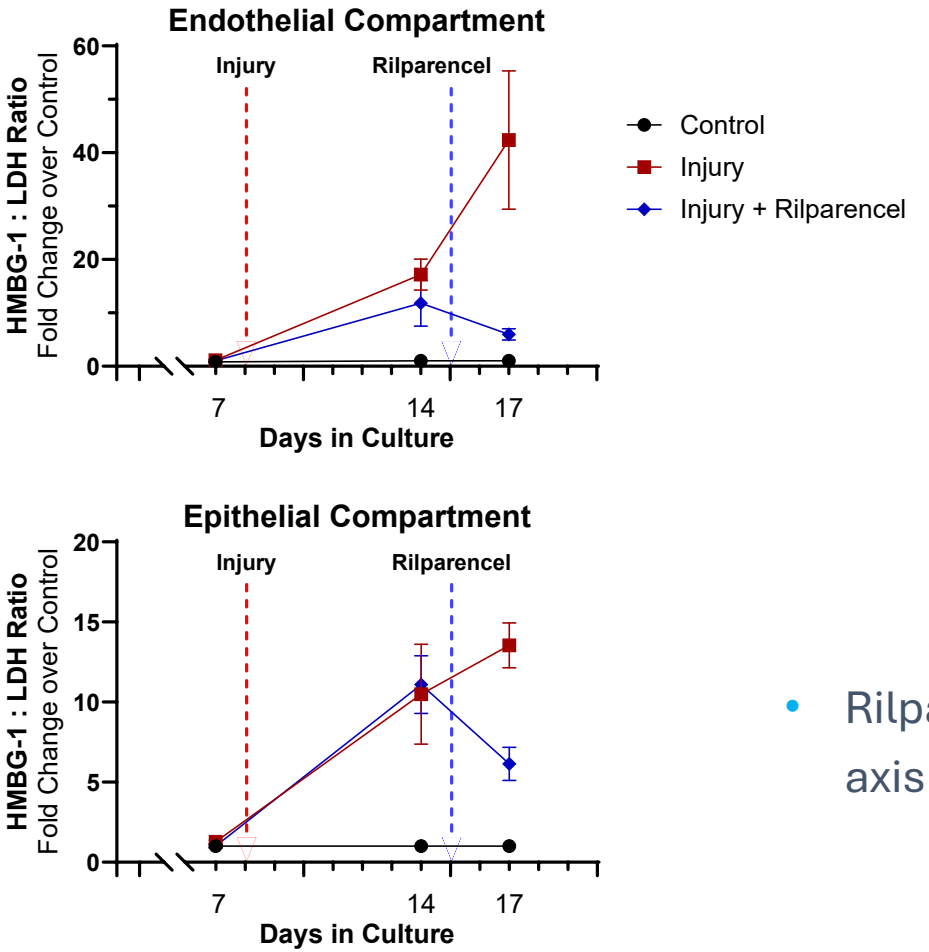
ProKidney

Rilparencel attenuates pro-inflammatory signaling & recruitment cues



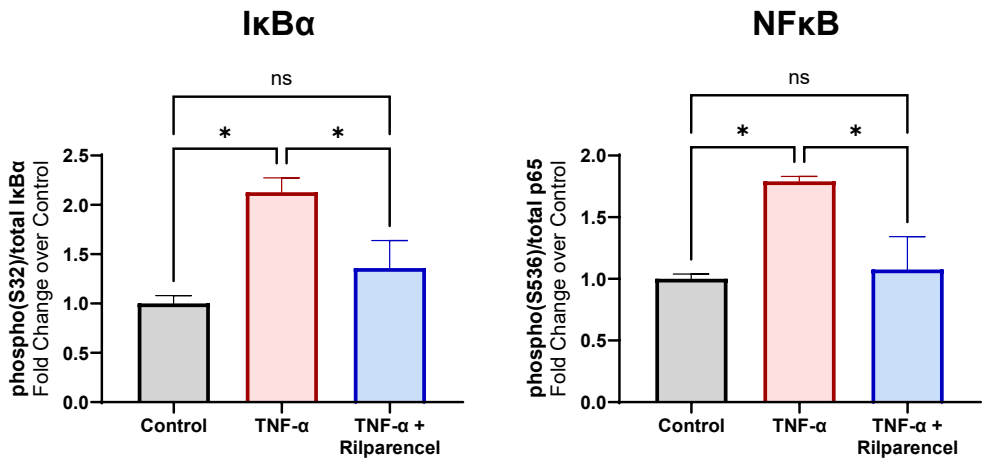
Kidney-on-chip 3D *in vitro* testing platform

(DAMP secretion assay)



2D *In vitro* testing platform

(ELISA)

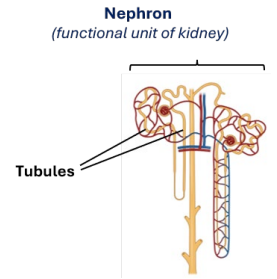


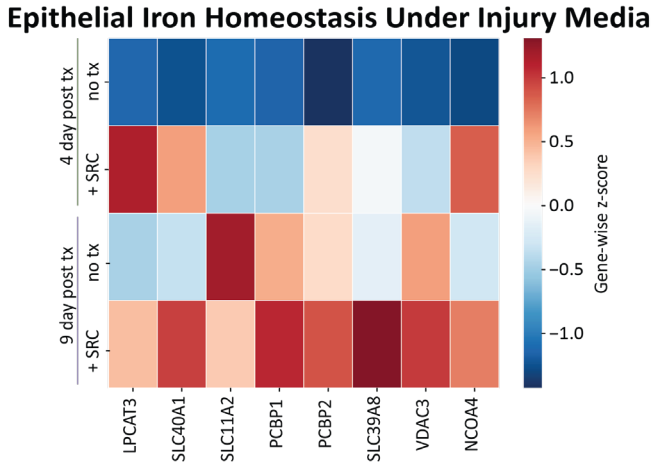
Epithelial cells, 3 days post-rilparencel treatment

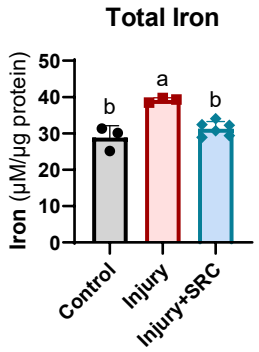
- Rilparencel treatment attenuates immunogenic & broad NF-κB axis signaling *in vitro* in a CKD-relevant stress environment

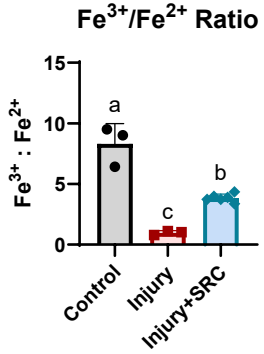
ProKidney

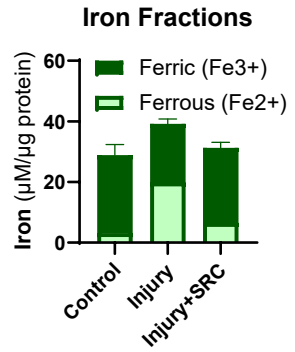
Rilparencel lowers reactive iron species & activates a cytoprotective lipid peroxidation repair program in injured renal epithelial cells

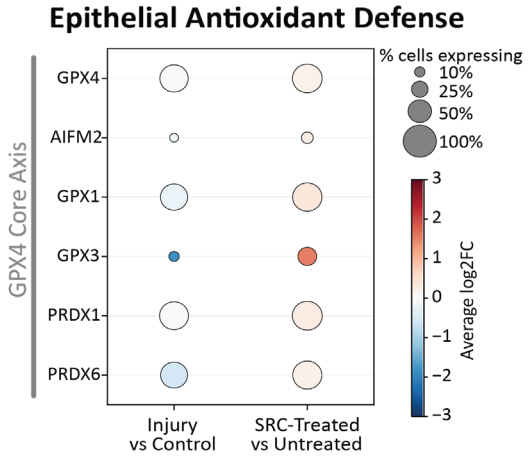










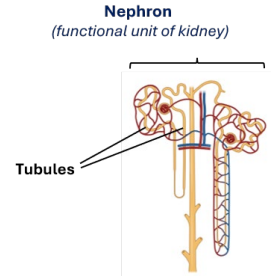


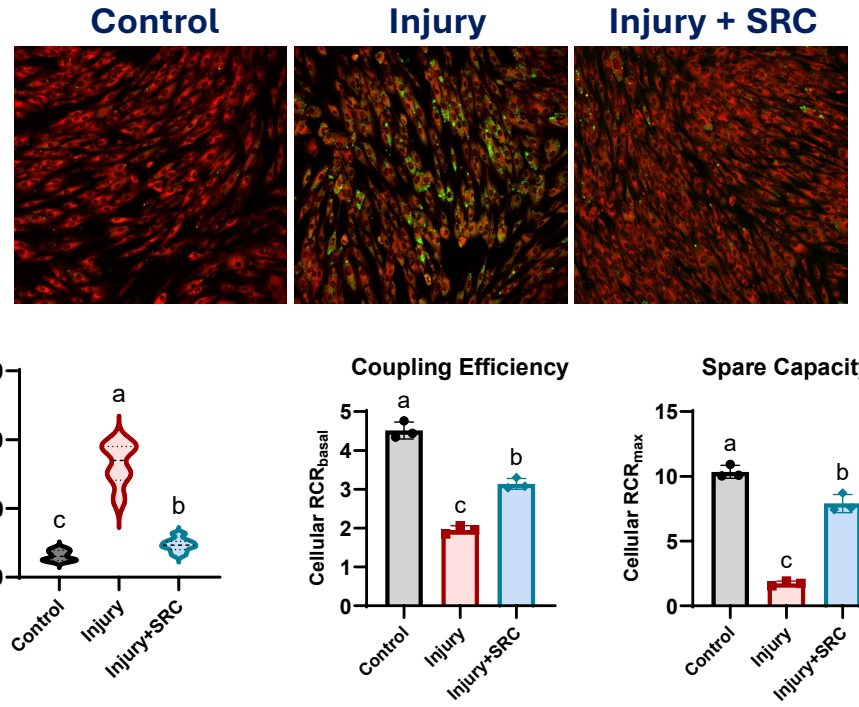
Key Findings

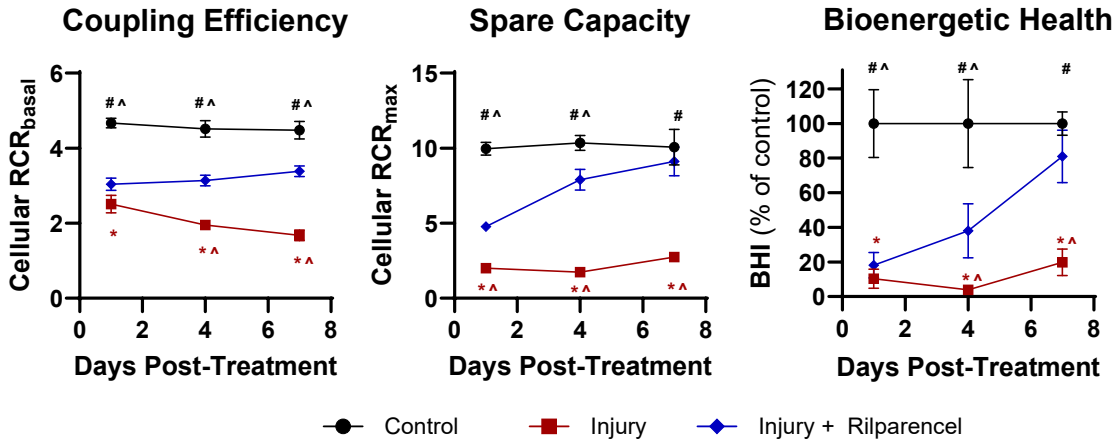
- Rilparencel administration limits the pool of reactive iron (Fe^{2+}) available to drive oxidative damage via the Fenton reaction
- Rilparencel administration transcriptionally activates a cytoprotective lipid peroxidation repair program in injured RPTEC

PROKIDNEY

Rilparencel rescues oxidative damage & mitochondrial dysfunction in continuously injured renal epithelial cells







Key Finding

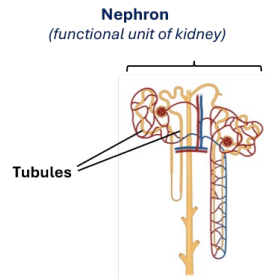
- Rilparencel can promote host cell stress-adaptive regulation that preserves proximal tubular epithelial cellular functions, alleviating injury-induced metabolic dysregulation

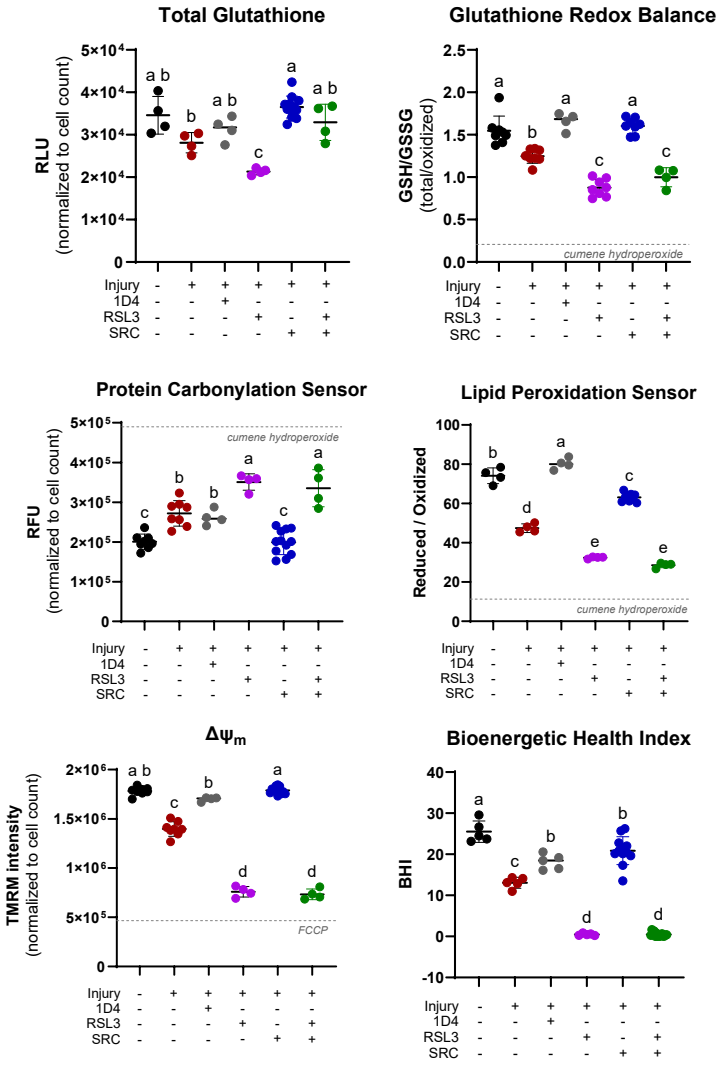
Rilparencel treatment:

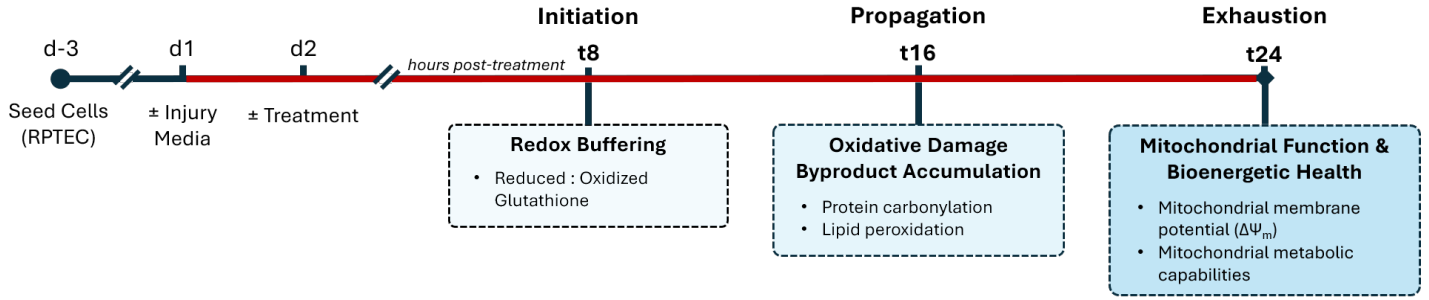
- Preserves mitochondrial coupling efficiency
- Expands & improves spare respiratory capacity
- Progressively improves overall bioenergetic health

ProKidney

GPX4 activity is required for rilparencel-mediated rescue of oxidative damage & mitochondrial dysfunction in epithelial cells







Key Findings

- Rilparencel-mediated lipid peroxidation detoxification serves as an essential component for RPTEC mitochondrial stabilization, restricting active oxidative damage & supporting adaptive cell survival
- Parallel pharmacological studies confirm these cytoprotective effects are not exclusively mediated through GPX4 activity, supporting that rilparencel operates via complex, multimodal & multifactorial mechanisms of action

1D4 = GPX4 activator

RSL3 = GPX4 inhibitor

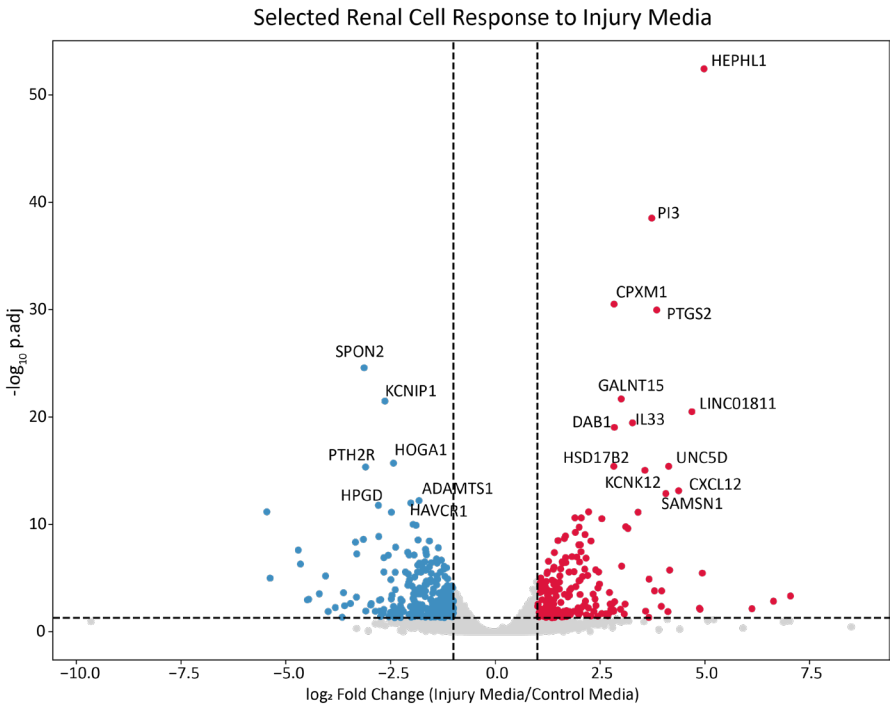
$\Delta\psi_m$ = Mitochondrial Membrane Potential

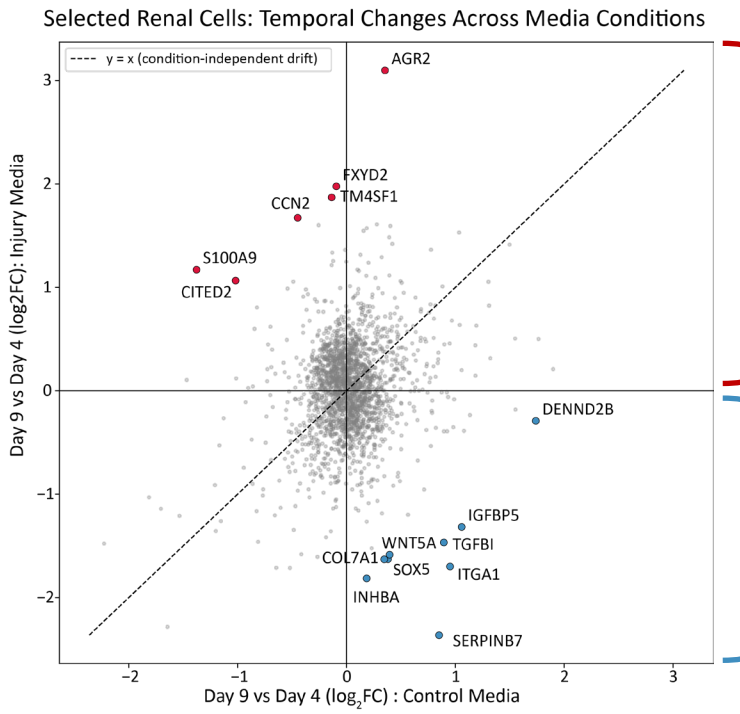
PROKIDNEY

Factors expressed by rilparencel with potential mechanistic relevance

Upregulation of chemotactic, cytoprotective, & stress-adaptation factors

Downregulation of baseline prostaglandin catabolism, amino acid metabolism, & steady-state matrix/receptor pathways





Increased expression of protective paracrine & microenvironmental regulators

Decreased expression of pro-fibrotic & growth factor signaling ligands

Key Findings

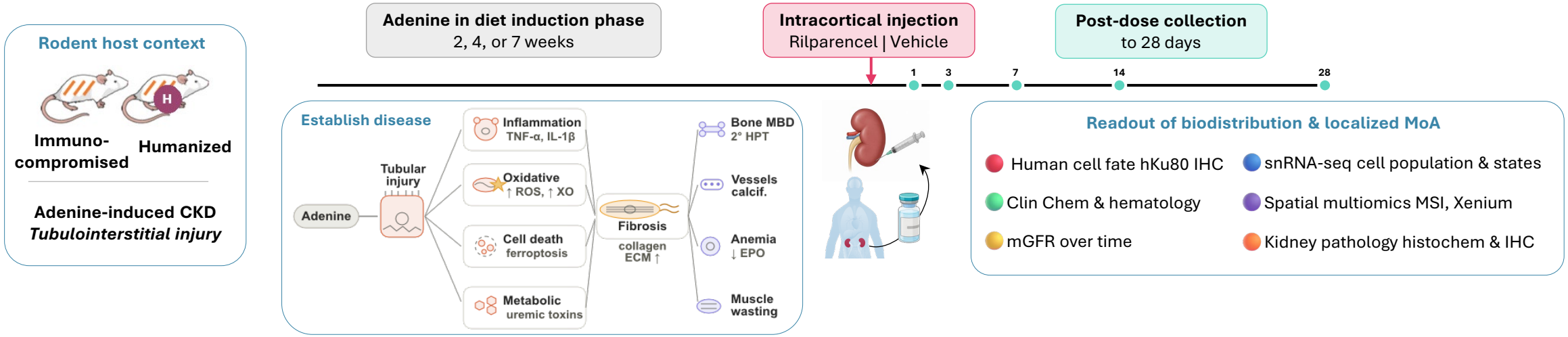
- High-dimensional transcriptomics allow us to map global gene expression changes in rilparencel within a human injury context, **uncovering what intrinsic factors may be critical for MoA**
  - Rilparencel upregulates a network of acute cytoprotective & chemotactic pathways, while progressively increasing the expression of chronic tissue repair support factors as the injury model advances
- These data will inform future gene editing of identified DEGs to determine whether they are active or passive **drivers of potency**

DEG = Differentially Expressed Gene

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)



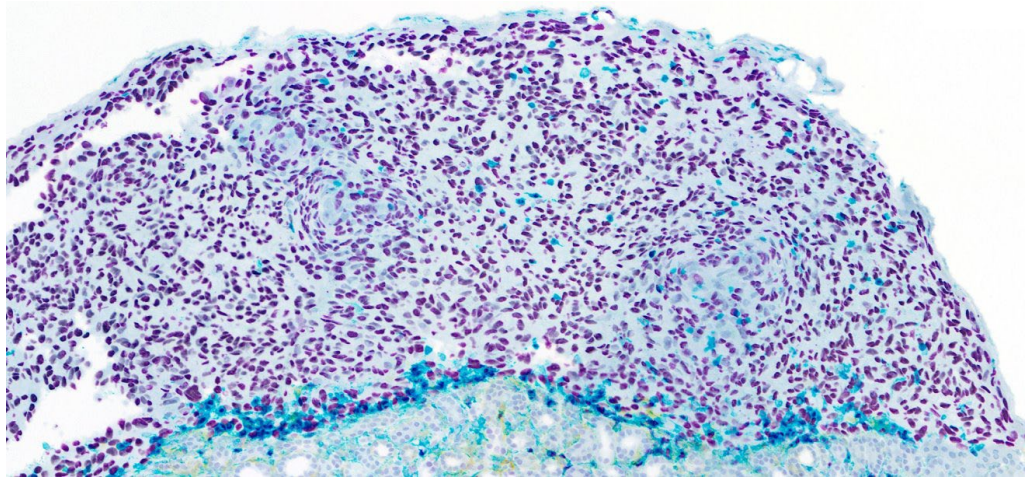
- Adenine feeding in immunocompromised / humanized rodent models demonstrated reliable kidney injury
  - **Rat models tested:** RNU, SRG; **Mouse models:** NSG-IL15 ± cord blood $CD34^{+}$ humanization
- Vehicle controls were similarly injected intracortically with the excipient of rilparencel without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

PROKIDNEY

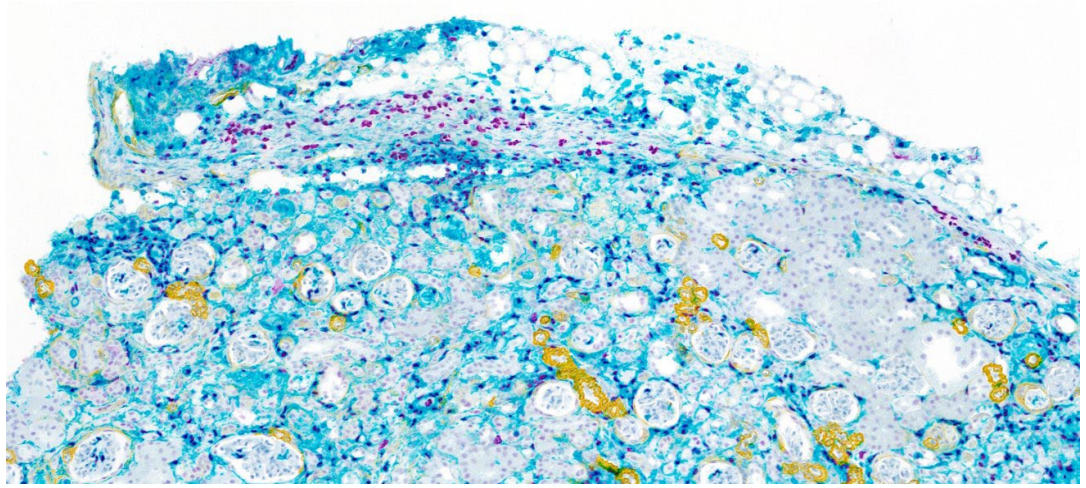
Rilparencel distributes to subcapsular & intraparenchymal renal compartments, partially persists through Day 28

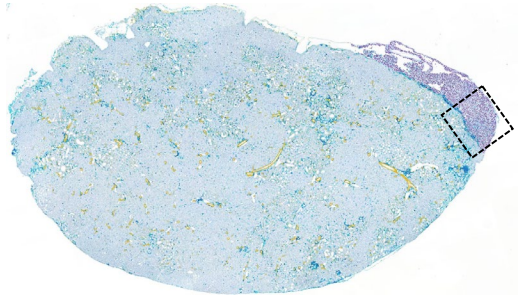
Humanized NSG-IL15 mice fed adenine

1-day post-dose

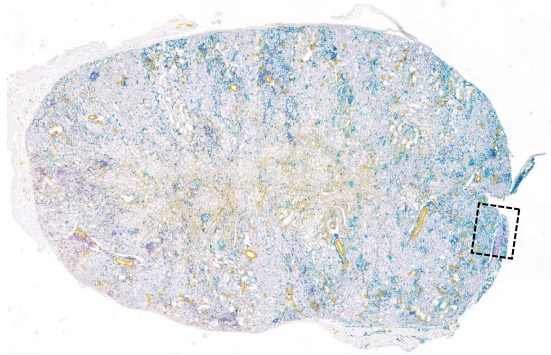


28 days post-dose

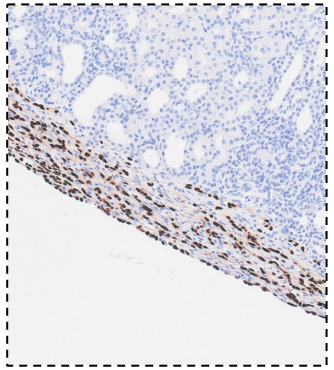




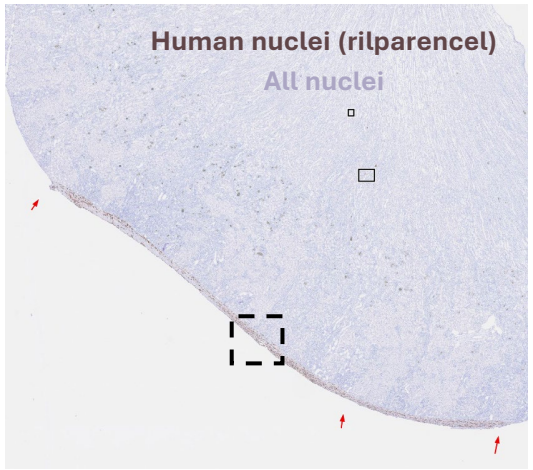
hKu80+ hmCD45- = **Rilparencel**
hKu80+ hmCD45+ = **Human immune cells**
hKu80- hmCD45+ = **Mouse immune cells**
Vascular smooth muscle cells / Myofibroblasts (αSMA)



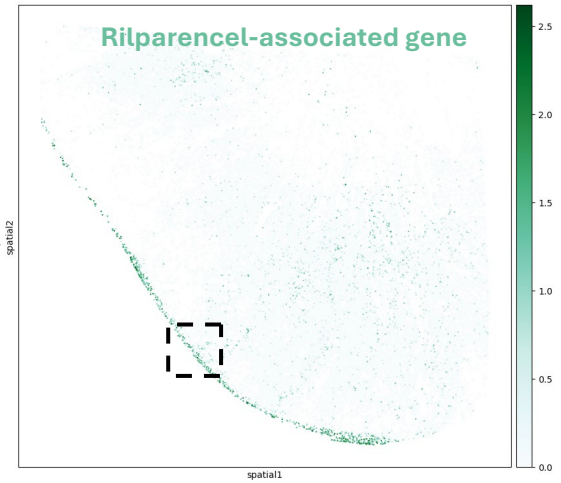
Aligning multiomic analytical modalities after rilparencel injection



IHC



Spatial transcriptomics



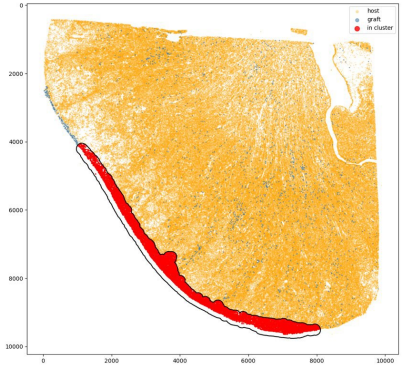
Single nuclei RNA-seq

Mass Spec Imaging (MSI)

PROKIDNEY

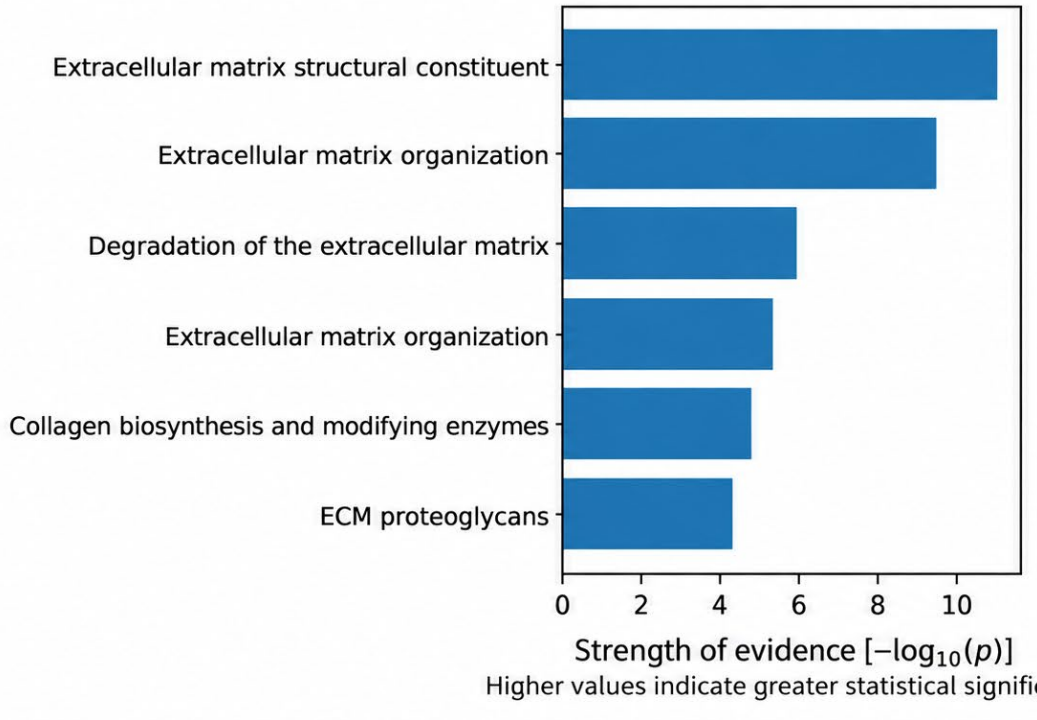
Graft-associated cells have a distinct transcriptional signature in injected rats

- 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

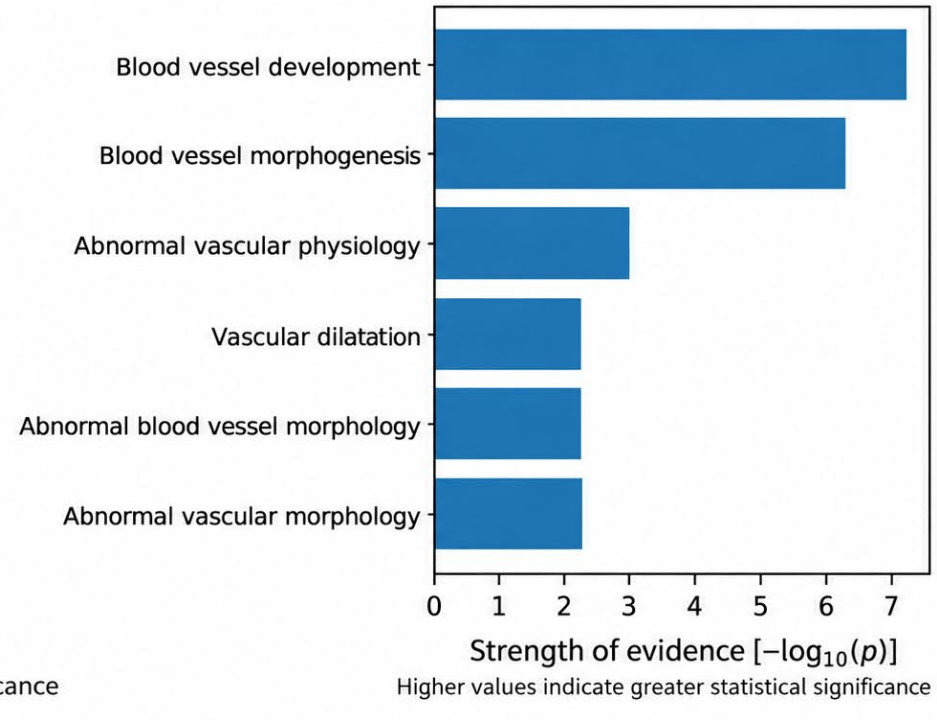


Rilparencel graft-associated gene signature

ECM remodeling

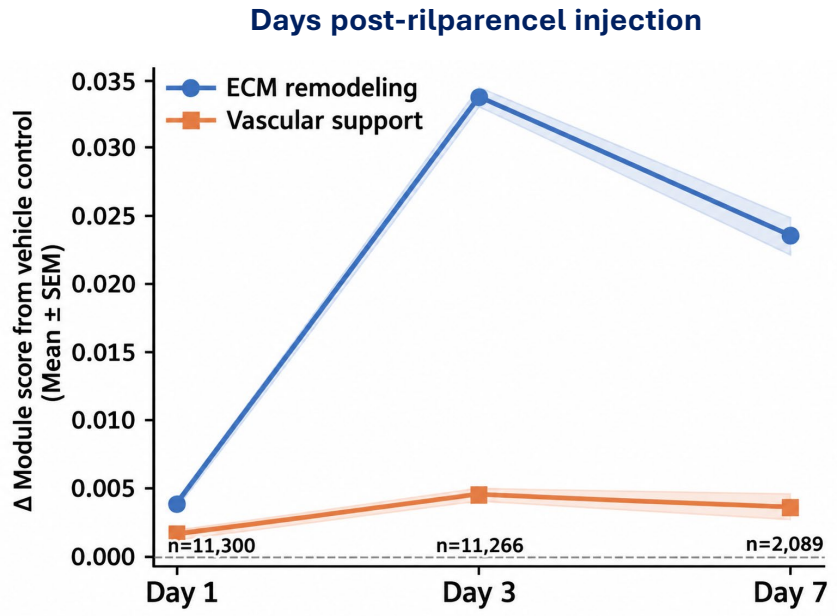


Vascular development & support

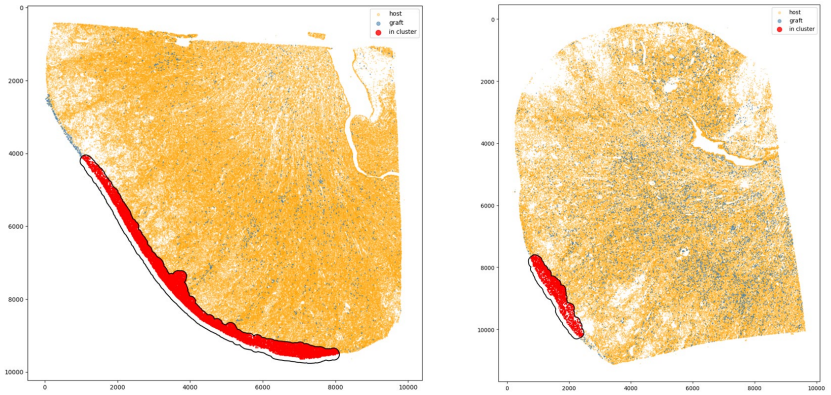


PROKIDNEY

Transcriptional signature of graft-associated cells evolves over time



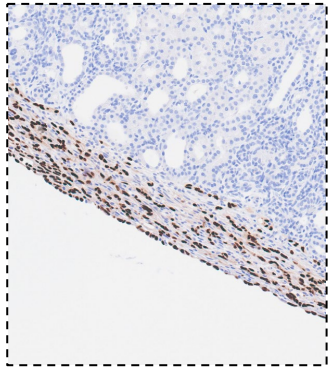
Rilparencel graft-associated gene signature



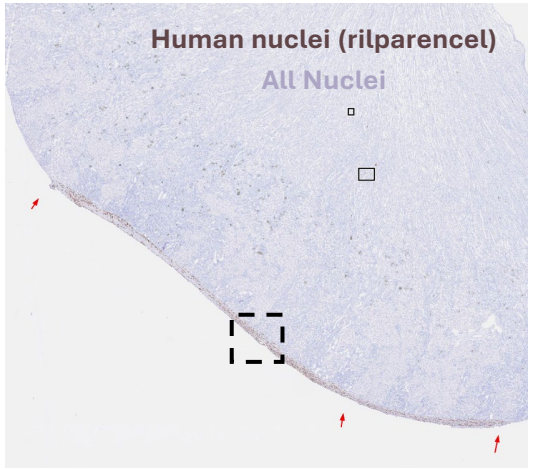
- The injured kidney's response to rilparencel is dynamic & evolves over time
- An initial higher upregulation in **ECM remodeling** gene expression drops over the first week after treatment but is maintained well above baseline
- Accompanying this matrix remodeling signal, population enrichment of **vascular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

PROKIDNEY

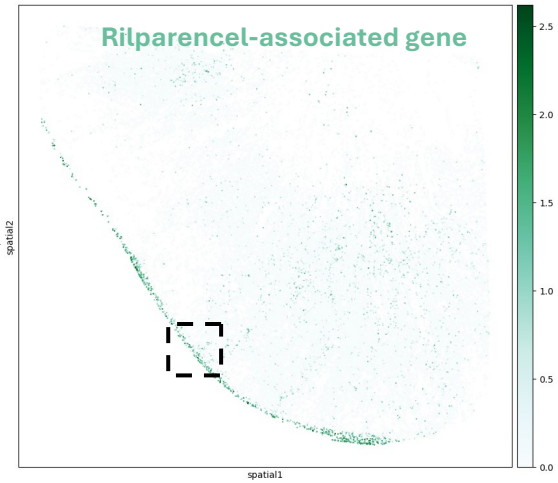
Aligning multiomic analytical modalities after rilparencel injection



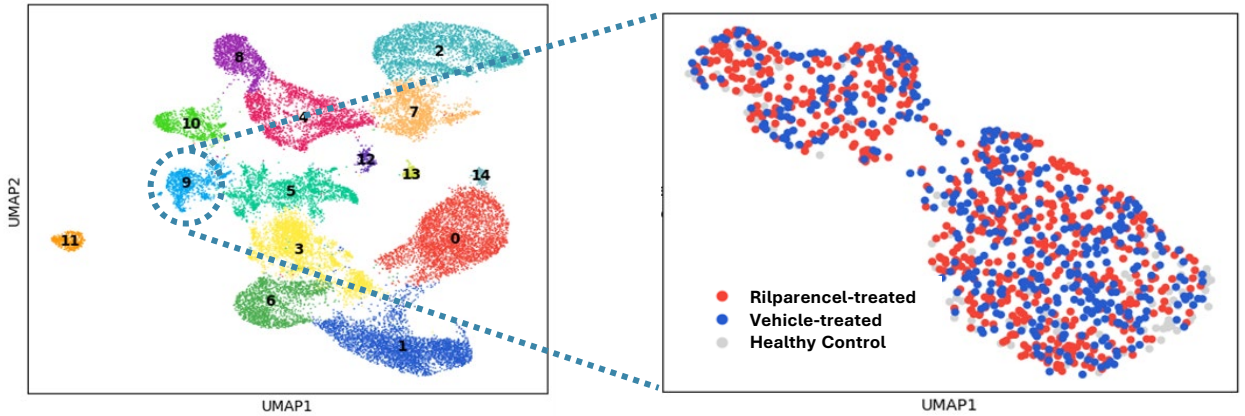
IHC



Spatial transcriptomics



Single nuclei RNA-seq

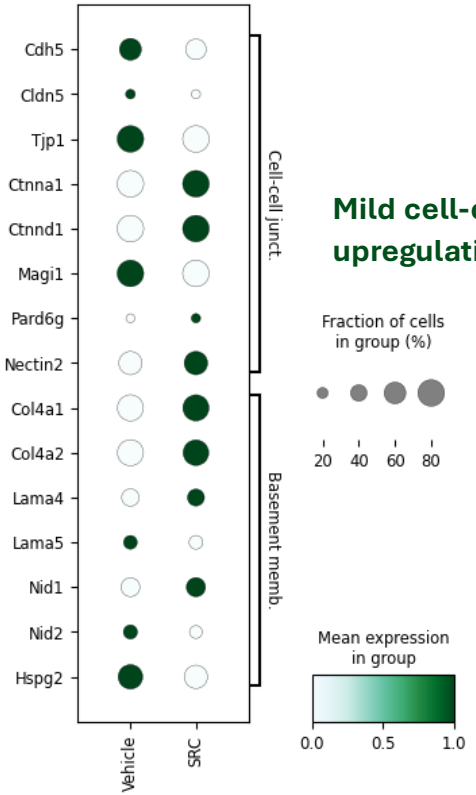


Mass Spec Imaging (MSI)

PROKIDNEY

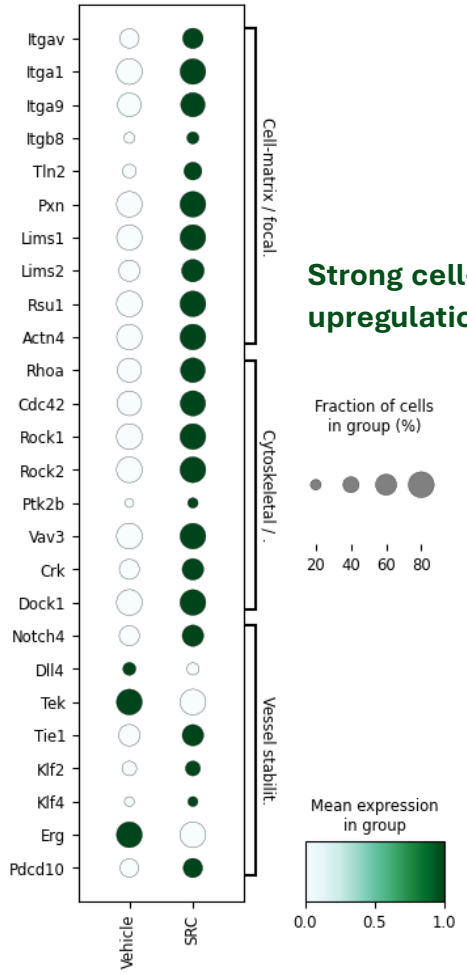
Cell junction & ECM adhesion signaling is upregulated in rat kidney endothelial cells

Endothelial junction & ECM programs



Mild cell-cell upregulation

Endothelial adhesion & stability programs

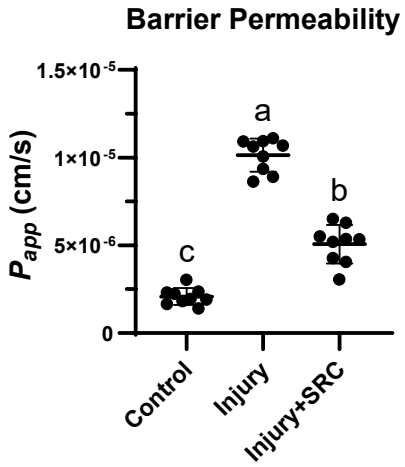


Strong cell-ECM upregulation

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

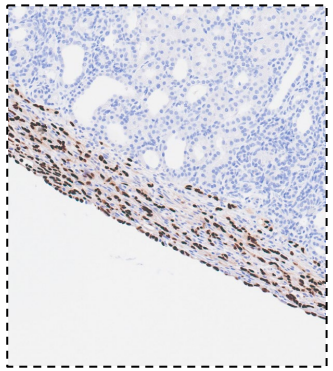
In Vitro Endothelial Cell Injury Rescue Model

- **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

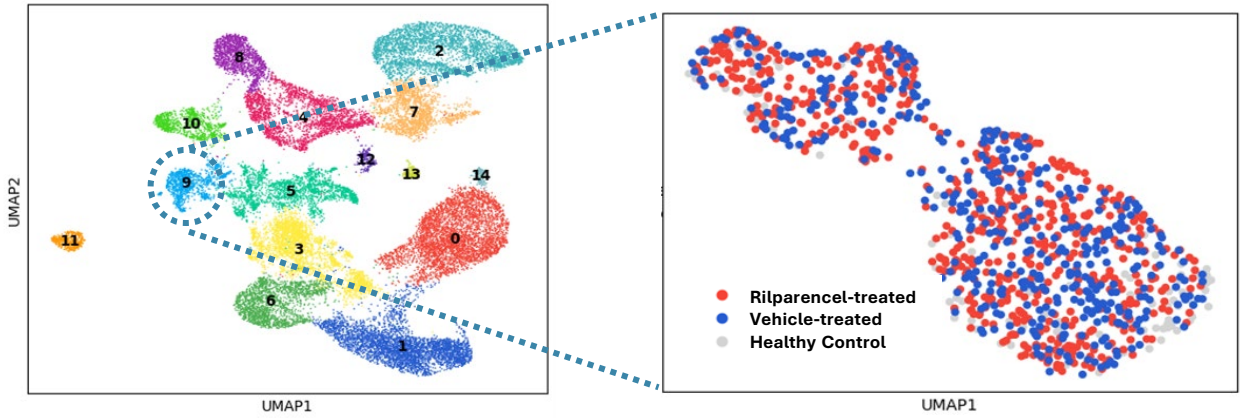


ProKidney

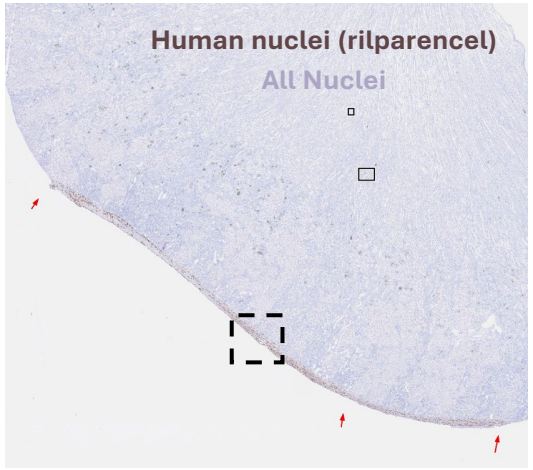
Aligning multiomic analytical modalities after rilparencel injection



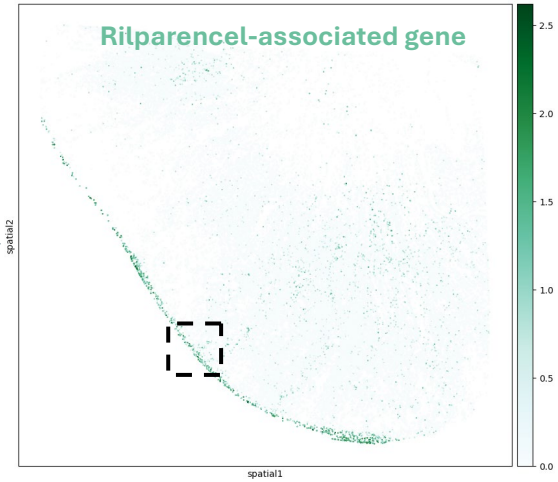
Single nuclei RNA-seq



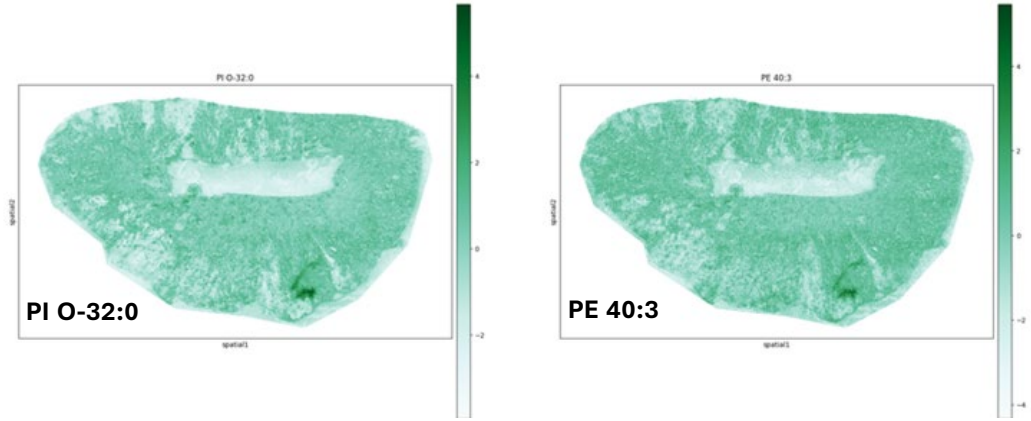
IHC



Spatial Transcriptomics



Mass spec imaging (MSI)

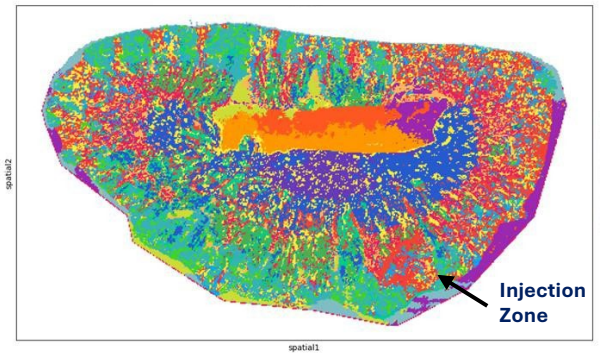


PROKIDNEY

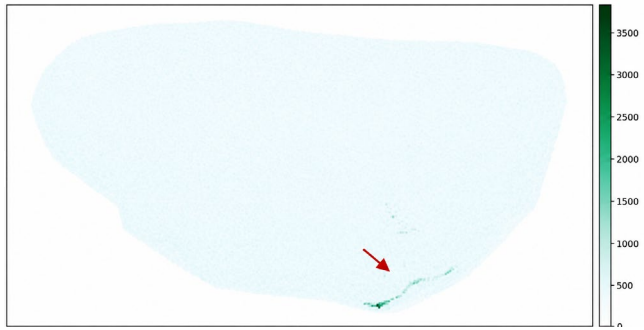
MSI reveals a distinct tissue remodeling signature at the rilparencel injection site

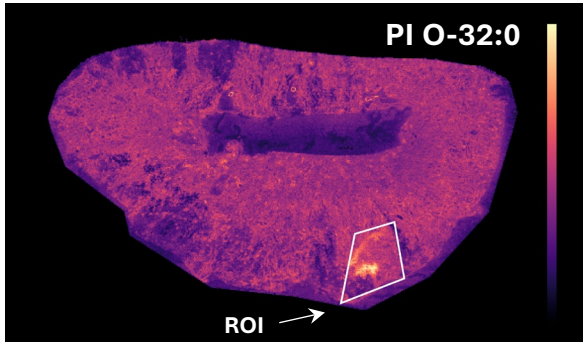
- MSI spatially resolved protein & lipid biomarkers within an injection-defined ROI encompassing the hKu80-associated rilparencel injection site at **day 3 post-injection**
- ROI showed enrichment of markers associated with immune responses, **stromal / perivascular remodeling** (↑ PDGFR-β, Vimentin), 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**

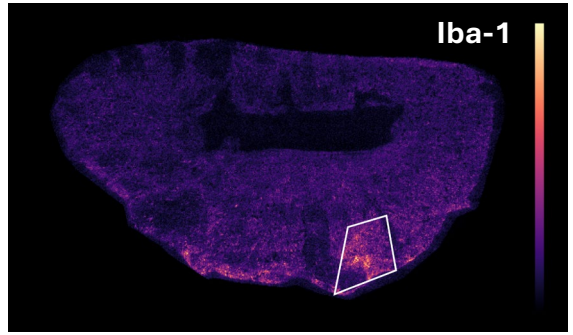
Signature domains



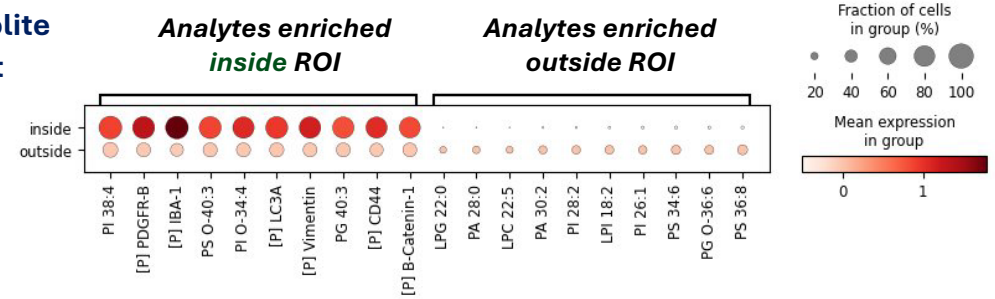
hKu80 (rilparencel)



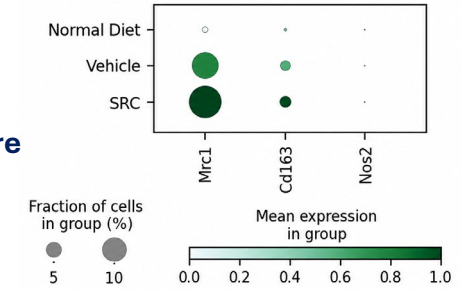




Differential lipid metabolite & protein enrichment
(MSI)



Scavenging & tissue repair & remodeling M2 macrophage signature
(snRNA-seq)



ROI = Region of Interest

PROKIDNEY

Translational studies suggest multifactorial MoA for rilparencel

Rilparencel

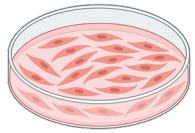


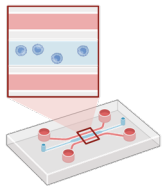
Transcriptomic analyses of REGEN-007 pre-formulation cell retains & patient biopsies, using the KPMP database (ASN poster SA-PO0014):

- **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





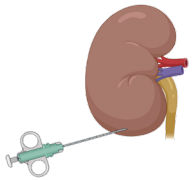
Kidney-on-chip

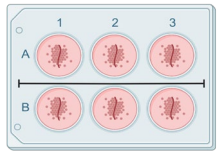
Human proximal tubule epithelial cell & glomerular vascular endothelial cell models of metabolic & inflammatory stress cultured with rilparencel showed (ASN poster TH-PO1128):

- **Lowered oxidative damage**
- **Improved redox balance & mitochondrial fitness**
- **Reduced pro-inflammatory signaling**
- **Improved barrier integrity**

Ex vivo

Kidney biopsy explant culture





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

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

In vivo (rodent)

Rodent models of CKD

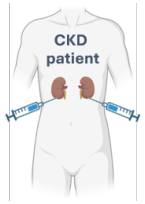


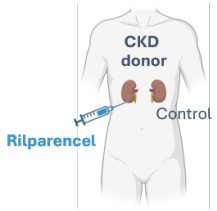
Whole-kidney multi-omics following rilparencel injection show signatures of (ASN talk FR-OR044):

- **Preserved vascular integrity & ECM remodeling**
- **Improved lipid & glucose metabolic programs**
- **Reduced pro-inflammatory signaling**

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**

How rilparencel may be able to preserve kidney function in patients with advanced CKD

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

ProKidney Publications

The Quest to Save Kidneys, Hearts, and Lives
Mechanisms Matter

Katherine R. Tuttle, MD, FASN, FACP, FNKF
Executive Director for Research
Providence Inland Northwest Health

Professor of Medicine
Nephrology Division and Kidney Research Institute
University of Washington School of Medicine

UNIVERSITY of WASHINGTON

Providence

In the spirit of honoring the composition of place, I acknowledge that I live and work on the homelands of the Spokane, Palouse, Nez Perce, Coeur d'Alene, and Kootenai Tribal People.

I am grateful to be on this land and ask for its support as we work to create an equitable, diverse, and inclusive community.

DIABETIC KIDNEY DISEASE COLLABORATIVE

CKD Is A Global Public Health Crisis

Worldwide

Extremely common

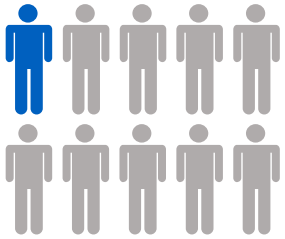
850 MILLION

2017-2023

Increasing death rate

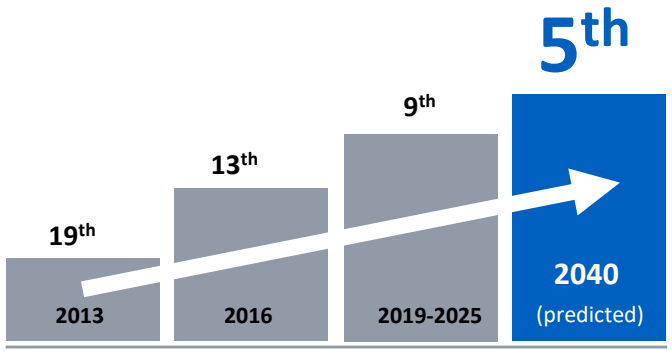
41.5%

from 1990 to 2017



1 in 10

people in the general population have CKD



Rank in cause of death

Western Europe

USA

44 MILLION

40 MILLION

and caused

in 2023

144,000

147,000

deaths

in 2023

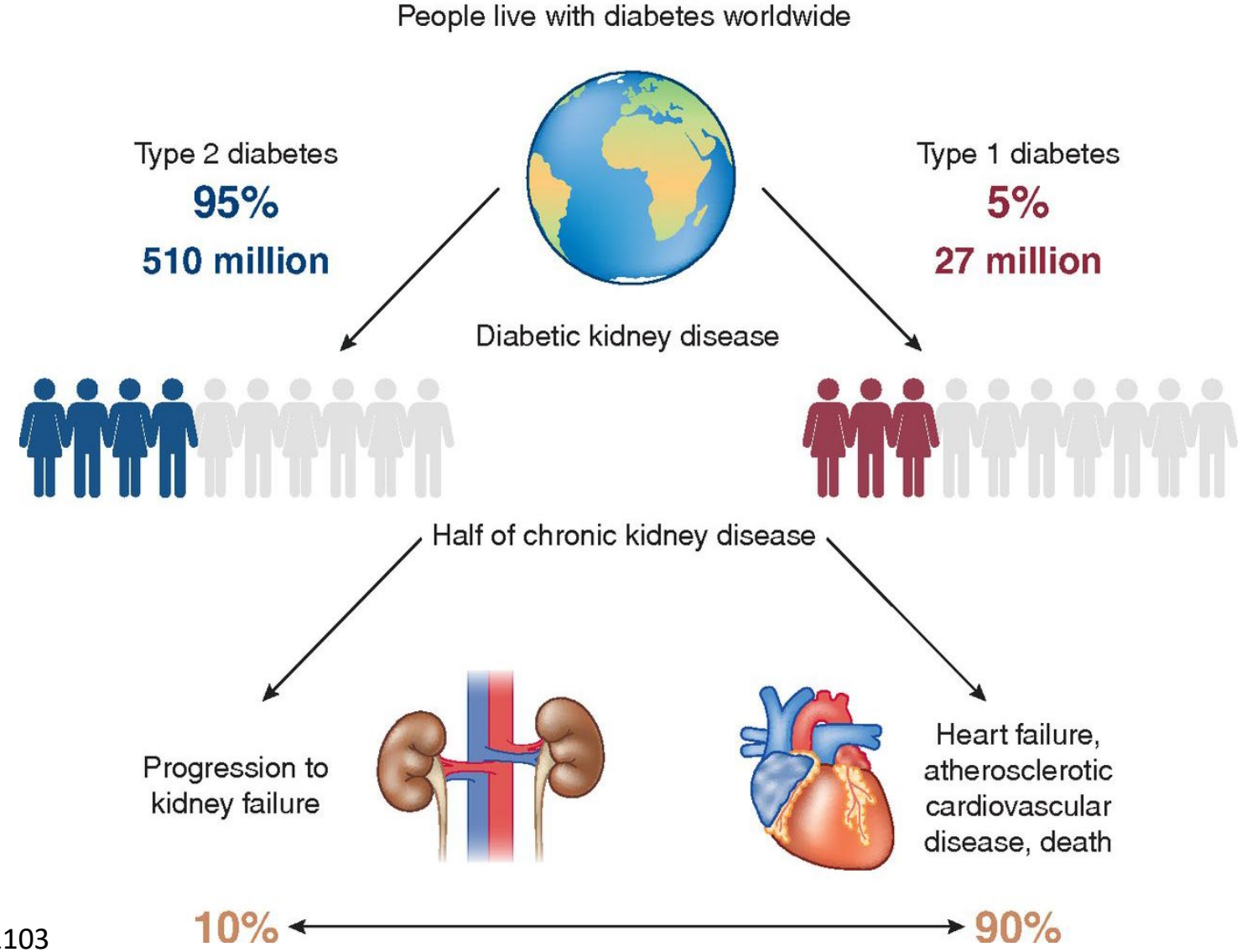
Kovesdy CP. *Kidney Int Suppl* 2022;12:7–11

Global Burden of Disease, Chronic Kidney Disease Collaboration. *Lancet* 2025;406:2461-2482

Global Burden of Disease, Causes of Death Collaborators. *Lancet* 2024;403:2100-2132

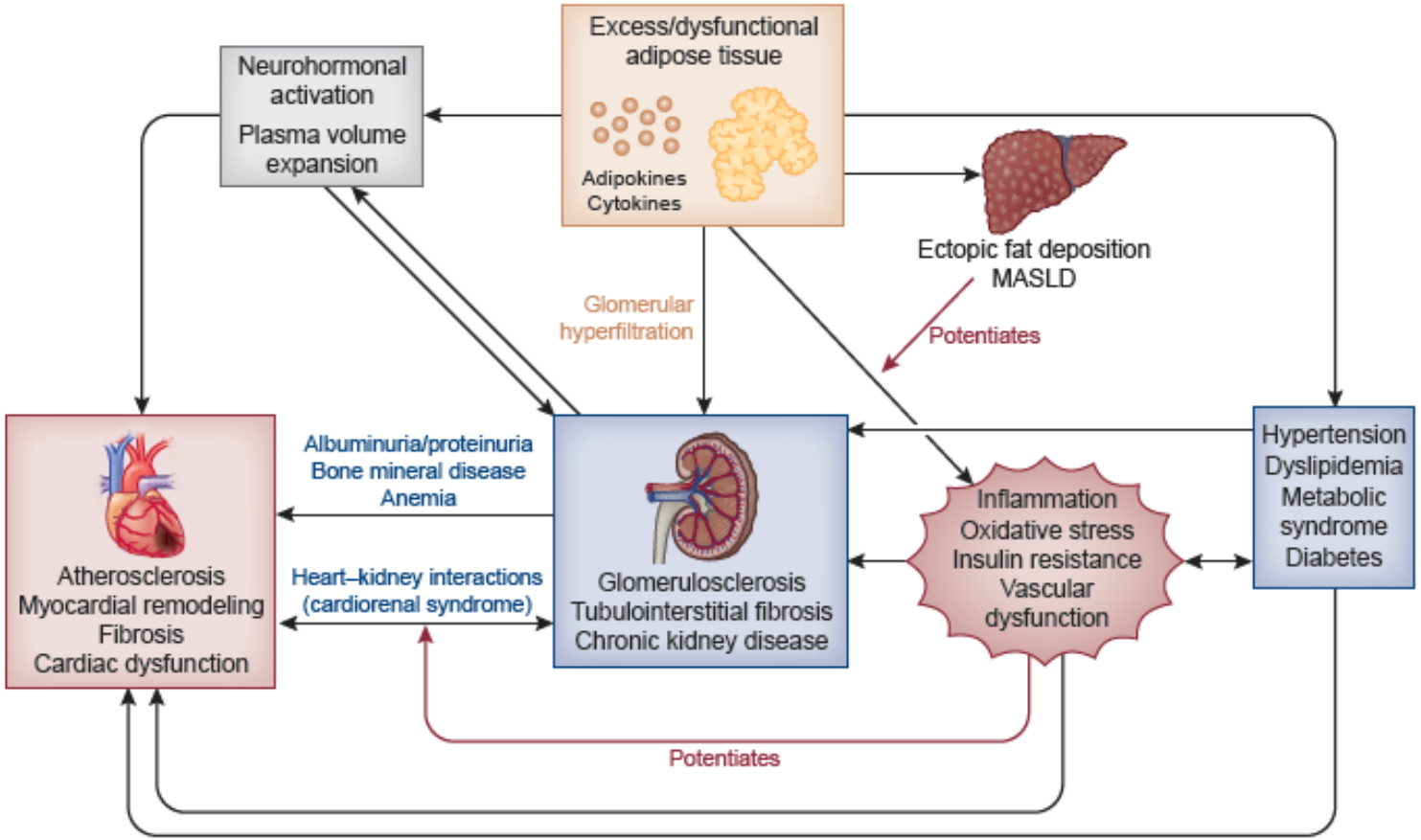
What Problem are We Trying to Solve?

589 million 2024 and 850 million 2050



Tuttle KR *et al. CJASN* 2022;17:1092-1103
International Diabetes Federation Atlas 11th edition, 2025

Cardiovascular-Kidney-Metabolic Syndrome
Kidney in the Middle



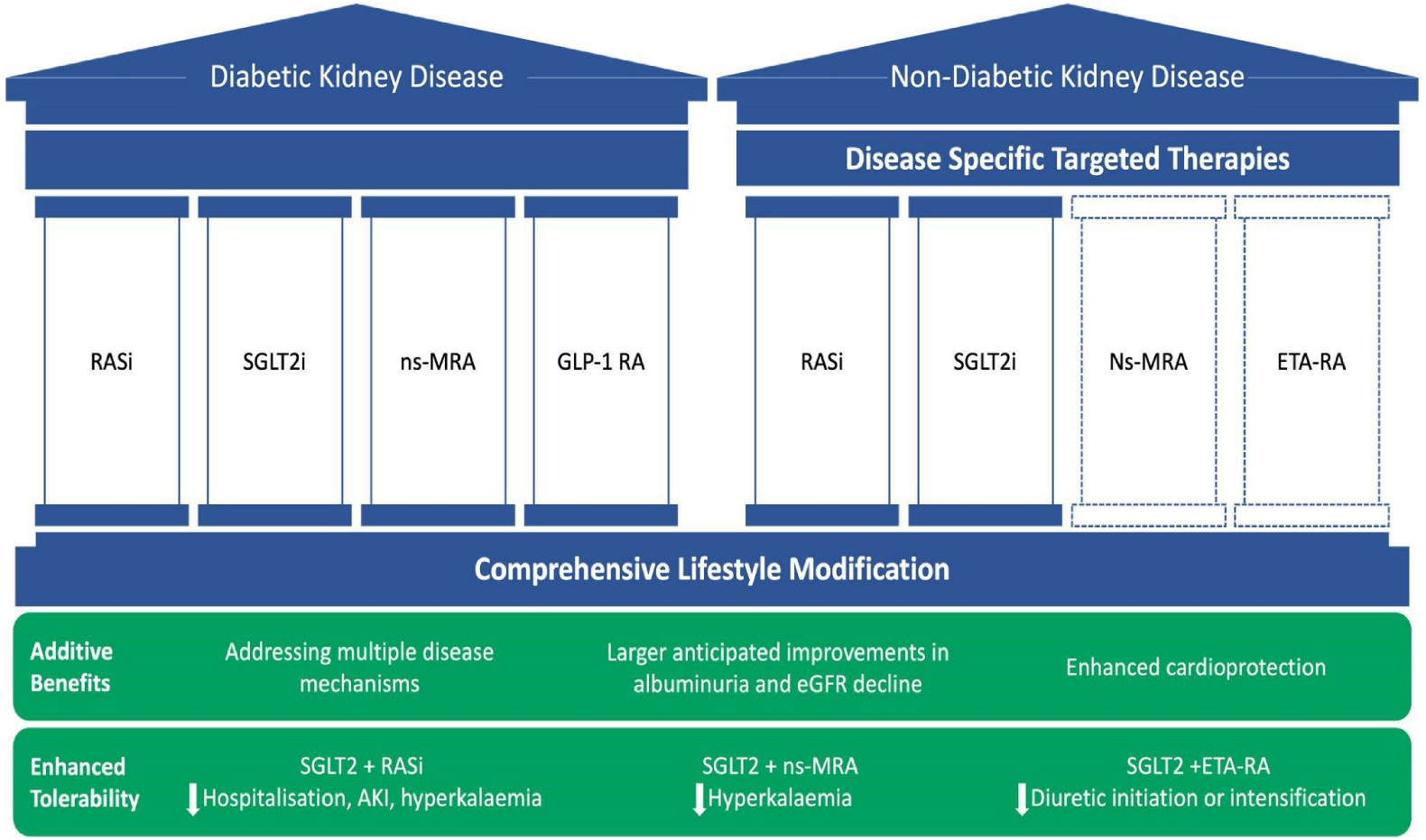
Tuttle KR *et al. Clin J Am Soc Nephrol* 2026; online ahead of print
Ndumele CE *et al. Circulation* 2023; 148:1636-1664

GOAL: MITIGATE HIGH KIDNEY & CARDIOVASCULAR RISK

	Urine albumin to creatinine ratio, mg/g					Urine albumin to creatinine ratio, mg/g				
	<10	10-29	30-299	300-999	≥1000	<10	10-29	30-299	300-999	≥1000
eGFR, mL/min/1.73 m^2 using creatinine alone	Cardiovascular mortality: 76 cohorts 26 022 346 participants; 776 441 events					Stroke: 68 cohorts 24 746 436 participants; 461 785 events				
≥105	1.4	2.0	3.0	4.1	5.4	1.2	1.6	2.2	3.1	4.3
90-104	Reference	1.3	1.9	2.7	3.6	Reference	1.3	1.6	2.4	3.1
60-89	1.0	1.4	1.7	2.4	3.2	1.1	1.3	1.7	2.2	3.0
45-59	1.4	1.7	2.2	2.8	3.8	1.4	1.6	1.9	2.3	2.9
30-44	2.0	2.3	2.8	3.7	4.6	1.6	1.7	2.0	2.4	3.0
15-29	3.2	3.1	3.5	5.0	6.5	1.8	2.1	2.1	2.7	3.0
<15	6.1	6.4	6.4	7.3	8.2	3.2	2.8	2.9	3.2	3.8
eGFR, mL/min/1.73 m^2 using creatinine alone	Kidney failure with replacement therapy: 57 cohorts 25 466 956 participants; 158 846 events					Heart failure: 61 cohorts 24 603 016 participants; 1 132 443 events				
≥105	0.5	1.2	2.9	7.7	25	1.2	1.7	2.7	4.2	6.9
90-104	Reference	1.8	4.3	12	43	Reference	1.3	2.0	2.8	4.2
60-89	2.3	4.9	10	27	85	1.1	1.4	1.9	2.7	4.2
45-59	13	19	37	89	236	1.6	1.8	2.4	3.4	5.0
30-44	50	58	115	240	463	2.2	2.5	3.1	4.2	6.5
15-29	283	301	443	796	1253	3.6	3.5	4.1	5.8	8.1
<15	770	1040	1618	2297	2547	5.1	5.7	5.8	7.9	9.9

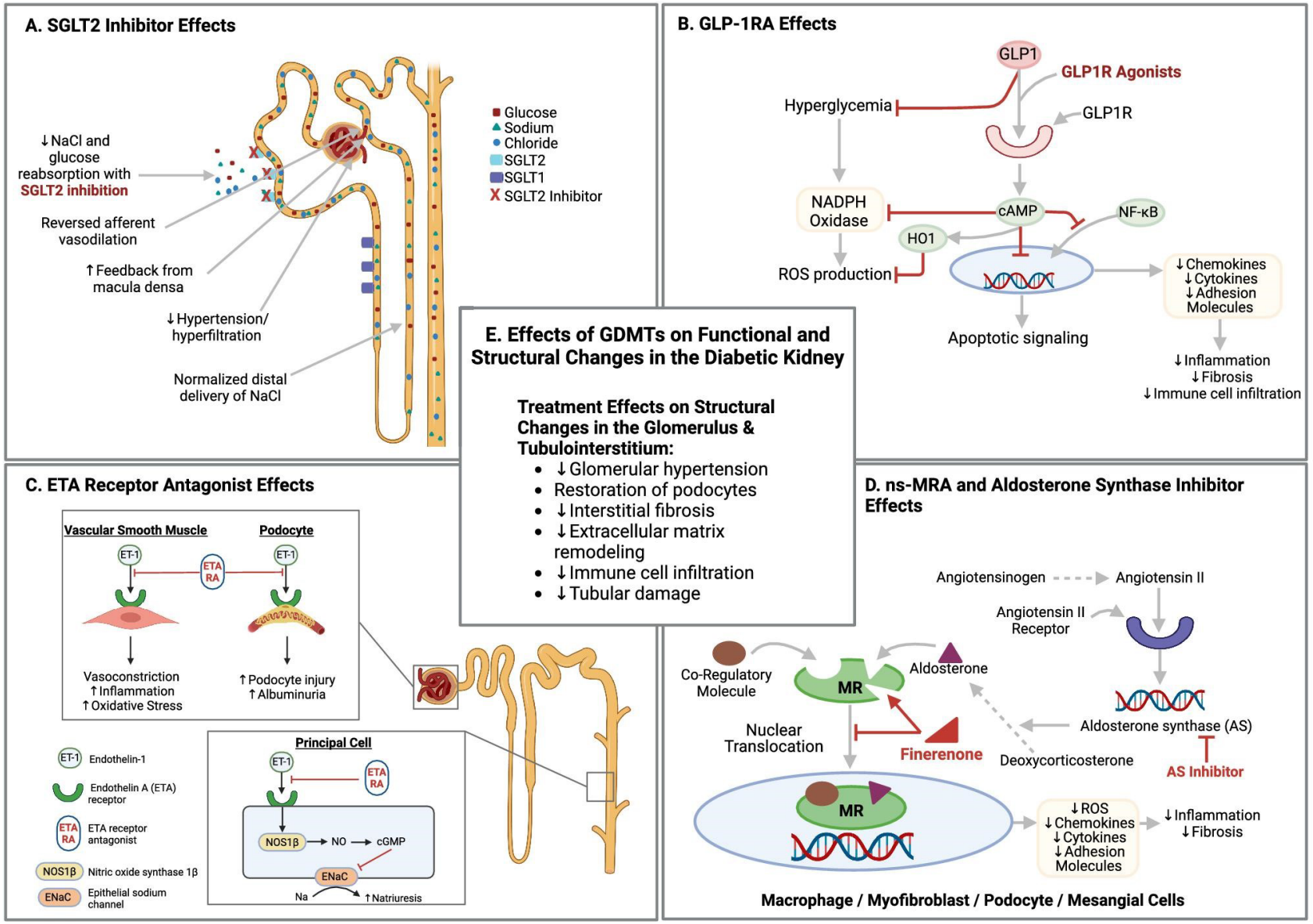
Grams ME *et al. JAMA* 2023;330:1266-1277

Combination Therapy and the 4-Pillars Diabetic and Non-Diabetic CKD



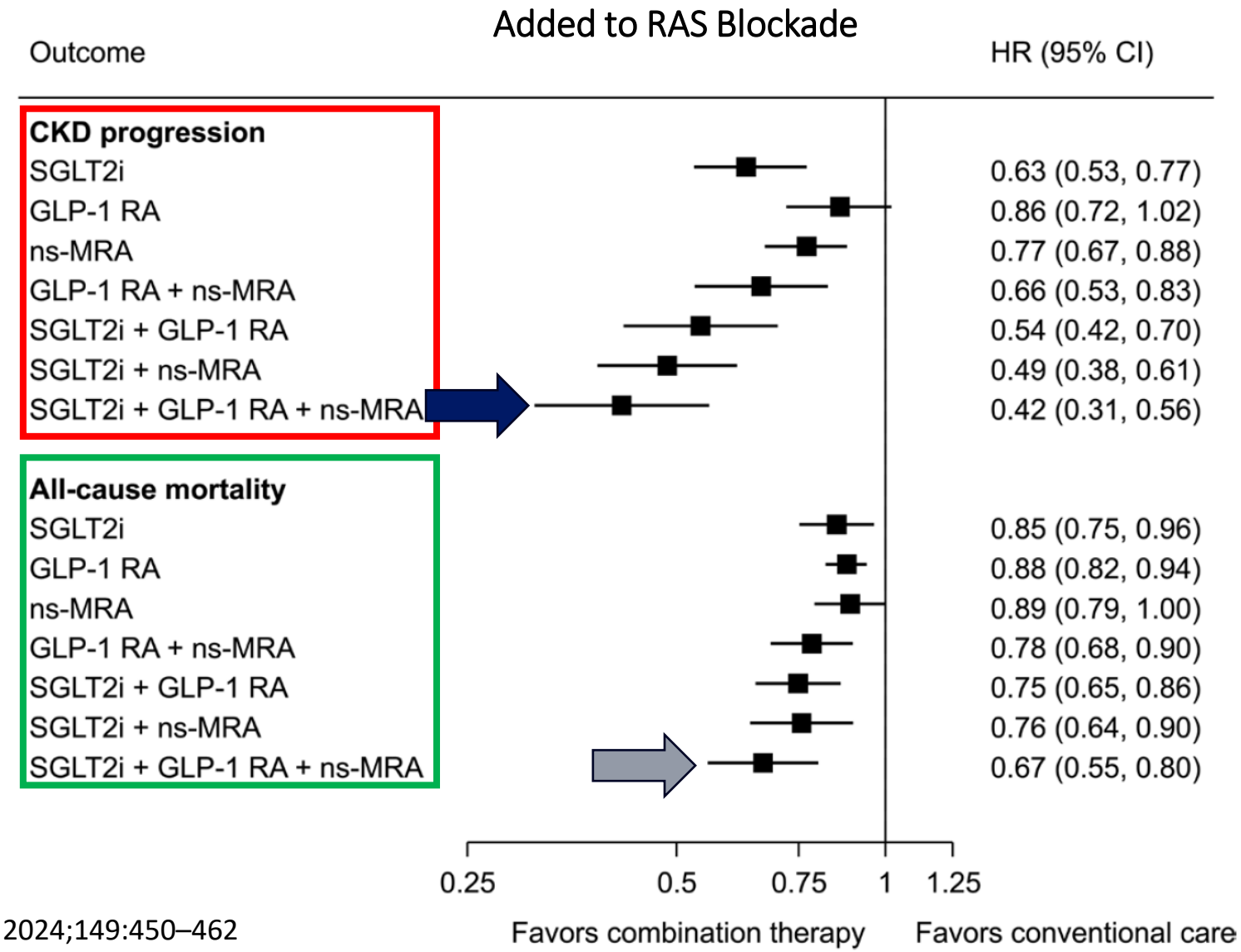
Neuen B *et al. Nephrol Dial Transplant* 2025:40 (S1):i59-i69

Complementary Mechanisms for CKM Therapies



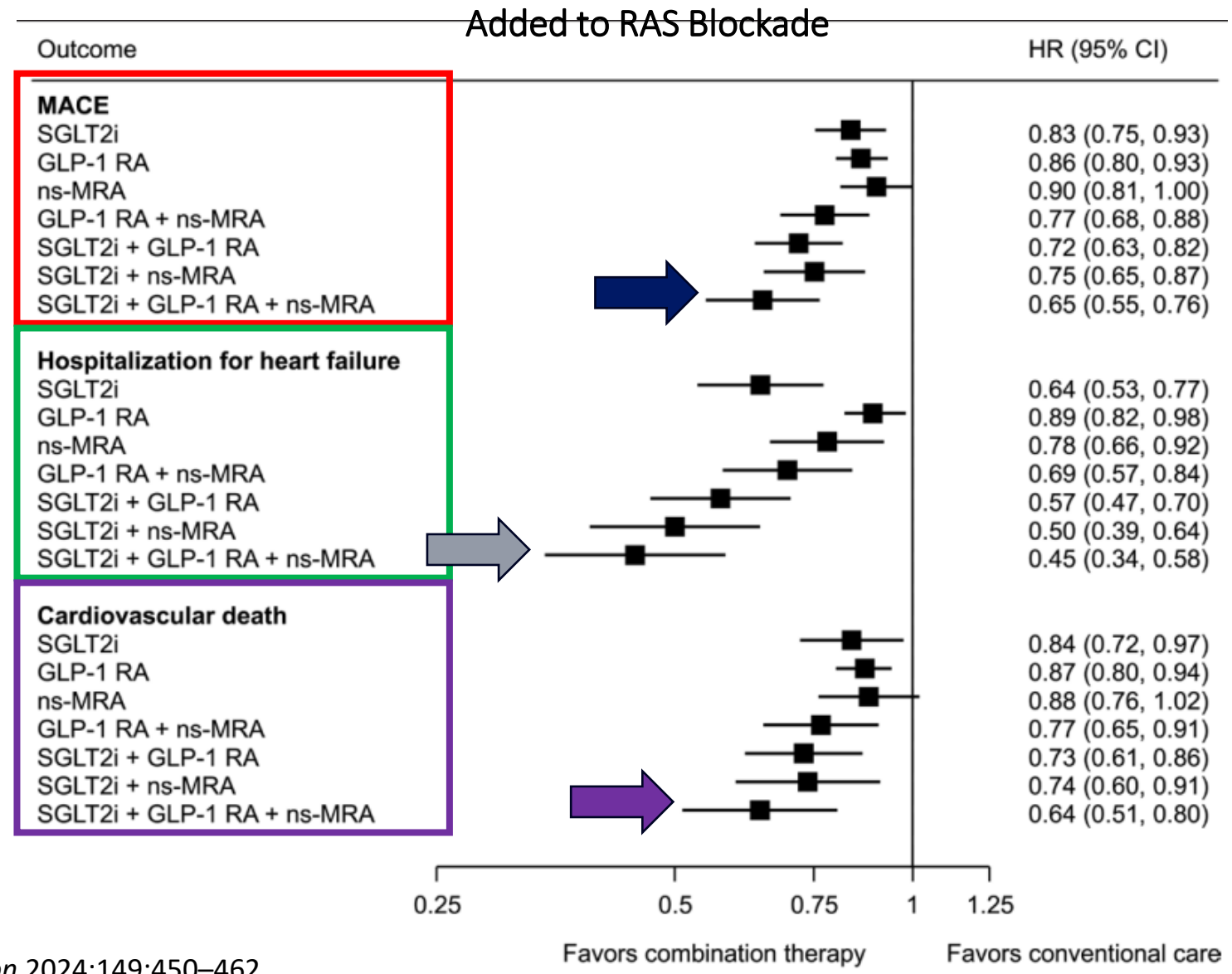
Alicic RZ, Neumiller JJ, Tuttle KR. *Nephrol Dial Transplant* 2025; 40 (S1):i3–i17

Combination Therapy and Kidney Outcomes



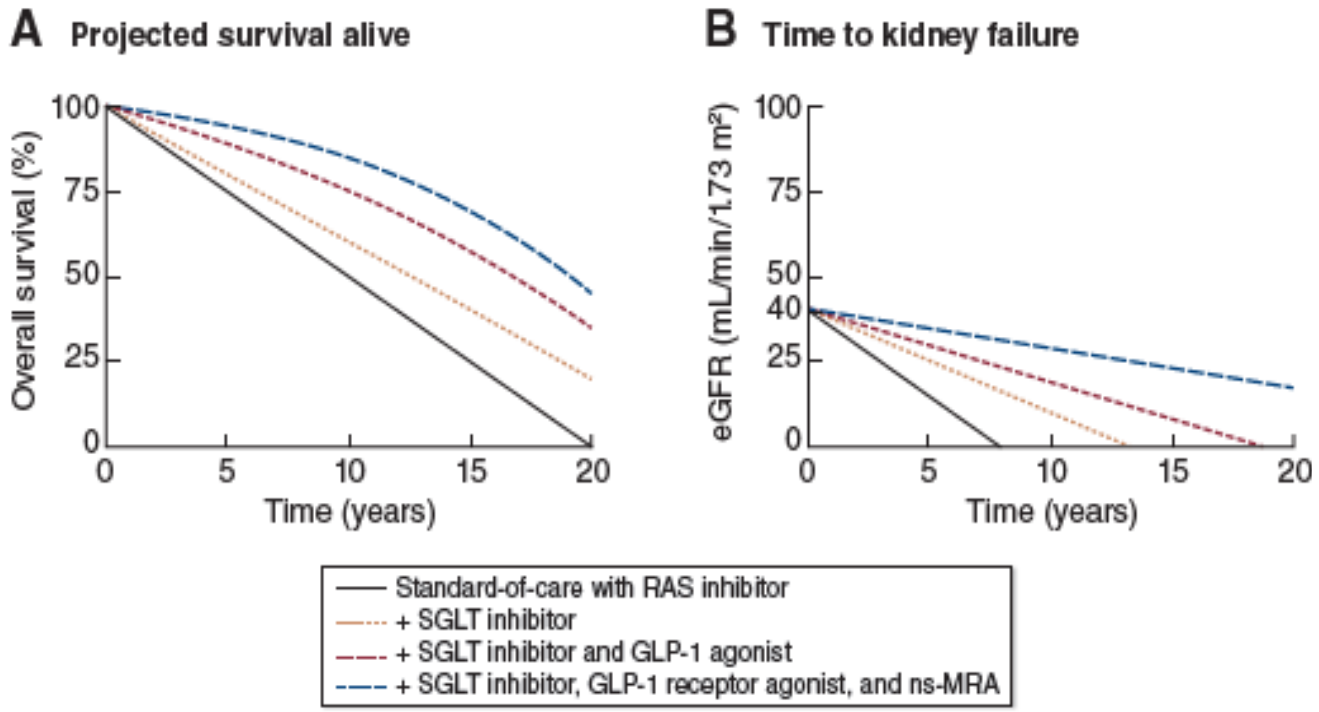
Neuen BL *et al. Circulation* 2024;149:450–462

Combination Therapy and Cardiovascular Outcomes



Neuen BL *et al. Circulation* 2024;149:450–462

Time to Events for Survival and Kidney Function in CKD Population Level and Person Level

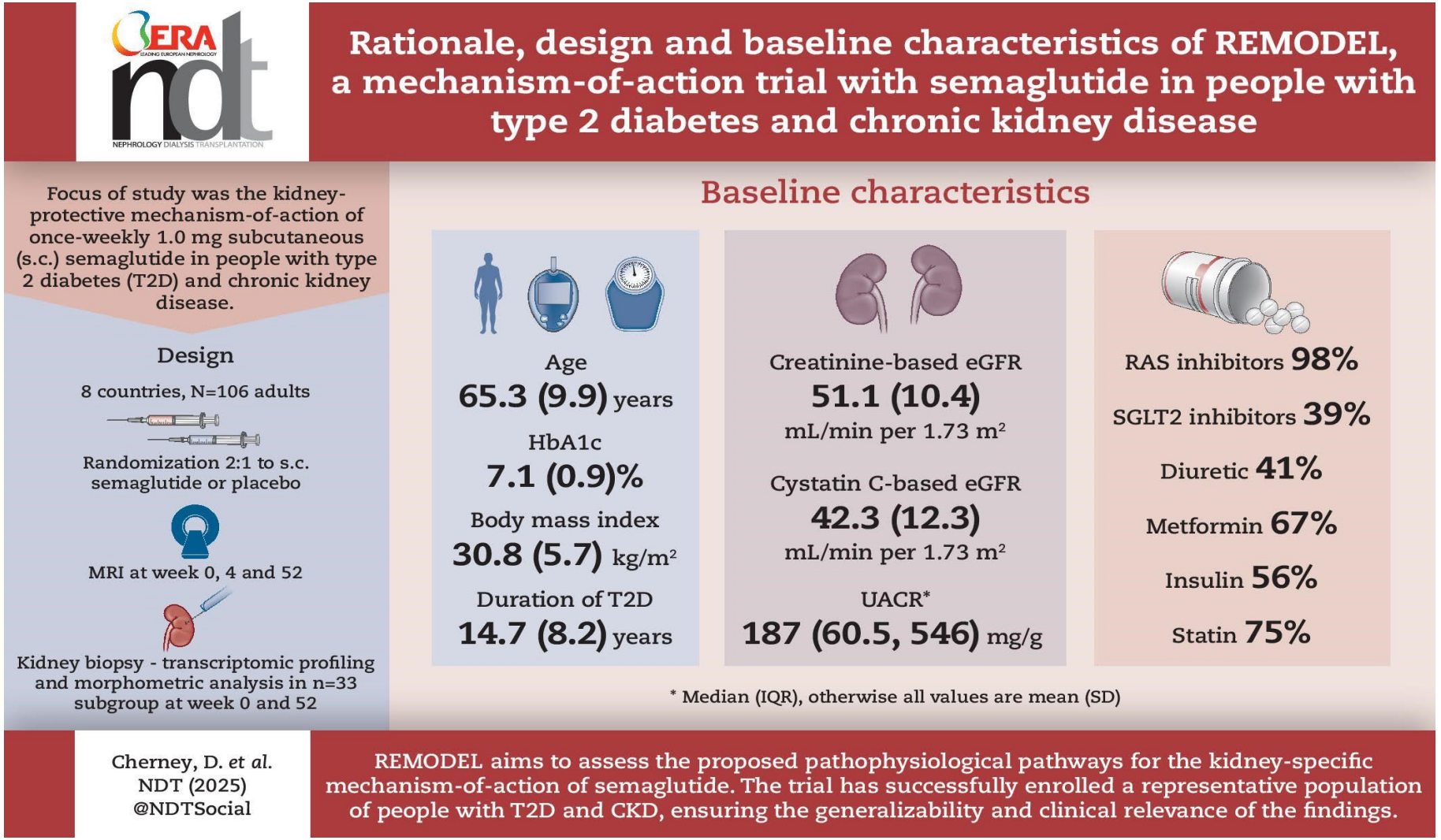


Tuttle KR *et al. Clin J Am Soc Nephrol* 2026; online ahead of print

Residual Risks with Current CKD Therapies
Questions and Potential Roles for Rilparencel

- Who are treatment responders and non-responders?
  - *TBD*
- What therapy or combination will work best?
  - *TBD*
- When is the right time to deploy therapy?
  - *Rilparencel as a reparative tool*
- Why does a therapy work or not work?
  - *Rilparencel as rescue treatment*
- Where can therapies be sourced?
  - *Rilparencel from a person's own body*
- How to make treatment fit-for-purpose?
  - *Rilparencel is designed for CKD*

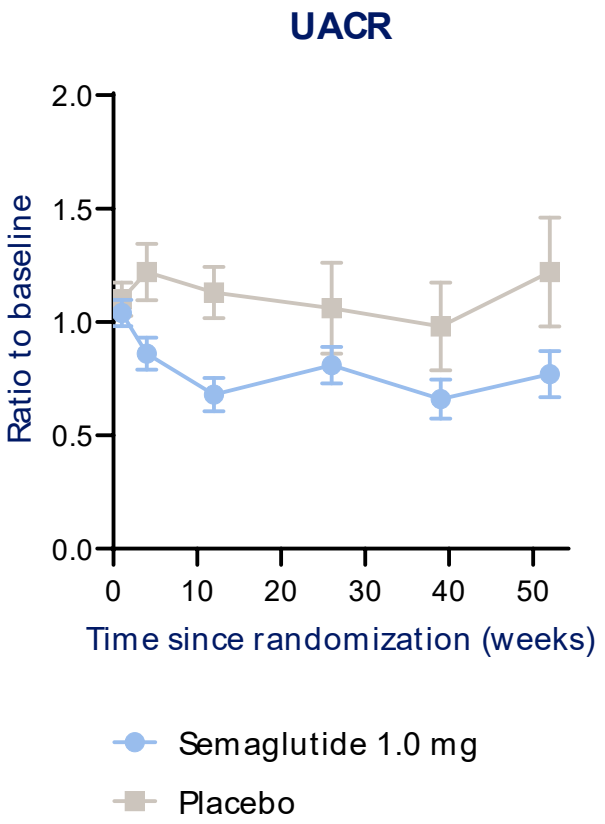
What Can We Learn from Mechanistic Studies?

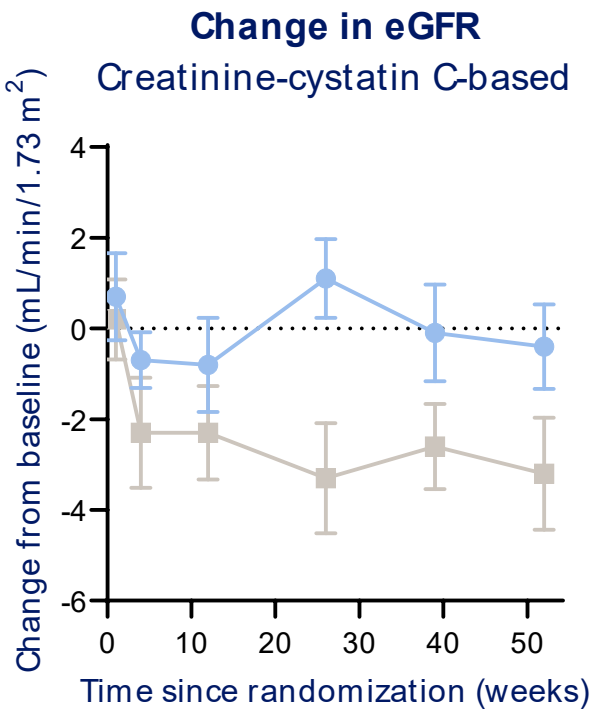


Reduced Albuminuria and Stabilized eGFR

Semaglutide treatment compared to placebo after 52 weeks:

- **UACR** reduced **40%**
  (ETR 0.60, 95% CI 0.41;0.88, p=0.008)
- **eGFR differences**
  - **Creatinine-based:**
    ETD 3.4 mL/min/1.73 m^2
    (95% CI -0.2;6.9, p=0.063)
  - **Cystatin C-based:**
    ETD 2.3 mL/min/1.73 m^2
    (95% CI -0.4;5.0, p=0.096)
  - **Creatinine-cystatin C-based:**
    ETD 2.9 mL/min/1.73 m^2
    (95% CI -0.2;6.1, p=0.069)



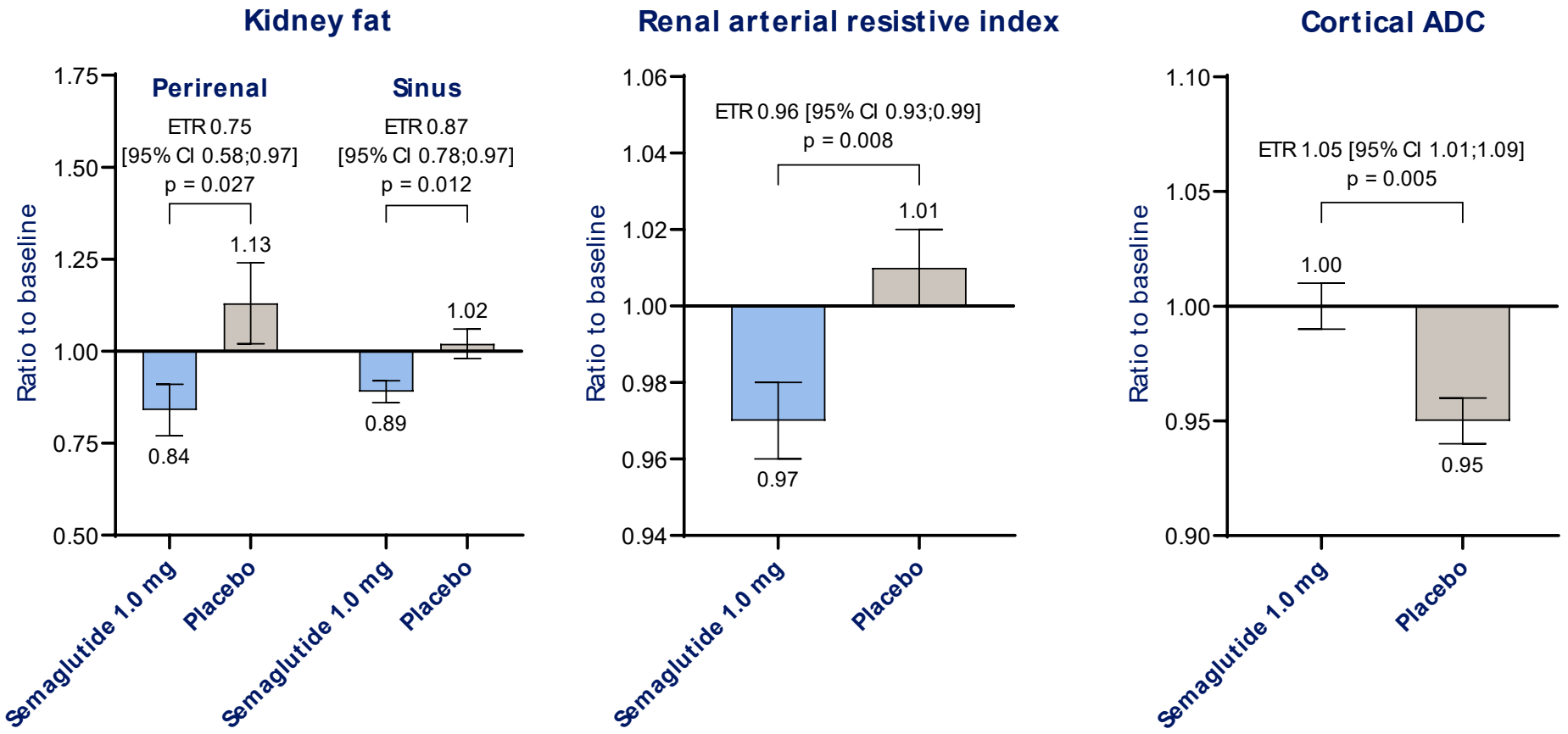


Tuttle KR, Bjornstad P… Kretzler M *et al. Nat Med* 2026 Oct 1. Online ahead of print. PMID: 42823485

Reduced Kidney Fat and Renal Arterial Resistance with Stabilized Cortical Fibrosis

Semaglutide treatment compared to placebo after 52 weeks:

- **25%** and **13% lower perirenal** and **sinus fat volumes**, respectively
- **Reduced** renal arterial resistive index (**RARI**) reflecting **lower renal vascular resistance**
- **No decrease in cortical** apparent diffusion coefficient (**ADC**) reflecting **stabilized fibrosis in the kidney cortex**

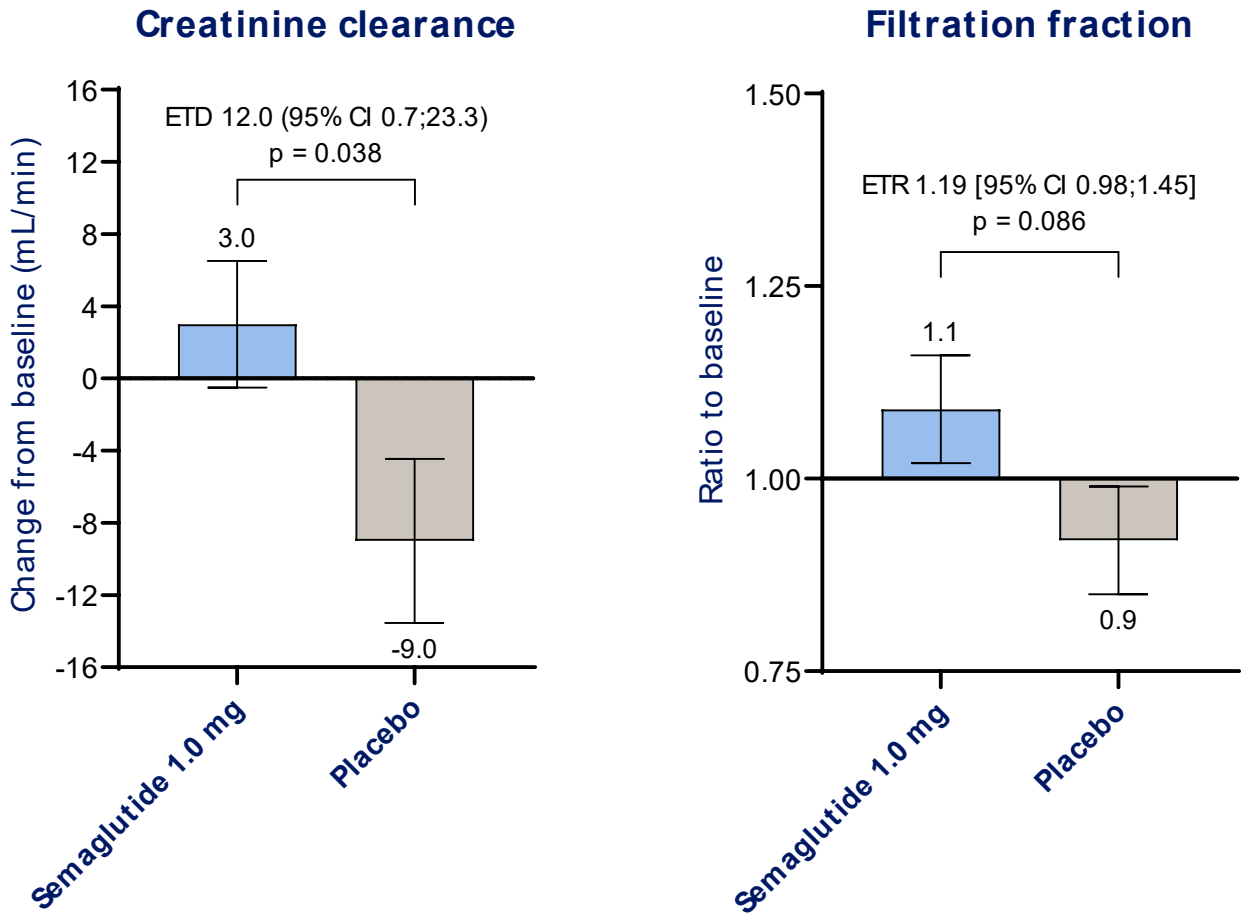


Tuttle KR, Bjornstad P… Kretzler M *et al. Nat Med* 2026 Oct 1. Online ahead of print. PMID: 42823485

Indicators of Improved Glomerular Filtration and Barrier Function

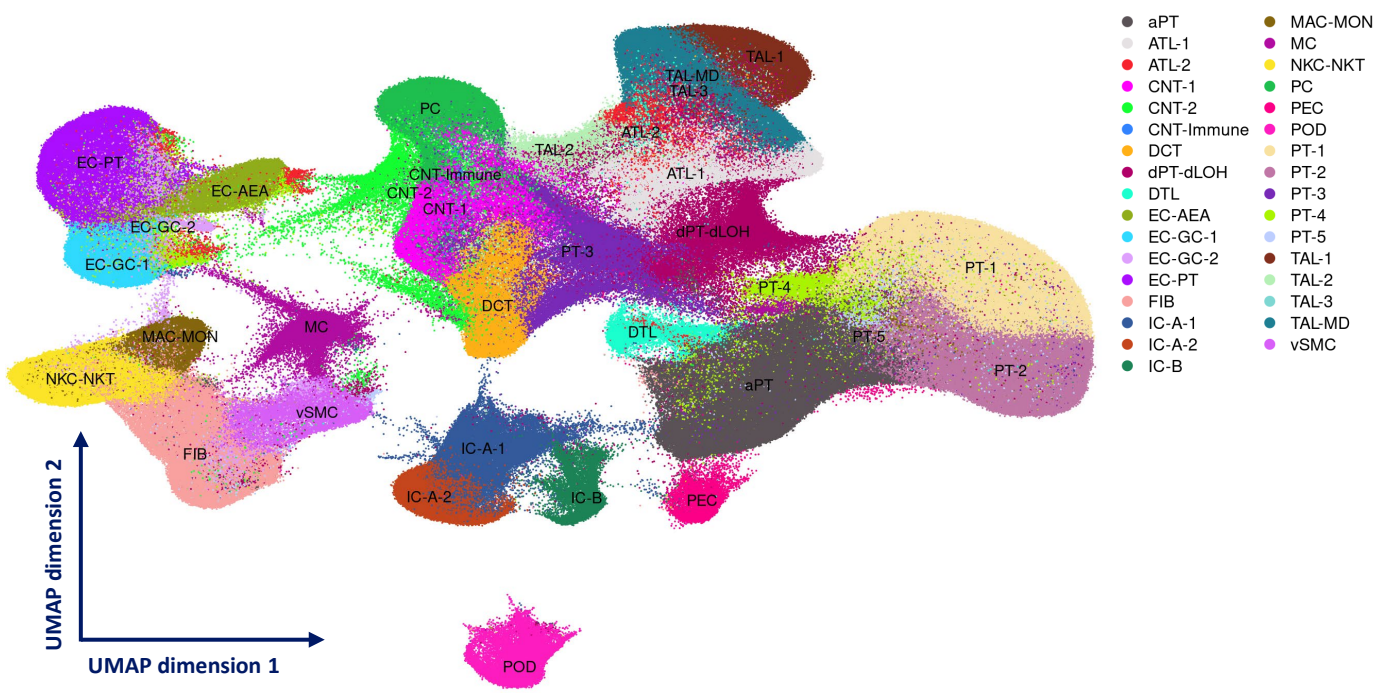
Semaglutide treatment compared to placebo after 52 weeks:

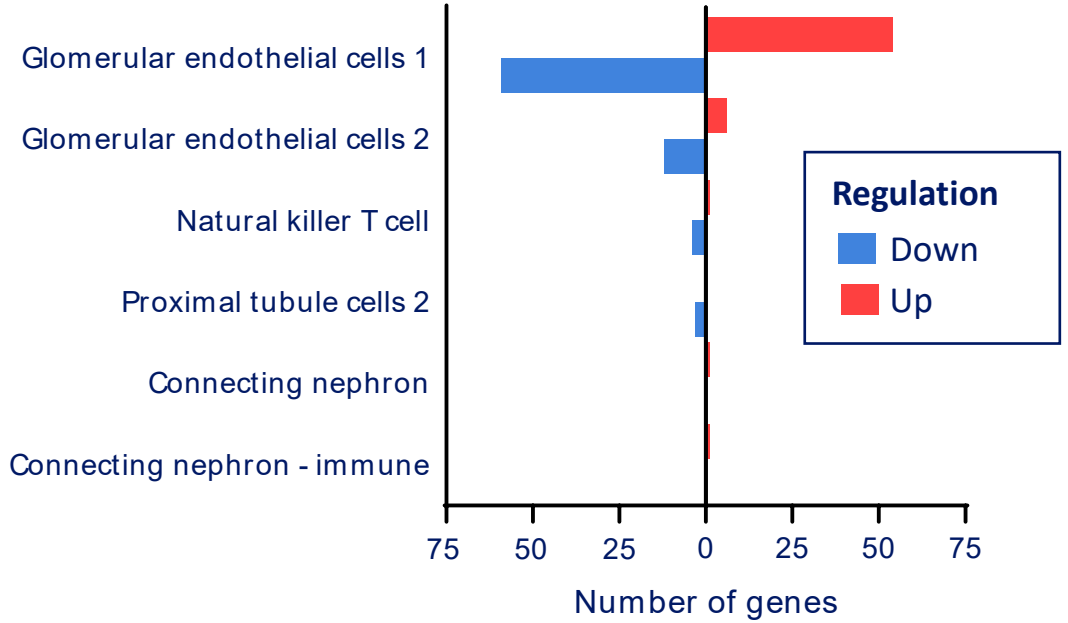
- **24-hour creatinine clearance** was **higher** by a mean ETD of **12 mL/min**
- **Filtration fraction** was **numerically higher** by **19%**



Tuttle KR, Bjornstad P… Kretzler M *et al.* ASN Kidney Week 2025*;* Late Breaking Abstract: FR-OR089

Transcriptomic Reprogramming in Glomerular Endothelial Cells





Fifty-five kidney-biopsy samples (794,000 nuclei) underwent snRNAseq with 31 canonical cell clusters, representing all major cell types in the nephron (identified using reference markers)

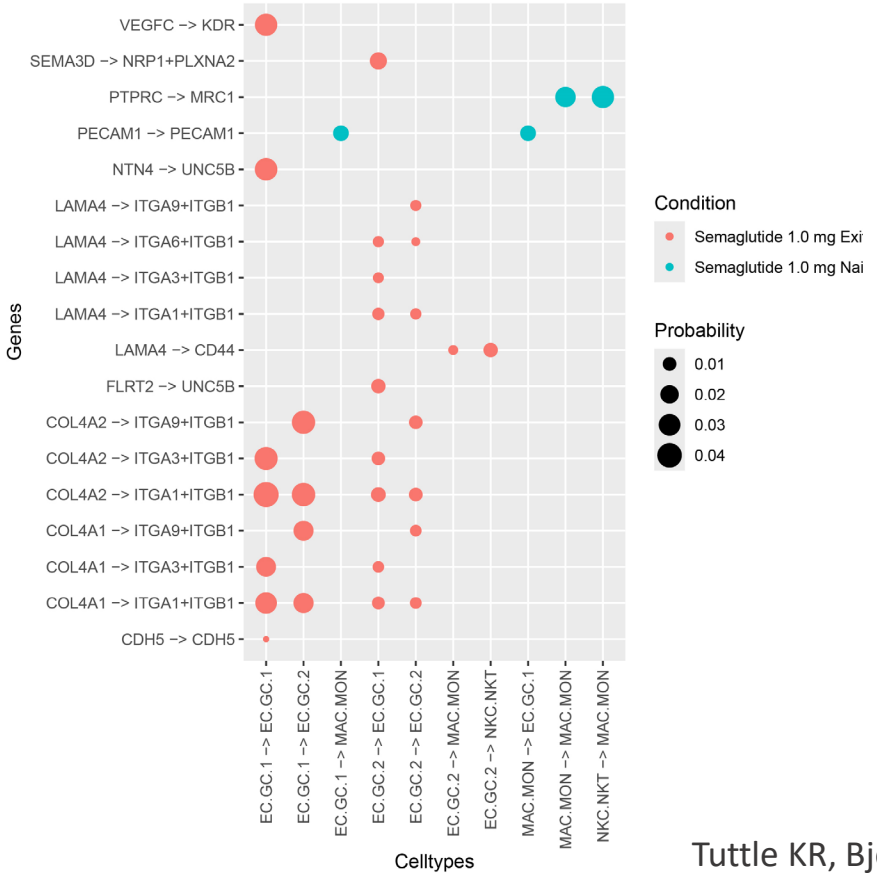
Glomerular endothelial cells were the most semaglutide-responsive cell type:

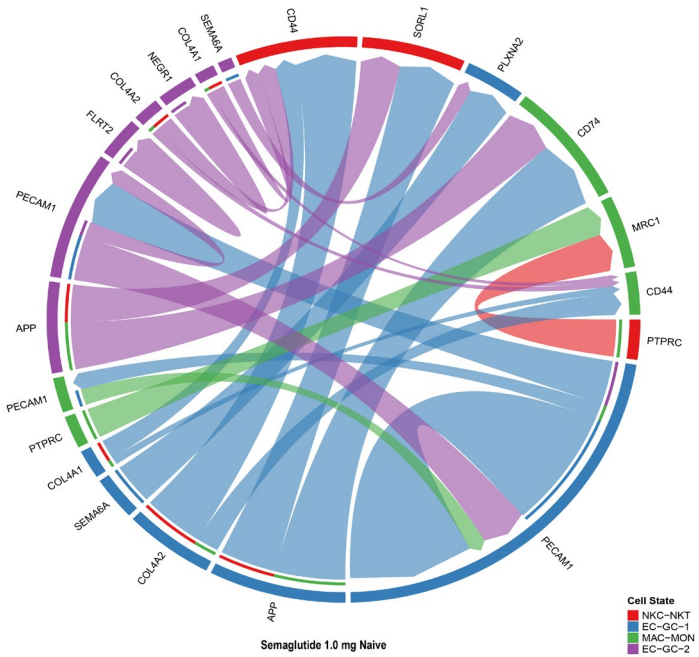
- 63% of metabolic stress genes down-regulated
- 60% of fibro-inflammatory genes down-regulated

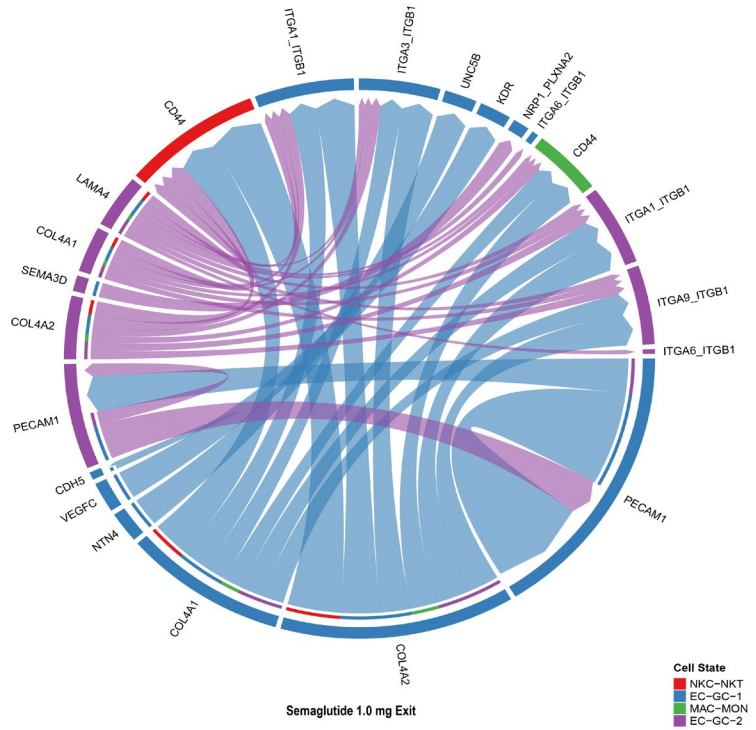
Tuttle KR, Bjornstad P… Kretzler M *et al.* *Nat Med* 2026 Oct 1. Online ahead of print. PMID: 42823485

Ligand-Receptor Interactions between Glomerular Endothelial Cells and Immune Cells – snRNAseq

Semaglutide promotes glomerular endothelial repair and remodeling programs:
Type 4 collagen, integrins, PECAM1 (CD31), CDH5 (VE cadherin)

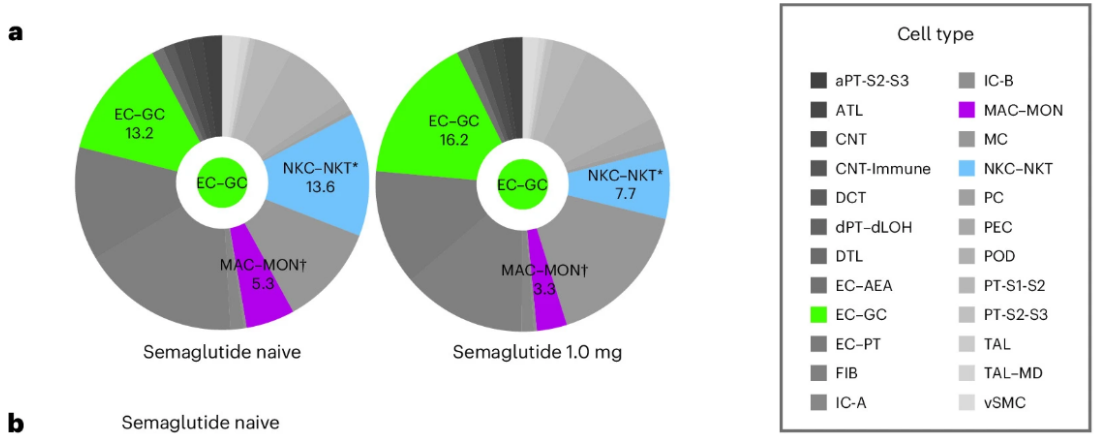


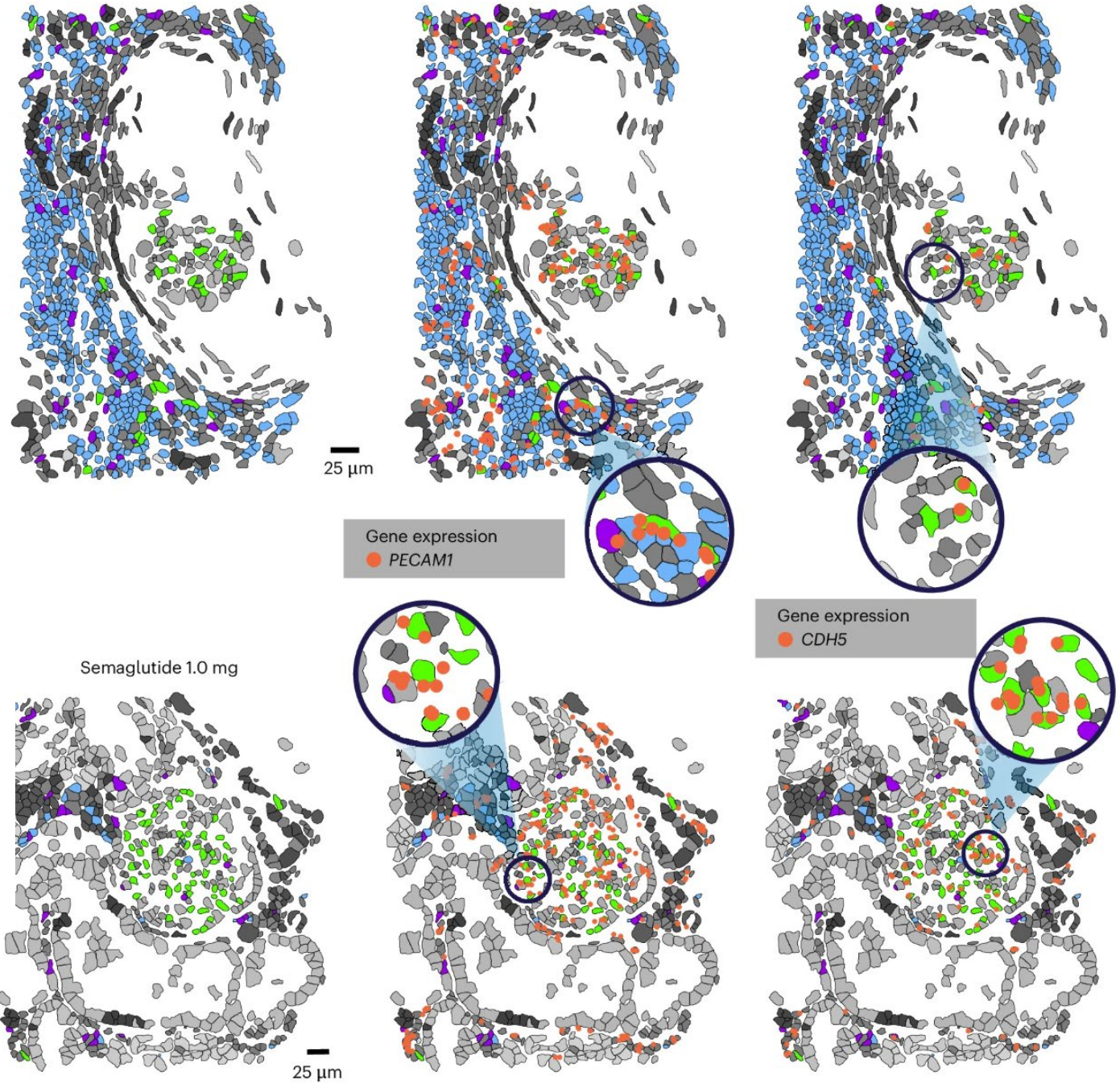




Tuttle KR, Bjornstad P… Kretzler M *et al.* *Nat Med* 2026 Oct 1. Online ahead of print. PMID: 42823485

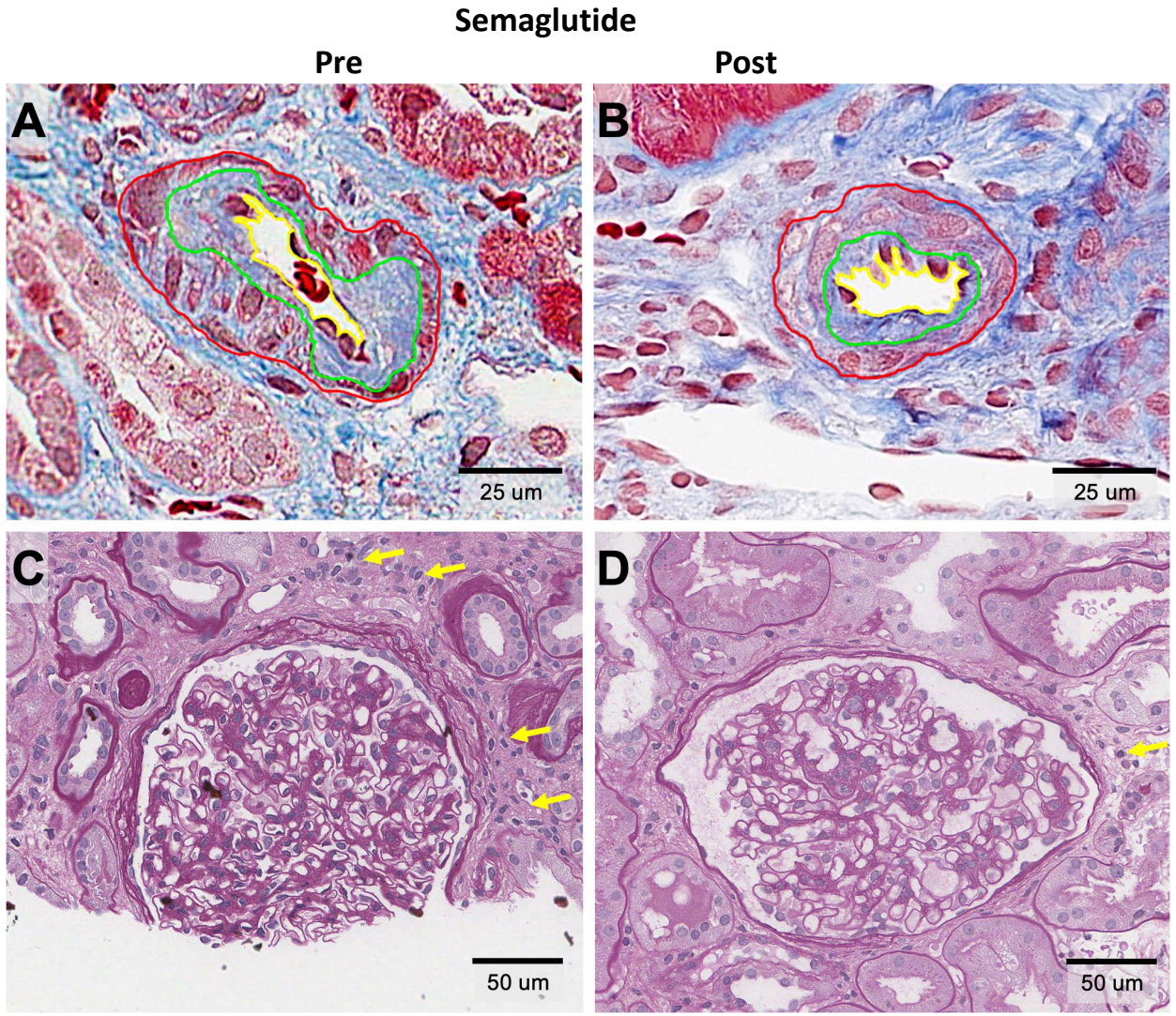
Spatial Transcriptomics Glomerular Endothelial and Natural Killer T Cells, Monocytes/Macrophages





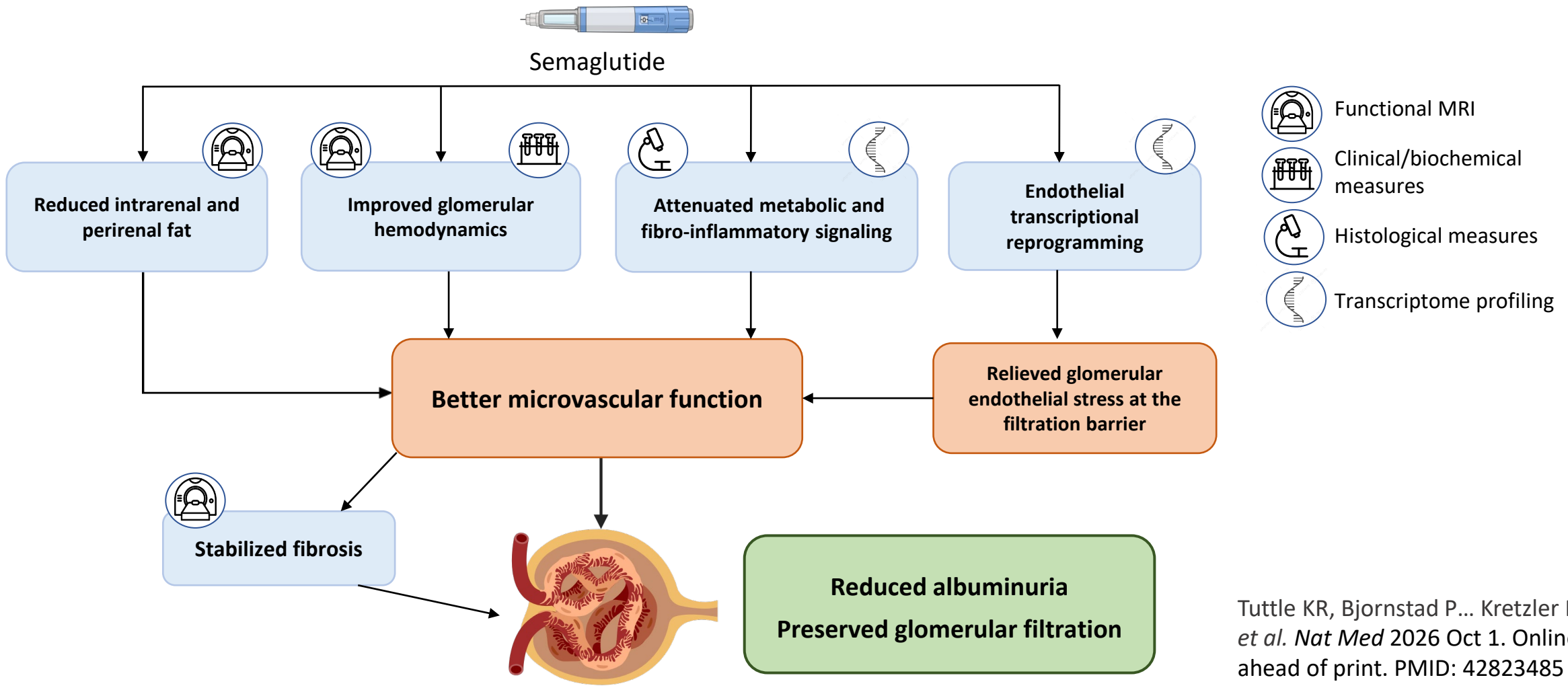
Tuttle KR, Bjornstad P… Kretzler M *et al. Nat Med* 2026 Oct 1. Online ahead of print.
PMID: 42823485

Reduced Fractional Intimal Area of Most Diseased Arterioles and Periglomerular Immune Cells



Tuttle KR, Bjornstad P… Kretzler M *et al. Nat Med* 2026 Oct 1. Online ahead of print. PMID: 42823485

Pathophysiological Interpretation of Semaglutide's Mechanisms-of-Action in CKD and T2D



Tuttle KR, Bjornstad P… Kretzler M *et al. Nat Med* 2026 Oct 1. Online ahead of print. PMID: 42823485

Q&A