ACTUALIZACION ENFERMEDAD RENAL DIABETICA PARA INTERNISTAS

David León Jiménez
Internal Medicine
Diabetes, Obesity and Vascular Risk Specialist
Virgen del Rocío University Hospital. UCAMI
QuironSalud Sevilla
@drleonjimenez

35º Congreso Sociedad Andaluza de Medicina Interna (SADEMI)
6º Encuentro de Enfermería de Medicina Interna de Andalucía

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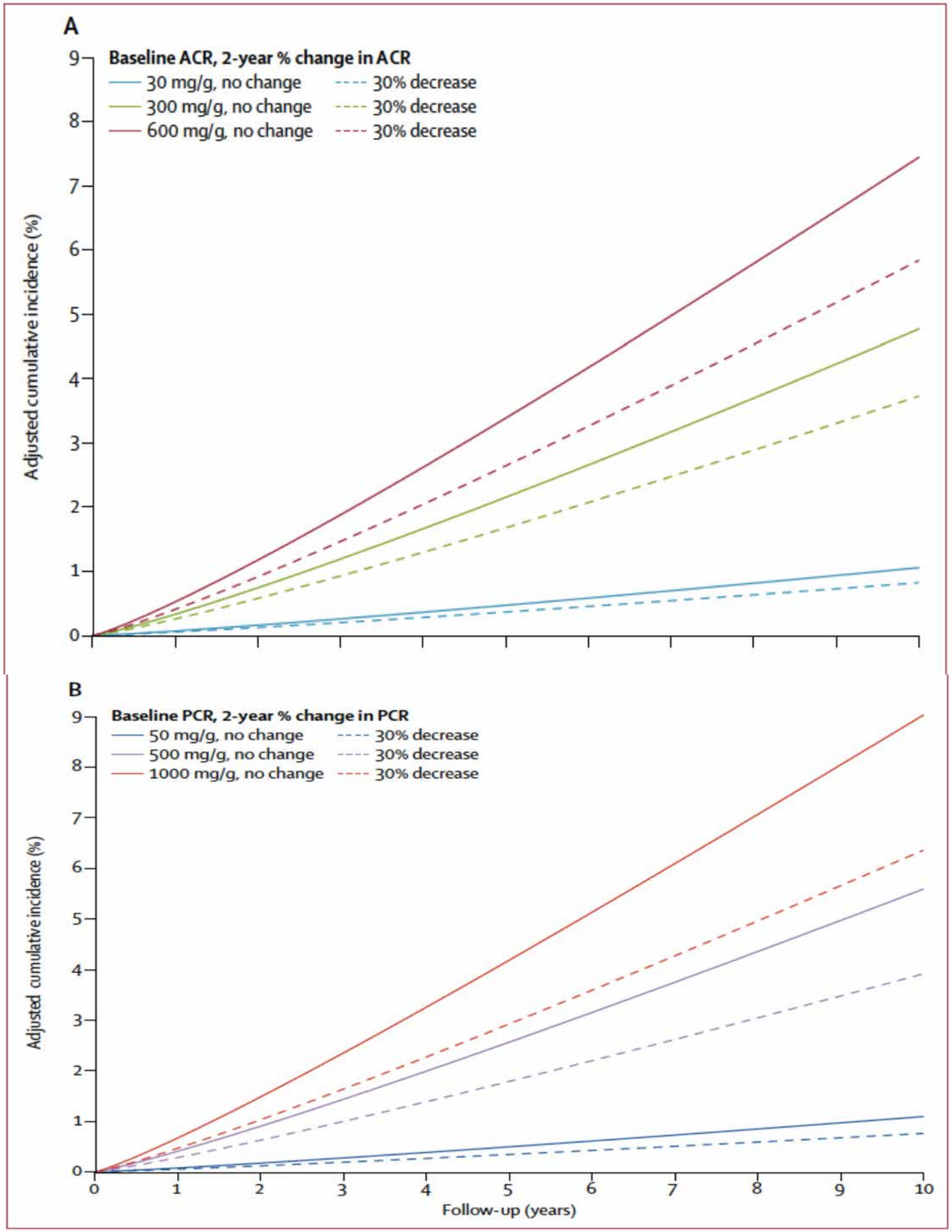
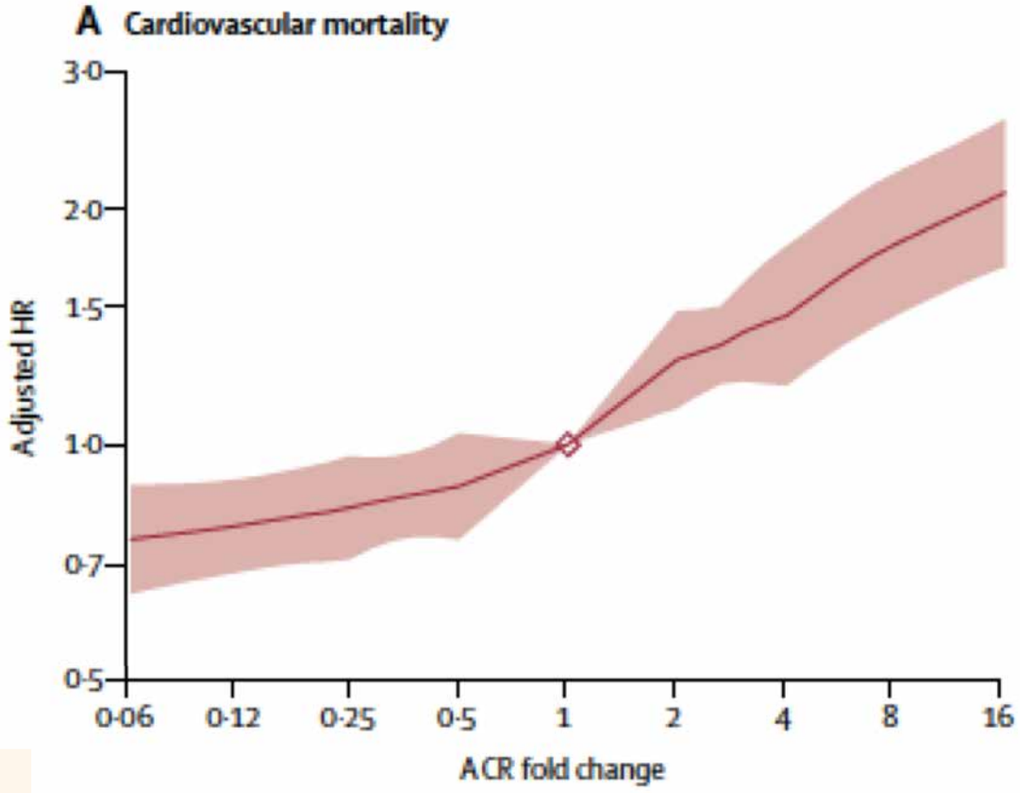
Campus Docente y Hospital S. Juan de Dios del Aljarafe
Bormujos, Sevilla

CONFLICTO INTERESES

Ponente: AstraZeneca Pharmaceuticals LP; Boehringer Ingelheim Pharmaceuticals, Inc.; Eli Lilly and Company; Janssen Pharmaceuticals, Inc.; Sanofi; Esteve y NovoNordisk.

IP: Ensayos clínicos multicéntricos internacionales de Sanofi.





ACR=urine albumin-to-creatinine ratio
HR=hazard ratio
PCR=urine protein-to-creatinine ratio

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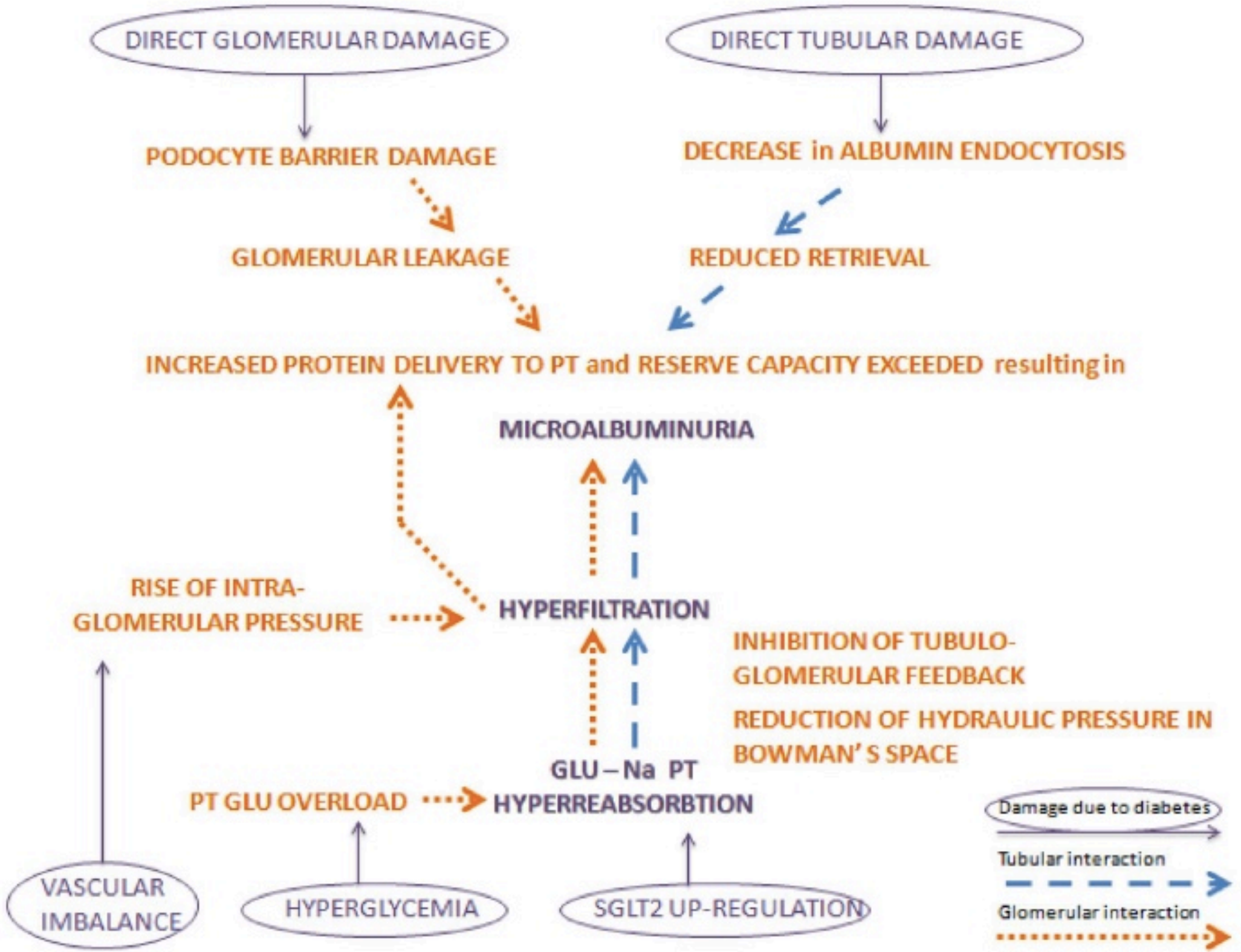

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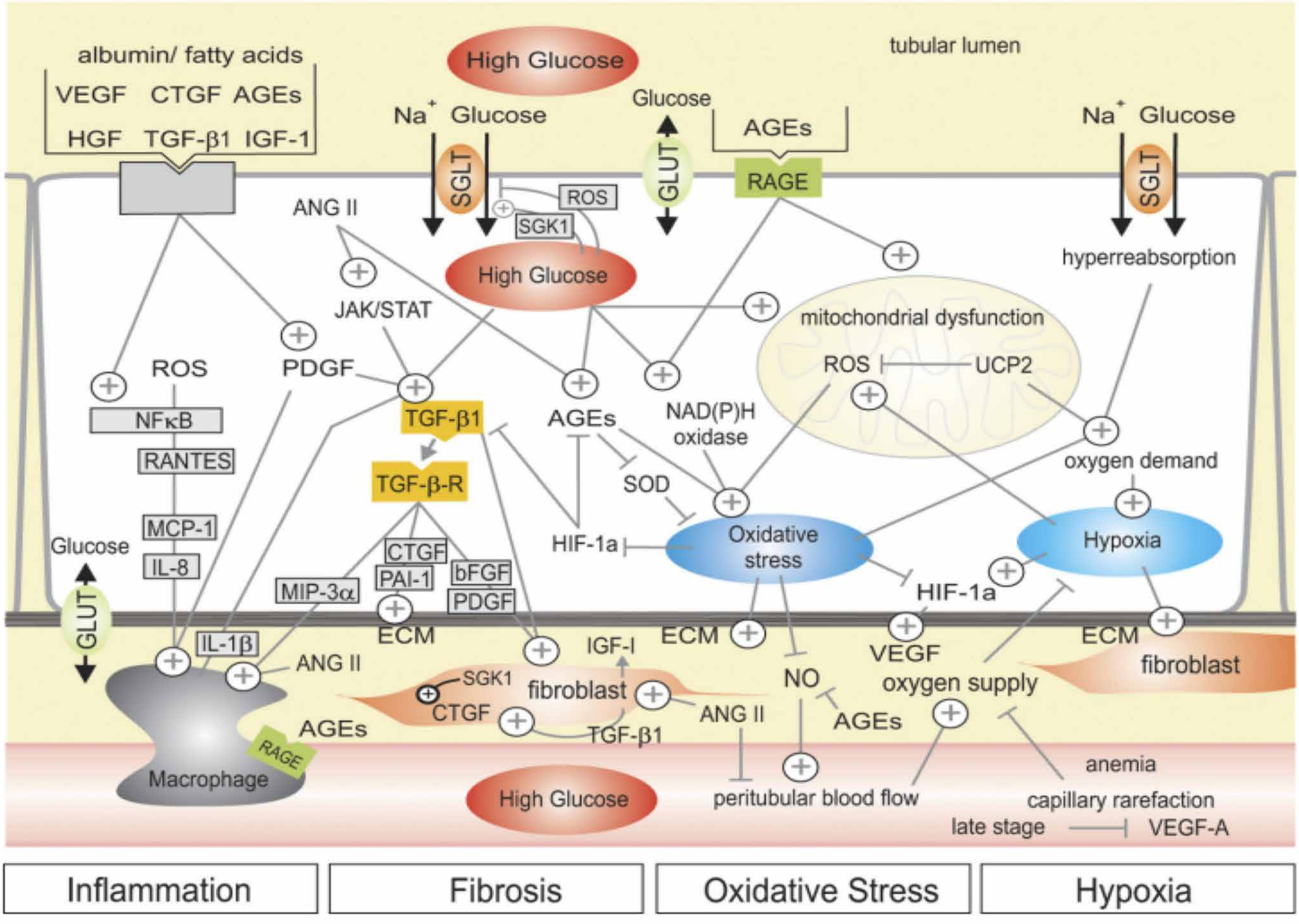

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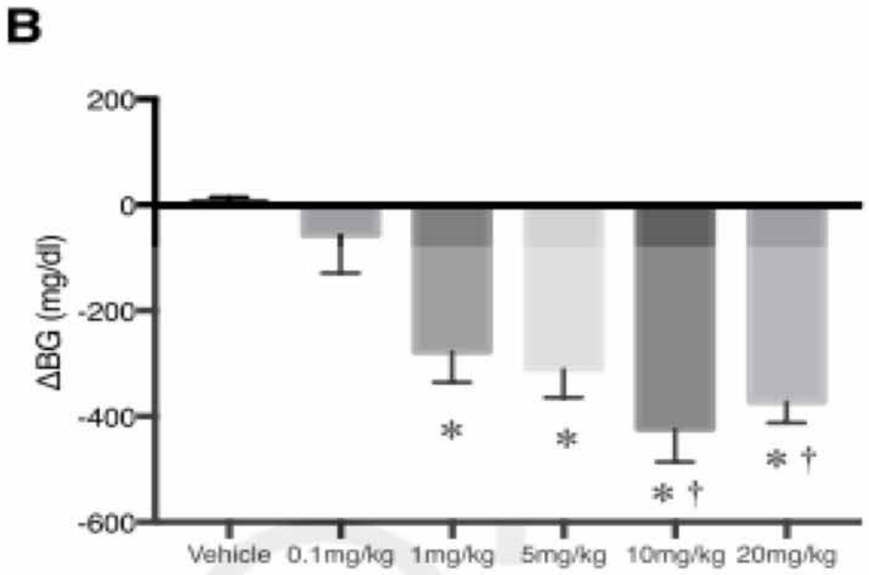

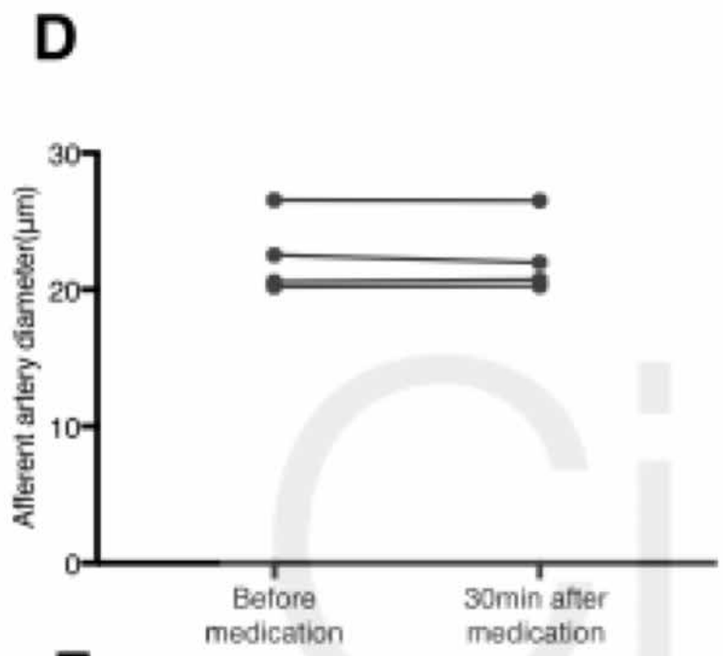

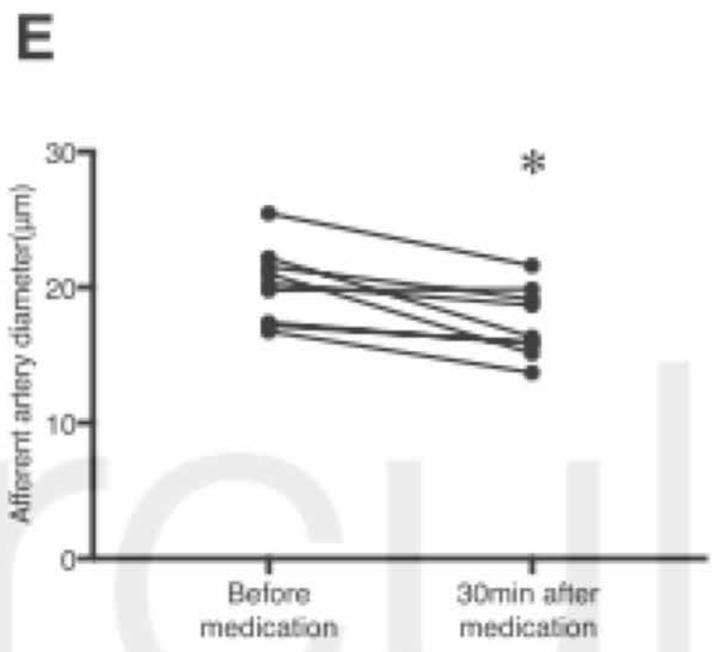

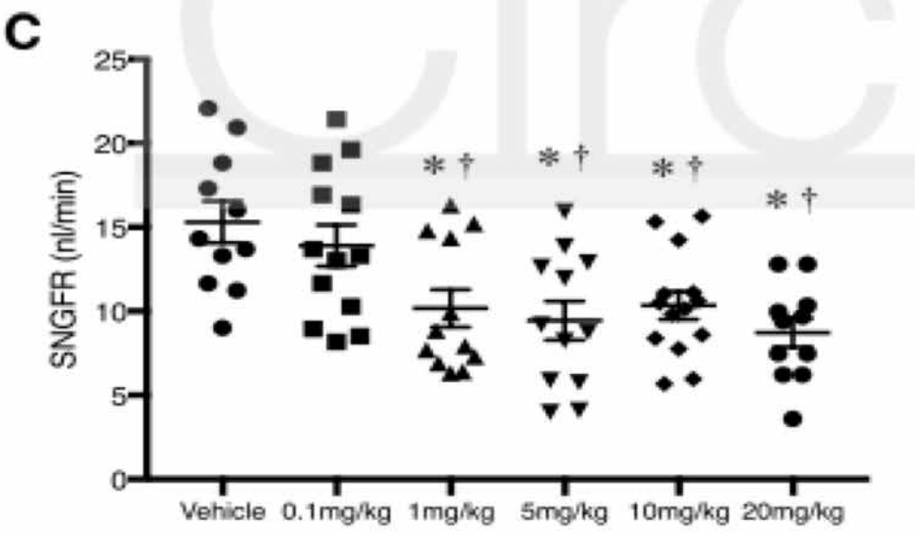

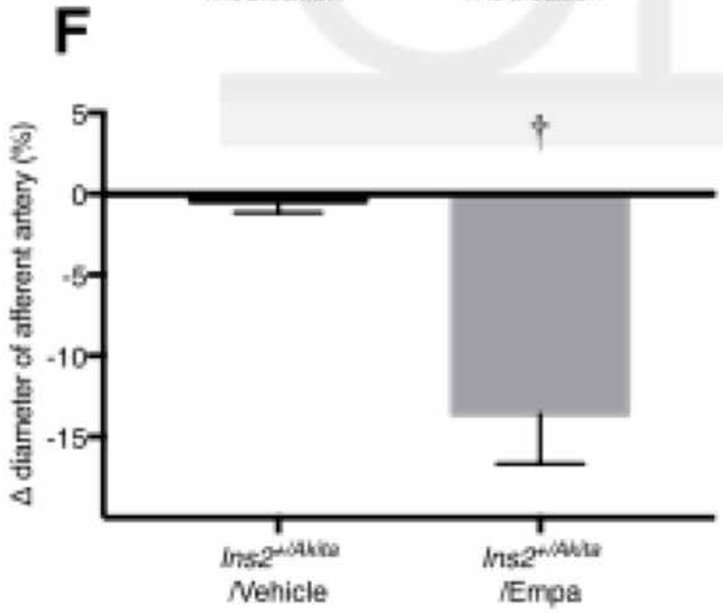

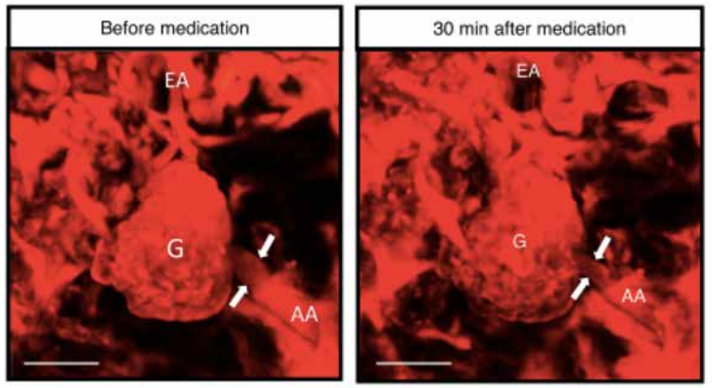

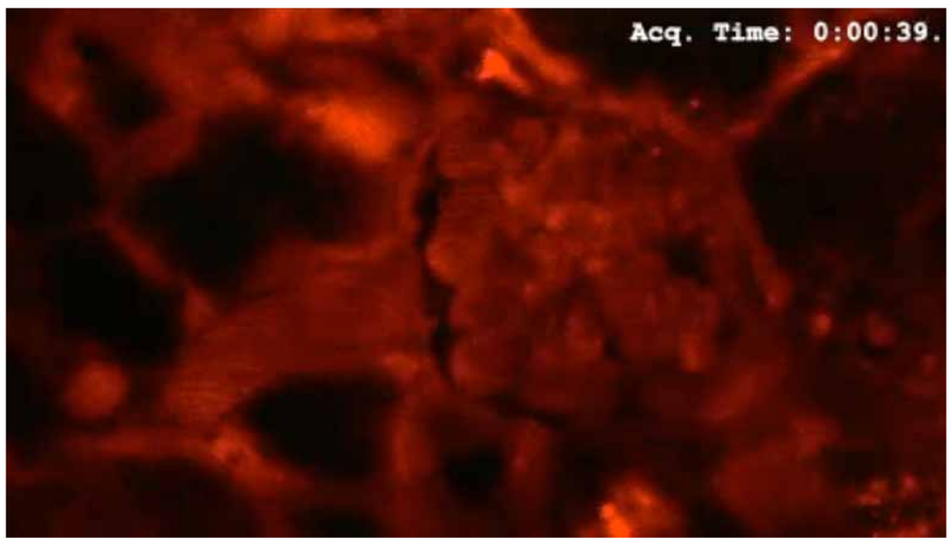

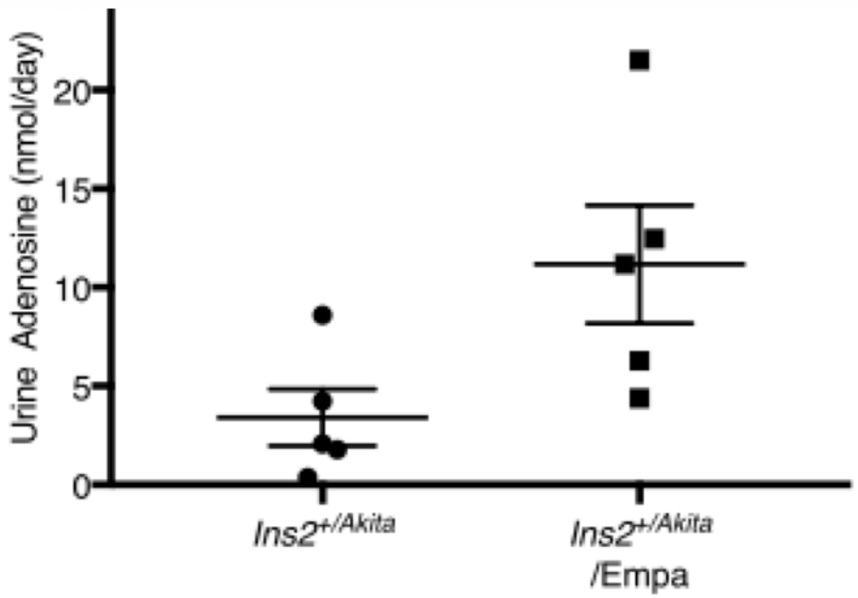

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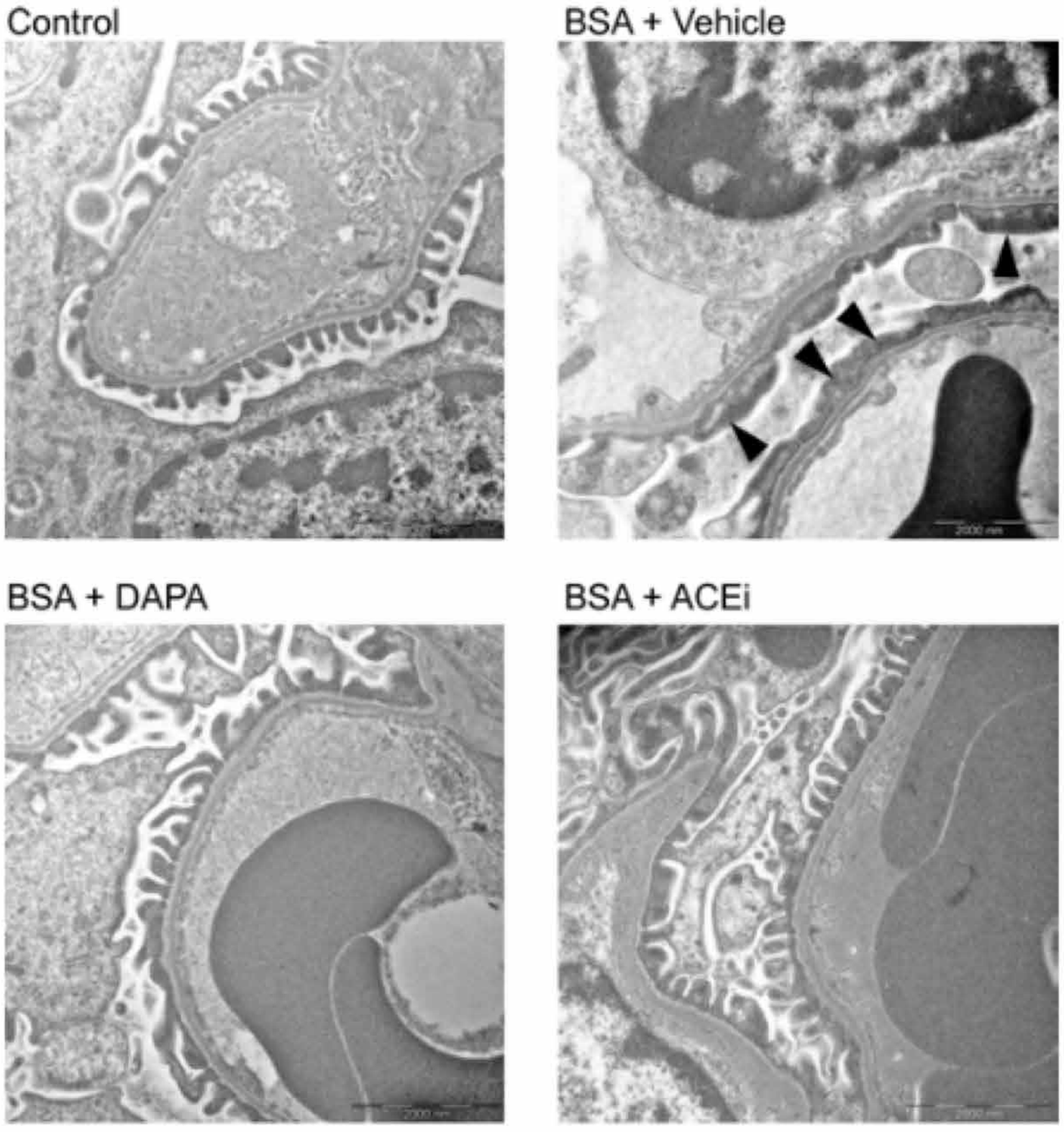

Figure 3. Dapagliflozin limits ultrastructural podocyte damage in mice with protein overload. Representative electron micrographs of glomeruli from control mouse and BSA-mice treated with vehicle, dapagliflozin (DAPA), or ACE inhibitor (ACEi). Focal areas of podocyte damage with effacement of foot processes are indicated by arrowheads in a mouse treated with BSA + vehicle. Scale bars: 2,000 nm.

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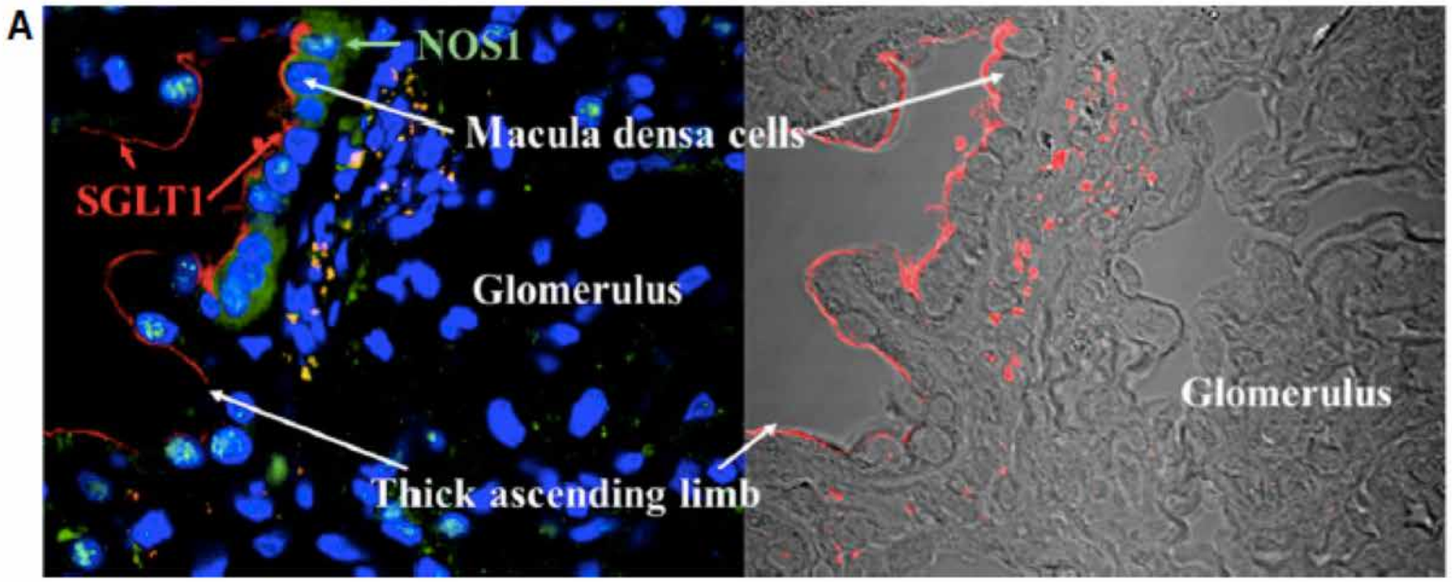

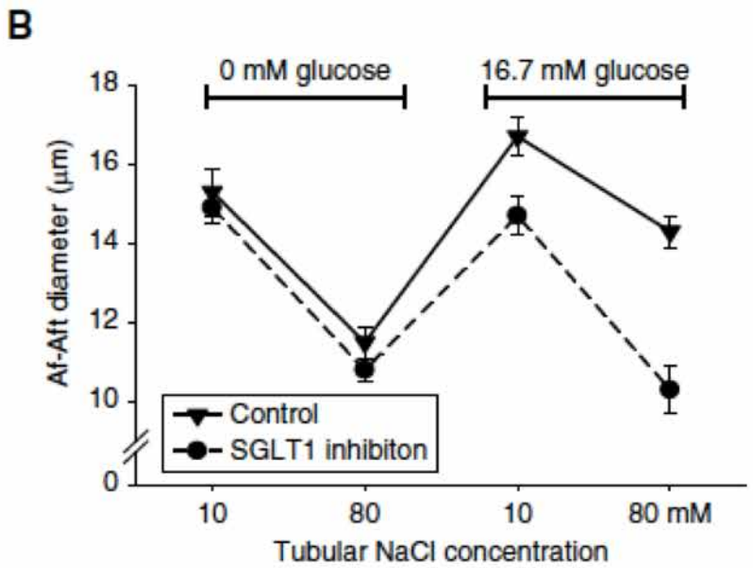

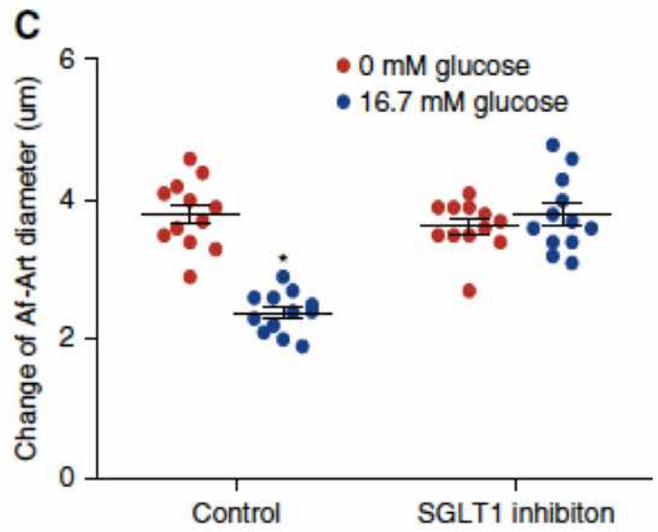

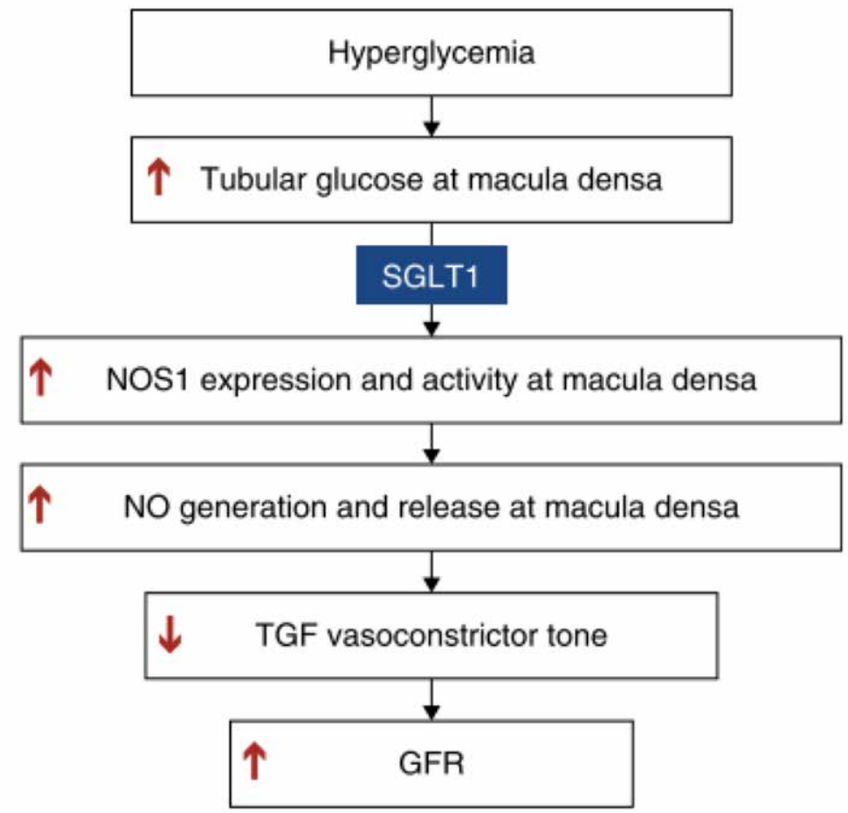

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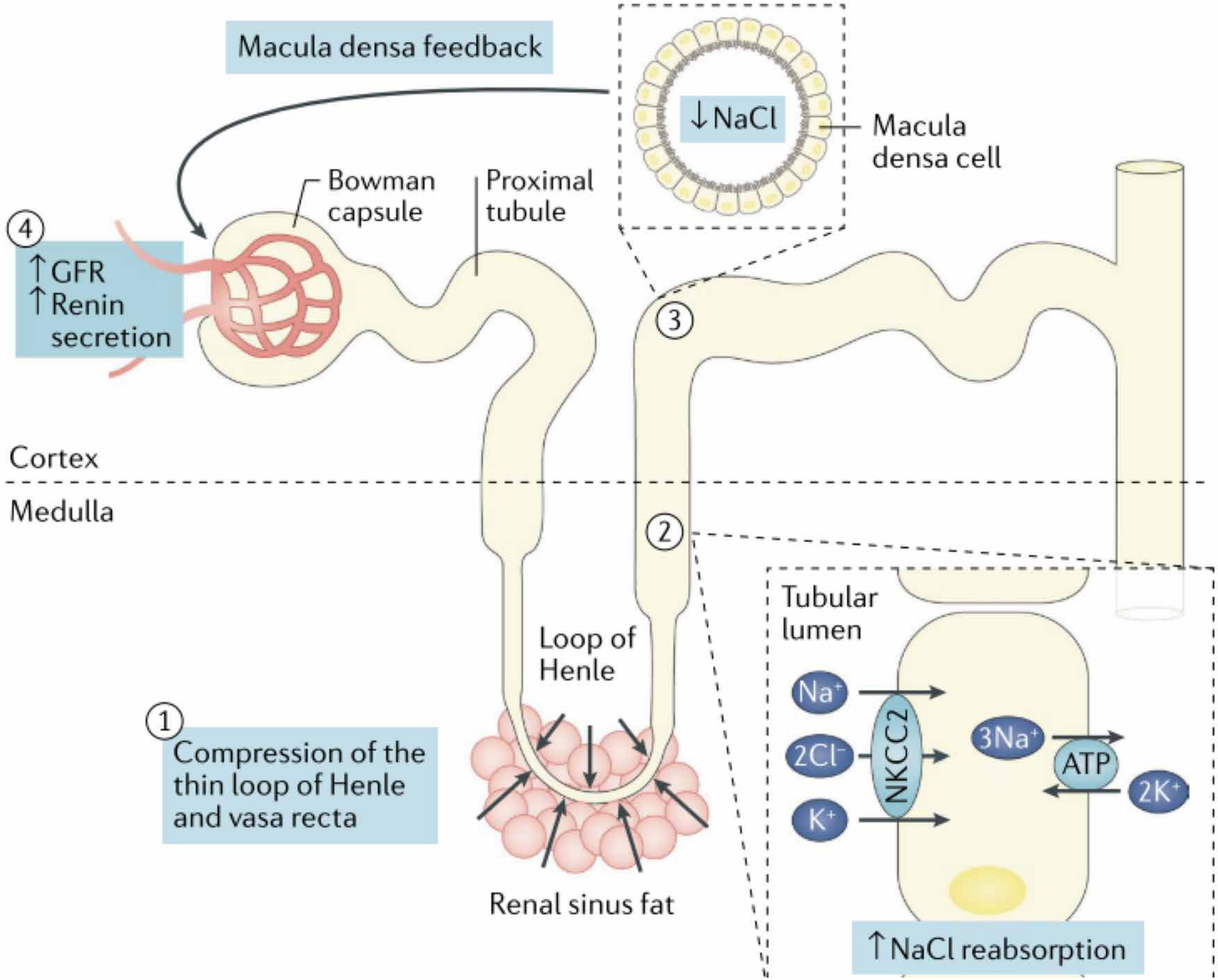

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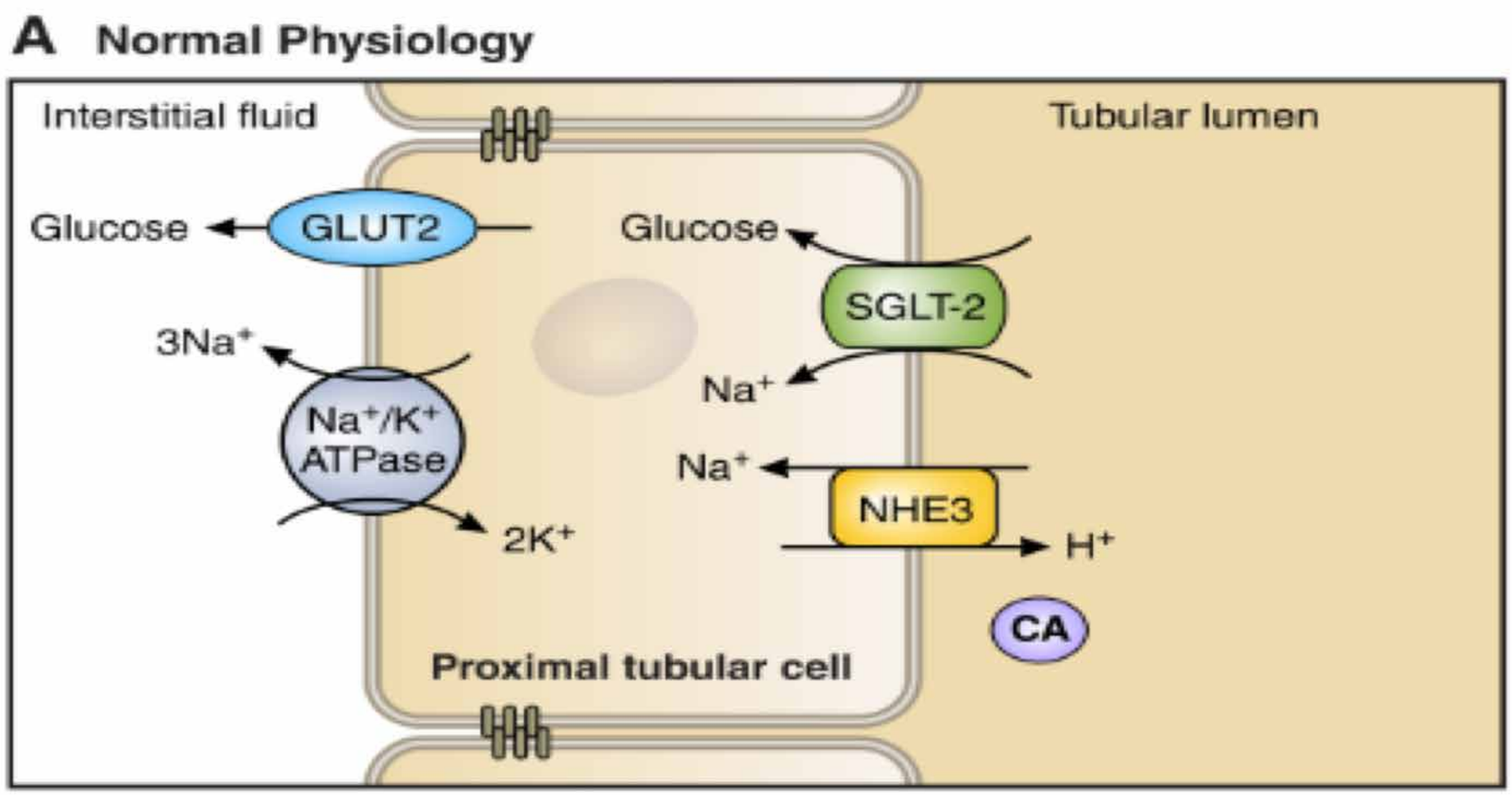

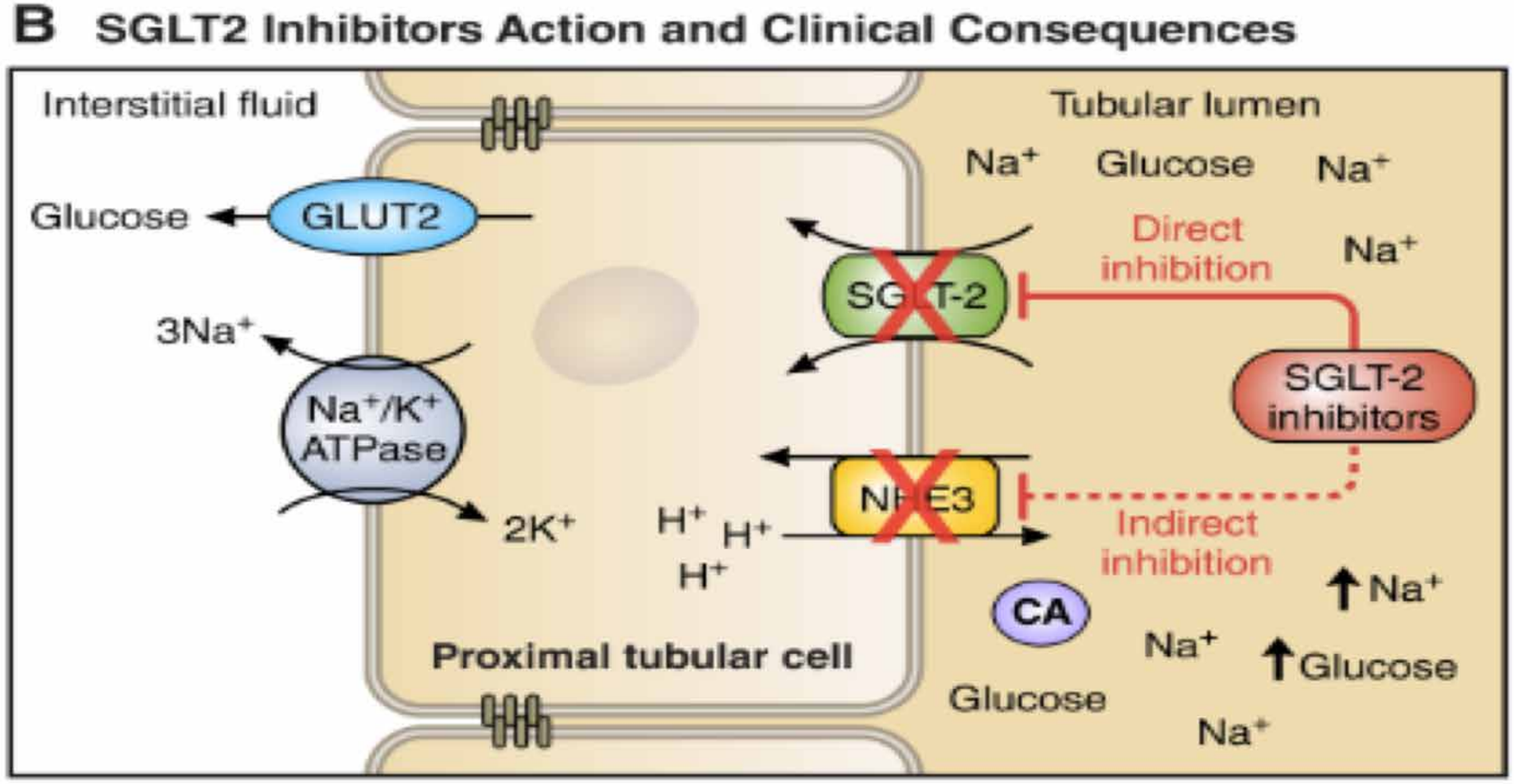

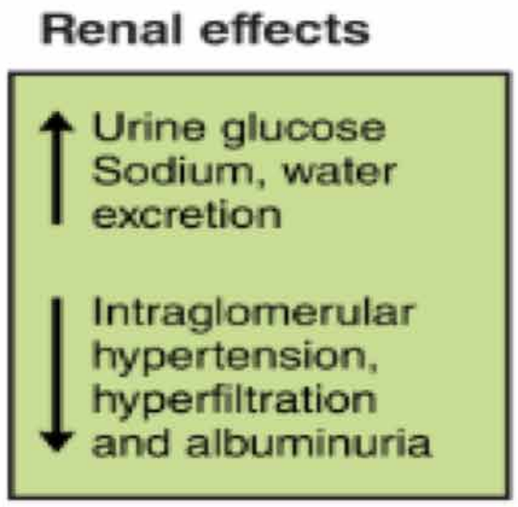

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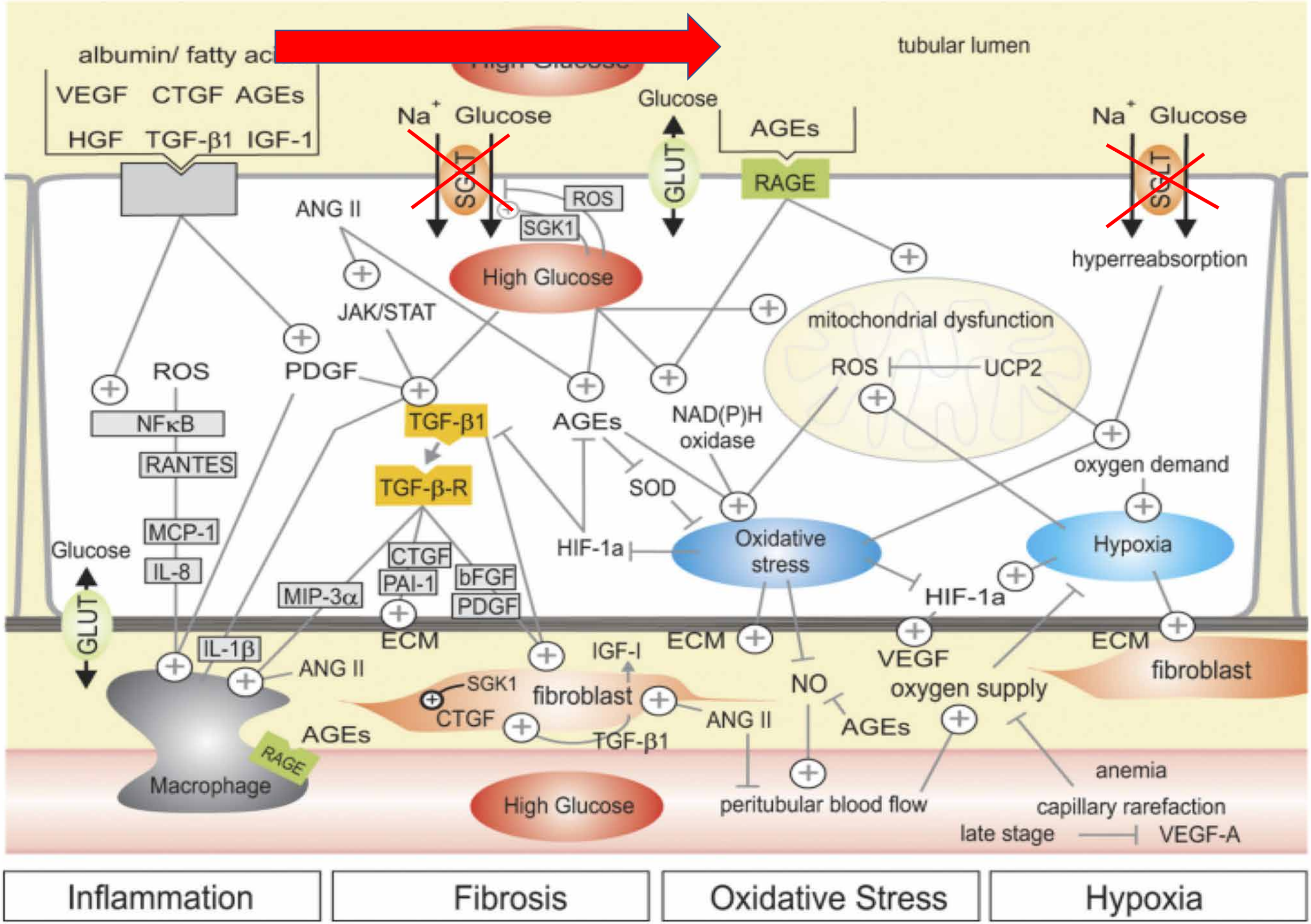

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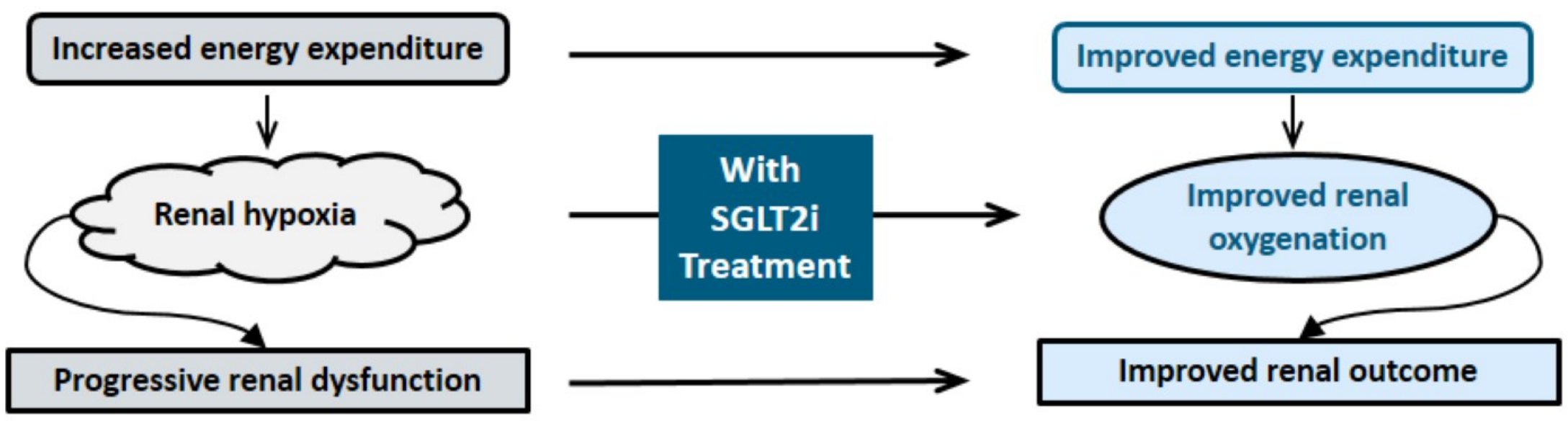
Suggested Changes in Renal Fuel Metabolism Before and After SGLT2 Inhibitor Therapy

T2DM Kidney	Preferred Substrate	With SGLT2i Treatment
Lactate/FFA Glutamate	S1/S2 segments	↓ Lactate/FFA ↔ Glutamate
Lactate/FFA Glutamate/glucose β-HB	S3 segment	↓ Lactate/FFA ↓ Glutamate/glucose ↑ β-HB
Lactate/FFA Glucose β-HB	Distal collecting tubules/cortical collecting tubules	↓ Lactate/FFA ↓ Glucose ↑ β-HB



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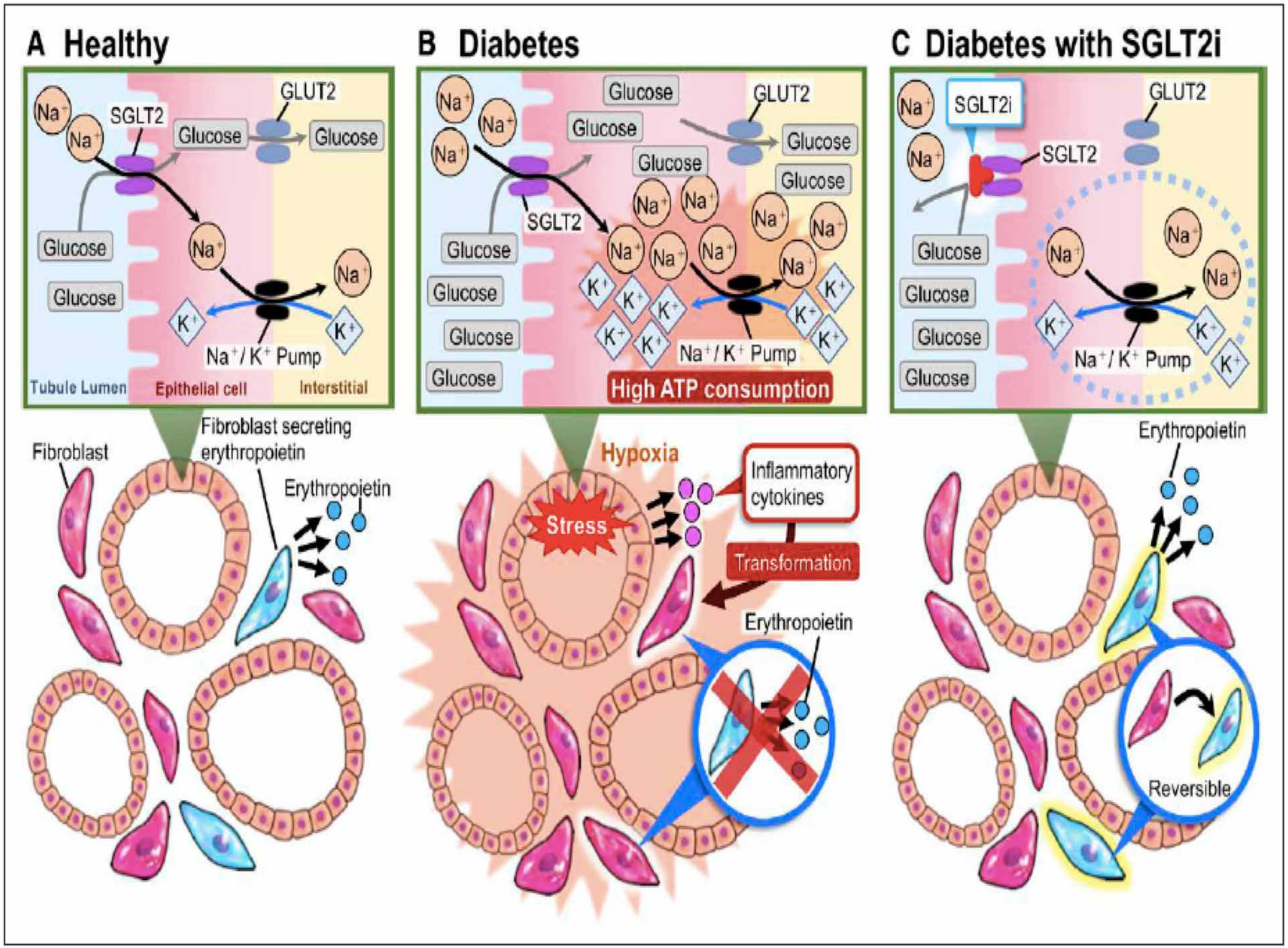

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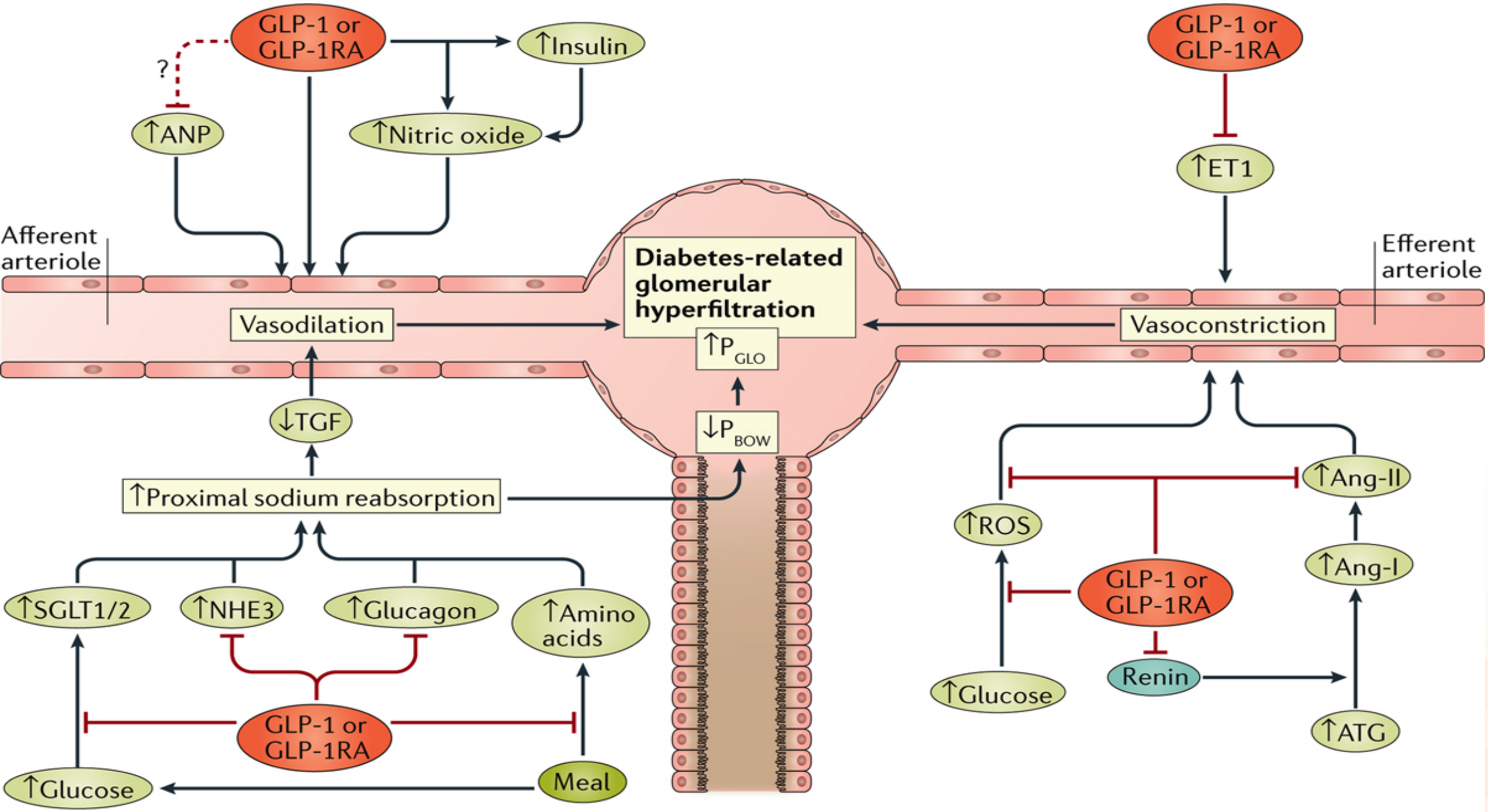
Effects of glucagon-like peptide 1 (GLP-1) and GLP-1 receptor agonists (GLP-1RAs) on renal haemodynamics in diabetes mellitus



Nature Reviews | Nephrology

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Muskiet, M. H. A. *et al.* (2017) GLP-1 and the kidney: from physiology to pharmacology and outcomes in diabetes. *Nat. Rev. Nephrol.* doi:10.1038/nrneph.2017.123

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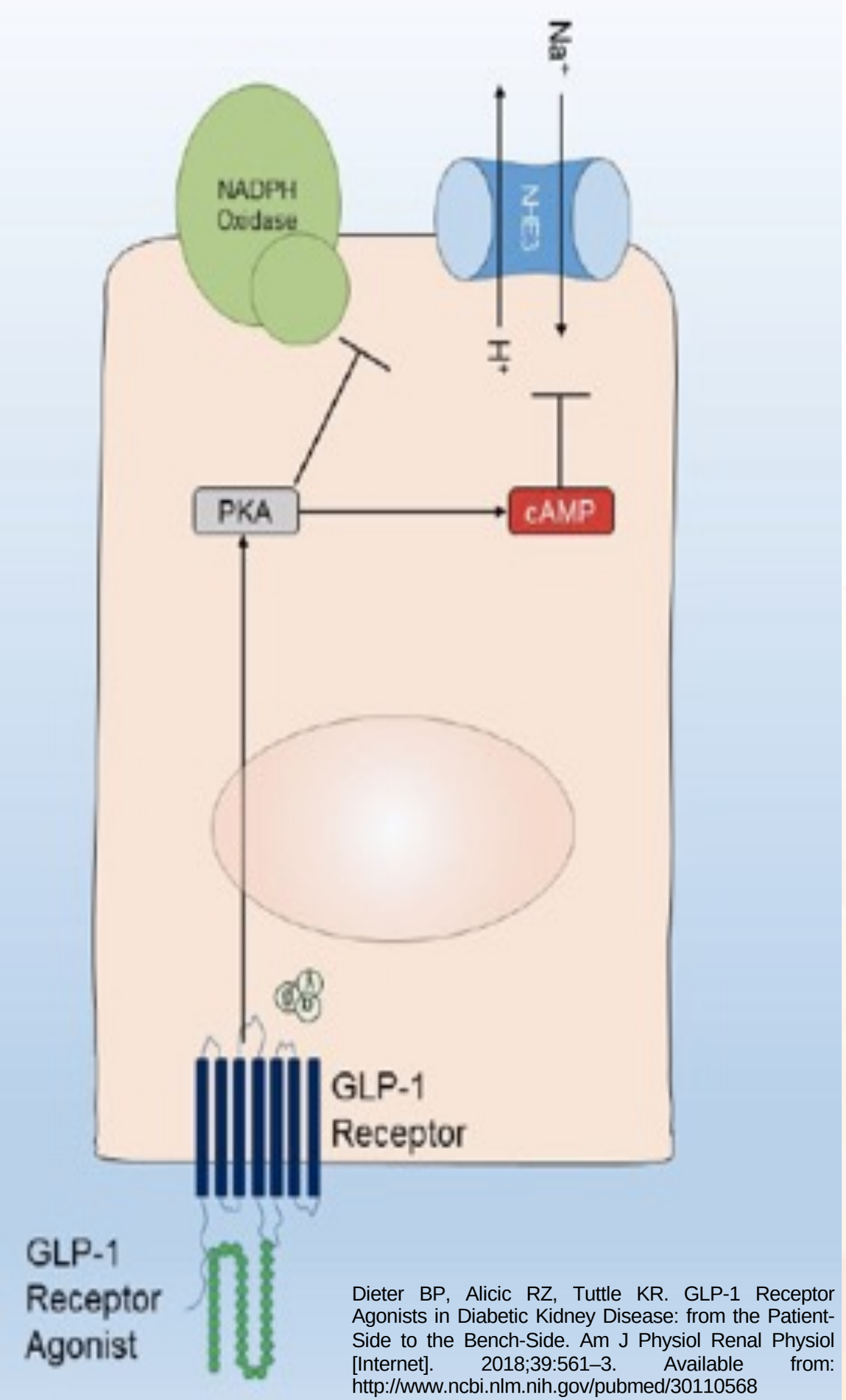
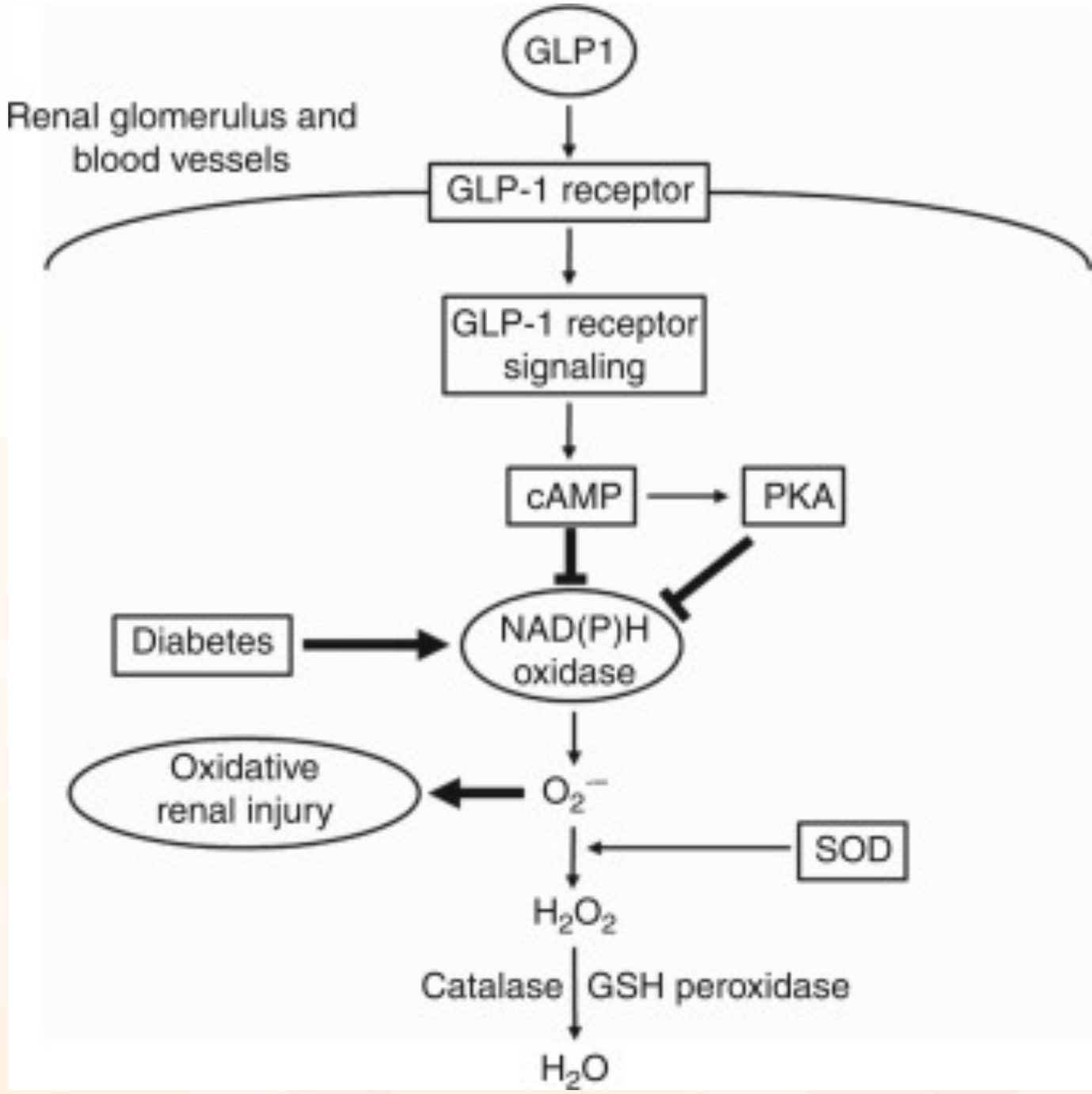


Dieter BP, Alicic RZ, Tuttle KR. GLP-1 Receptor Agonists in Diabetic Kidney Disease: from the Patient-Side to the Bench-Side. Am J Physiol Renal Physiol [Internet]. 2018;39:561–3. Available from: http://www.ncbi.nlm.nih.gov/pubmed/30110568

A conceptual model of hypothesized mechanisms for activation of natriuretic and anti-oxidant mechanisms by GLP-1 receptor agonists.



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WILEY

BRIEF REPORT

Effects of the SGLT-2 inhibitor dapagliflozin on glomerular and tubular injury markers

Claire C. J. Dekkers MD[1] | Sergei Petrykiv MD[2] | Gozewijn D. Laverman MD[3] | David Z. Cherney MD[4,5] | Ron T. Gansevoort MD[1] | Hiddo J. L. Heerspink PhD[1]

[1]Department of Clinical Pharmacy and Pharmacology, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands

[2]Department of Nephrology, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands

[3]Department of Nephrology, Ziekenhuisgroep Twente, Almelo and Hengelo, The Netherlands

[4]Department of Medicine, Division of Nephrology, Toronto General Hospital, University of Toronto, Toronto, Canada

[5]Department of Physiology and Banting and Best Diabetes Centre, University of Toronto, Toronto, Canada

Correspondence
Hiddo J. L. Heerspink, PhD, Department of Clinical Pharmacy and Pharmacology, University of Groningen, University Medical Center Groningen, Hanzeplein 1, 9700 RB Groningen, The Netherlands.
Email: h.j.lambers.heerspink@umcg.nl

The mechanisms by which SGLT-2 inhibitors lower albuminuria are incompletely understood. We assessed in a *post-hoc* analysis of a cross-over trial the effects of the SGLT2 inhibitor dapagliflozin on glomerular markers (IgG to IgG4 and IgG to albumin), tubular markers (urinary KIM-1, NGAL and LFABP) and inflammatory markers (urinary MCP-1 and IL-6) to provide more insight into kidney protective effects. Dapagliflozin decreased albuminuria by 43.9% (95% CI, 30.3%-54.8%) and eGFR by 5.1 (2.0-8.1) mL/min/1.73m^2 compared to placebo. Dapagliflozin did not change glomerular charge or size selectivity index compared to placebo. Dapagliflozin decreased urinary KIM-1 excretion by 22.6% (0.3%-39.8%; P = .05) and IL-6 excretion by 23.5% (1.4%-40.6%; P = .04) compared to placebo, whereas no changes in NGAL, LFABP and MCP-1 were observed. During dapagliflozin treatment, changes in albuminuria correlated with changes in eGFR (r = 0.36; P = .05) and KIM-1 (r = 0.39; P = .05). In conclusion, the albuminuria-lowering effect of 6 weeks of dapagliflozin therapy may be the result of decreased intraglomerular pressure or reduced tubular cell injury.

KEYWORDS
acute kidney injury, dapagliflozin, KIM-1, MCP-1, SGLT-2, type 2 diabetes

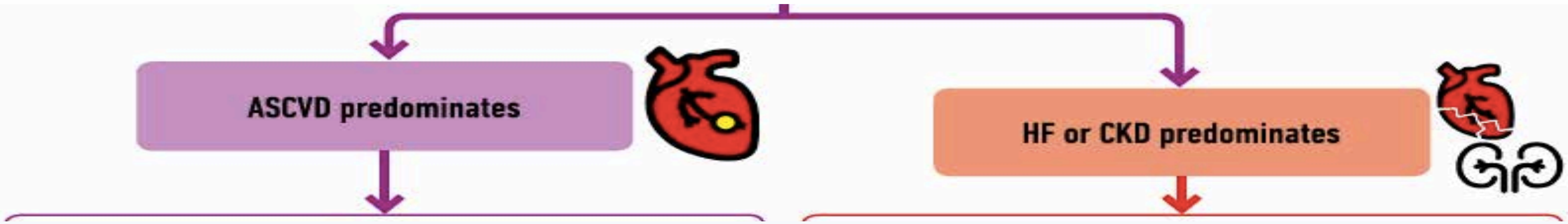
Dismuyó de manera significativa KIM-1 e IL-6

Urinary IgG and IgG4 glomerular damage

Urinary kidney injury molecule-1 (KIM-1), neutrophil gelatinase-associated lipocalin (NGAL) and liver-type fatty acid-binding protein (LFABP) tubular damage

Urinary monocyte chemo attractant protein-1 (MCP-1) and urinary interleukin-6 (IL-6) inflamation

CONCLUSIONES



- **11.3 For patients with type 2 diabetes and diabetic kidney disease, consider use of an SGLT2 inhibitor in patients with an eGFR ≥ 30 mL/min/1.73m² and particularly in those with > 300 mg/g albuminuria to reduce risk of CKD progression, cardiovascular events, or both.** ***Grade of evidence: A***

- **In patients with CKD who are at increased risk for cardiovascular events, use of a glucagon-like peptide 1 (GLP-1) receptor agonist may reduce risk of progression of albuminuria, cardiovascular events, or both.** ***Grade of evidence: C***

Davie … ensus
Repo…
2018…

GRACIAS POR SU ATENCIÓN

David León Jiménez
Internal Medicine
Diabetes, Obesity and Vascular Risk Specialist
Virgen del Rocío University Hospital. UCAMI
QuironSalud Sevilla
@drleonjimenez