



National Taiwan University
College of Medicine

Physiology and Pathophysiology of Kidney Pericytes

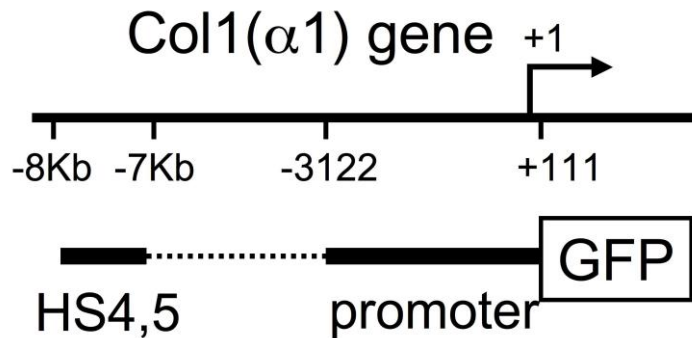
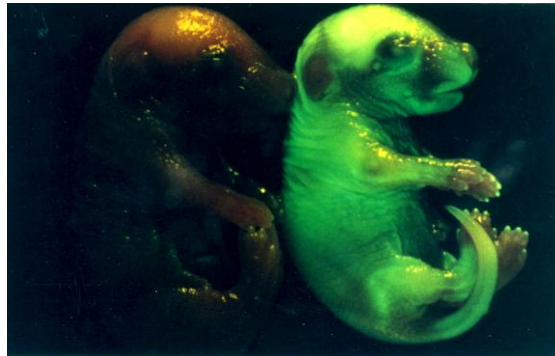


Shuei-Liong Lin, MD, PhD
National Taiwan University
Taipei, Taiwan

Collagen producing cells (fibroblasts) are perivascular in normal adult kidney

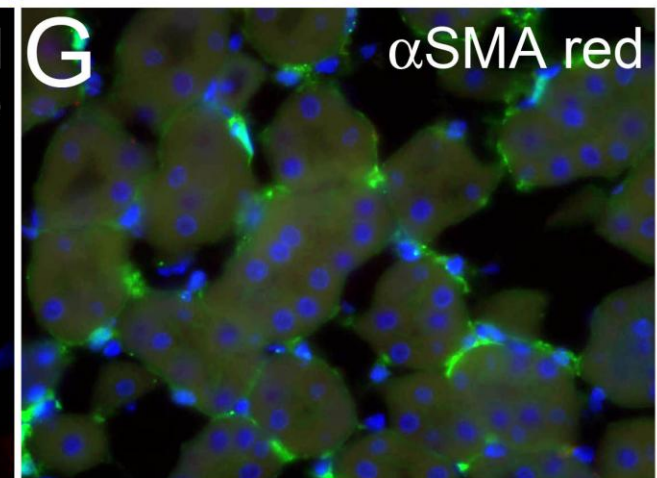
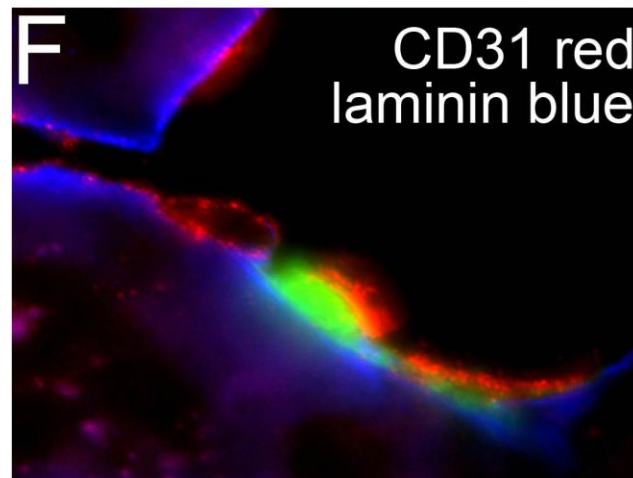
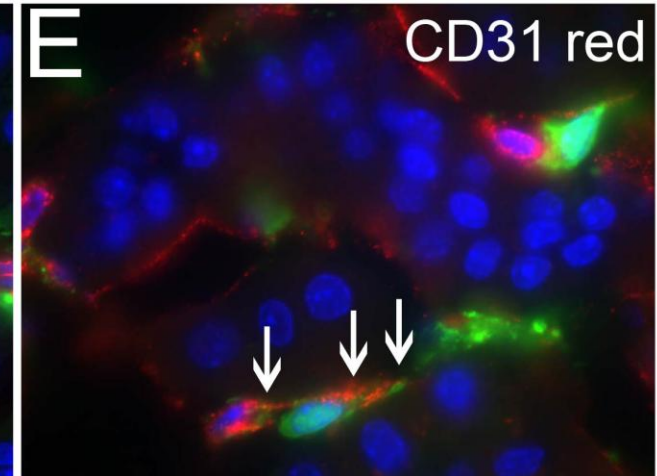
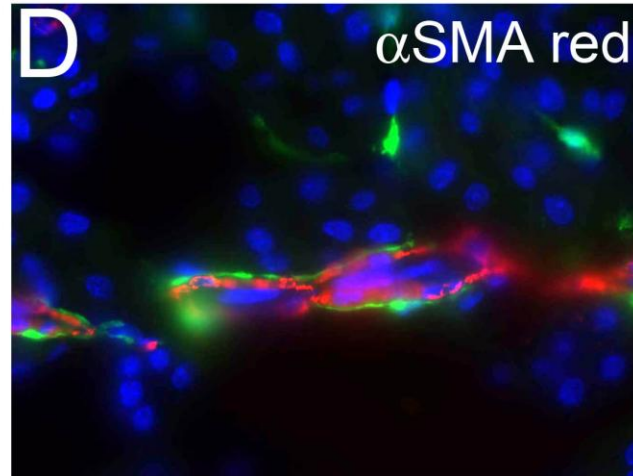
Gift from Dr. David Brenner (UCSD)

Col1a1-GFP^{Tg} mice



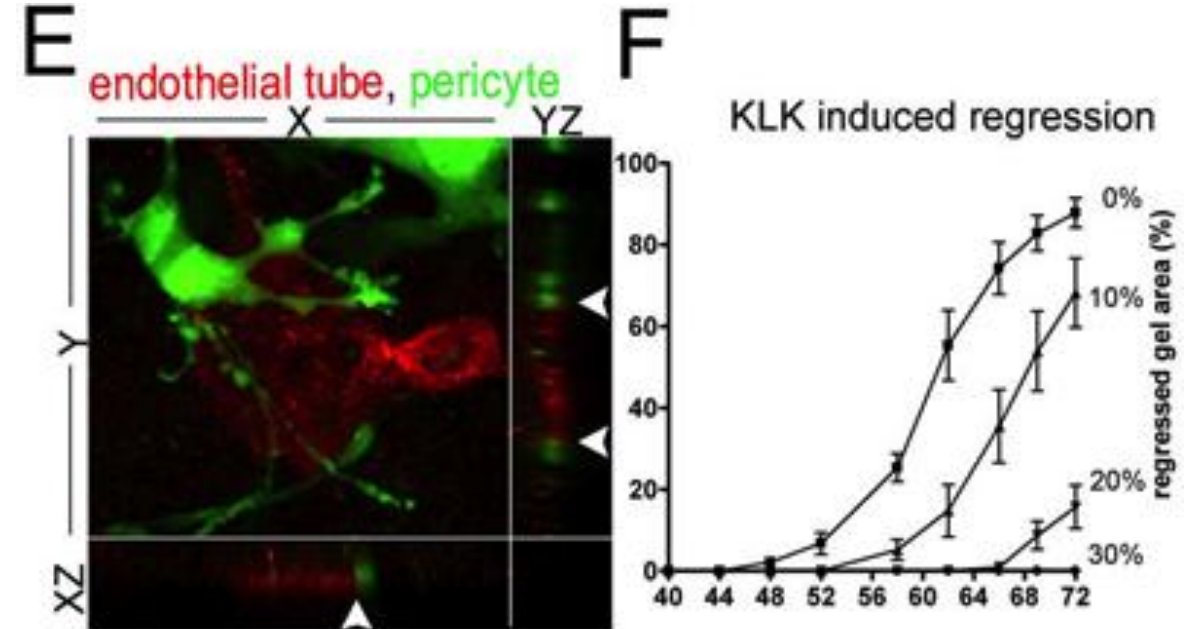
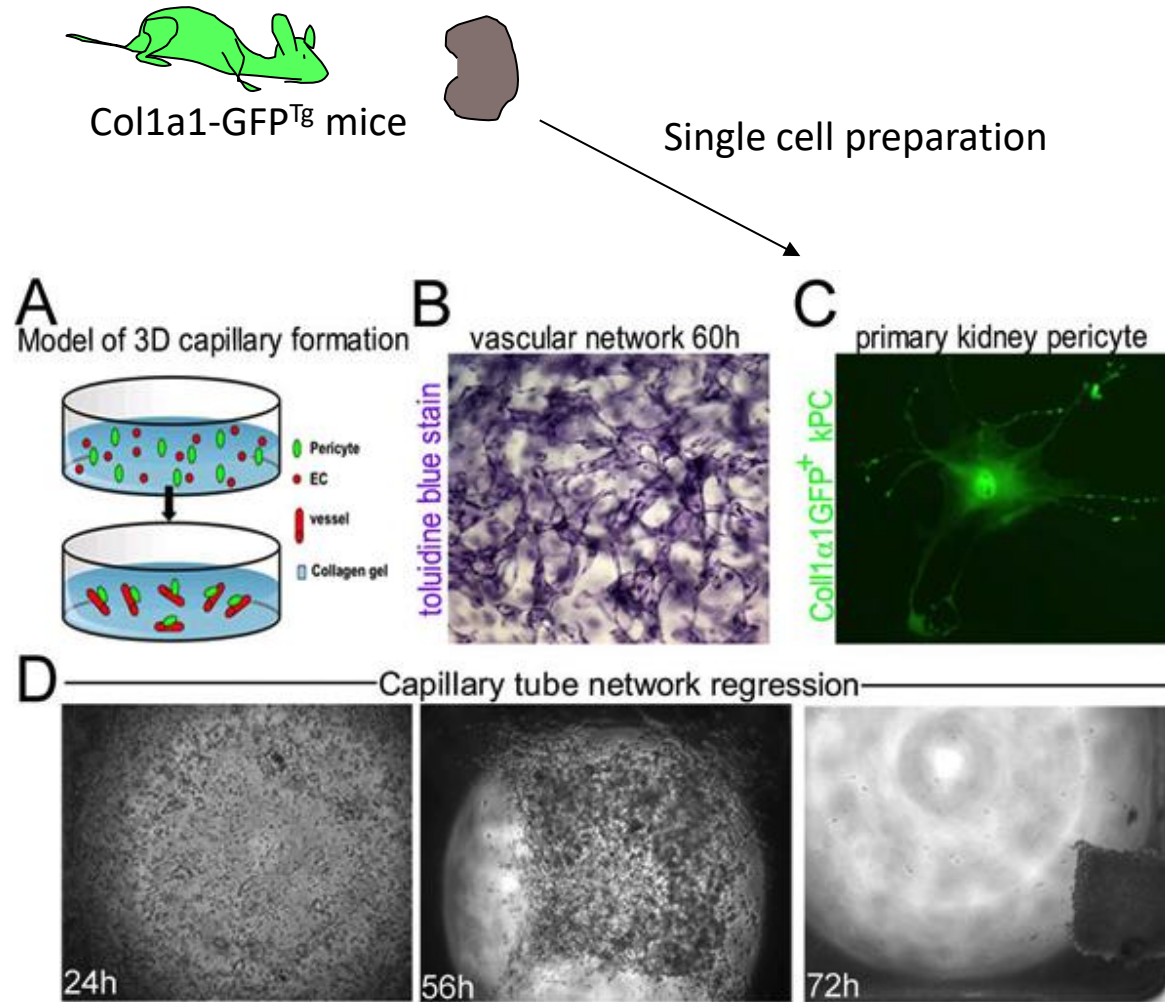
Am J Pathol. 2008;173(6):1617-27

Perivascular fibroblasts (Col1a1-GFP⁺)



Perivascular fibroblasts (pericytes) stabilize vascular tube

J Am Soc Nephrol 2012;23(5):868-83.



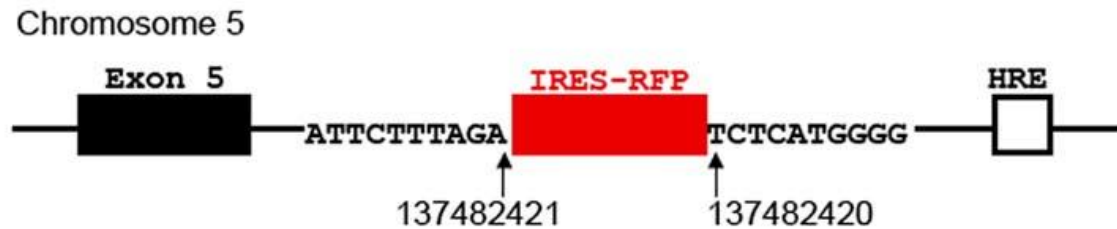


Pericytes produce erythropoietin (EPO)

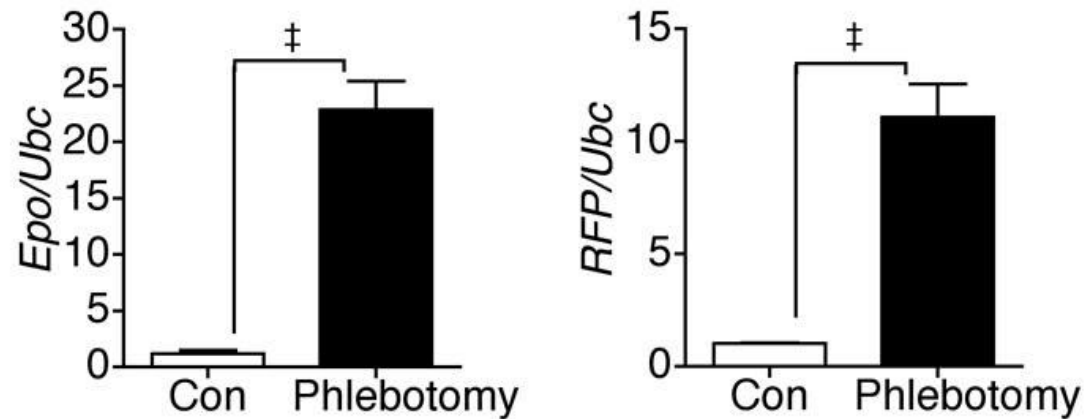
Chang YT

J Clin Invest. 2016 Feb;126(2):721-31.

A *Epo*^{IRES-RFP/+} mice



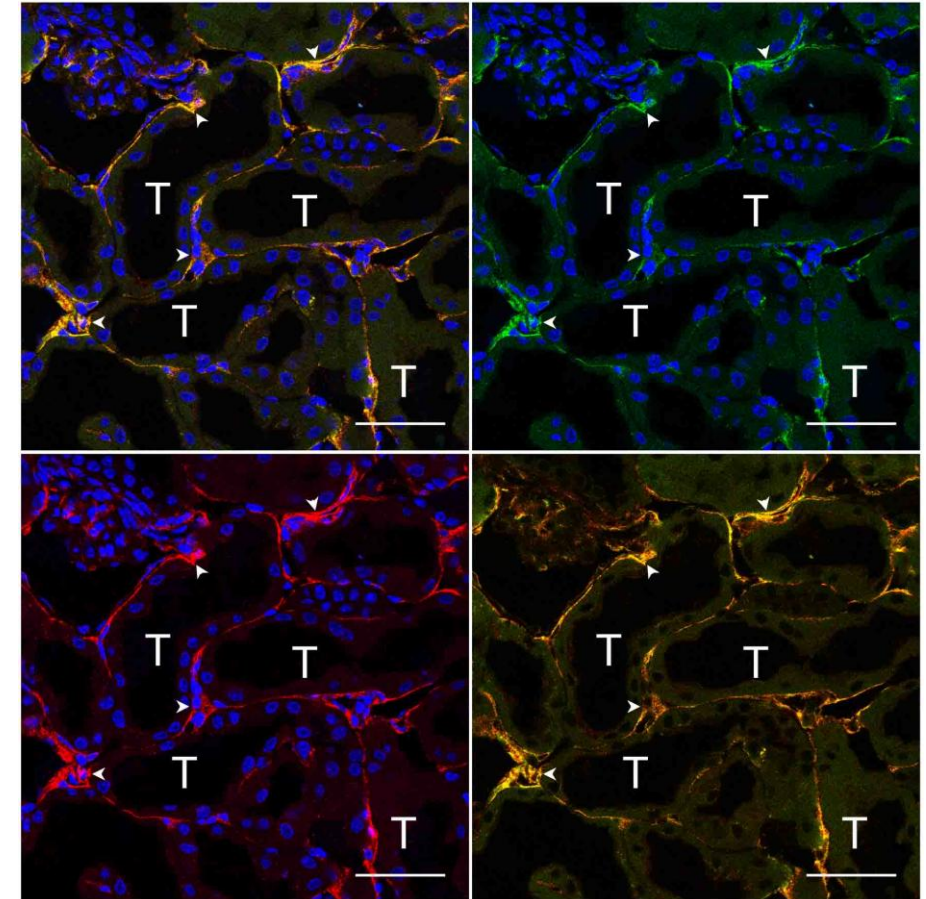
B *Epo*^{IRES-RFP/+} mice



Col1a1-GFP^{Tg}; *Epo*^{IRES-RFP/+} mice

merge

Col1a1-GFP

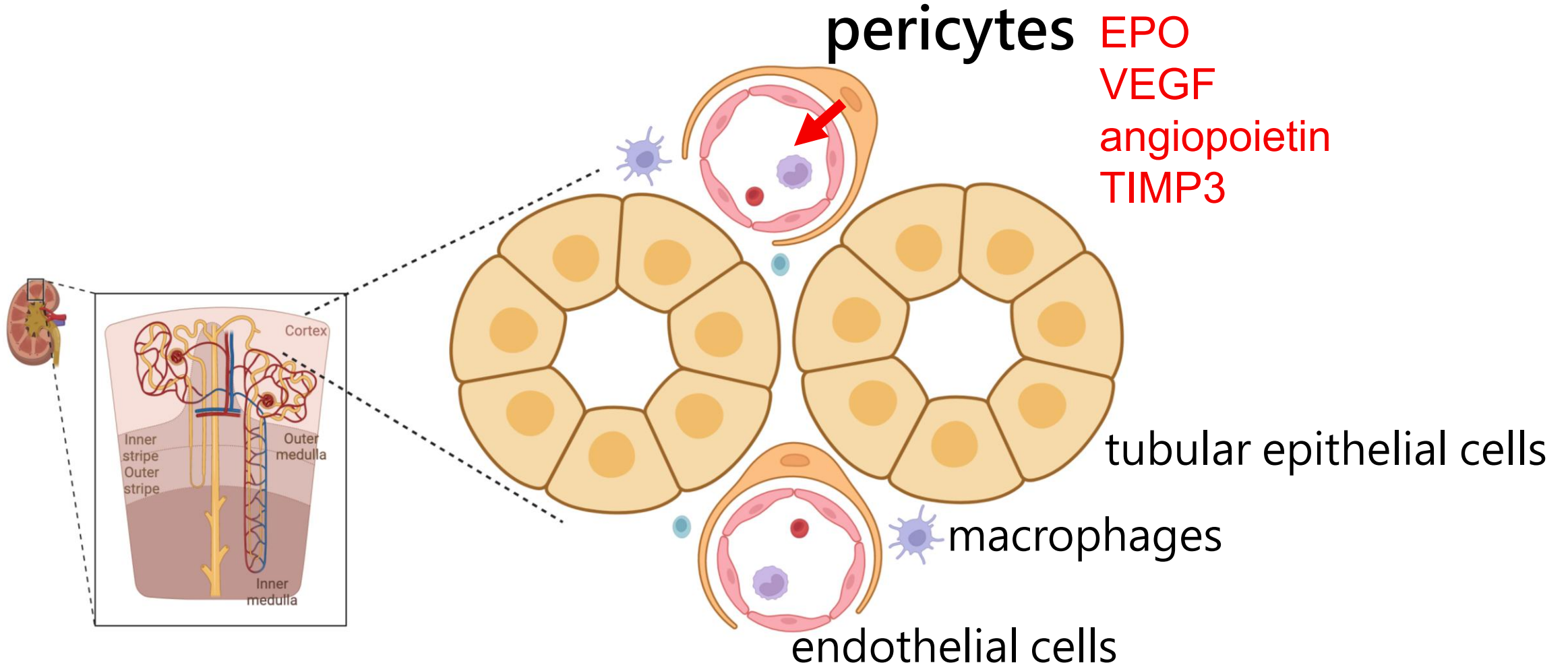


Epo-RFP

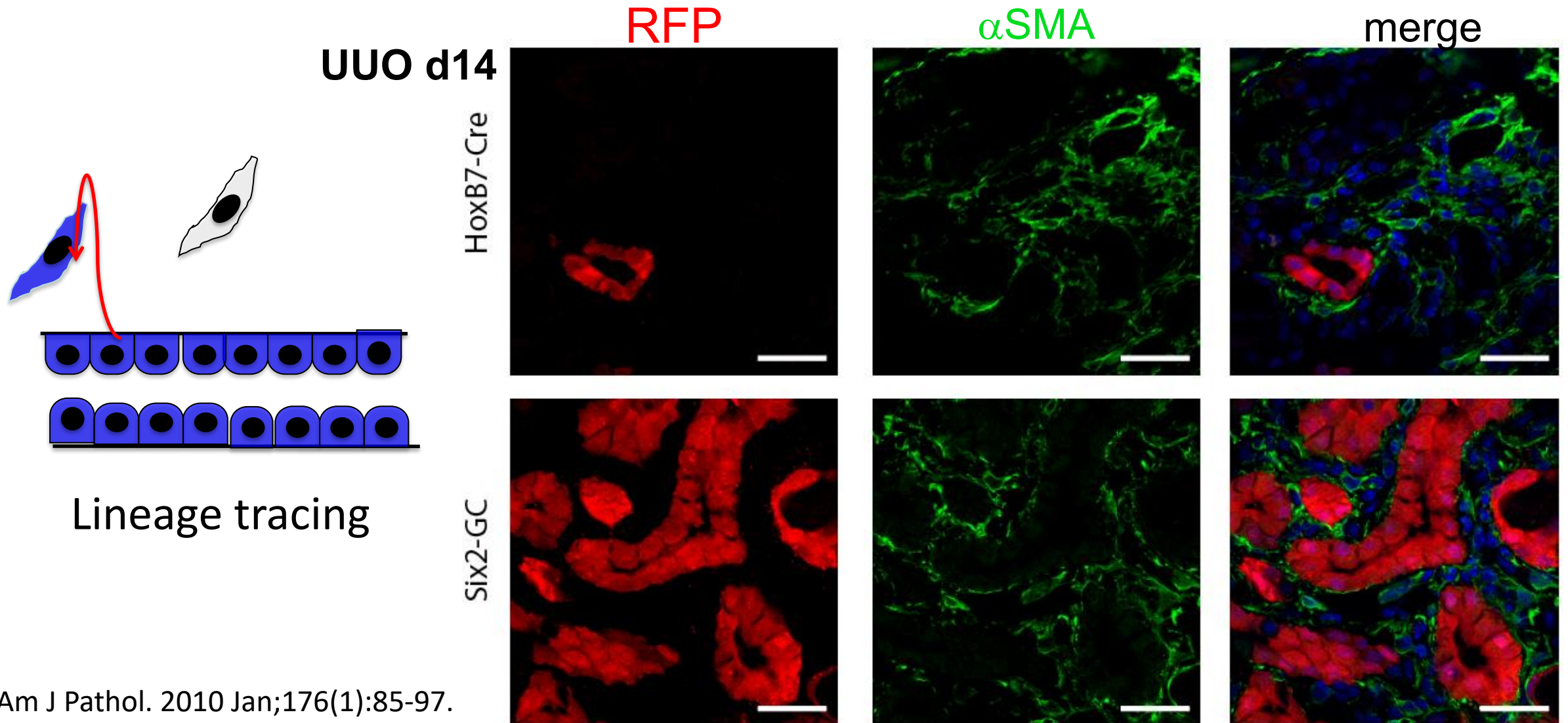
Col1a1-GFP Epo-RFP

Summary 1

Pericytes produce EPO and stabilize blood vessels

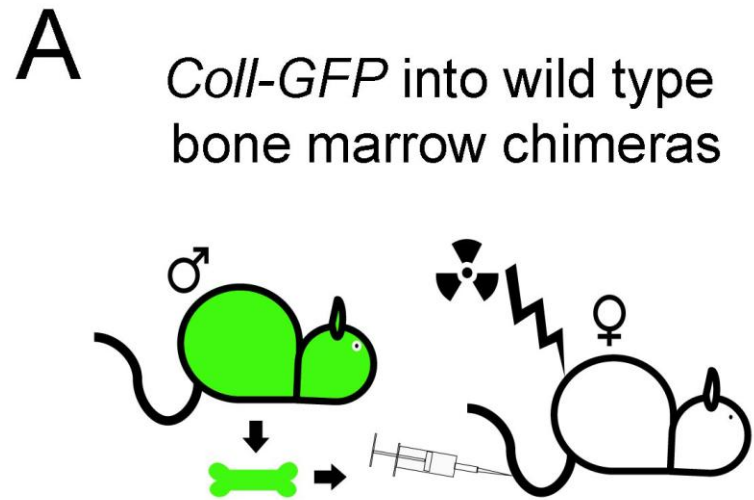


No EMT of renal tubular epithelial cells during kidney fibrosis

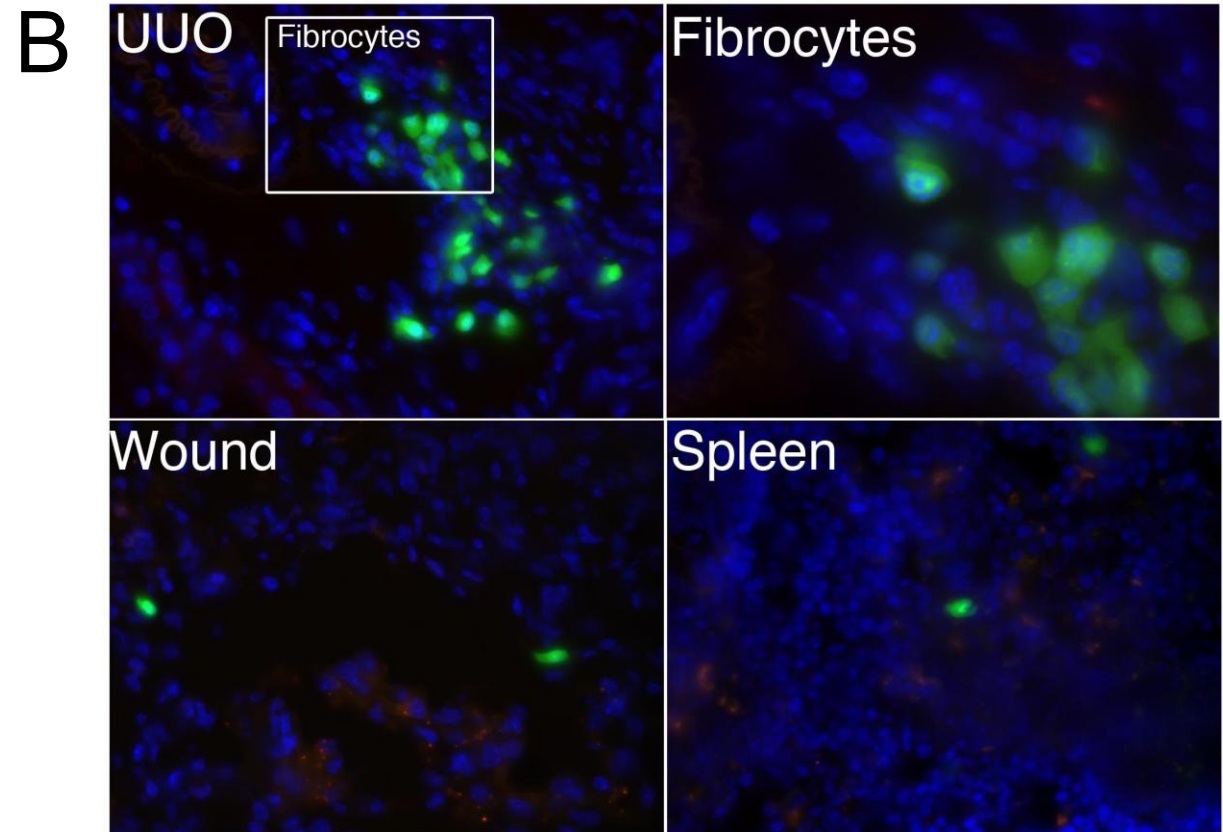


Am J Pathol. 2010 Jan;176(1):85-97.

Bone marrow-derived fibrocytes do not contribute to myofibroblasts



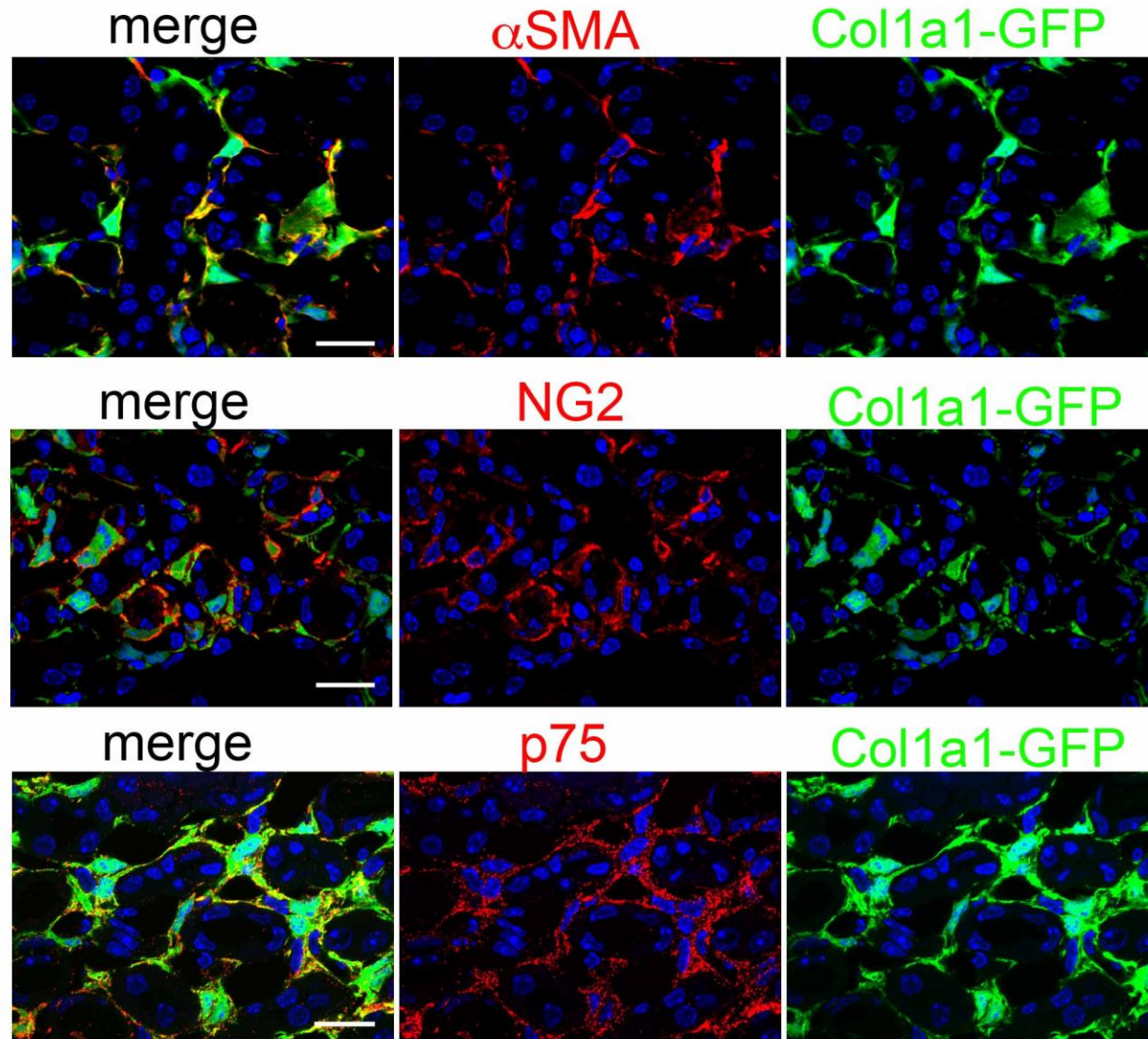
Am J Pathol. 2008 Dec;173(6):1617-27



Pericytes are activated to myofibroblasts after UUO



Col1a1-GFP^{Tg} mice



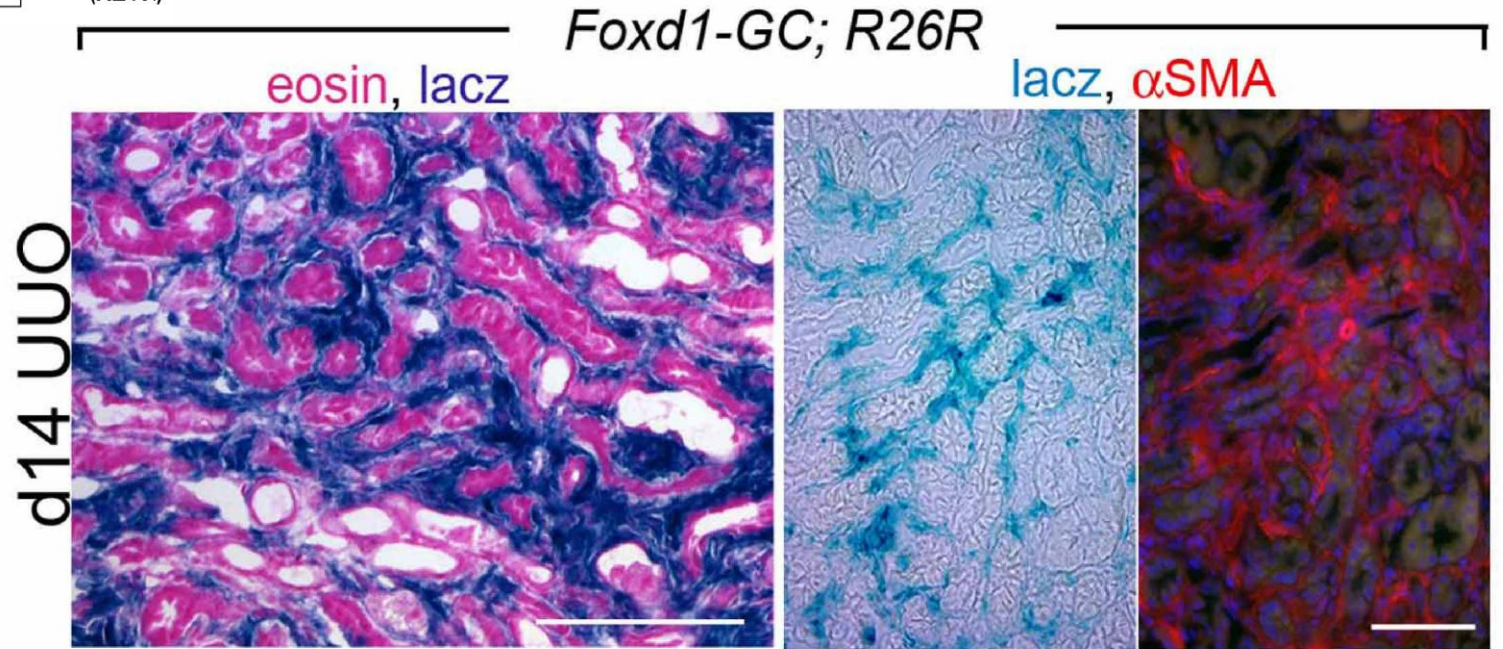
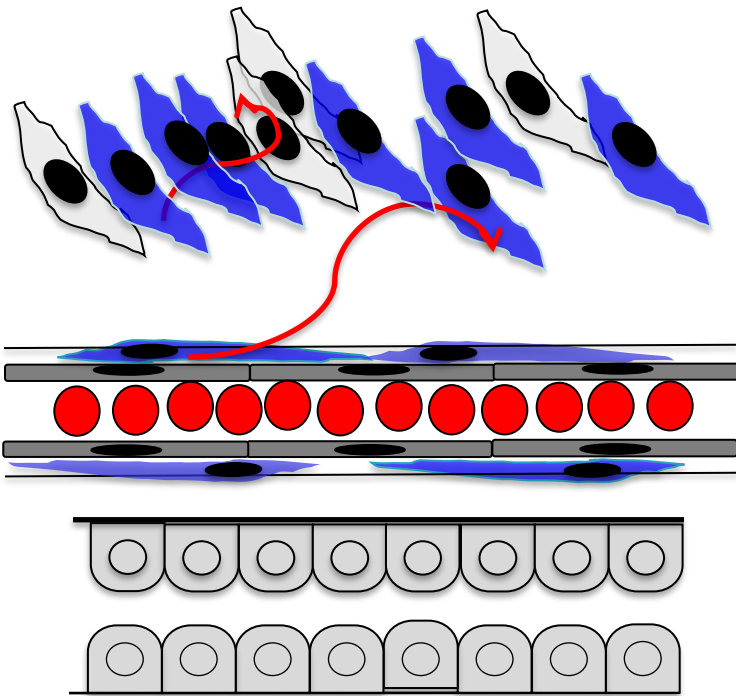
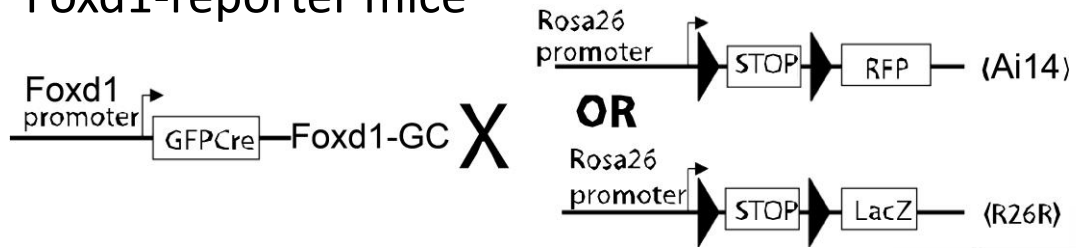
Chang FC

Am J Pathol.
2011;178(2):911-23.

Lineage tracing the fate of pericytes after progressive injury

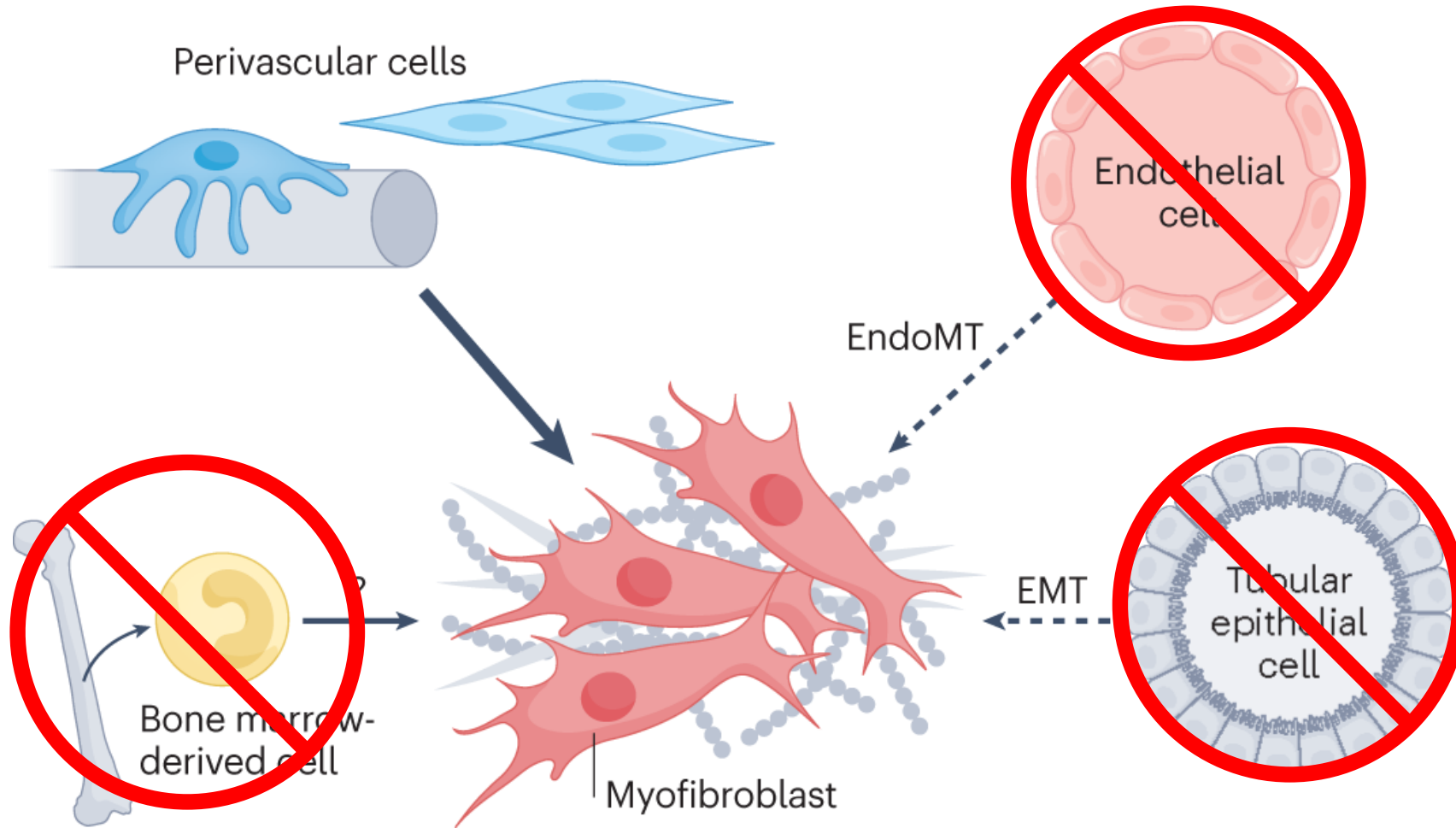
Am J Pathol. 2010;176(1):85-97.

Foxd1-reporter mice



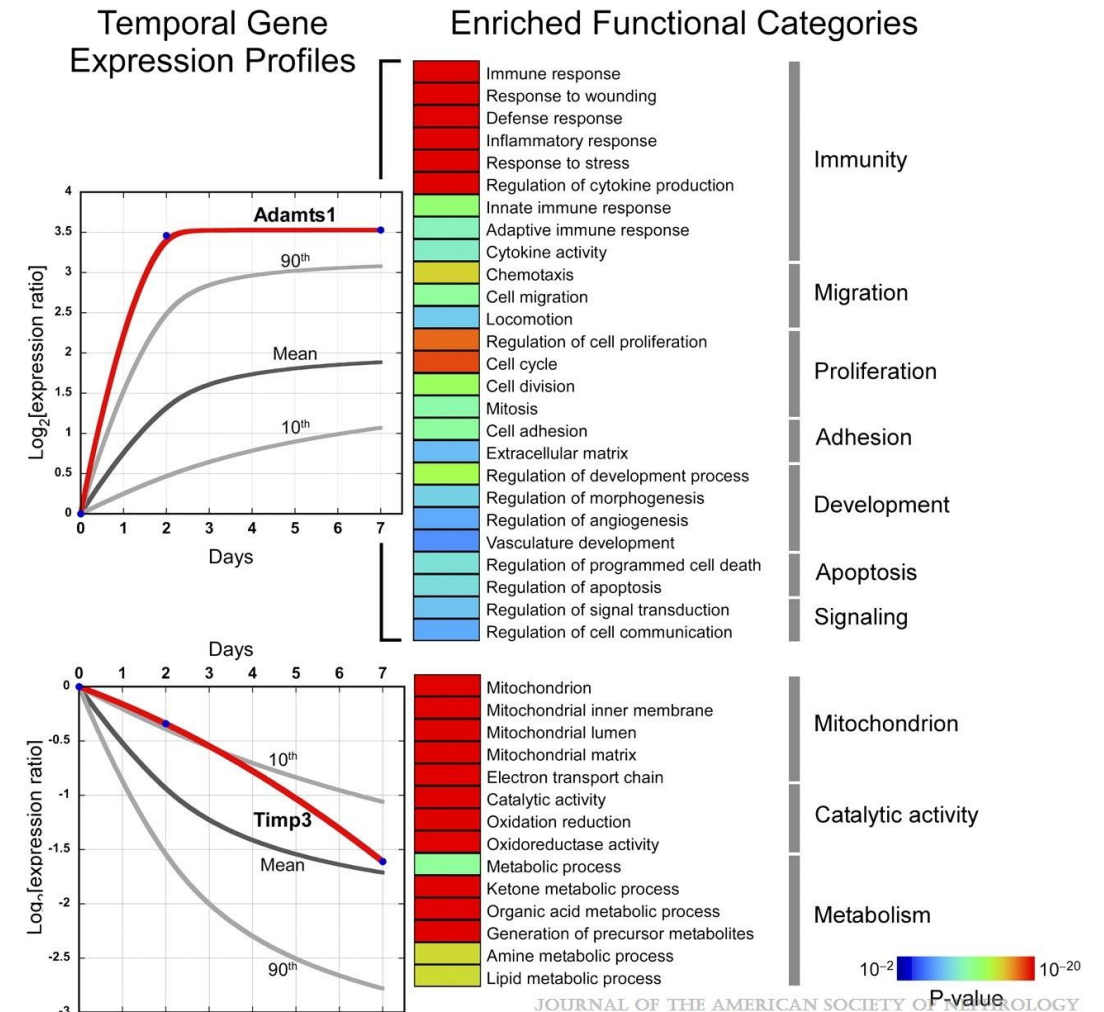
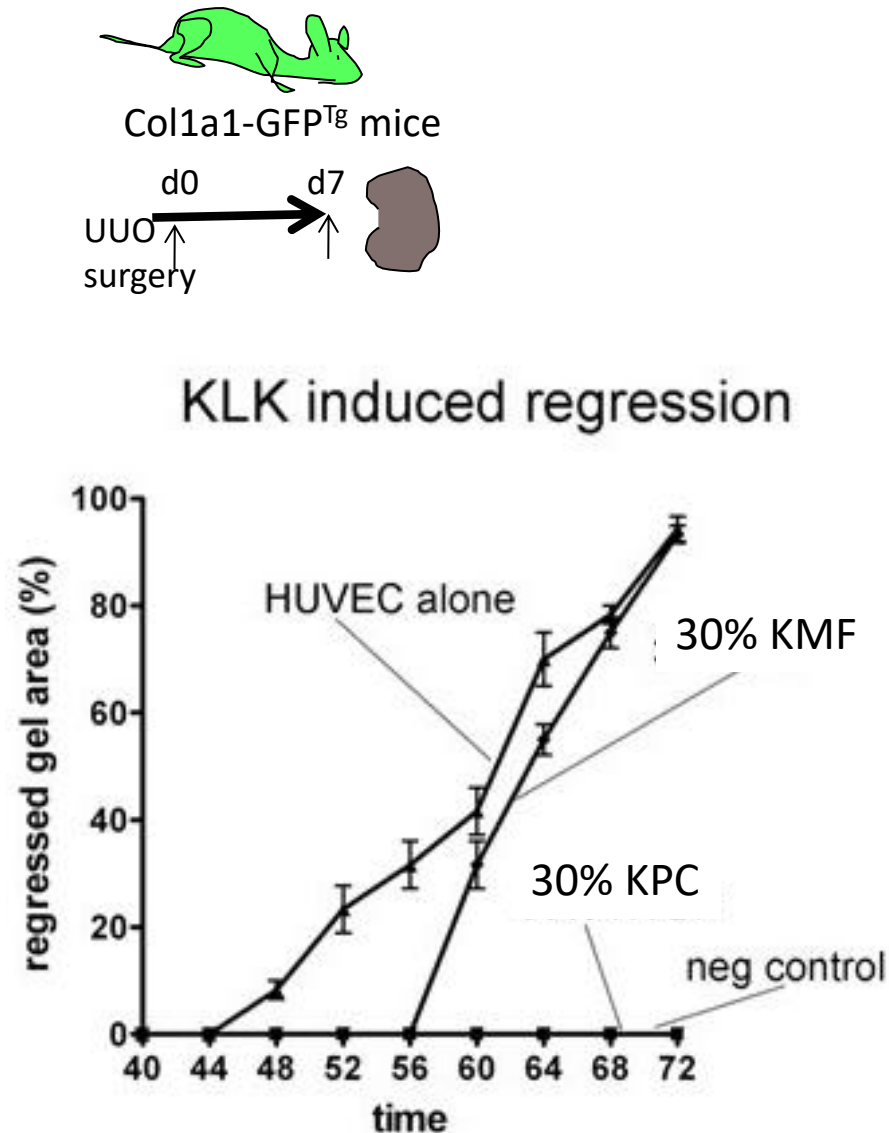
Summary 2

Pericytes: main cellular source of kidney myofibroblasts



Kidney myofibroblasts fail to stabilize vascular tube

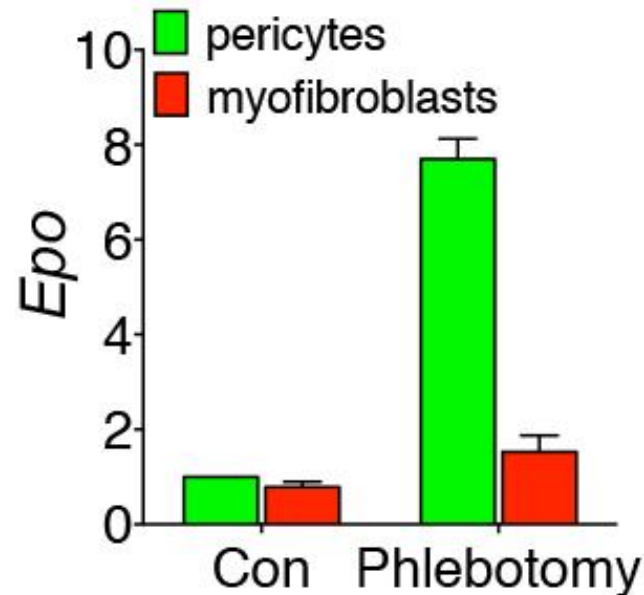
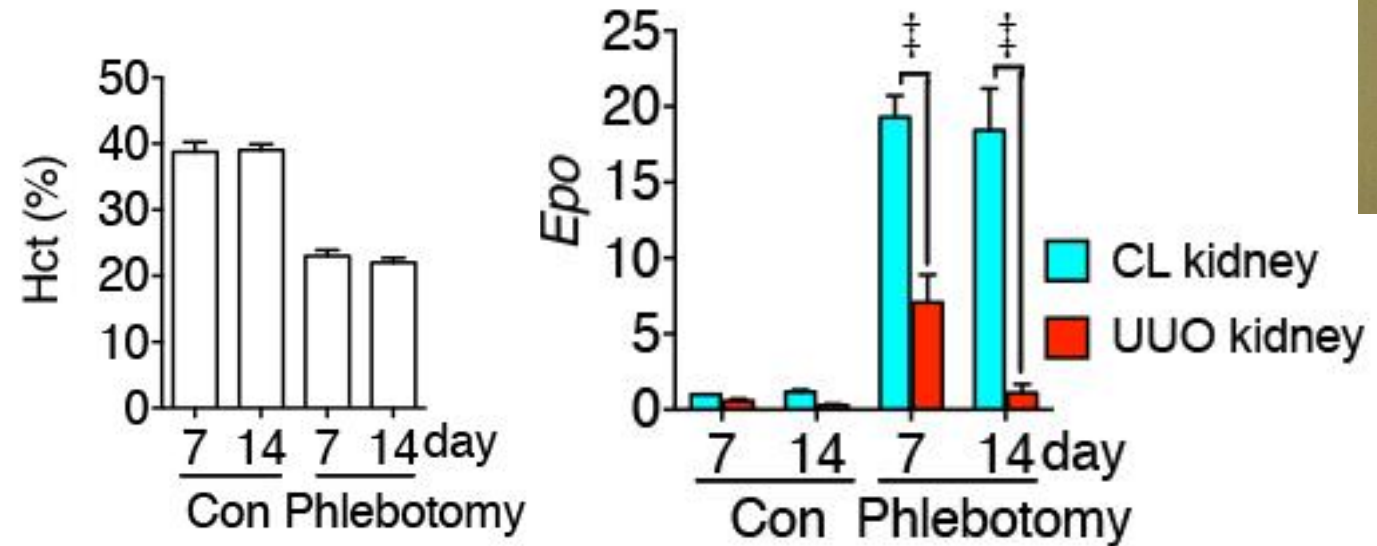
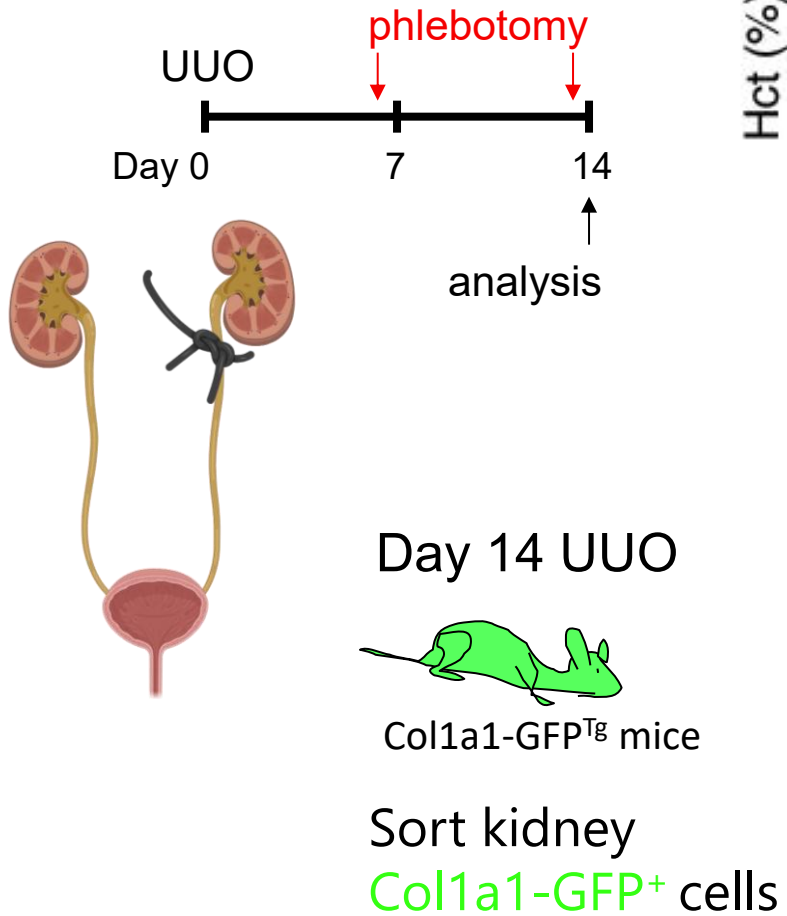
J Am Soc Nephrol 2012;23(5):868-83.



Myofibroblasts fail to produce EPO



Chang YT



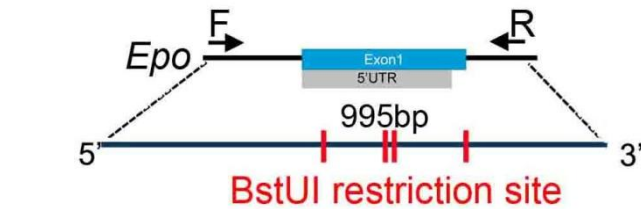
JCI 2016; 126(2):721-31.

Hypermethylation in *Epo* 5'-regulatory element of myofibroblasts



Chang YT

Bisulfite Genomic Sequencing (BGS)



pGEM-T easy

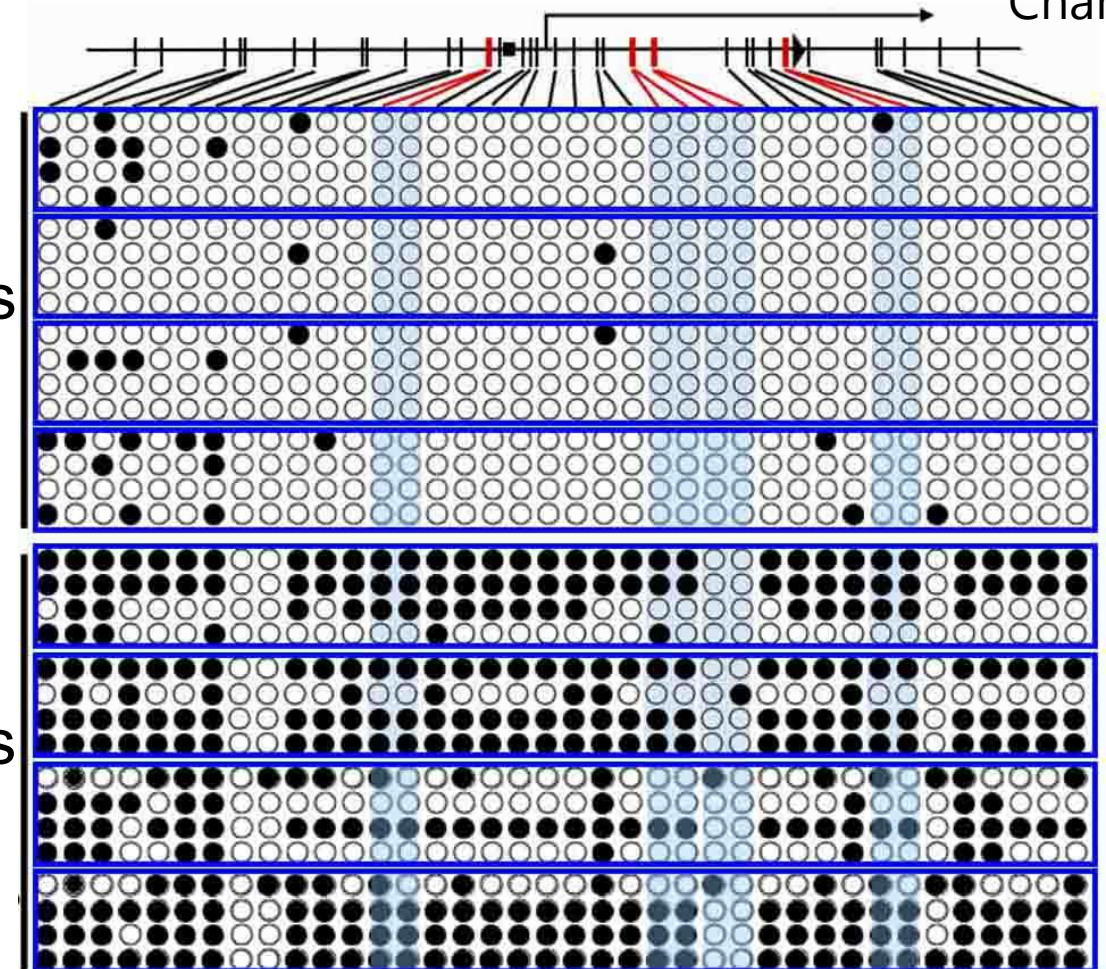
transformation

Sequencing

pericytes

myofibroblasts

JCI 2016; 126(2):721-31.

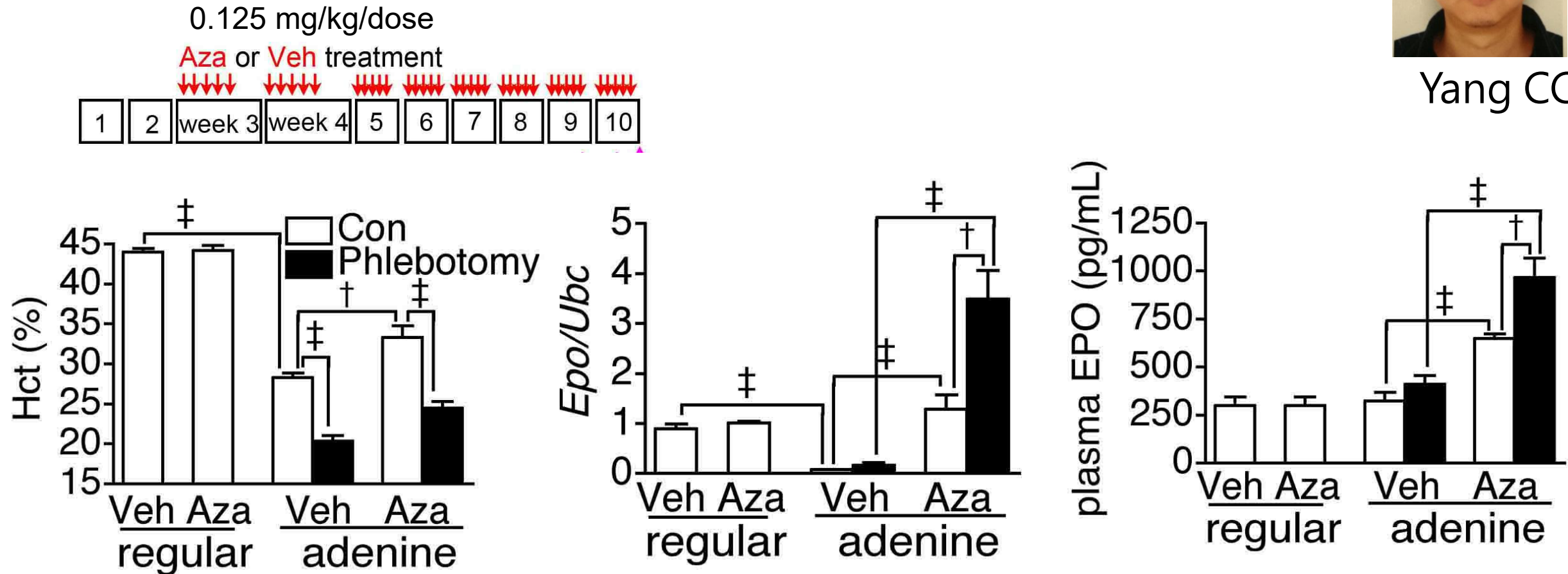


5-Azacytine restores EPO and ameliorates anemia in chronic adenine model

JCI 2016; 126(2):721-31.



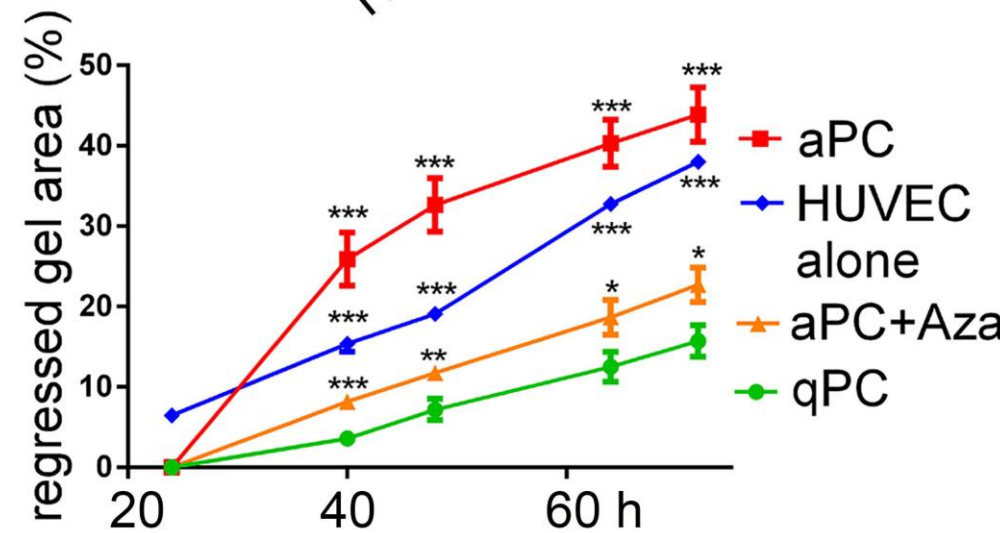
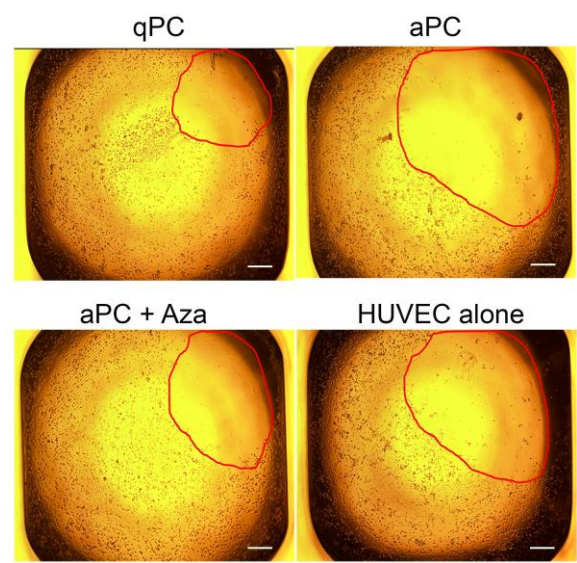
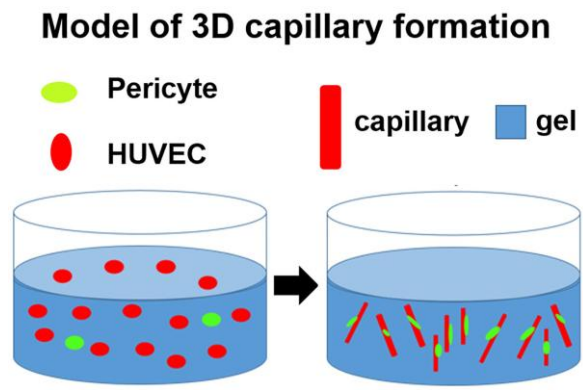
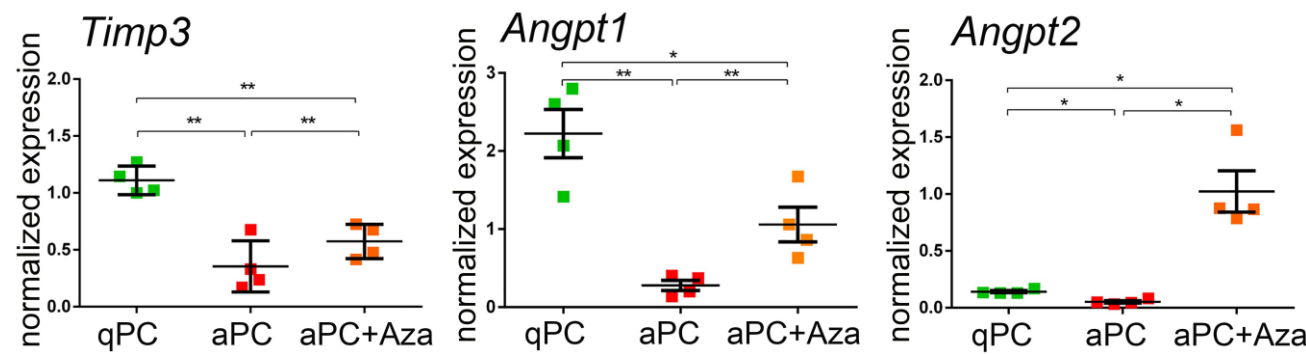
Yang CC



5-Azacytidine restores the vasculature-stabilizing function

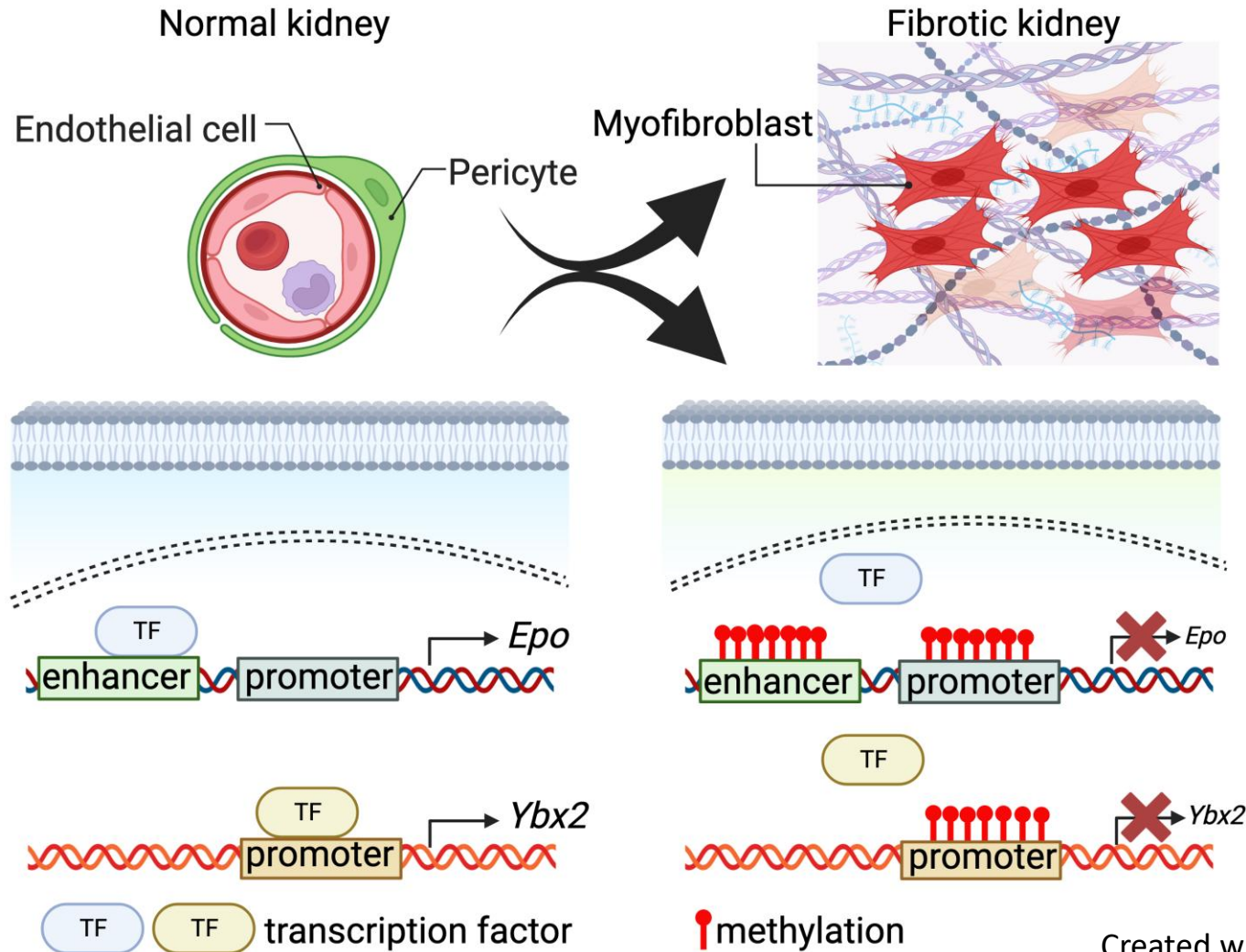


Chou YH

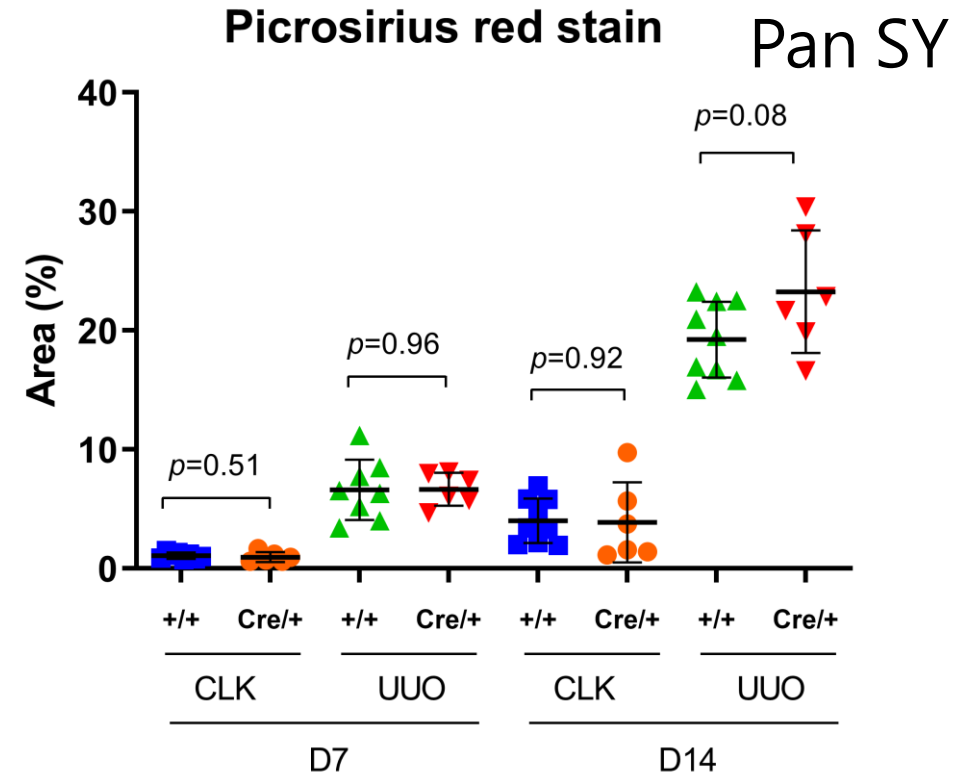
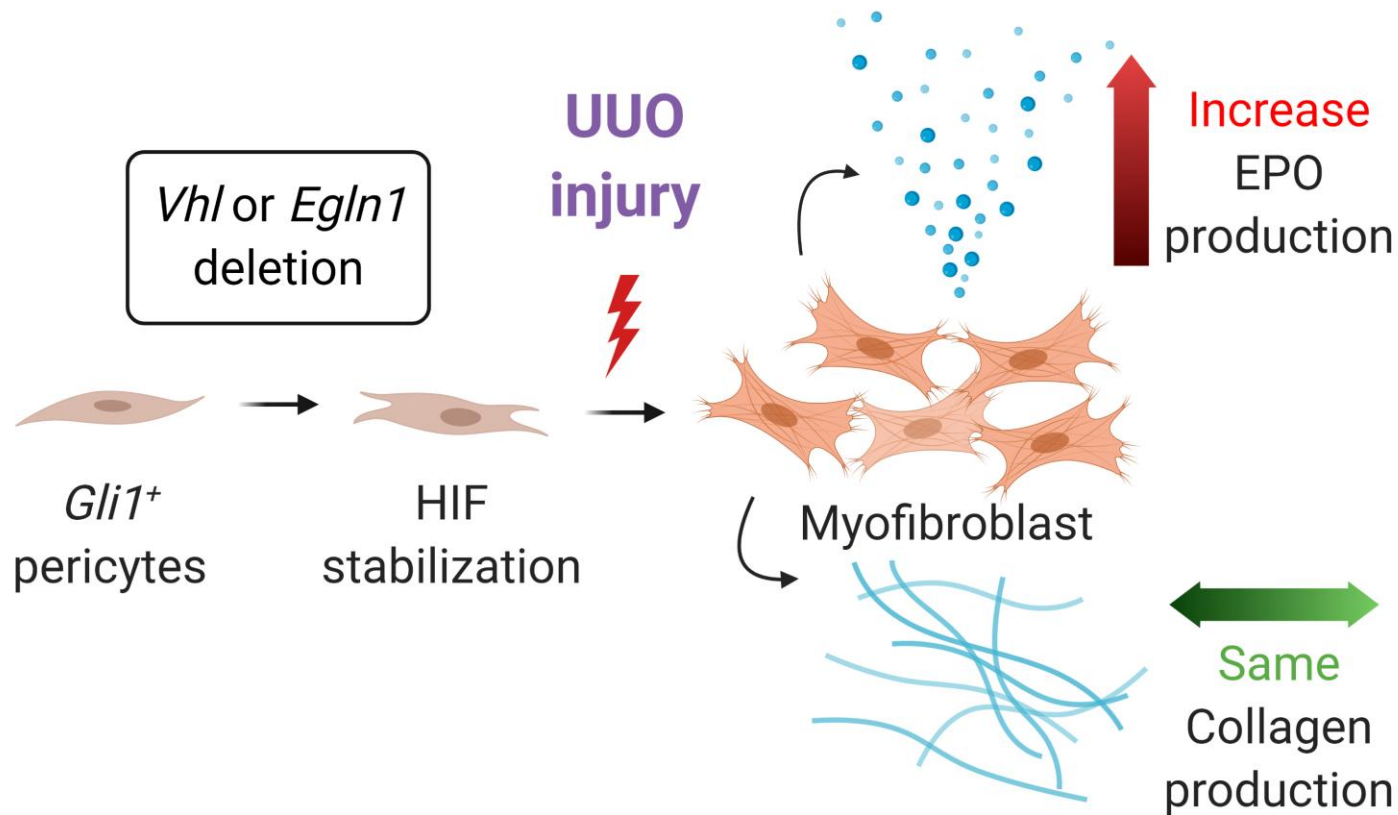


Summary 3

Pericyte-myofibroblast transition after kidney injury



Pericyte-specific HIF stabilization increases erythropoiesis but not renal fibrosis



Kidney Int 2021; 99(6):1354-1368.

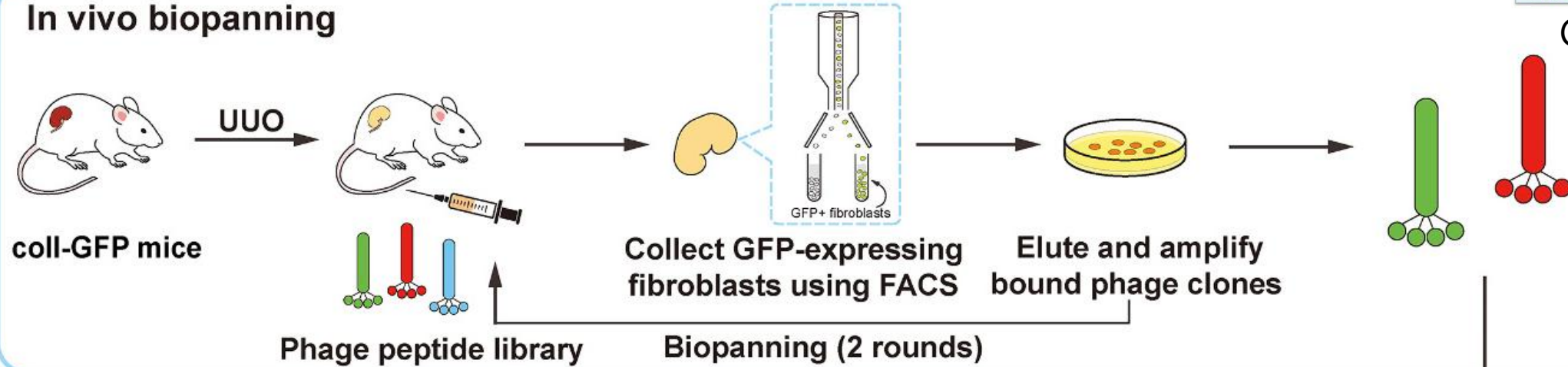
Myofibroblast-specific drug delivery system

J Control Release 2022;346:169-179

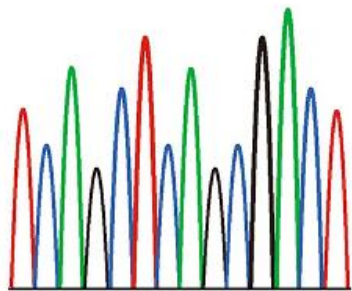


Cheng HT

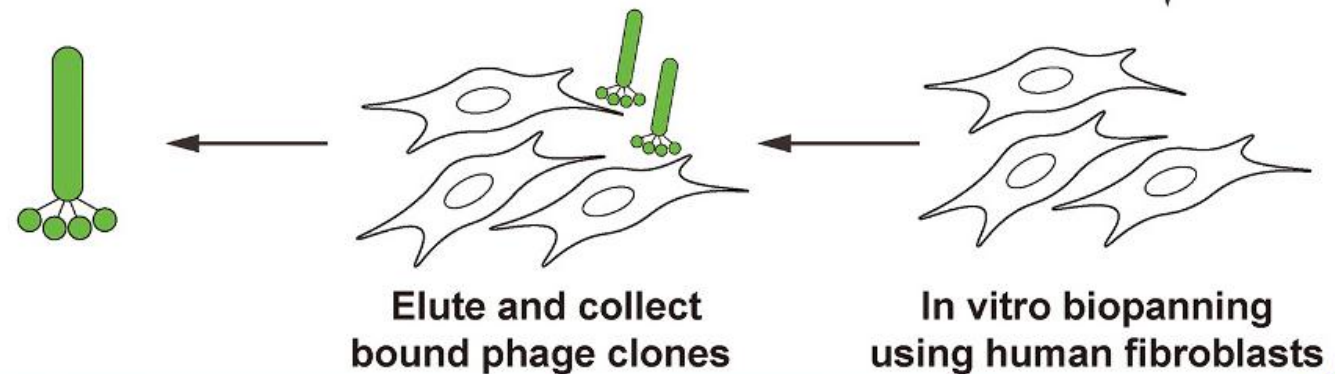
In vivo biopanning



Sequencing analysis



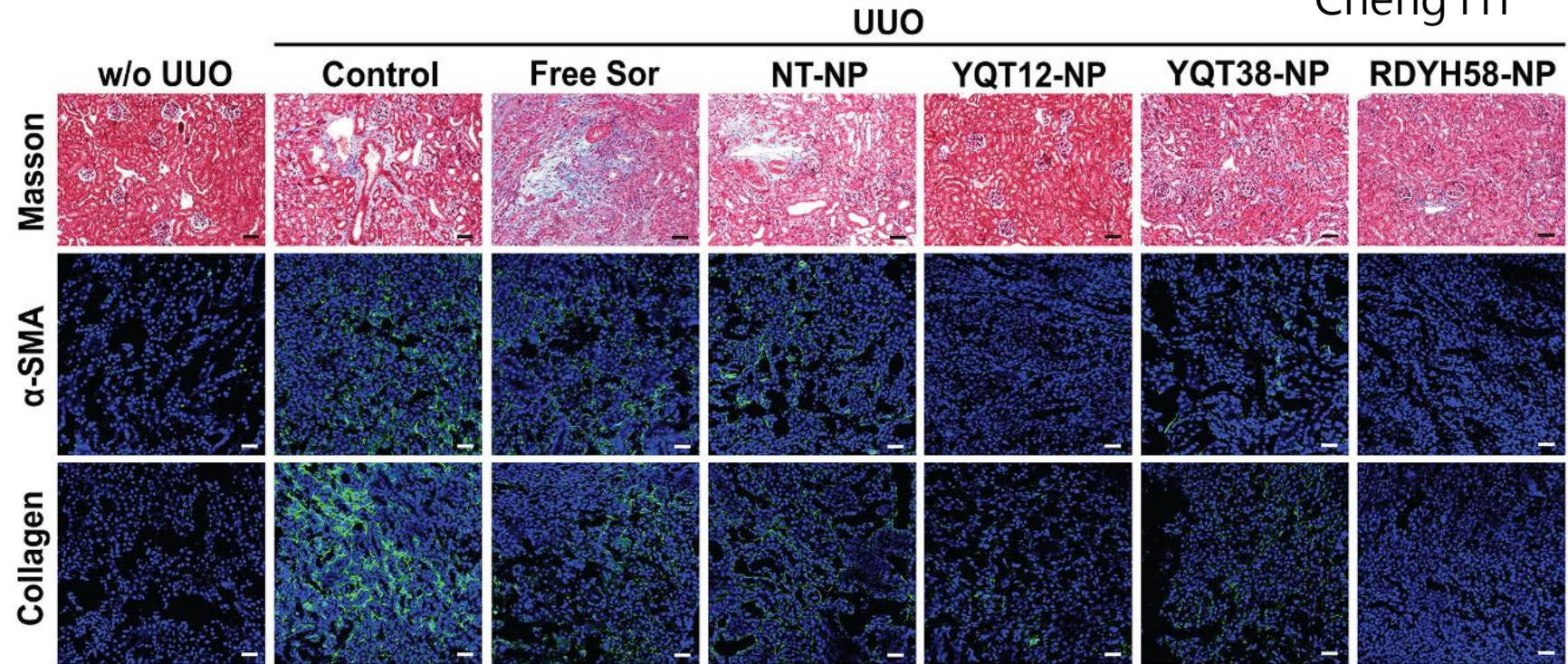
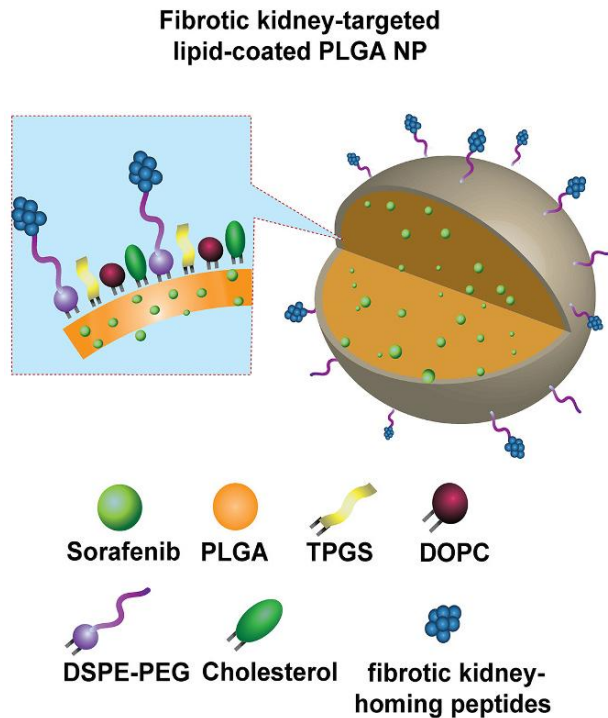
In vitro biopanning



Myofibroblast-targeted peptide-LNP-sorafenib attenuates renal fibrosis



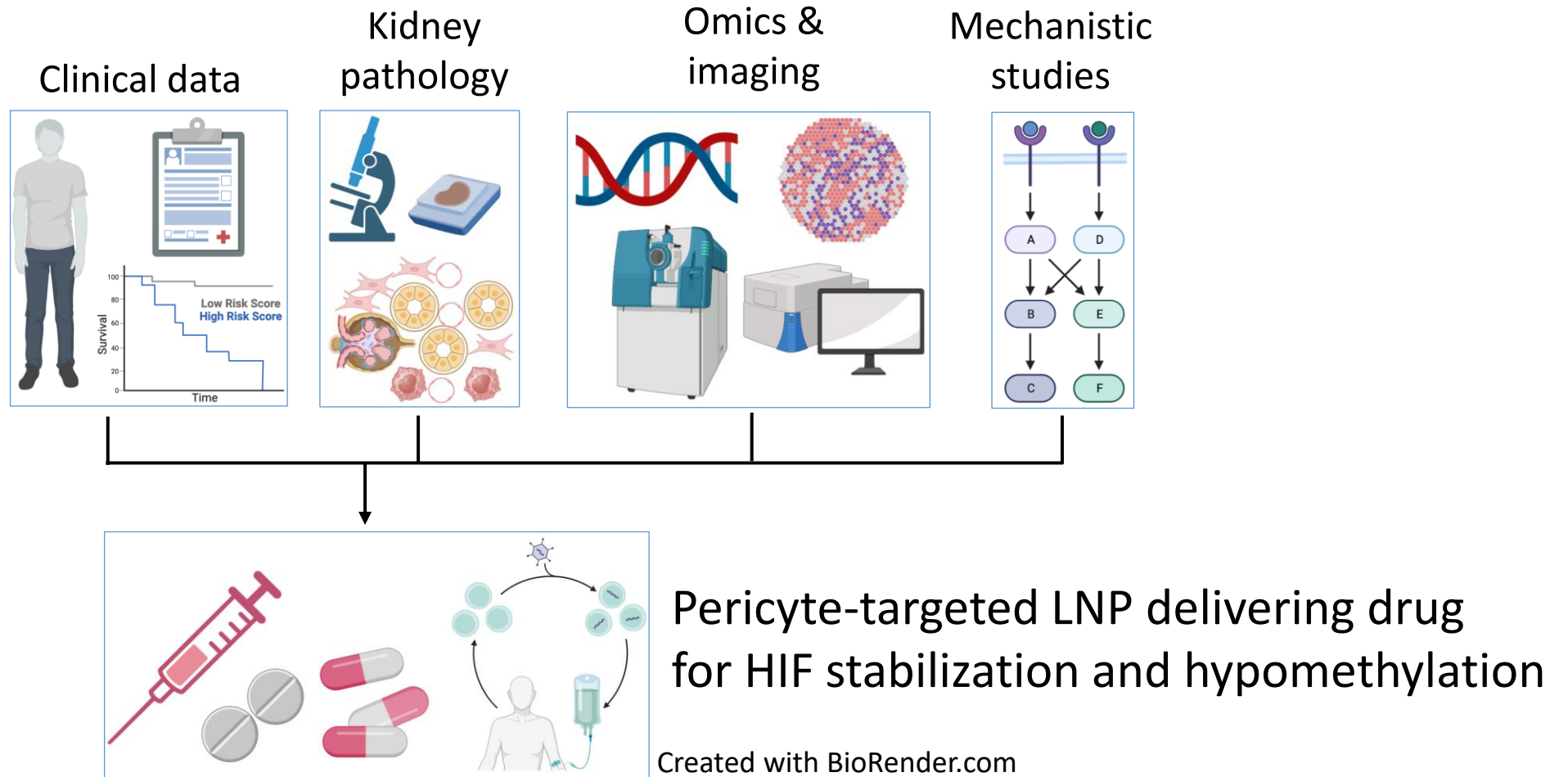
Cheng HT



YQT12
YQT38
RDYH58

Summary 4

Kidney Precision Medicine



Conclusion

In kidney,

- Pericytes: perivascular collagen- and EPO-producing cells
- Myofibroblasts: activated and scar-producing pericytes
- Pericyte-specific targeting and drug delivery as a precision medicine?