Μικροβίωμα και ΧΝΝ:

Η σημασία του μικροβιώματος στην εξέλιξη της ΧΝΝ

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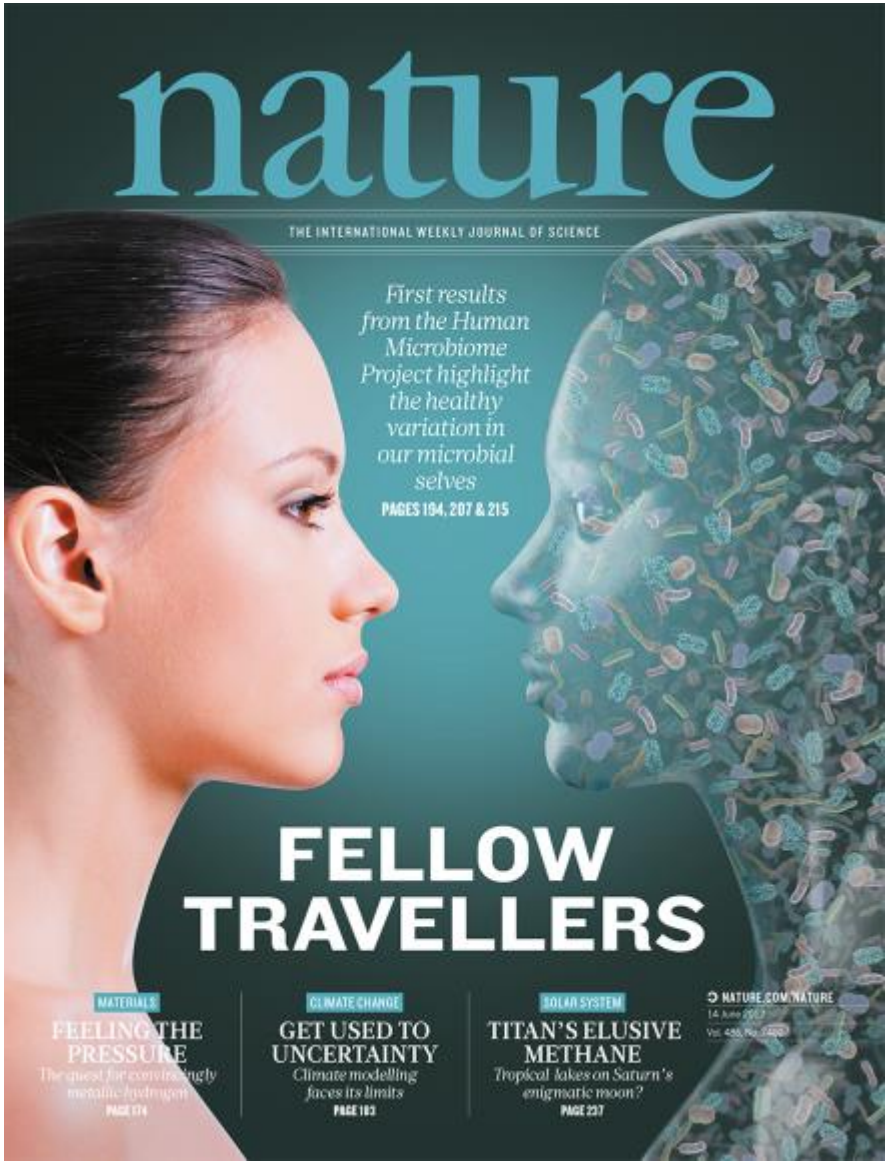
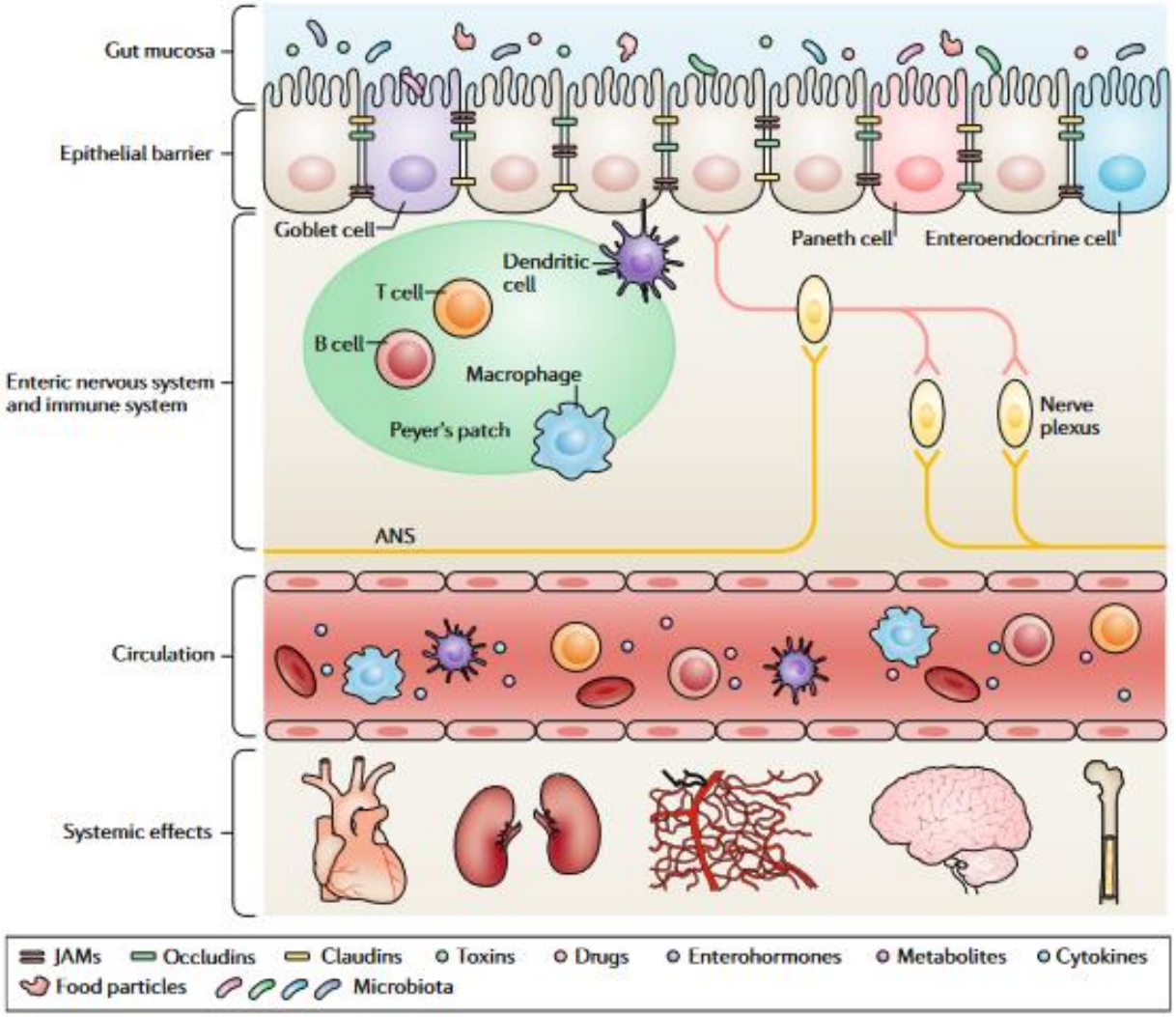
Νεφρολογική Κλινική
Γ.Ν.Α Γ.ΓΕΝΝΗΜΑΤΑΣ

Our Self-Portrait: The Human Microbiome



The anatomy of the gut and its interactions with multiple systems



Nat Rev Nephrol. 2018;14(7):442-456

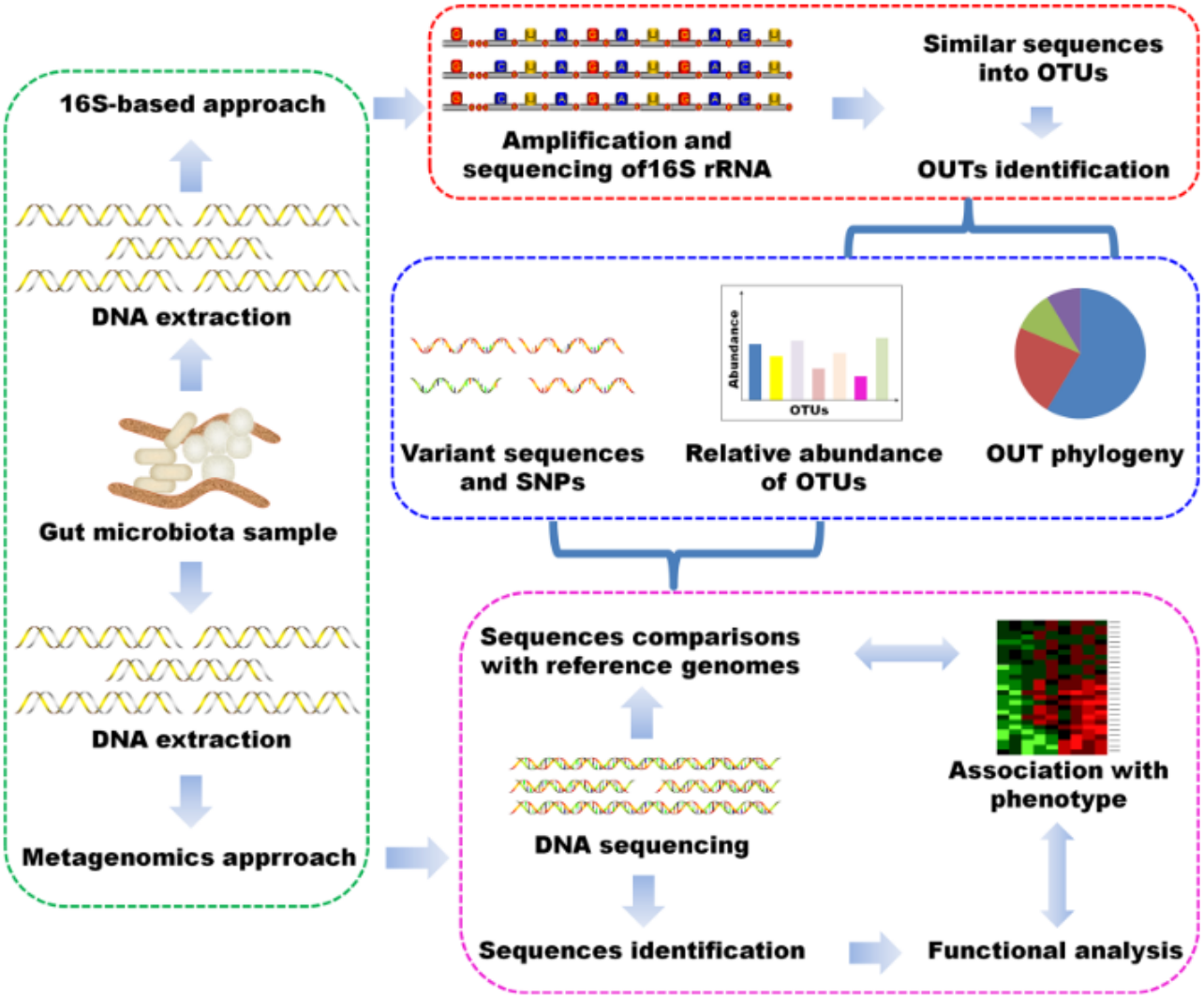
Enterotypes

Enterotype Name	Microbiological Diversity	The Main Source of Energy	Production of Vitamins	Diet or Diet Components
Enterotype I	The most common bacteria are *Bacteroides* spp.	sugars and protein fermentation	biotin, riboflavin, panthenol, ascorbic acid and thiamine.	meat and products such as mayonnaise, cream, cheese, and other products containing large amounts of saturated fat
Enterotype II	The most common bacteria are *Prevotella* spp.	high ability to break down glycoproteins, especially mucins	biotin, riboflavin, panthenol, ascorbic acid and thiamine.	simple sugars and in vegetarians, Mediterranean ones, rich in fruits and vegetables
Enterotype III	The most common bacteria are *Ruminococcus* and *Akkermansia* spp.	protein fermentation, decomposition of mucin and simple sugars	biotin, riboflavin, panthenol, ascorbic acid and thiamine, folic acid	excess of alcohol and products rich in polyunsaturated fatty acids

Formation and health consequences of selected uremic toxins

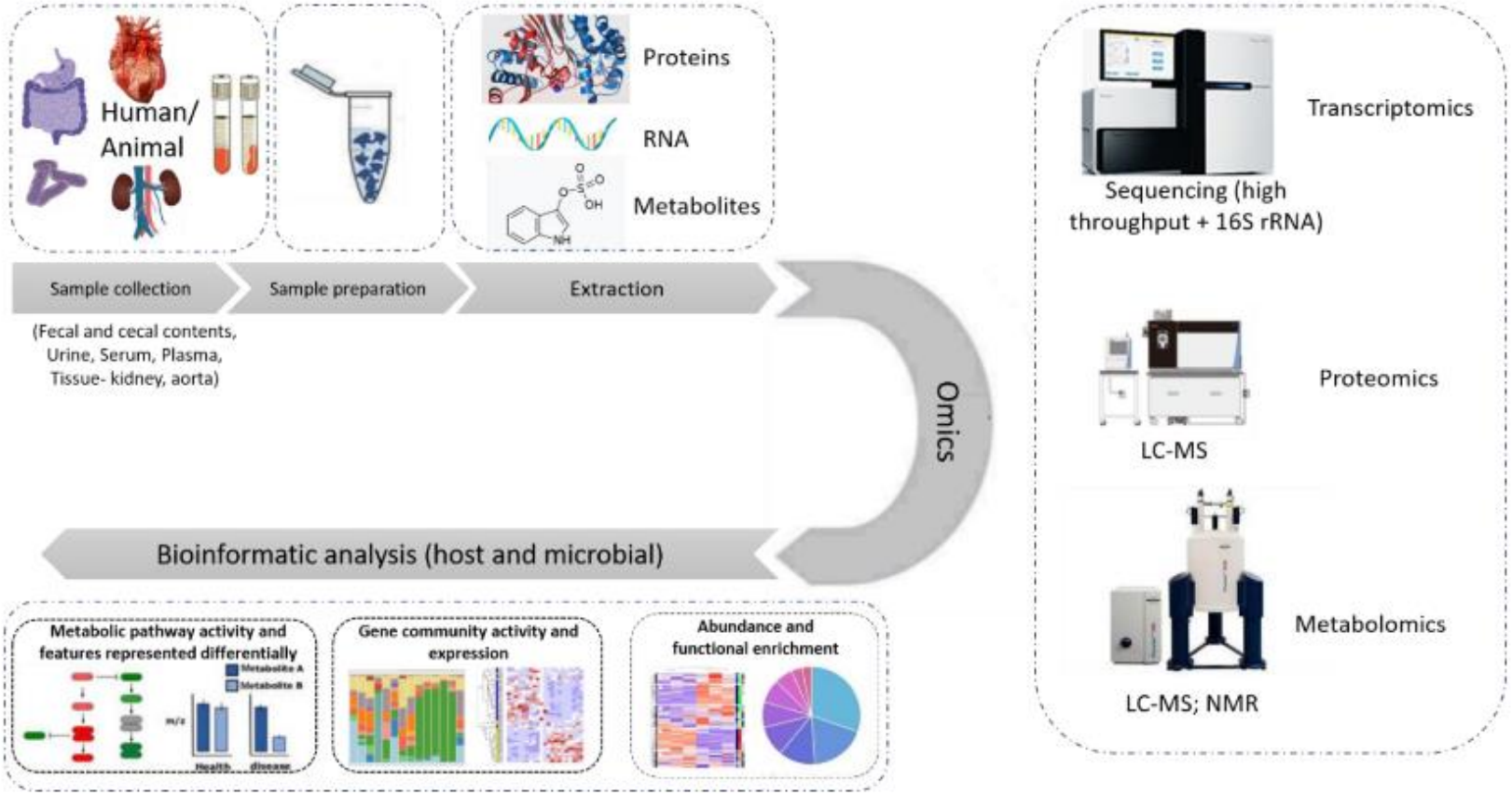
Compound	Source in the Diet	Compound by Microorganisms Transformation	Compound by Liver Metabolism	Health Consequences
Tyrosine	Turkey, chicken, beef, brown rice, fish, milk, nuts, yogurt, eggs, cheese, fruit and vegetables	p-cresol	p-cresol sulfate	Increased gene expression associated with tubular interstitial fibrosis, aorta and vascular calcification, endothelial cell damage. It lowers the production of erythropoietin and bone rotation
Tryptophan	Beef, poultry, pork, fish, milk, yoghurt, eggs, soy products	Indole	p-indoxyl sulfate	Renal fibrosis, oxidative stress, increased inflammation cytokines, mortality. Braking endothelial proliferation, increased endothelial permeability.
Phosphatidylcholine and choline	fish and seafood, meat and dairy products	Trimethylamine	Trimethylamine N-oxide (TMNO)	Associated with higher mortality
Protein and nitrogen compounds	Dairy products, eggs	Urea	Ammonia	Damage to intestinal epithelial cells due to an increase in the pH of the intestinal environment

Study of Microbiome

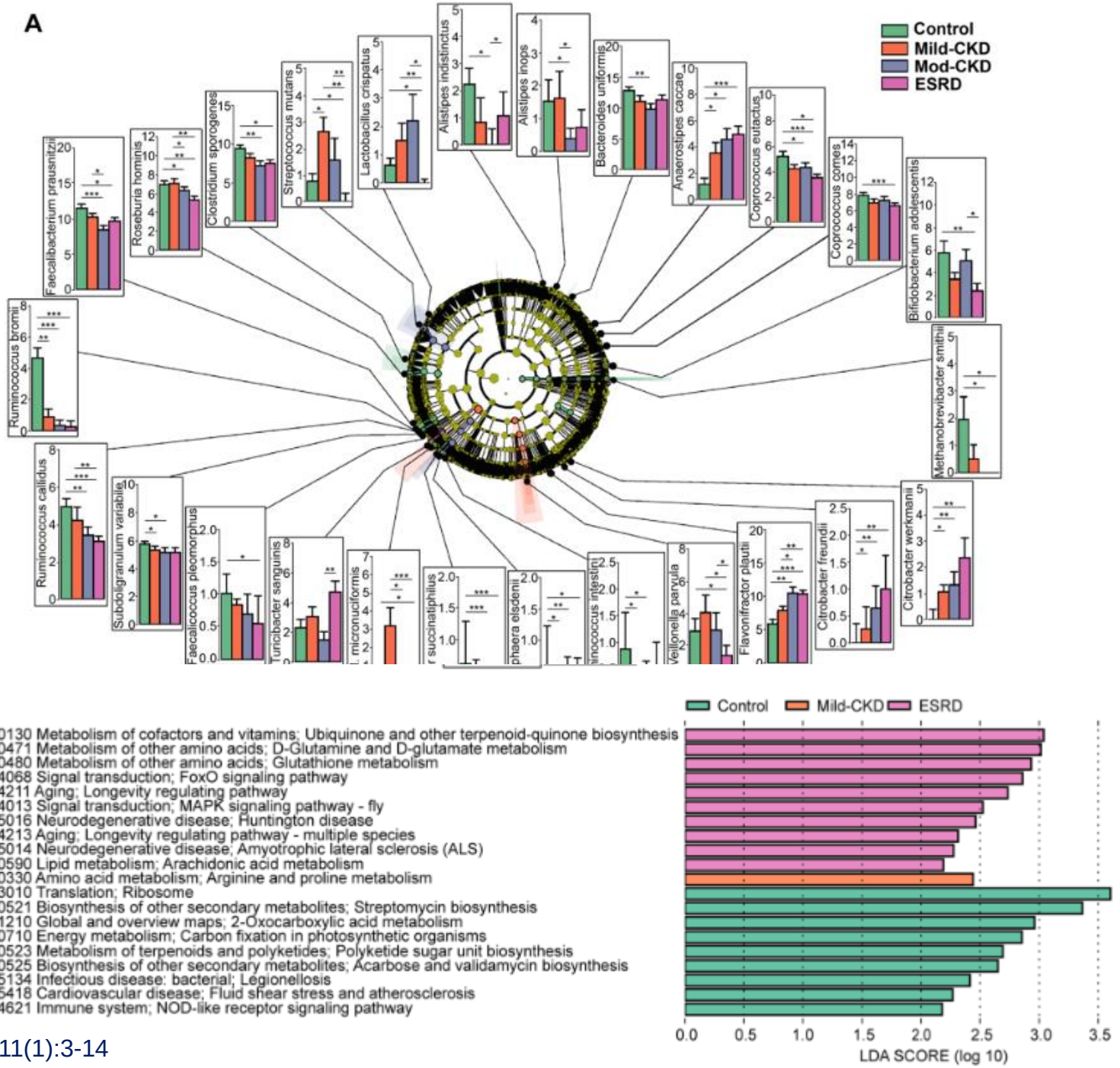


J Transl Med (2019) 17:5-15

Microbiome in Chronic Kidney Disease (CKD): An Omics Perspective

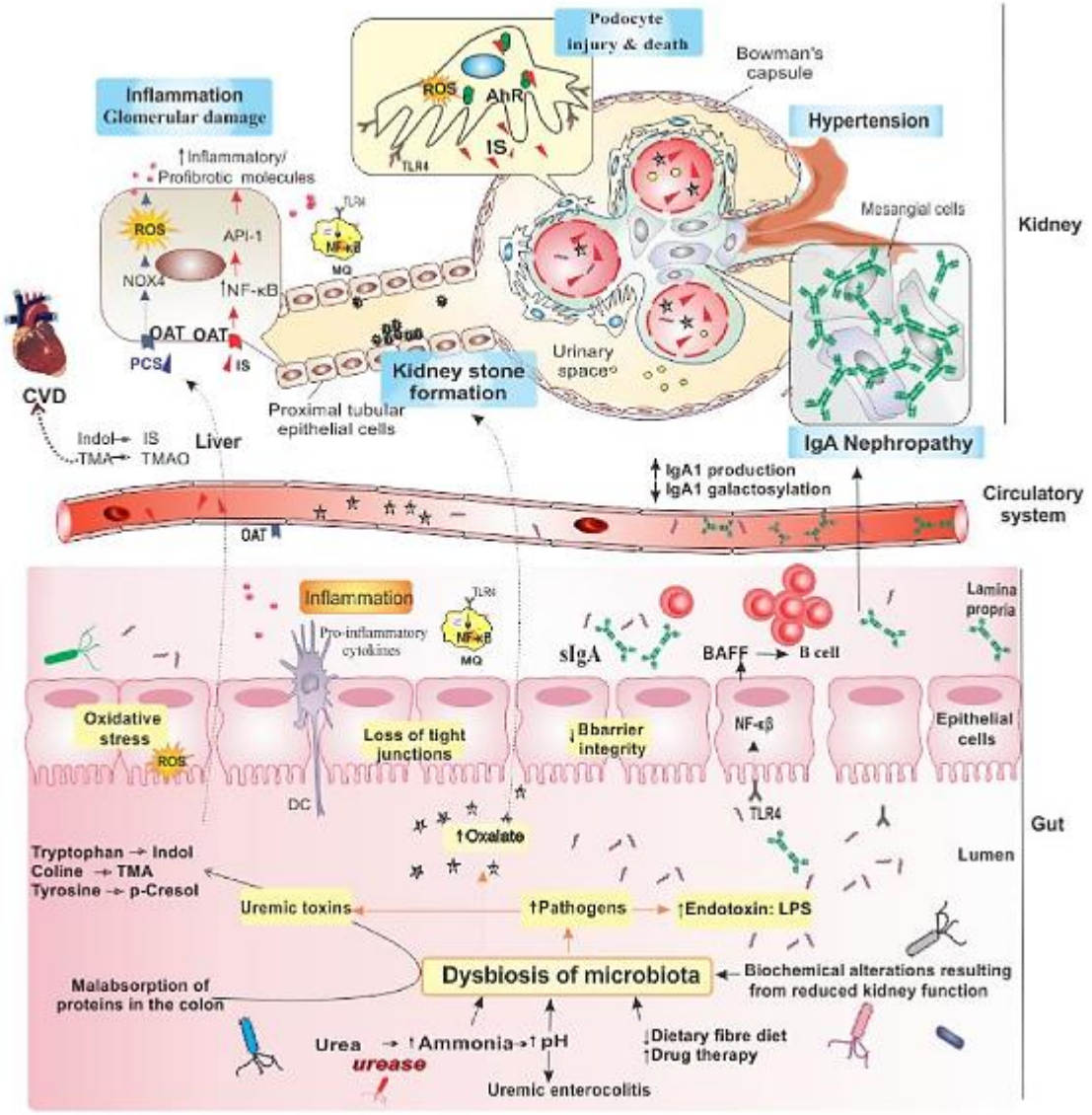


Toxins 2022;14:176-195



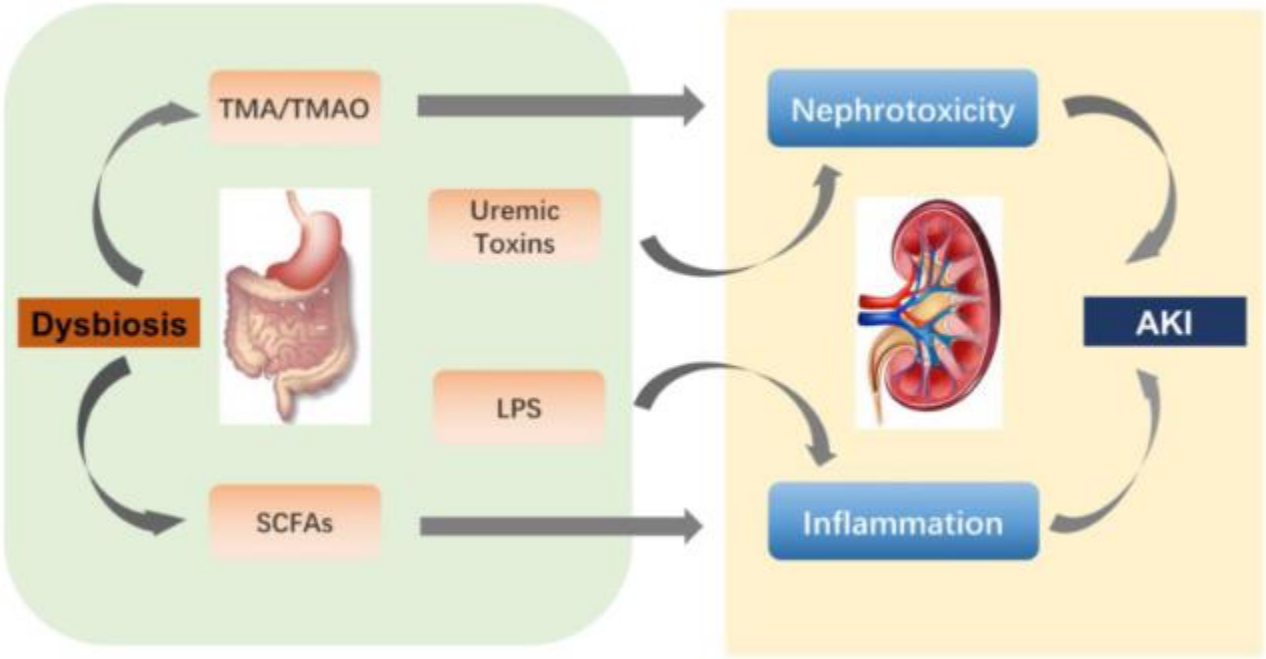
Microbiome 2023;9;11(1):3-14

The impact of gut microbiota on kidney function and pathogenesis



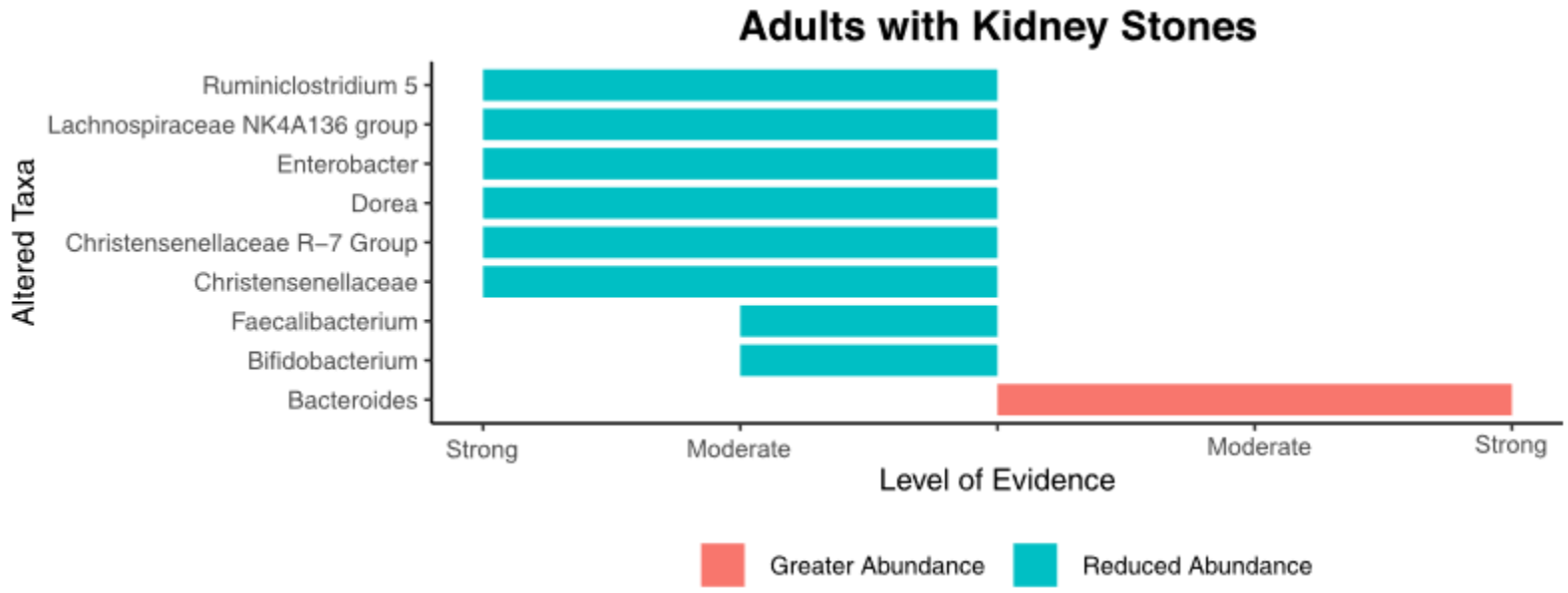
Biomed Pharmacother. 2017;93:412–9

Gut microbiota-kidney cross-talk in acute kidney injury



Semin Nephrol. 2019; 39(1):107–116

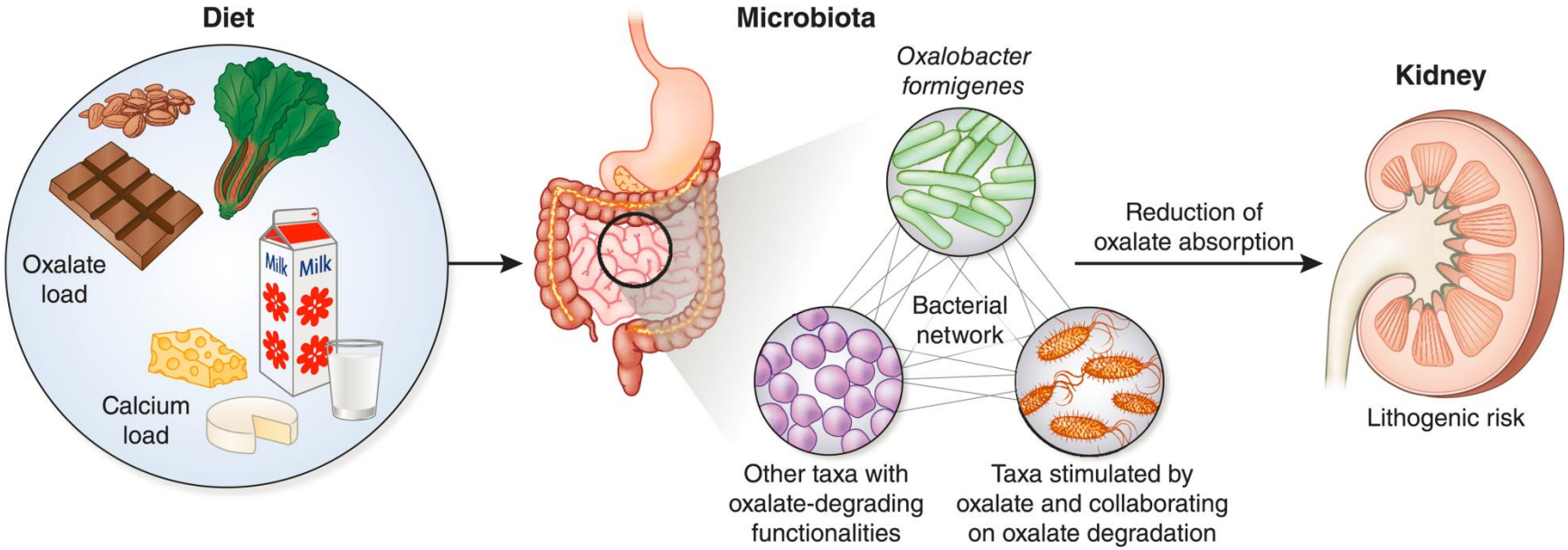
Gut microbiota – Kidney Stones



Altered taxa based on strong and moderate level of evidence for adults with kidney stones compared to controls

BMC Nephrol. 2020;21(1):215

Gut microbiota – Kidney Stones

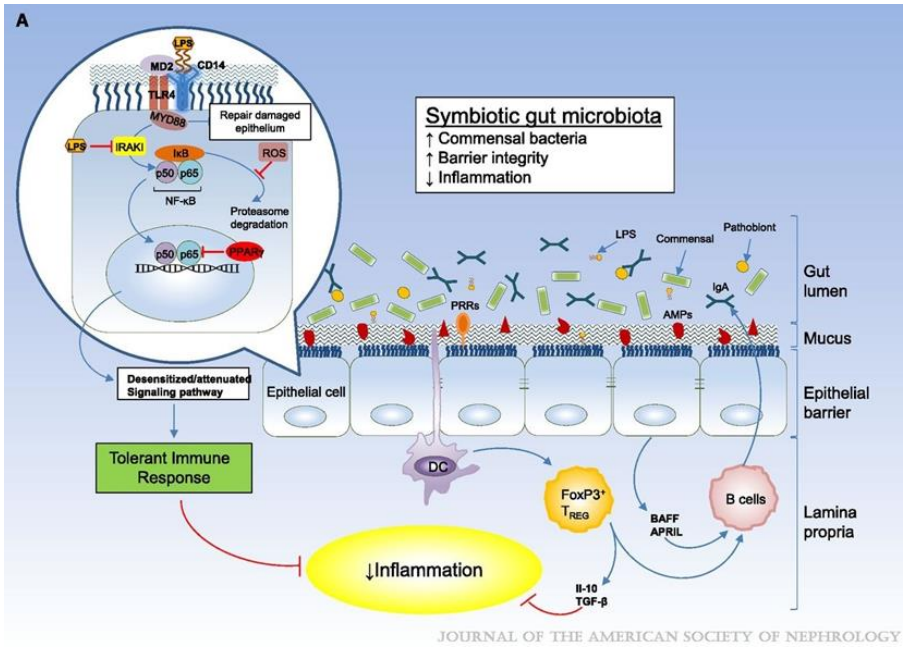


Overview of the possible gut–kidney axis in nephrolithiasis, with Oxalobacter formigenes at the center of a bacterial network involved in oxalate degradation and protecting against the onset of hyperoxaluria

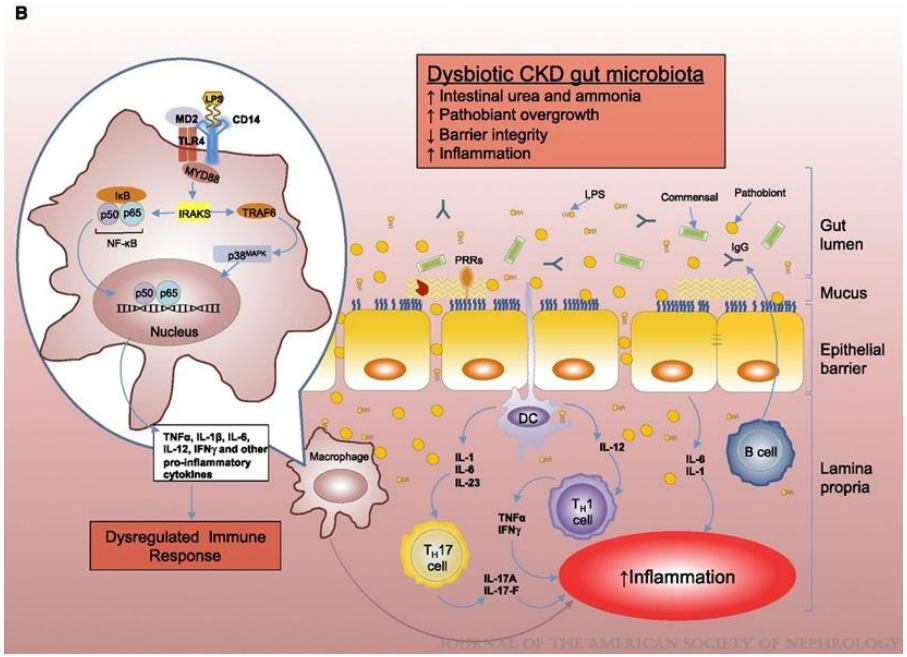
Kidney International 2019;96:13–30

Gut-Kidney Axis: Inflammation

Symbiotic gut microbioma

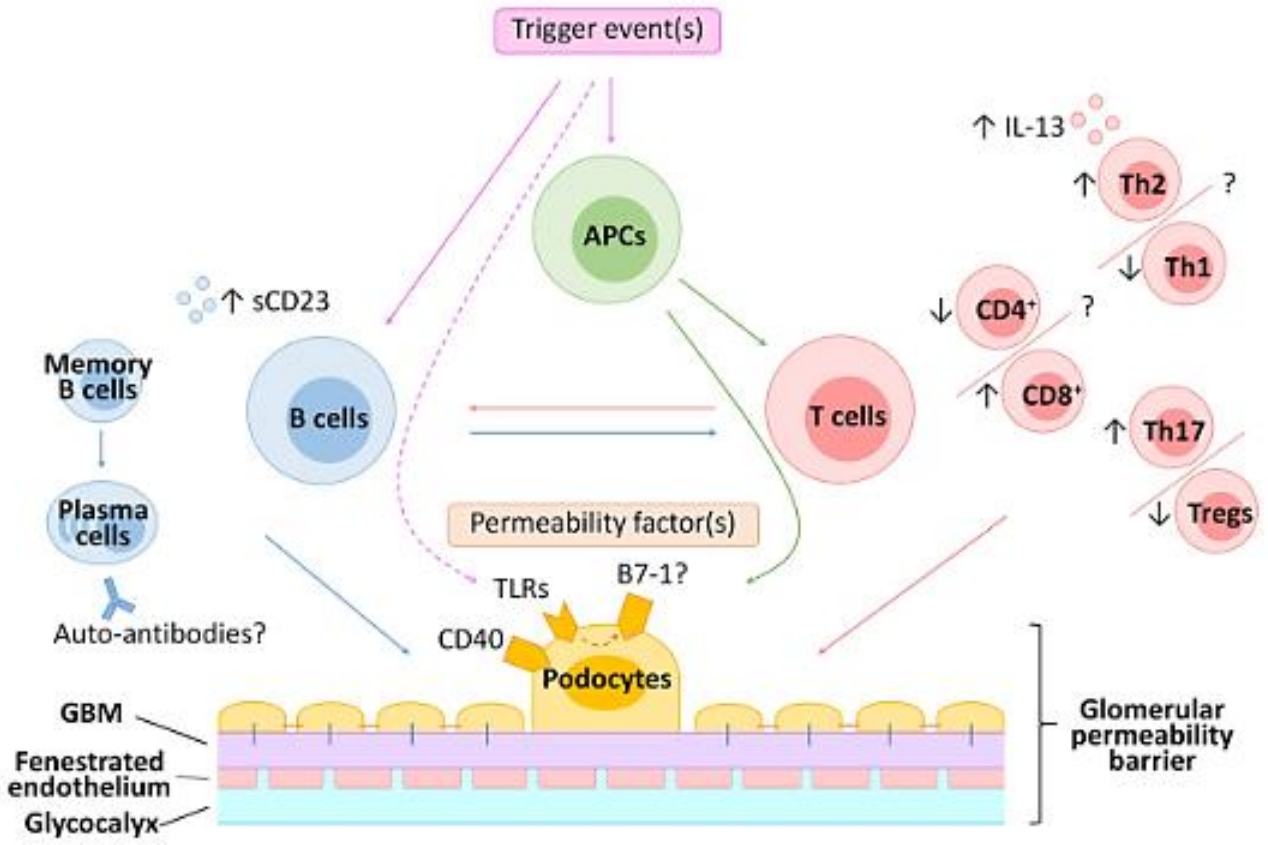


Dysbiotic gut microbioma



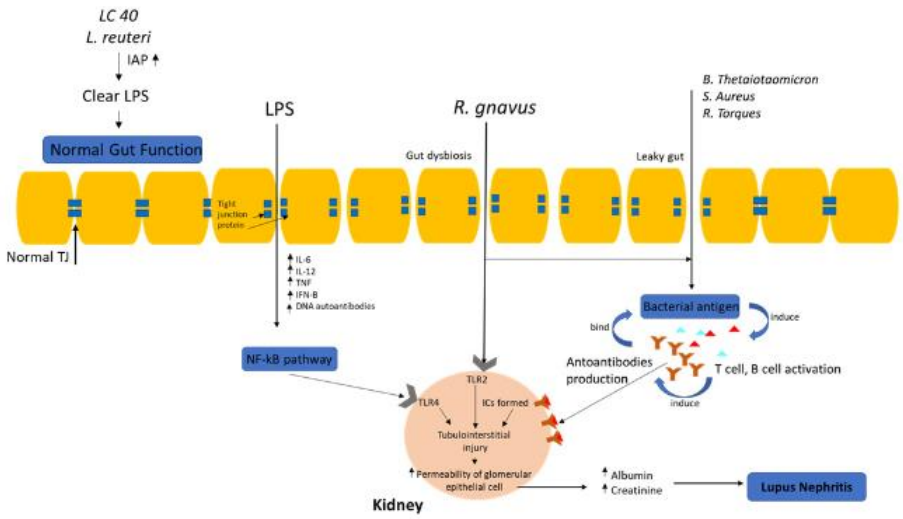
JASN 2014;25(4):657-670

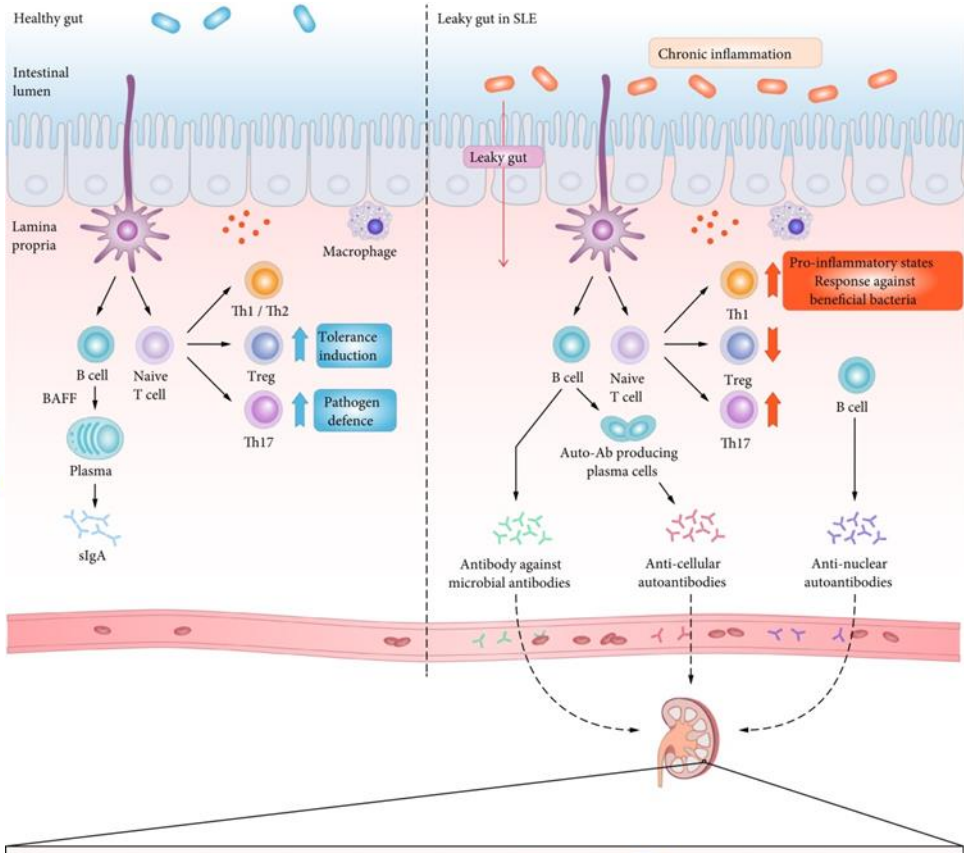
Immunology of idiopathic nephrotic syndrome

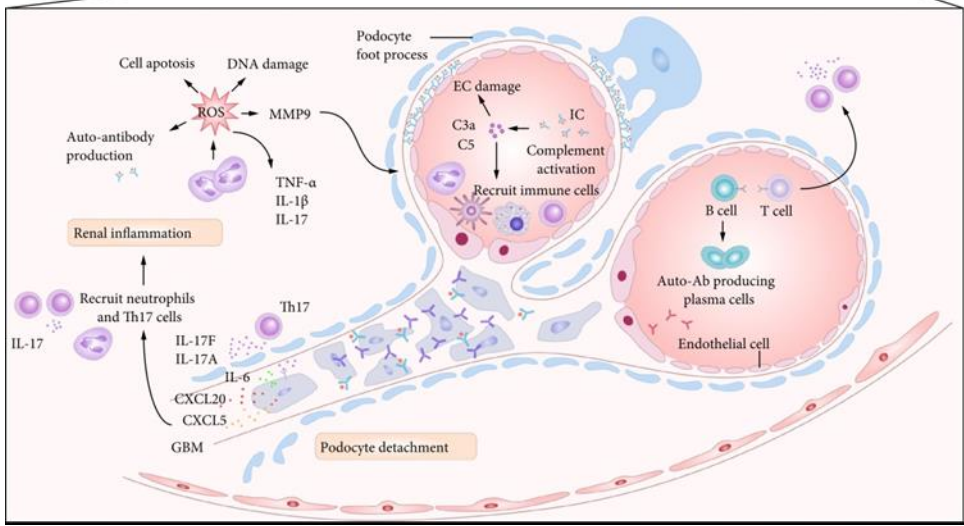


Pediatr Nephrol 2018;33:573–584

Involvement of Gut Microbiota in SLE and Lupus Nephritis

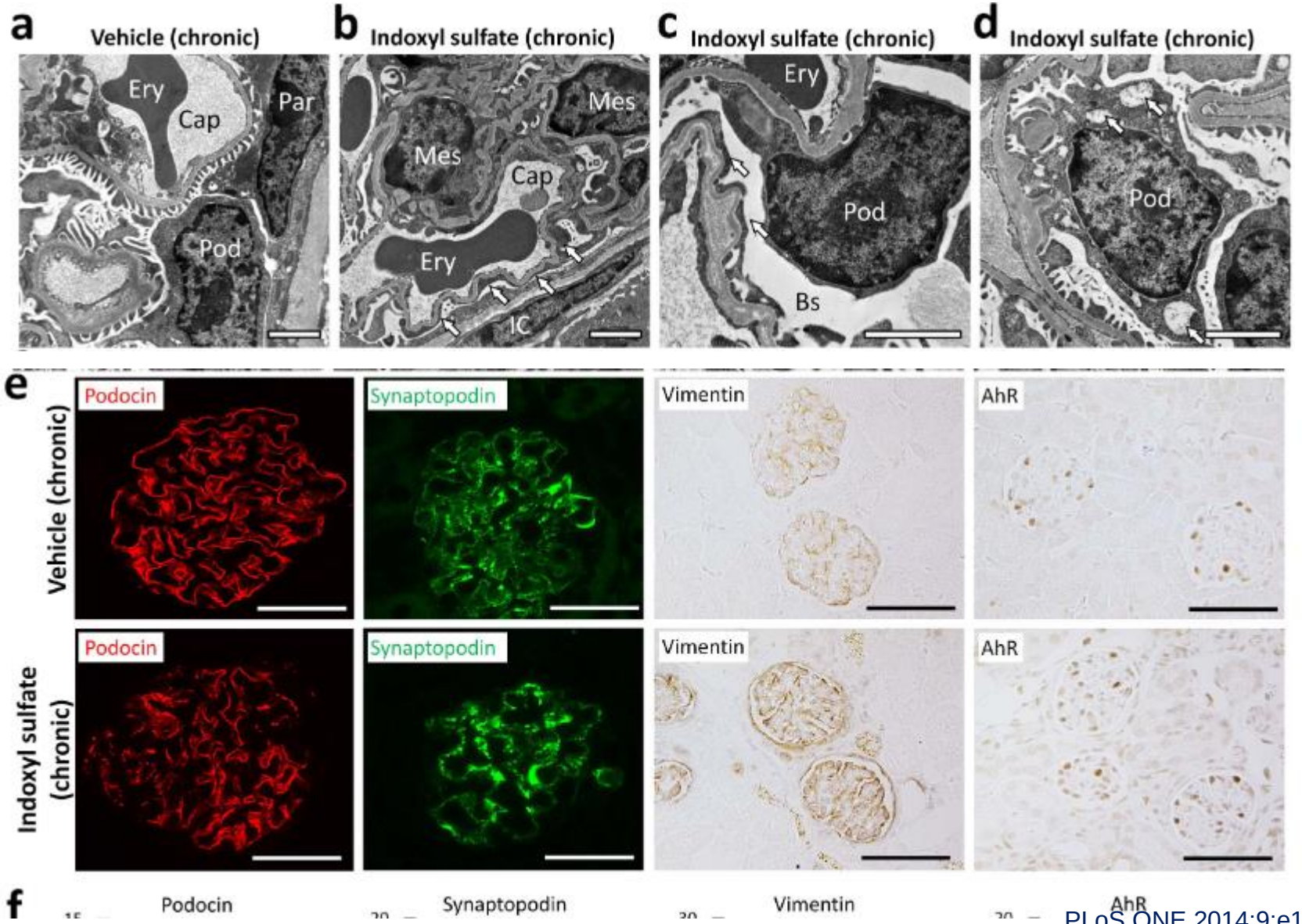






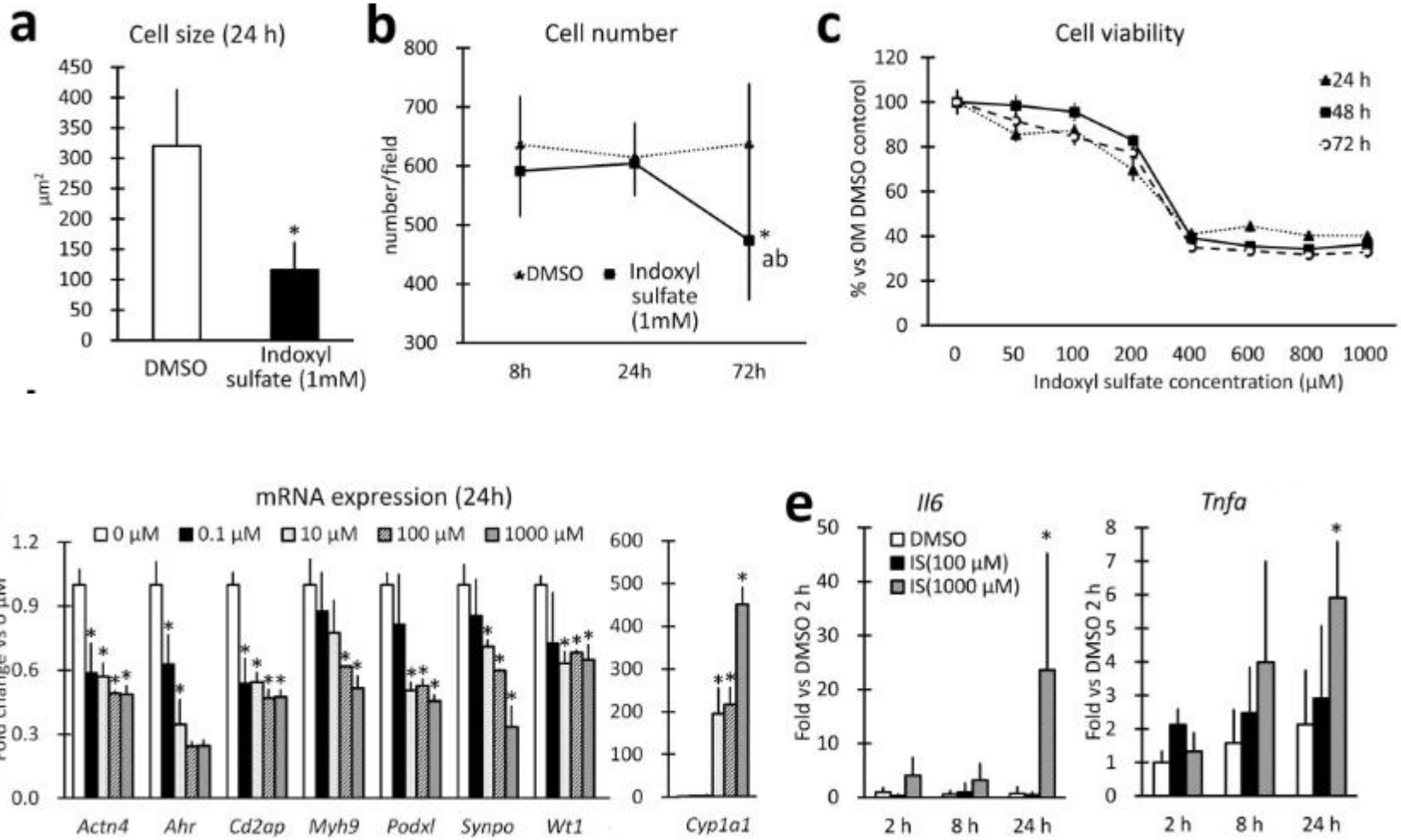
Biomedicines 2023;11(3):653

Indoxyl sulfate treatment induces podocyte injury



PLoS ONE 2014;9:e108448

Indoxyl sulfate altered differentiation marker expression in mouse podocytes



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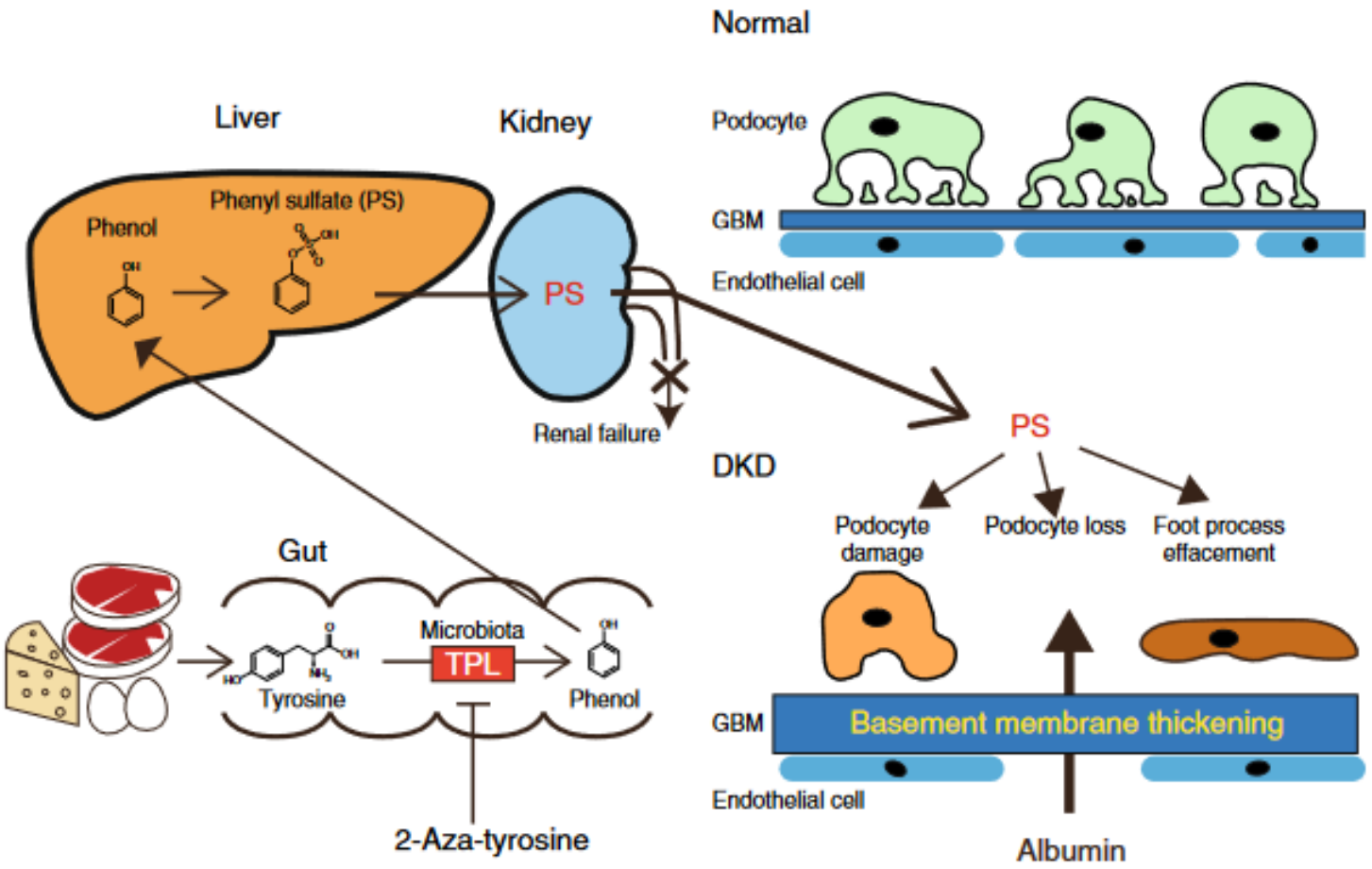
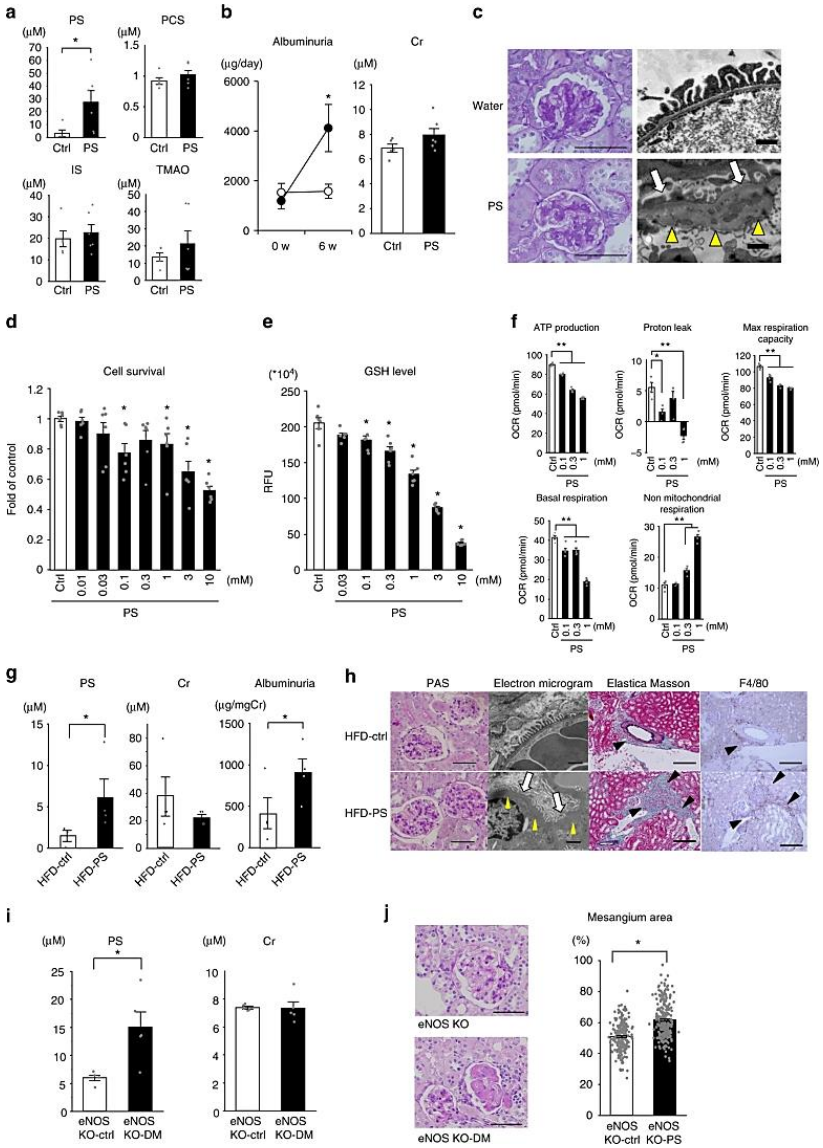
Gut microbiome-derived phenyl sulfate contributes to albuminuria in diabetic kidney disease



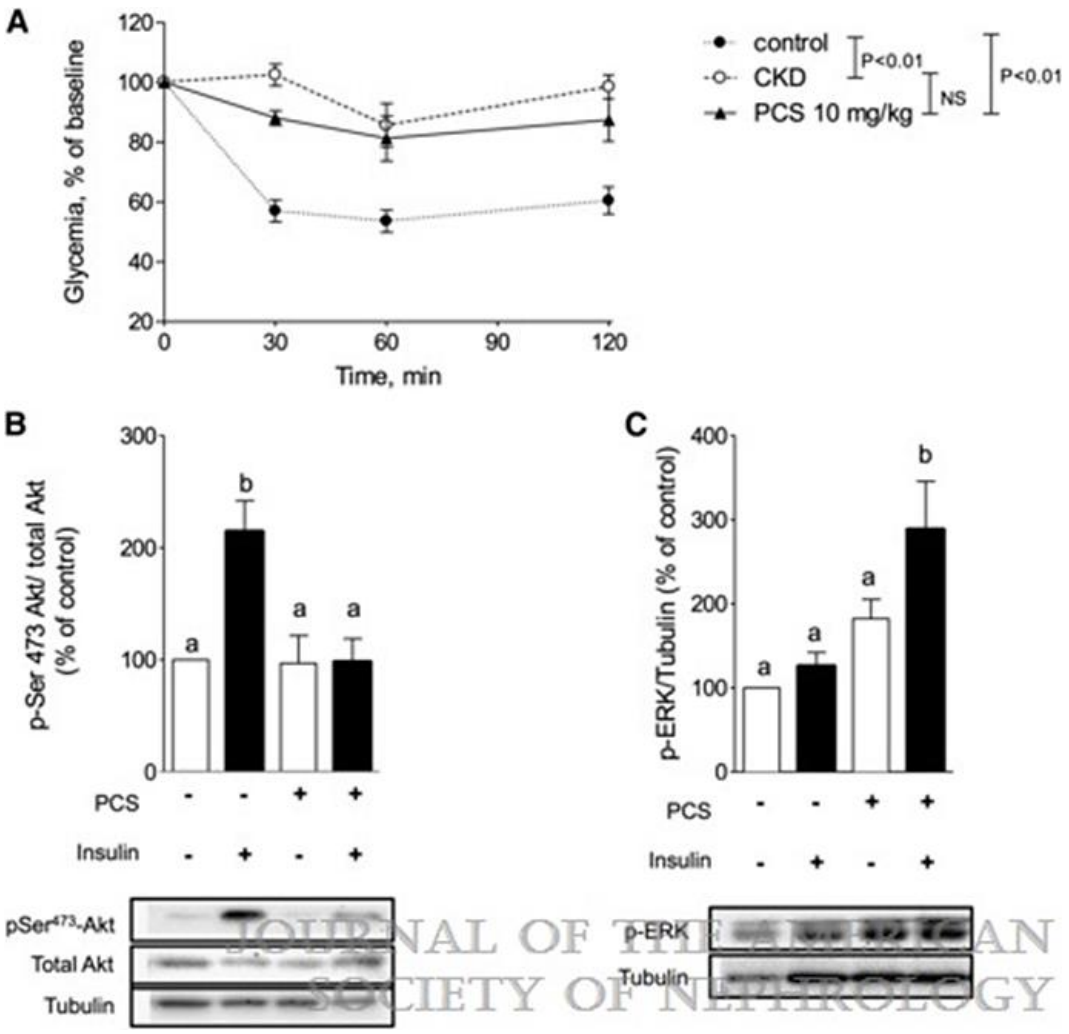
Nat Commun. 2019;10(1):1835

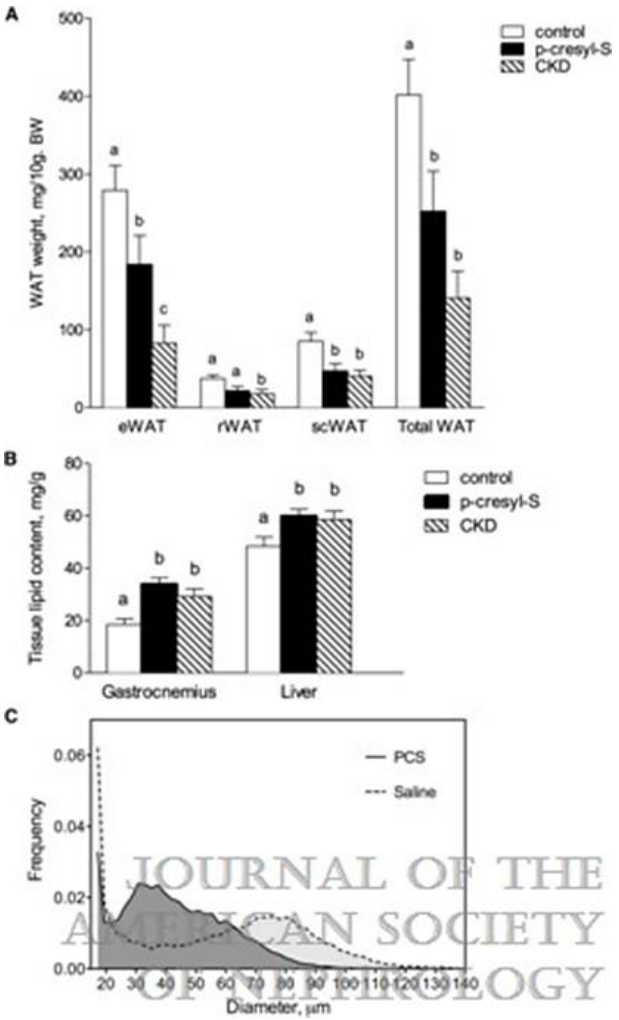
Gut microbiome-derived phenyl sulfate contributes to albuminuria in diabetic kidney disease



Nat Commun. 2019;10(1):1835

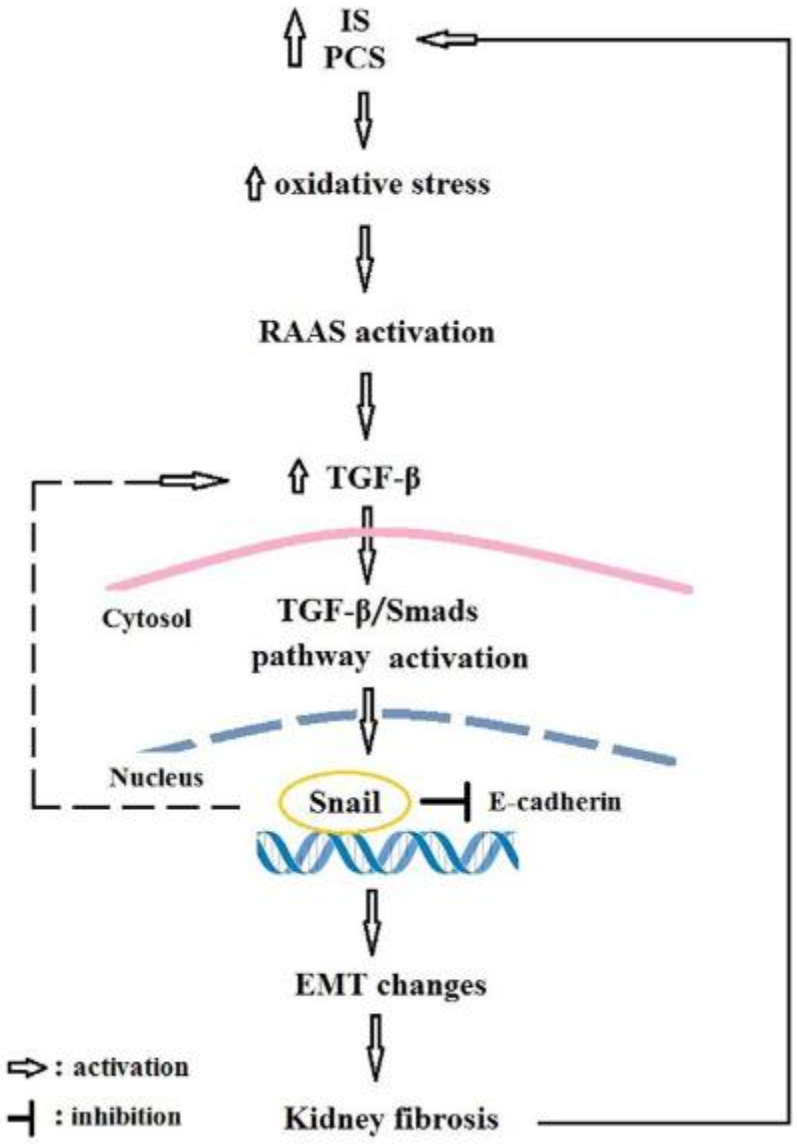
p-Cresyl sulfate promotes insulin resistance associated with CKD





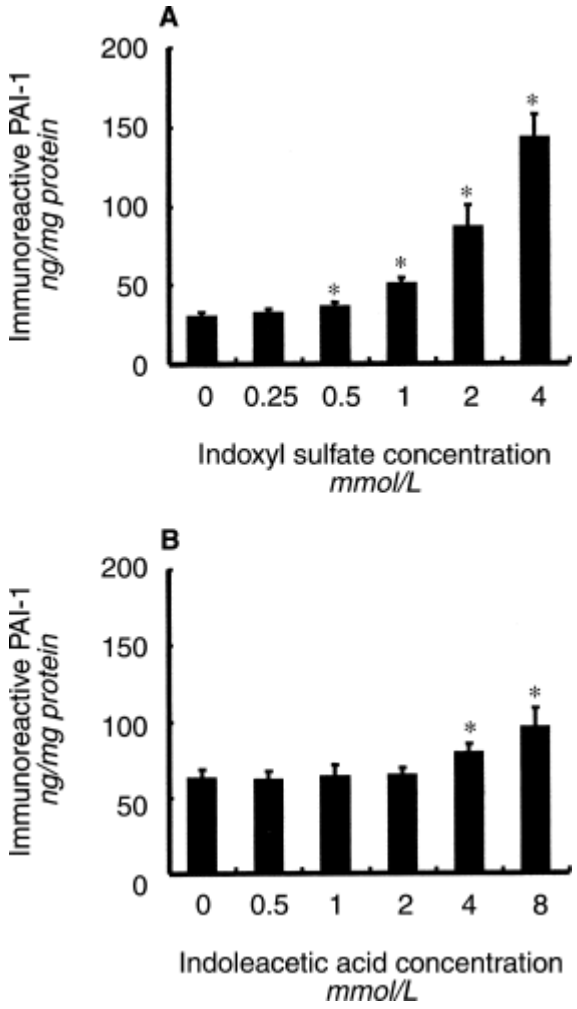
JASN 201;24(1):88-99

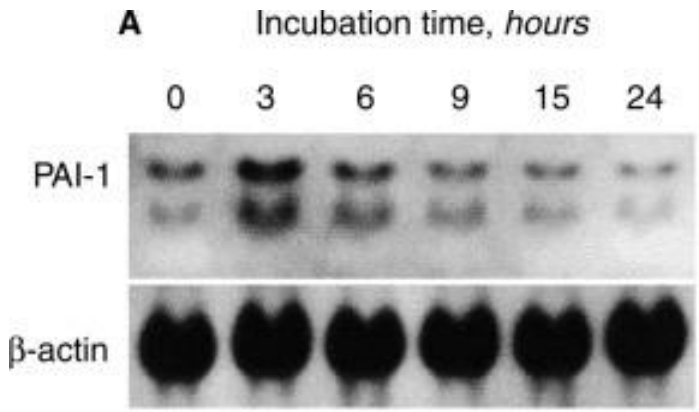
Uremic Toxins Induce Kidney Fibrosis by Activating Intrarenal RAAS Associated Epithelial-to-Mesenchymal Transition

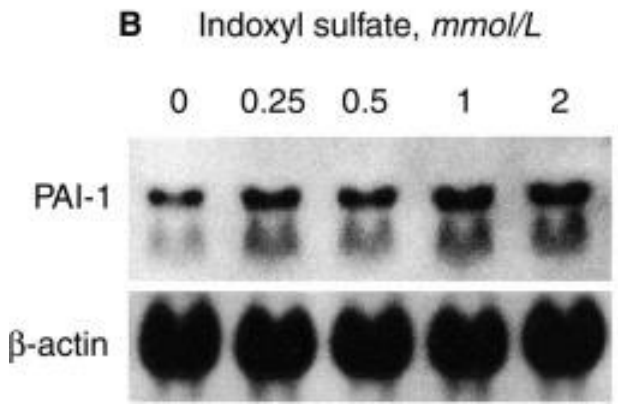


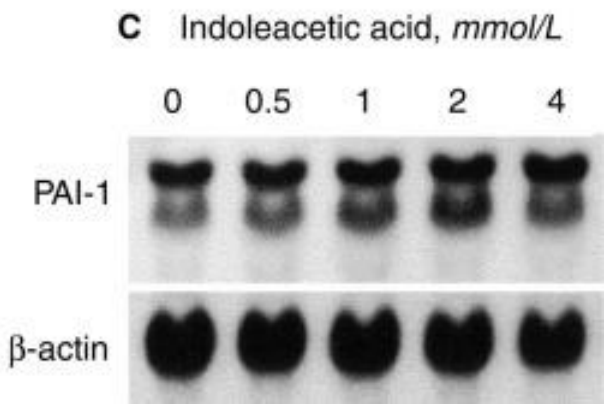
PLoS ONE 2012;7:e34026

Indoxyl Sulfate









Kidney International 2003;63:1671–1680

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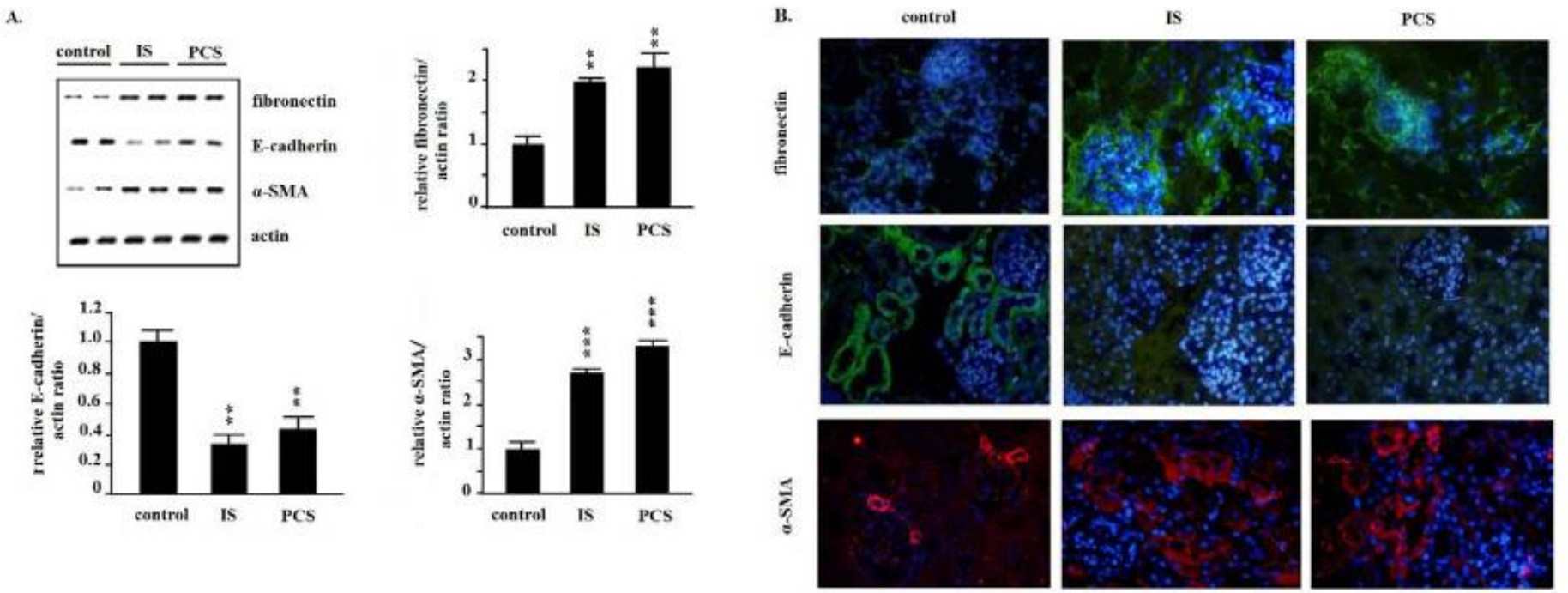
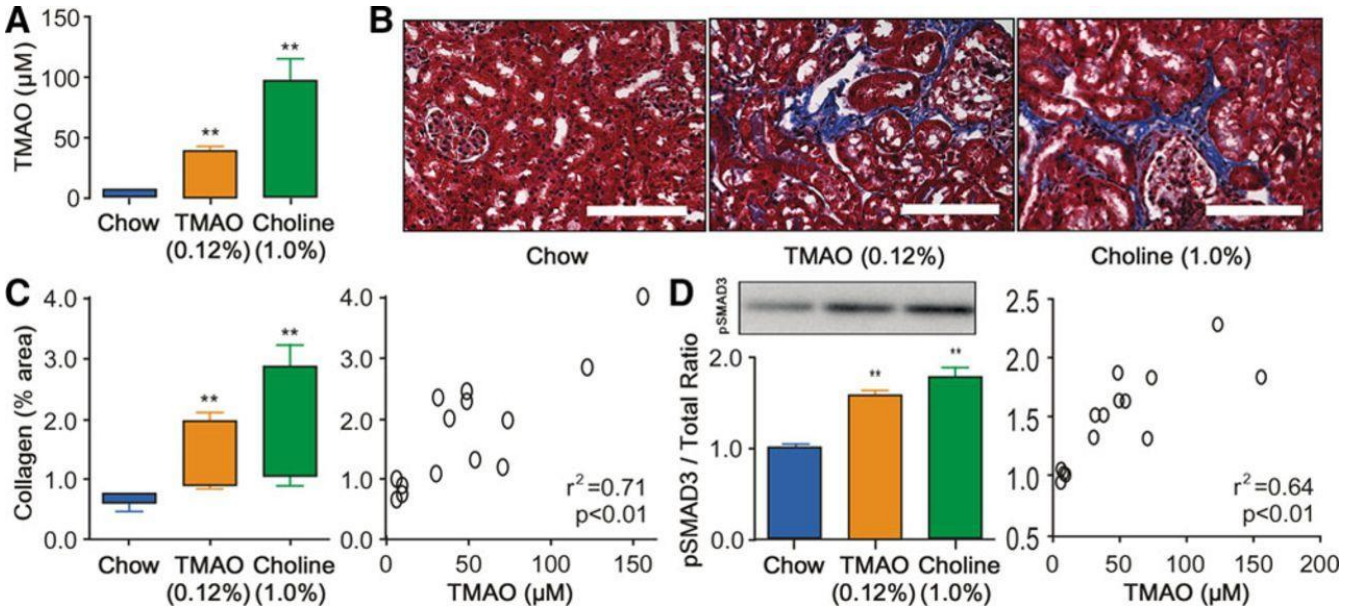
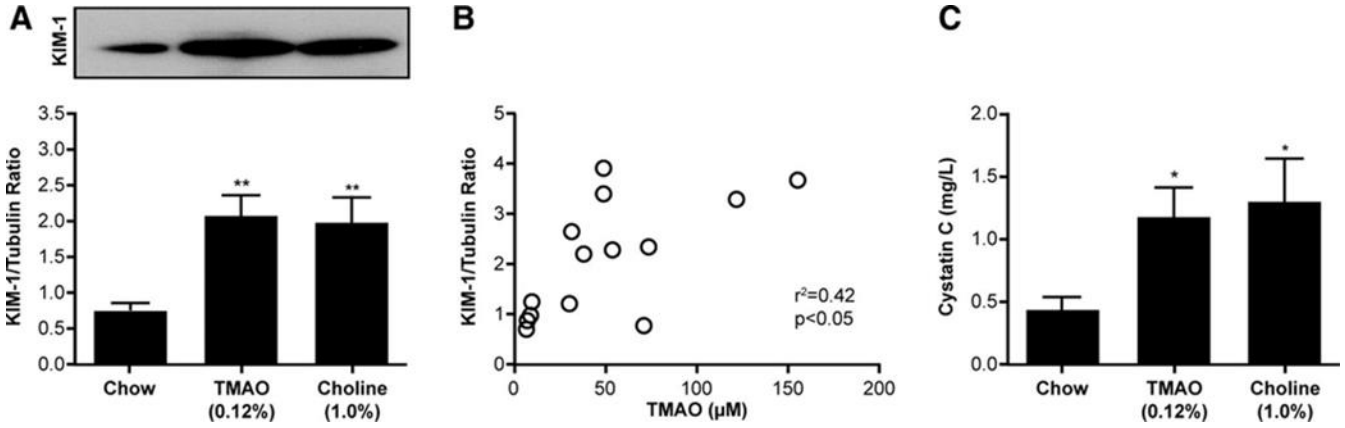


PLoS ONE 2012;7:e34026

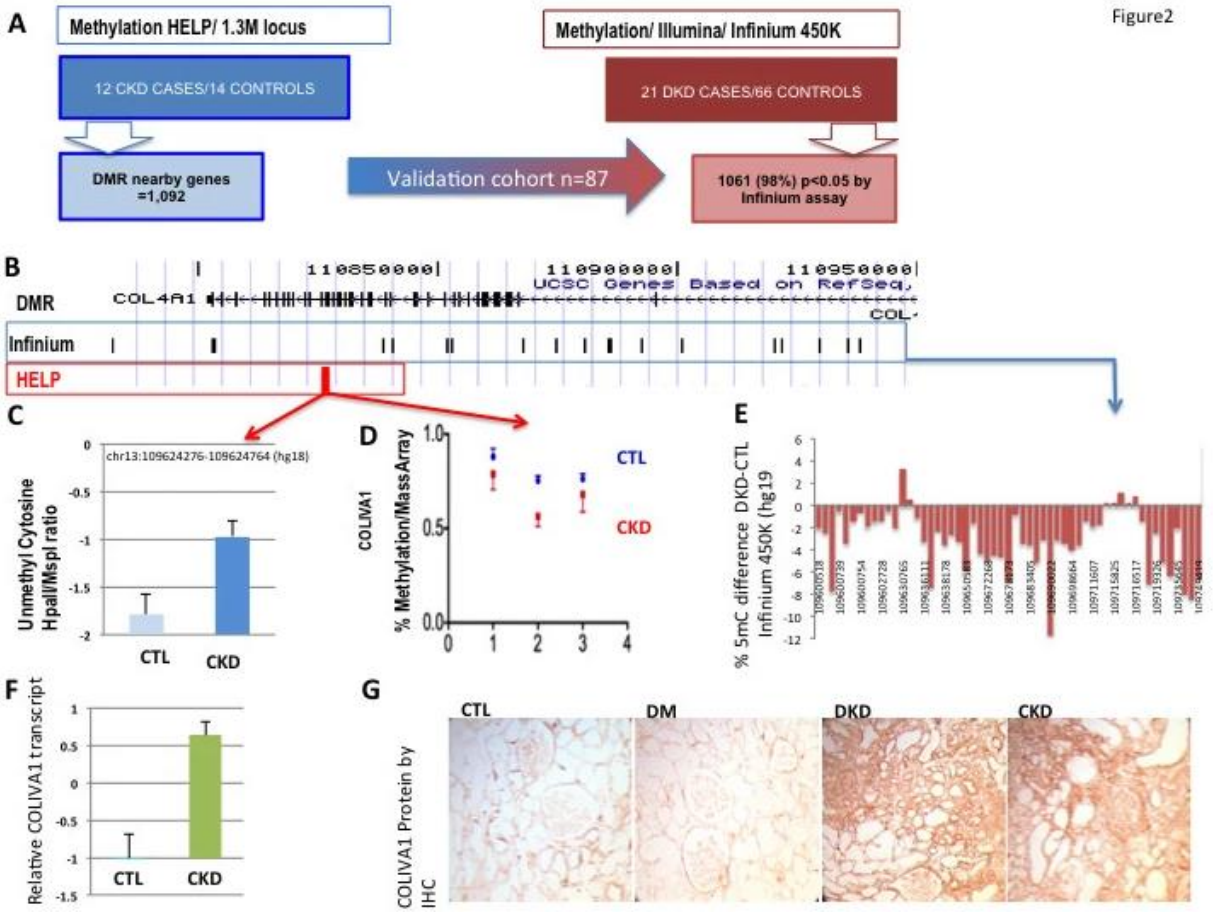
Gut Microbiota-Dependent Trimethylamine N-oxide (TMAO) Pathway Contributes Fibrosis





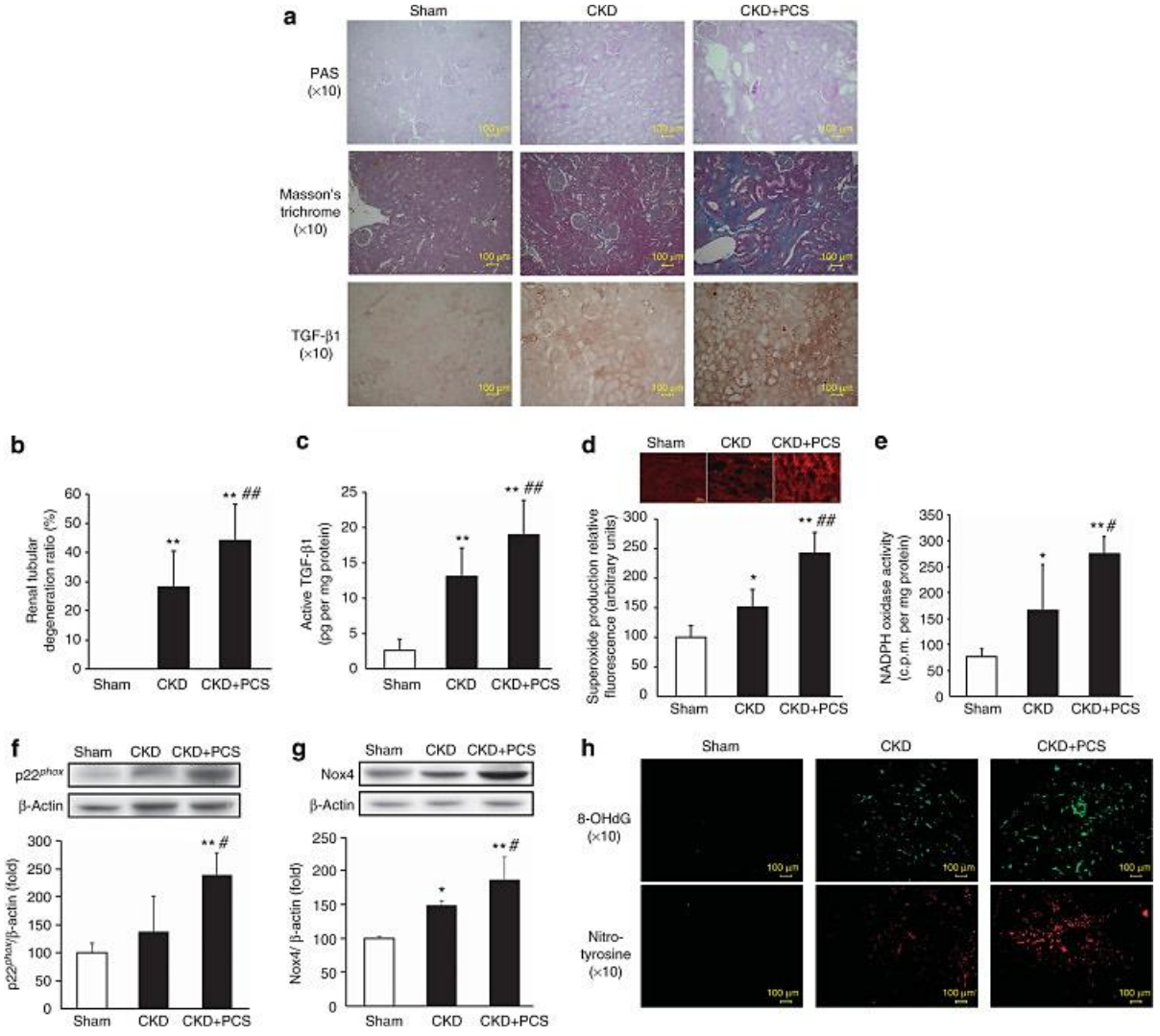
Circ Res. 2015;116(3):448-55

Cytosine methylation changes in enhancer regions of core pro-fibrotic genes characterize kidney fibrosis development



Genome Biol. 2013;14(10):R108

p-Cresyl sulfate causes renal tubular cell damage by inducing oxidative stress by activation of NADPH oxidase



Kidney Int. 2013;83(4):582-92

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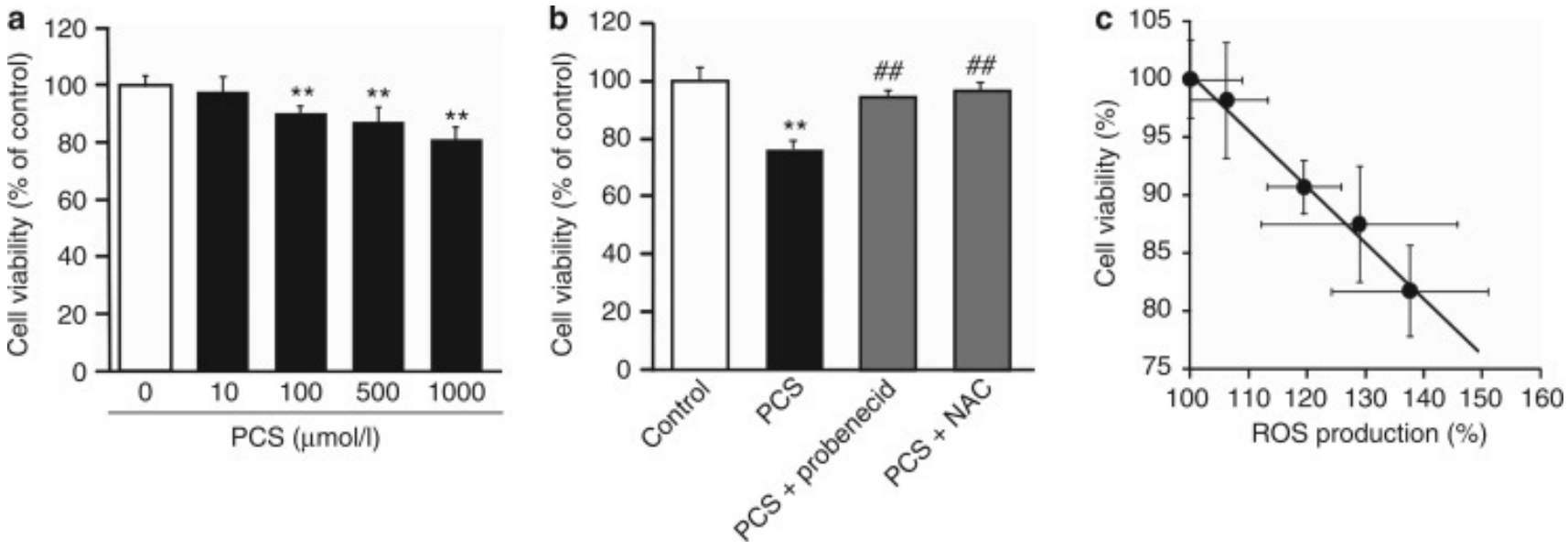
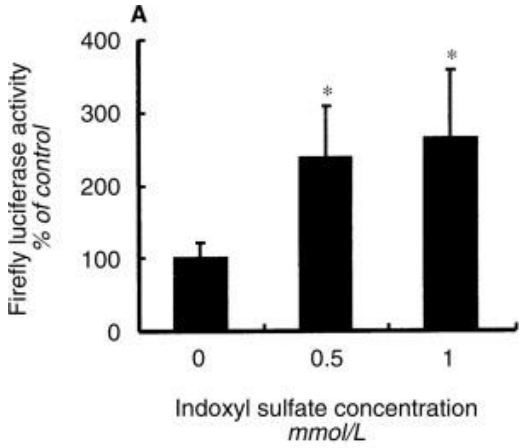
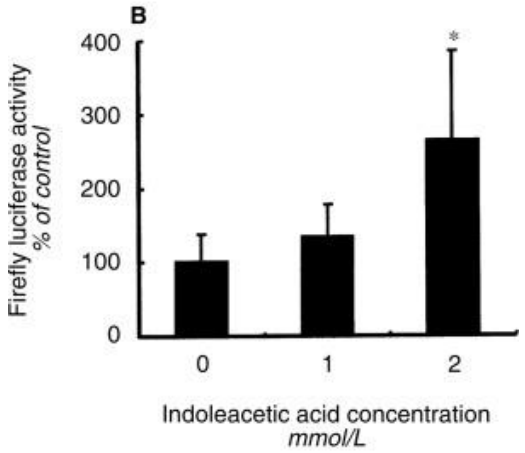
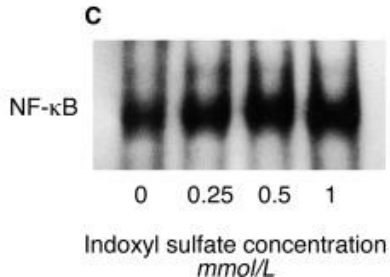


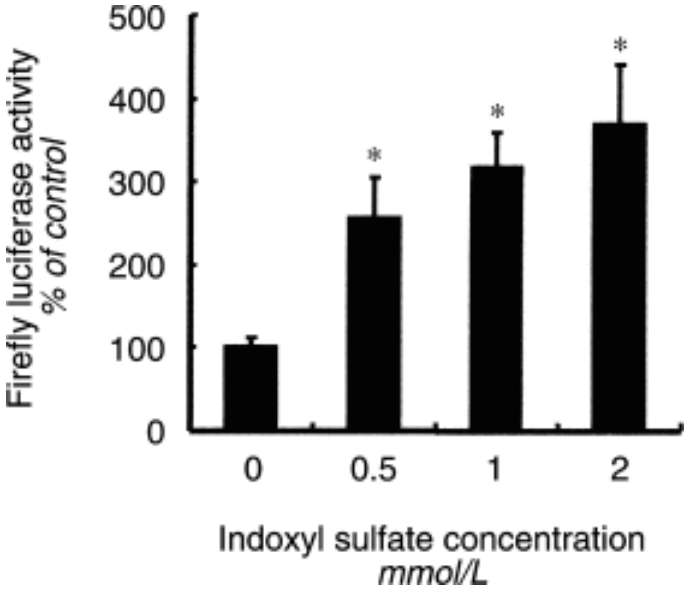
Kidney Int. 2013;83(4):582-92

Uremic toxins of organic anions up-regulate PAI-1 expression by induction of NF-B and free radical in proximal tubular cells



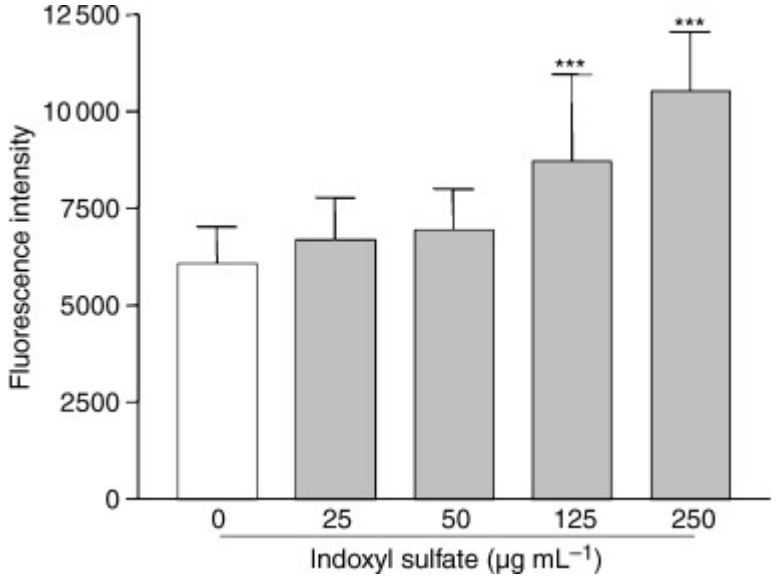


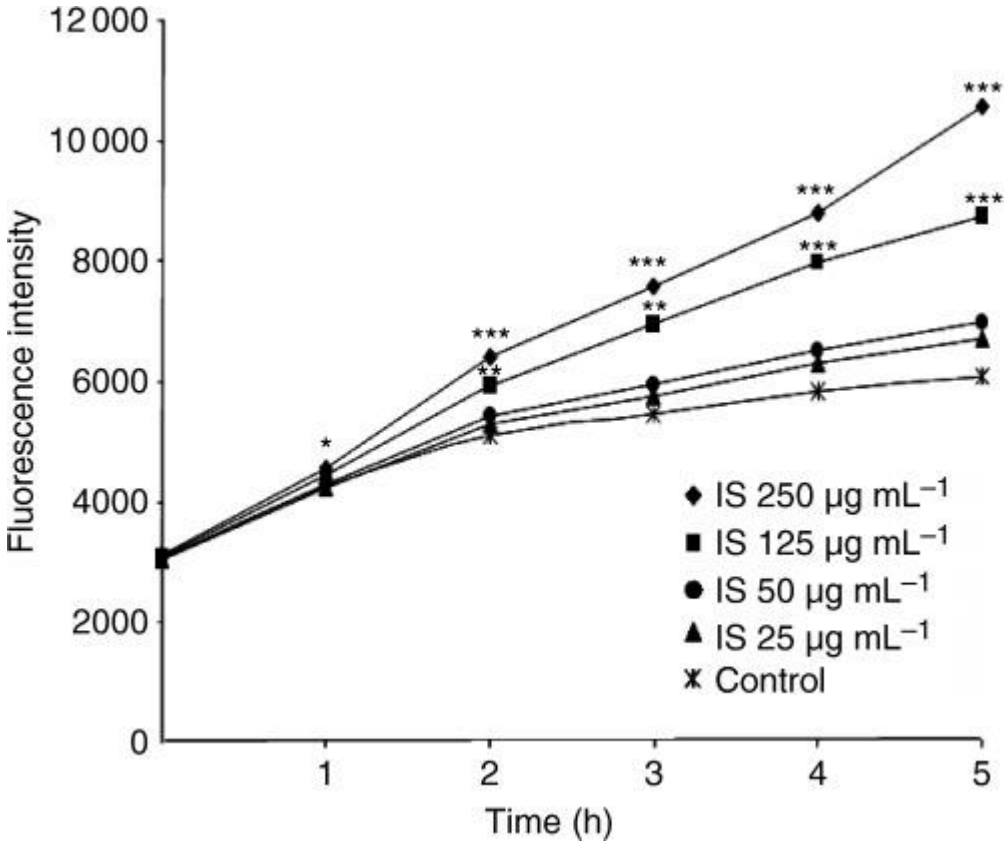




Kidney International 2003;63:1671–1680

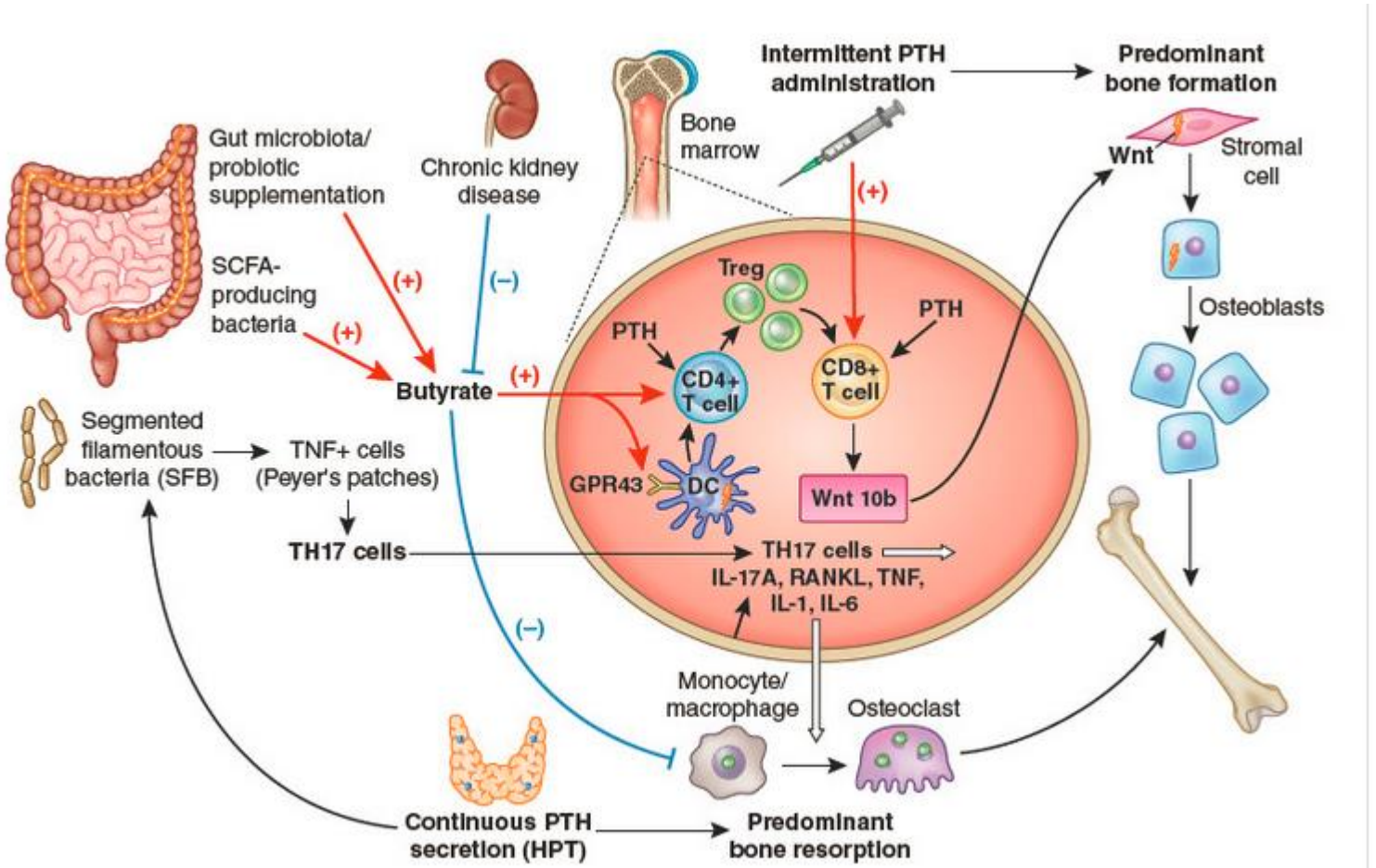
The uremic solute indoxyl sulfate induces oxidative stress in endothelial cells





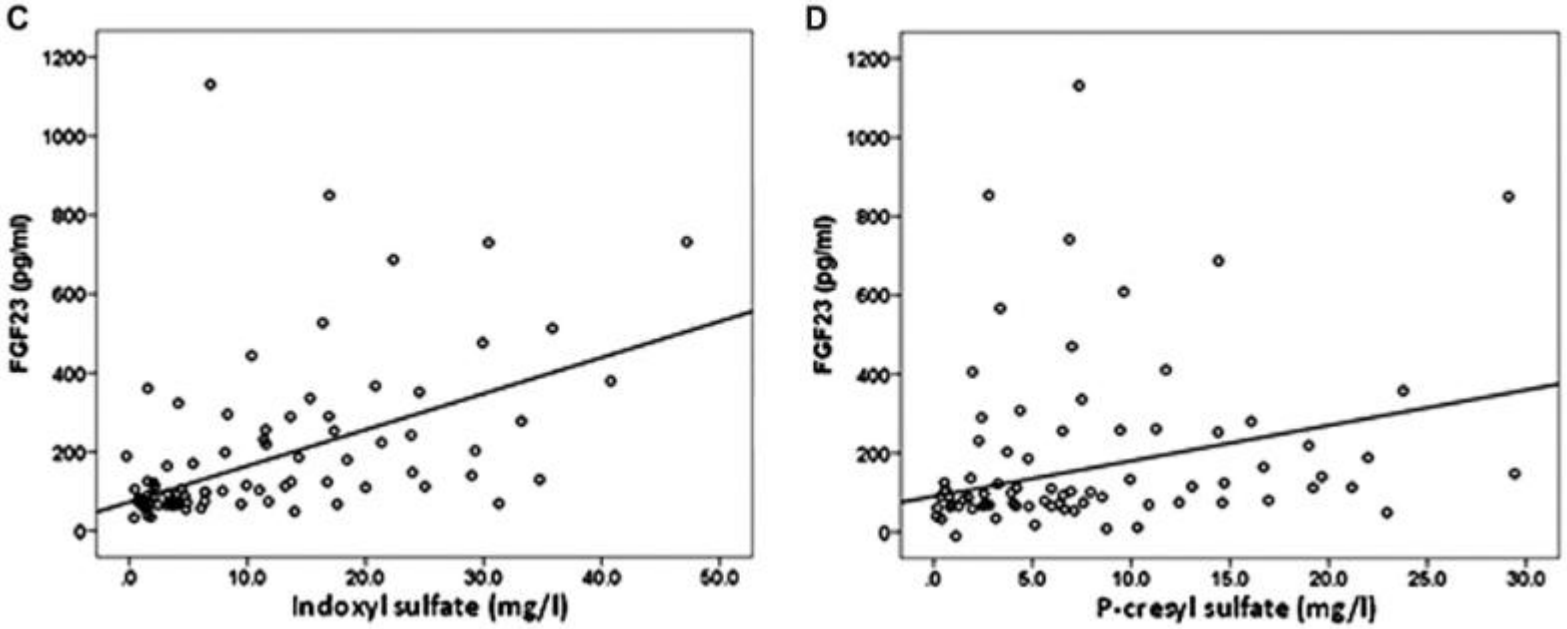
J Thromb Haemost. 2007;(6):1302-8

Gut microbiota orchestrates PTH action in bone: role of butyrate and T cells



Kidney International. 2020;98:269–272

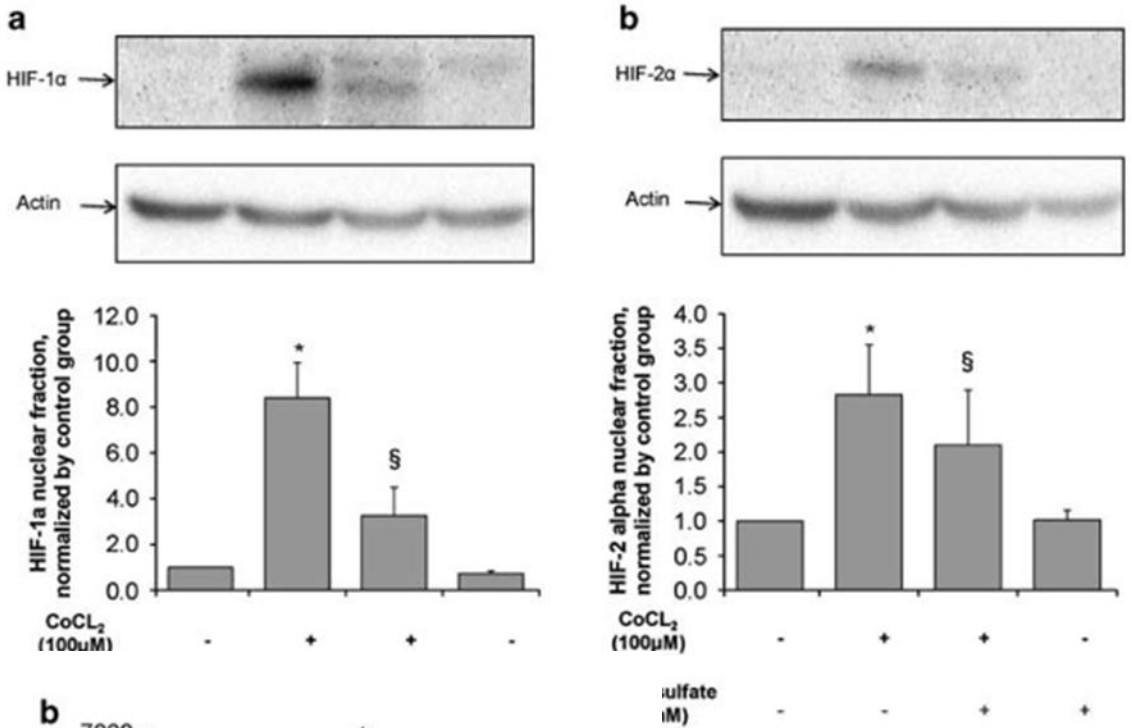
Association of Indoxyl Sulfate With Fibroblast Growth Factor 23 in Patients With Advanced Chronic Kidney Disease

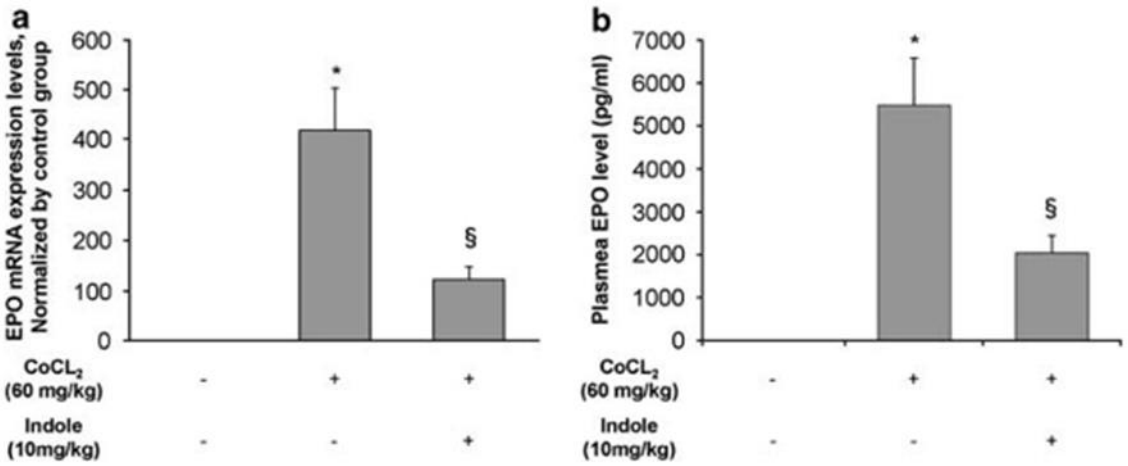


IS but not PCS correlated independently with FGF23 in worsening CKD. IS may be an independent factor involved in regulation of bone-mineral metabolism

Am J Med Sci. 2014;347(5):370-6

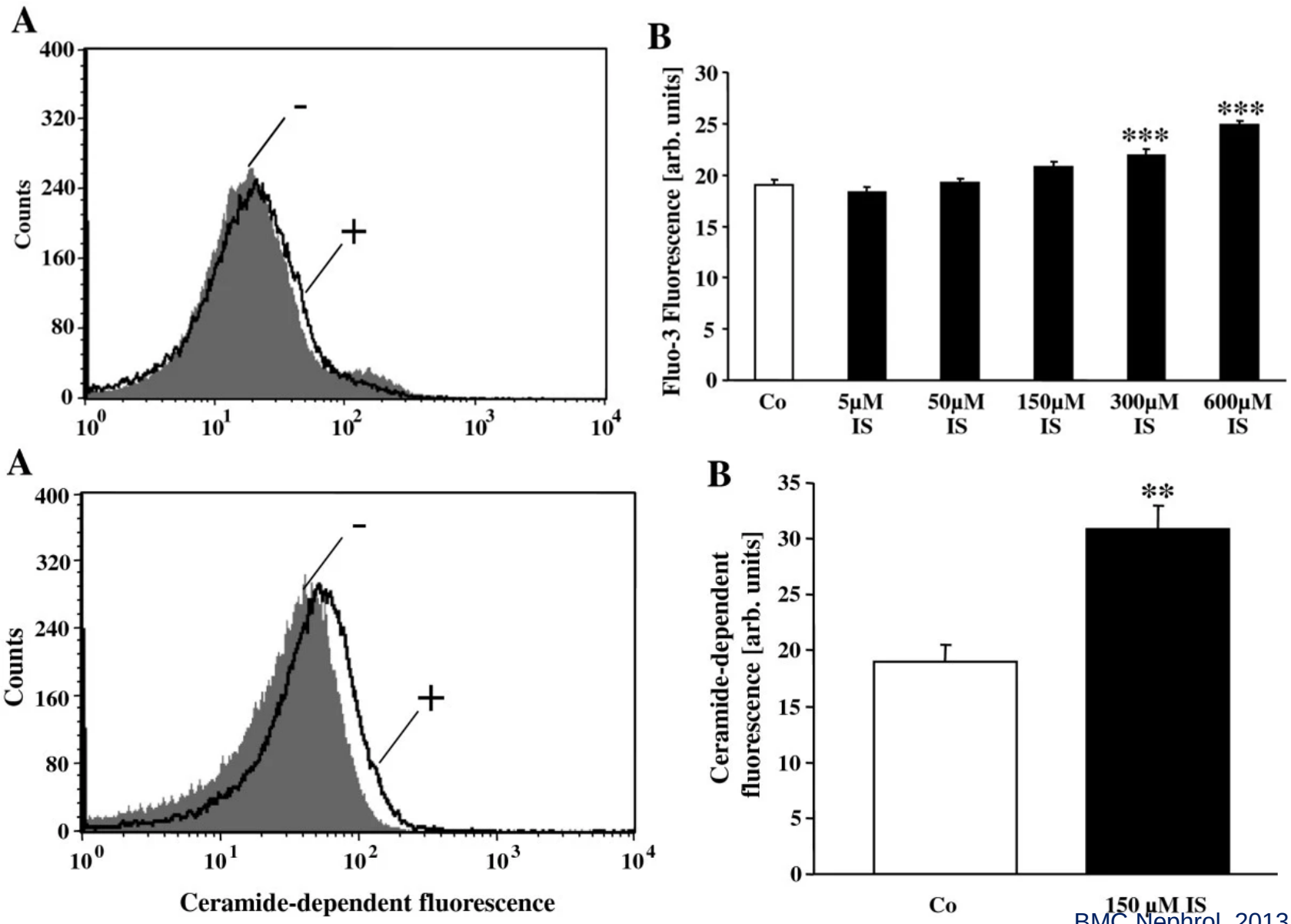
Indoxyl sulfate, a representative uremic toxin, suppresses erythropoietin production in a HIF-dependent manner





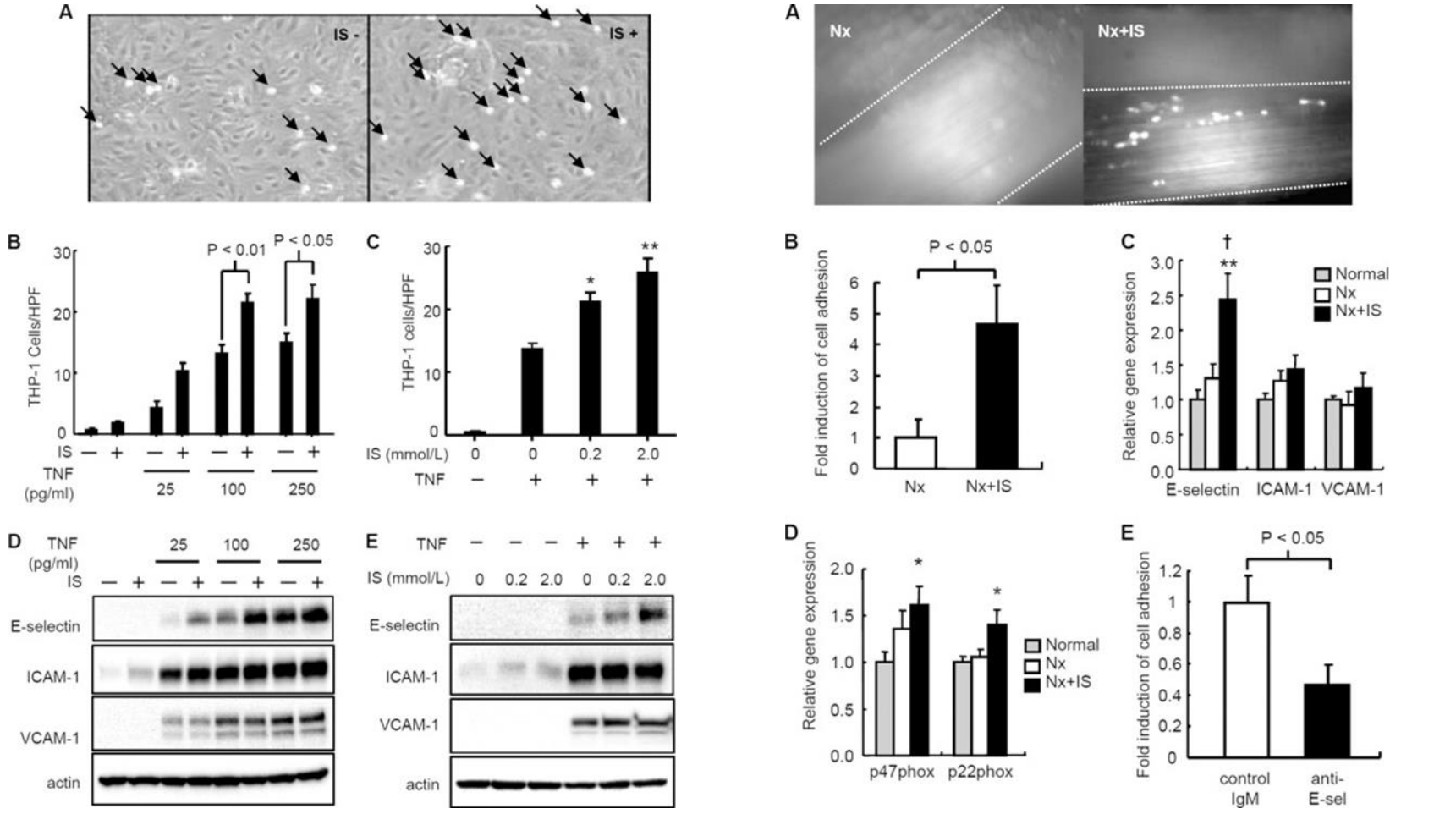
Lab Invest. 2011;91(11):1564-71

Triggering of suicidal erythrocyte death by uremic toxin indoxyl sulfate



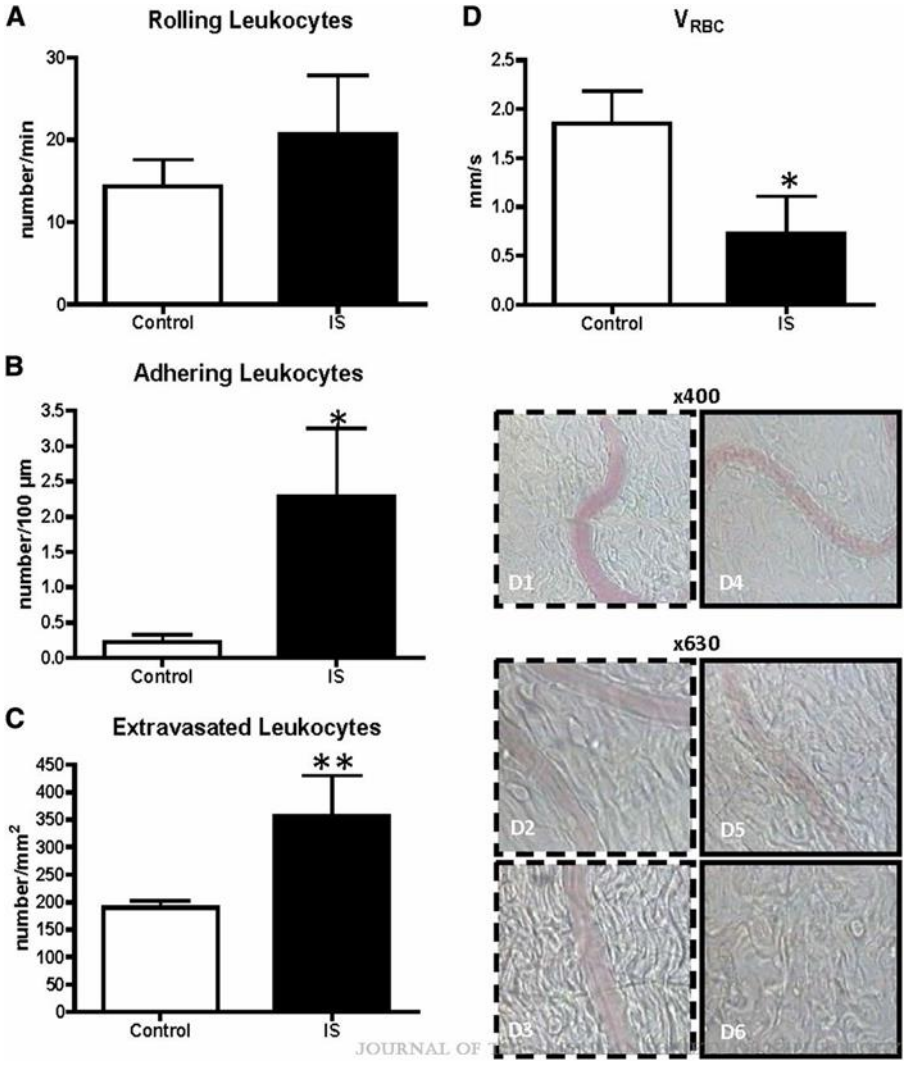
BMC Nephrol. 2013 ;4:14:244

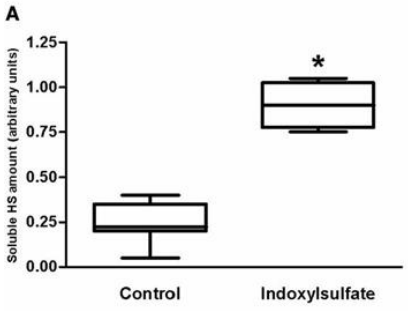
Indoxyl Sulfate Induces Leukocyte-Endothelial Interactions through Up-regulation of E-selectin

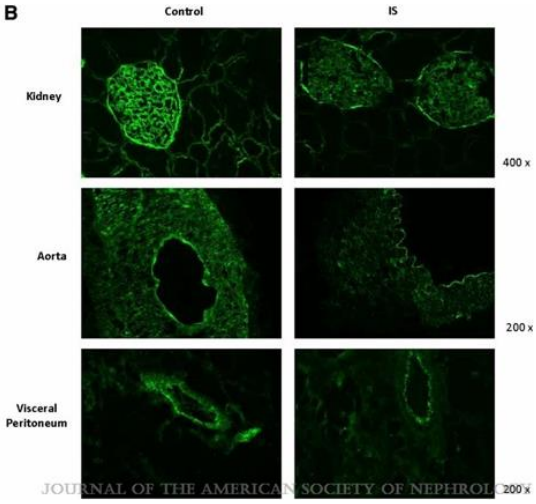


Biol Chem 2010;285:38869 –38875

Protein-Bound Uremic Toxins Stimulate Crosstalk between Leukocytes and Vessel Wall

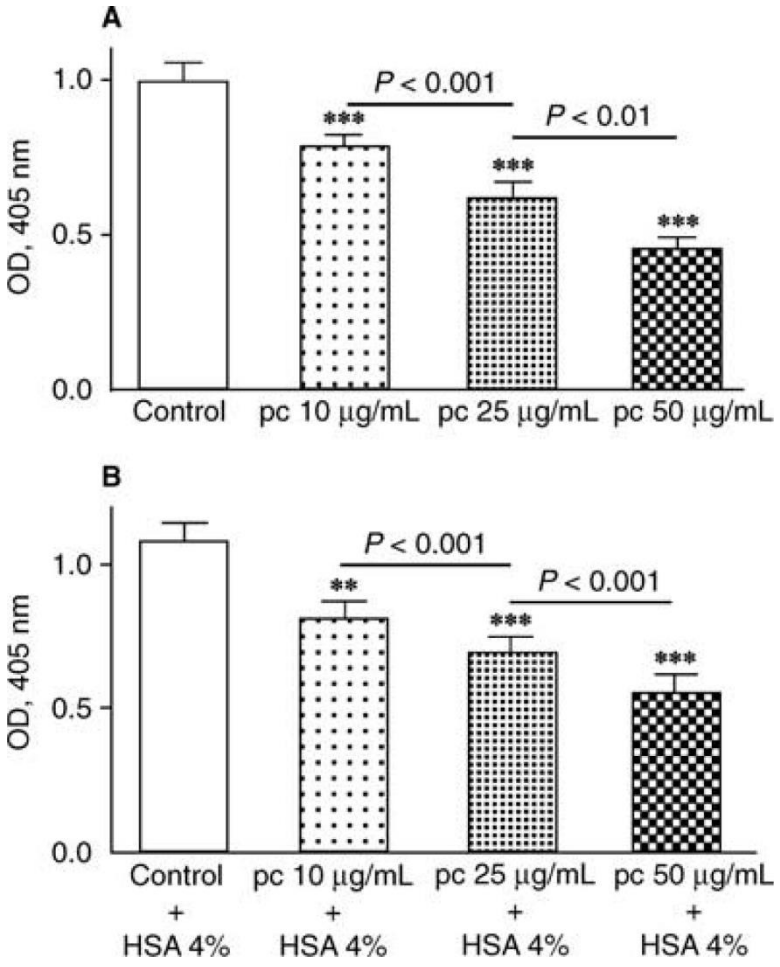


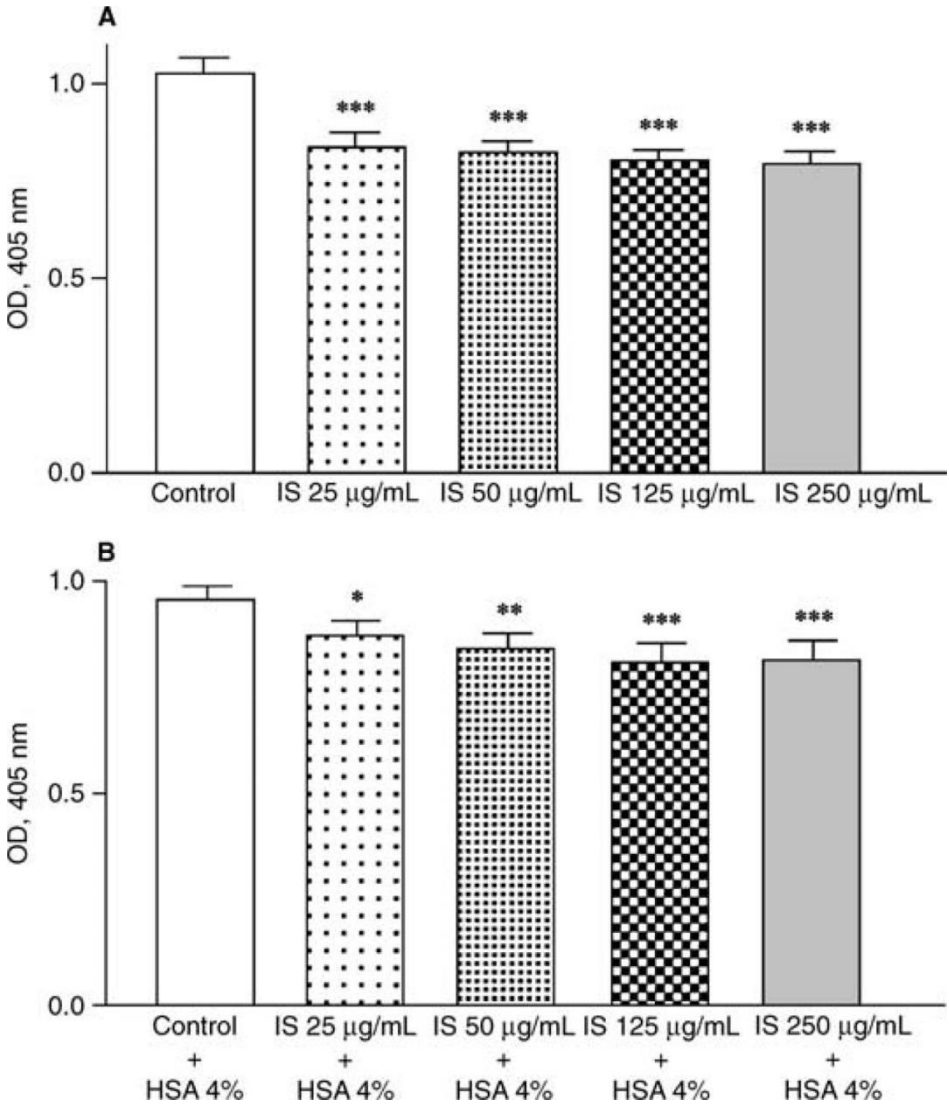




JASN 2013;24(12):1981-1994

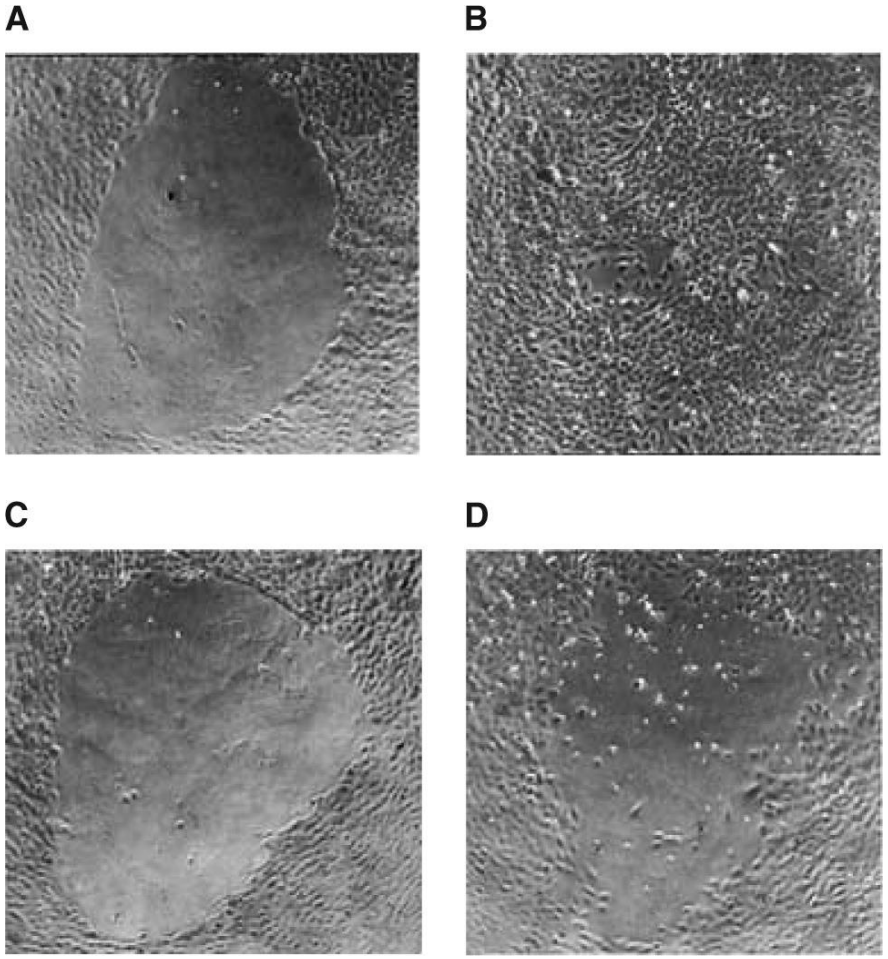
The uremic solutes p-cresol and indoxyl sulfate inhibit endothelial proliferation and wound repair





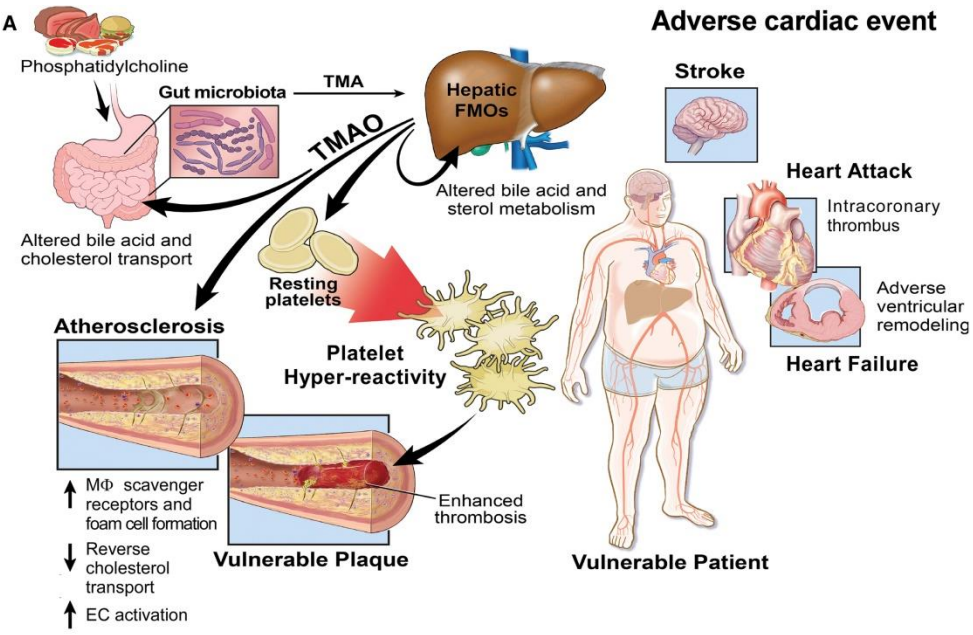
Kidney Int. 2004;65(2):442-51

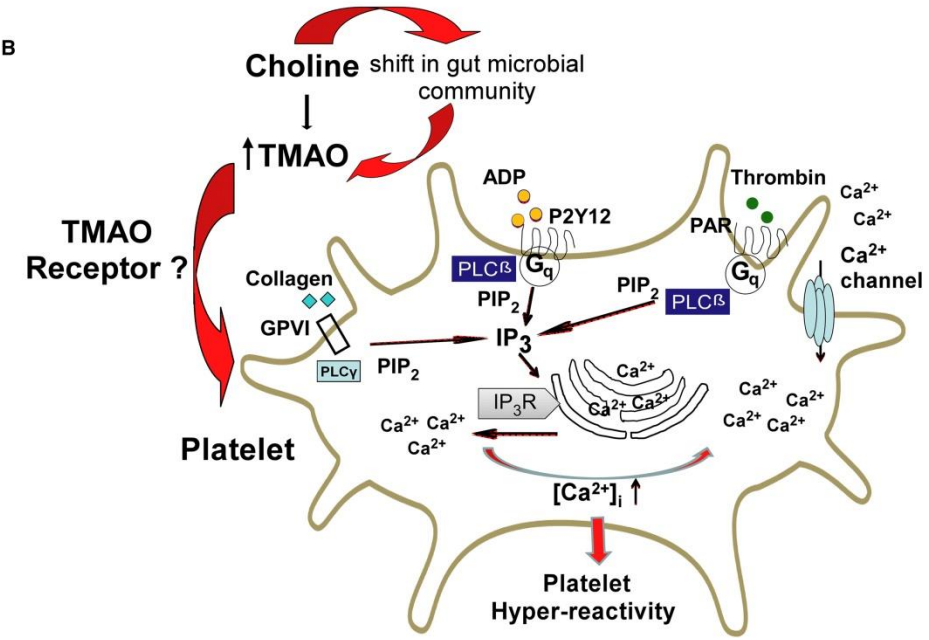
The uremic solutes p-cresol and indoxyl sulfate inhibit endothelial proliferation and wound repair

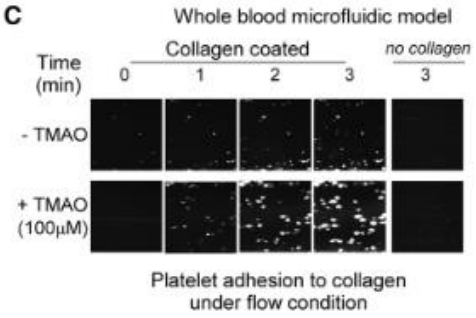


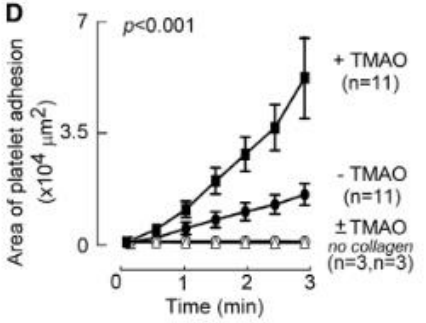
Kidney Int. 2004;65(2):442-51

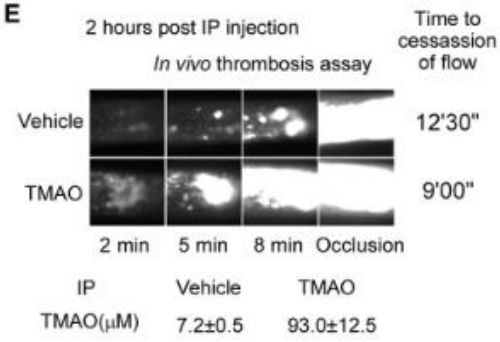
Gut-Microbial Involvement in Development of Platelet Hyperresponsiveness and Atherothrombotic Heart Disease

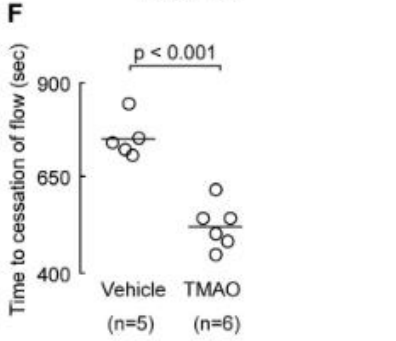






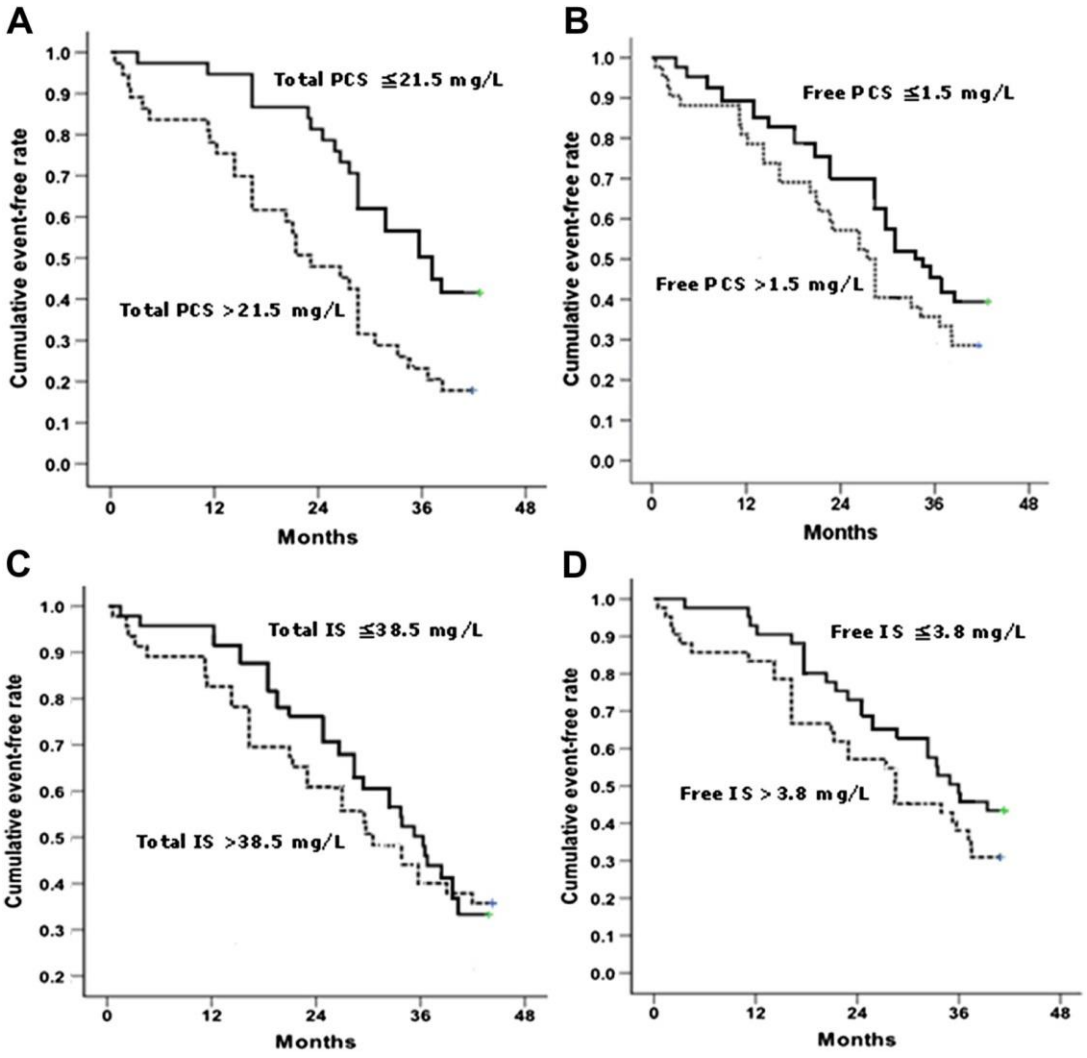






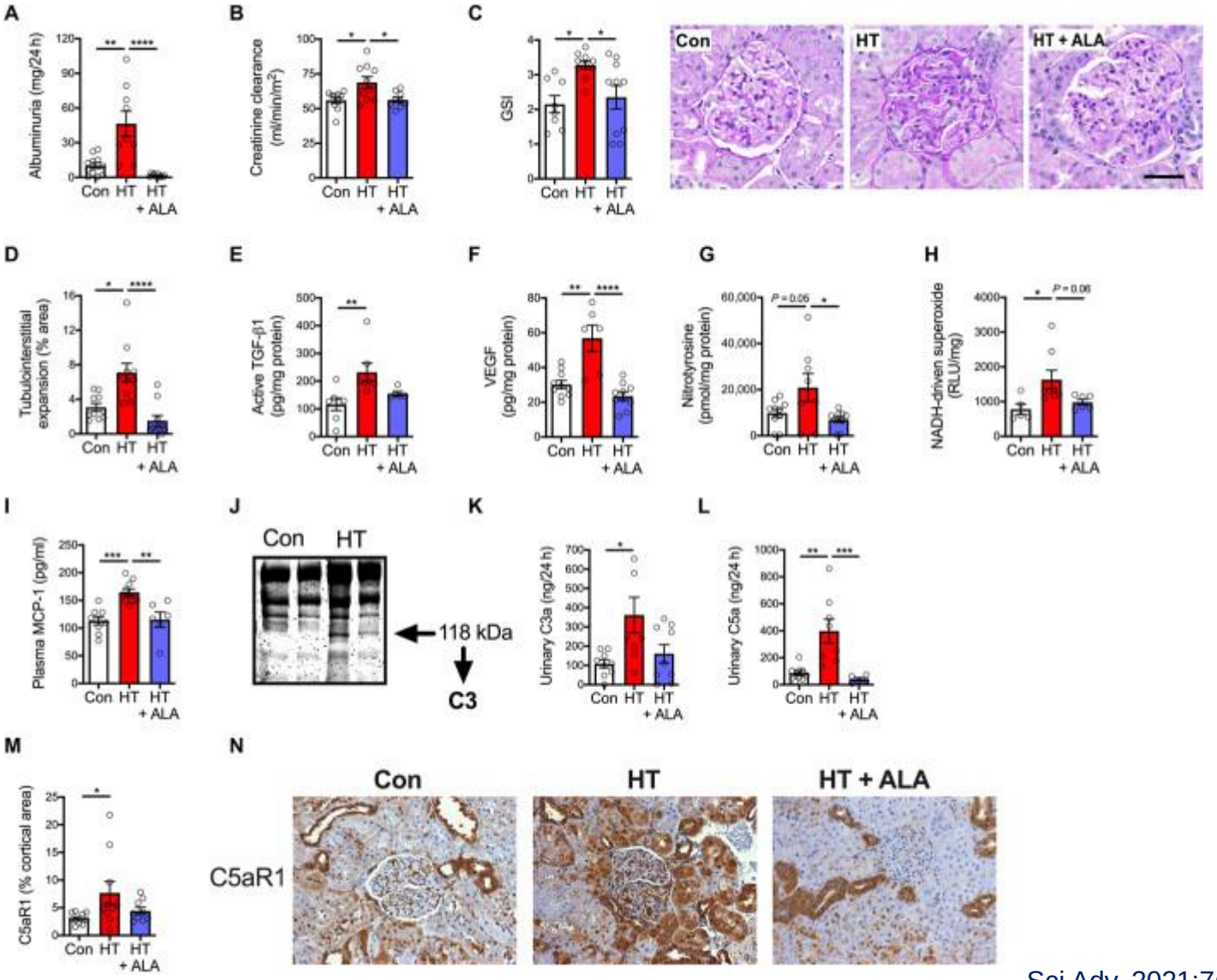
Cell 2016;165(1):111-124

The role of protein-bound uremic toxins on peripheral artery disease and vascular access failure in patients on hemodialysis



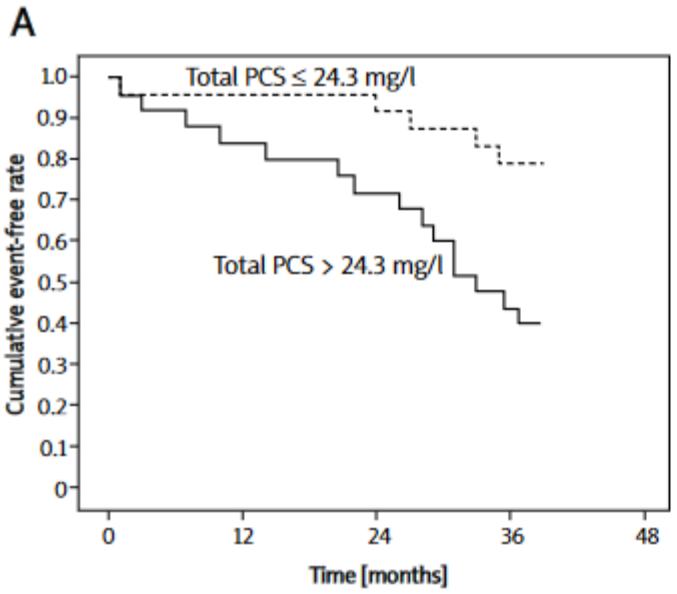
Atherosclerosis 2012;225(1):173-9

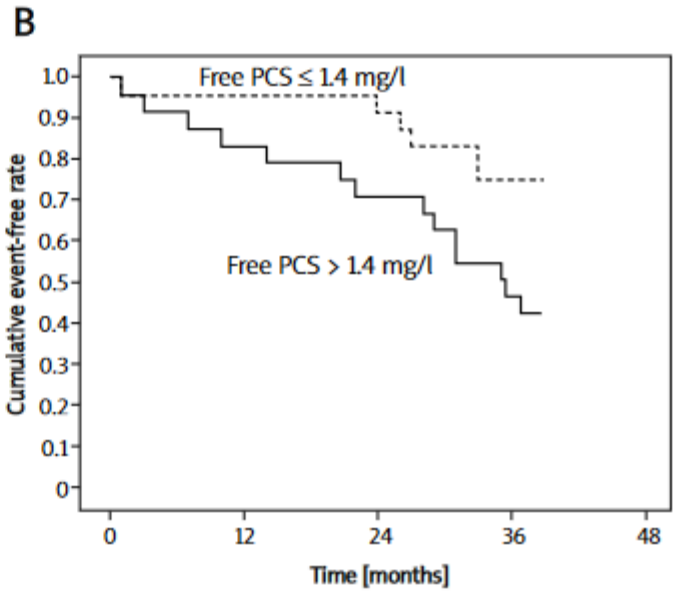
Processed foods drive intestinal barrier permeability and microvascular diseases

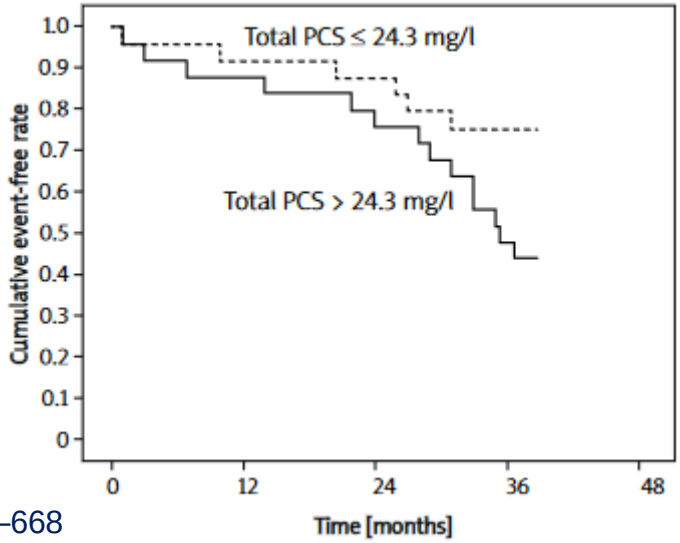


Sci Adv. 2021;7(14):eabe4841

Serum p-cresyl sulfate predicts cardiovascular disease and mortality in elderly hemodialysis patients



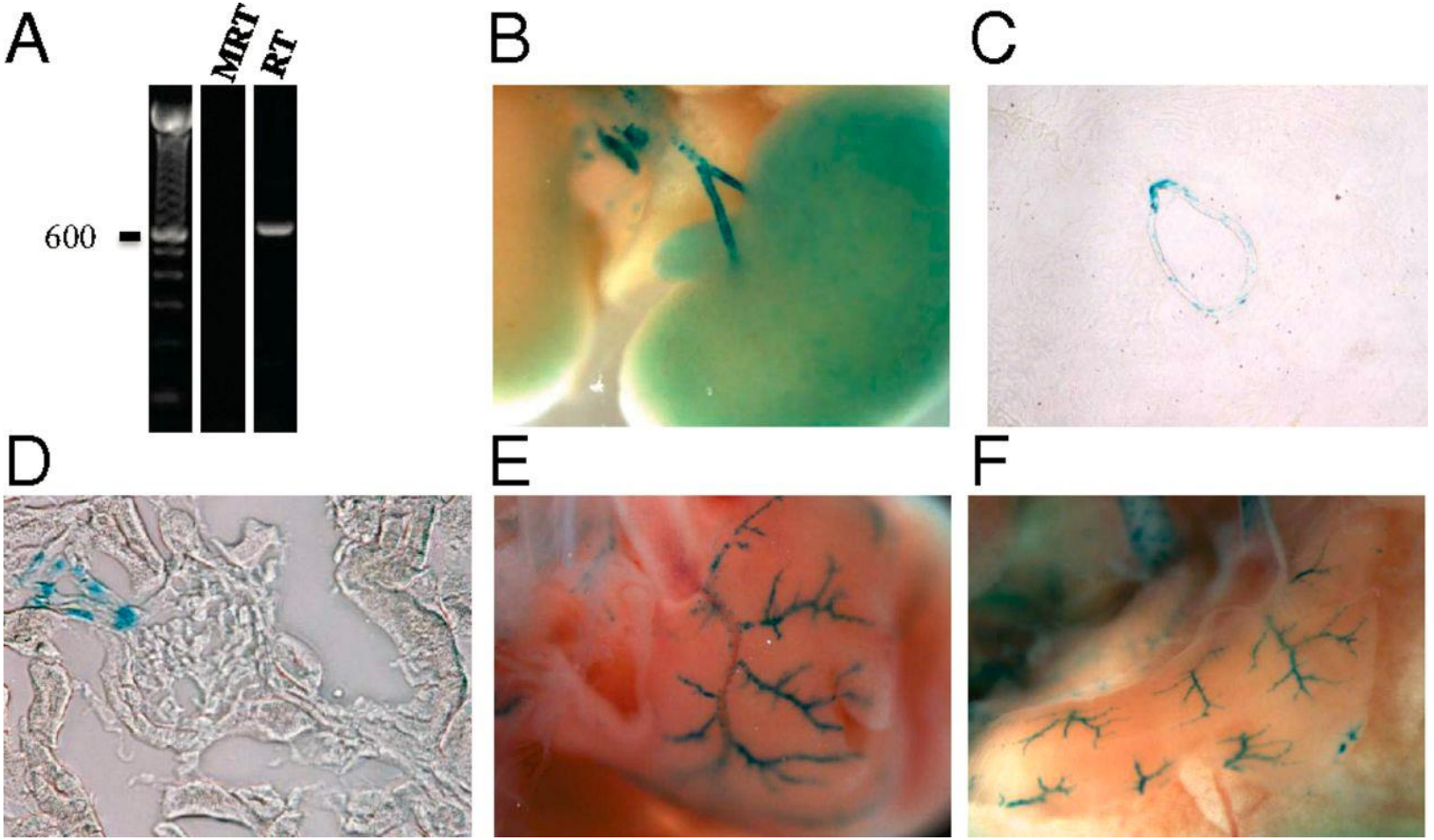




Single medical center
50 stable HD patients
>65 years old
Follow-up : 38 months
Clinical outcomes : cardiovascular events and all-cause mortality

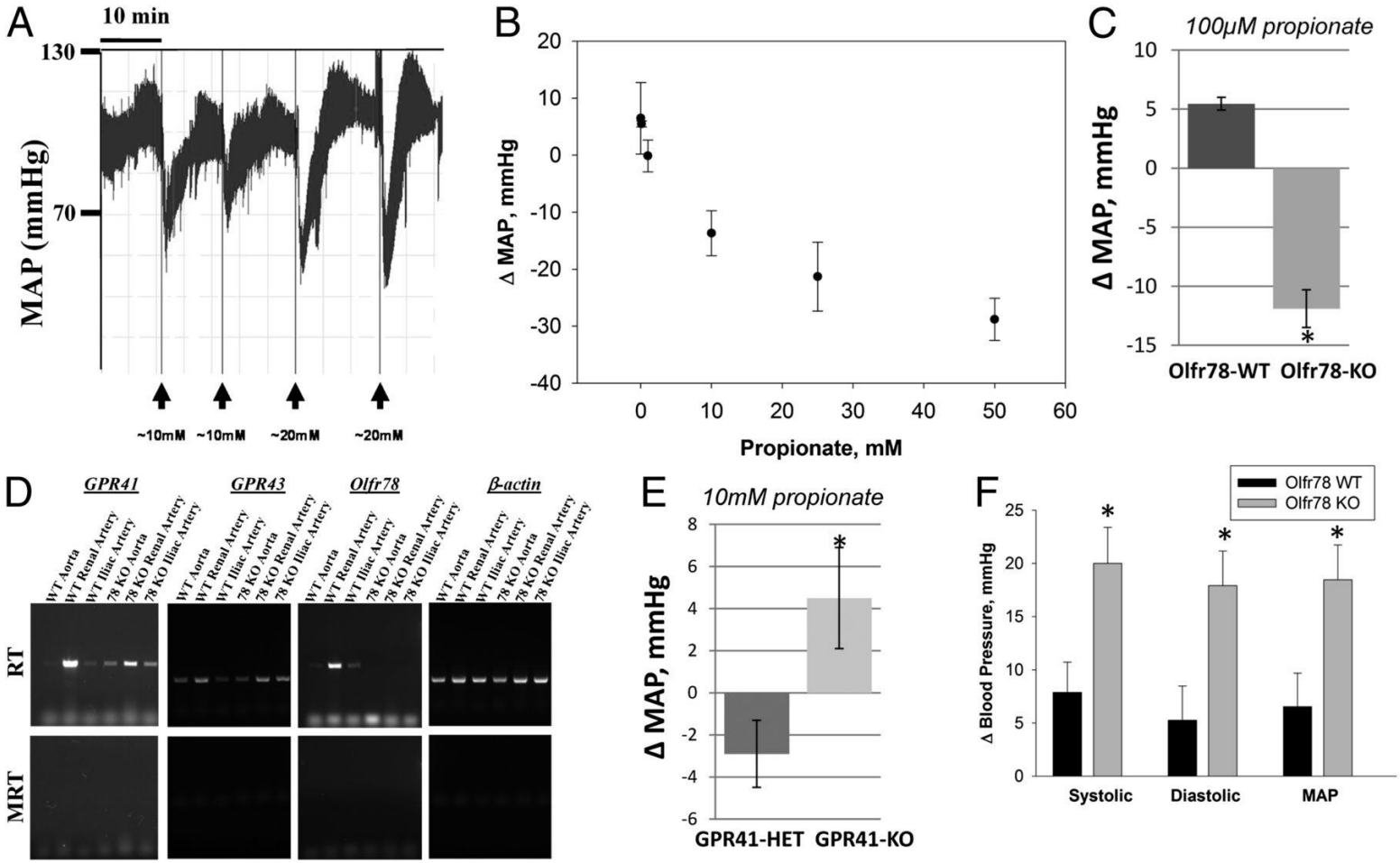
Arch Med Sci 2013;9(4): 662–668

Olfactory receptor responding to gut microbiota-derived signals plays a role in renin secretion and blood pressure regulation



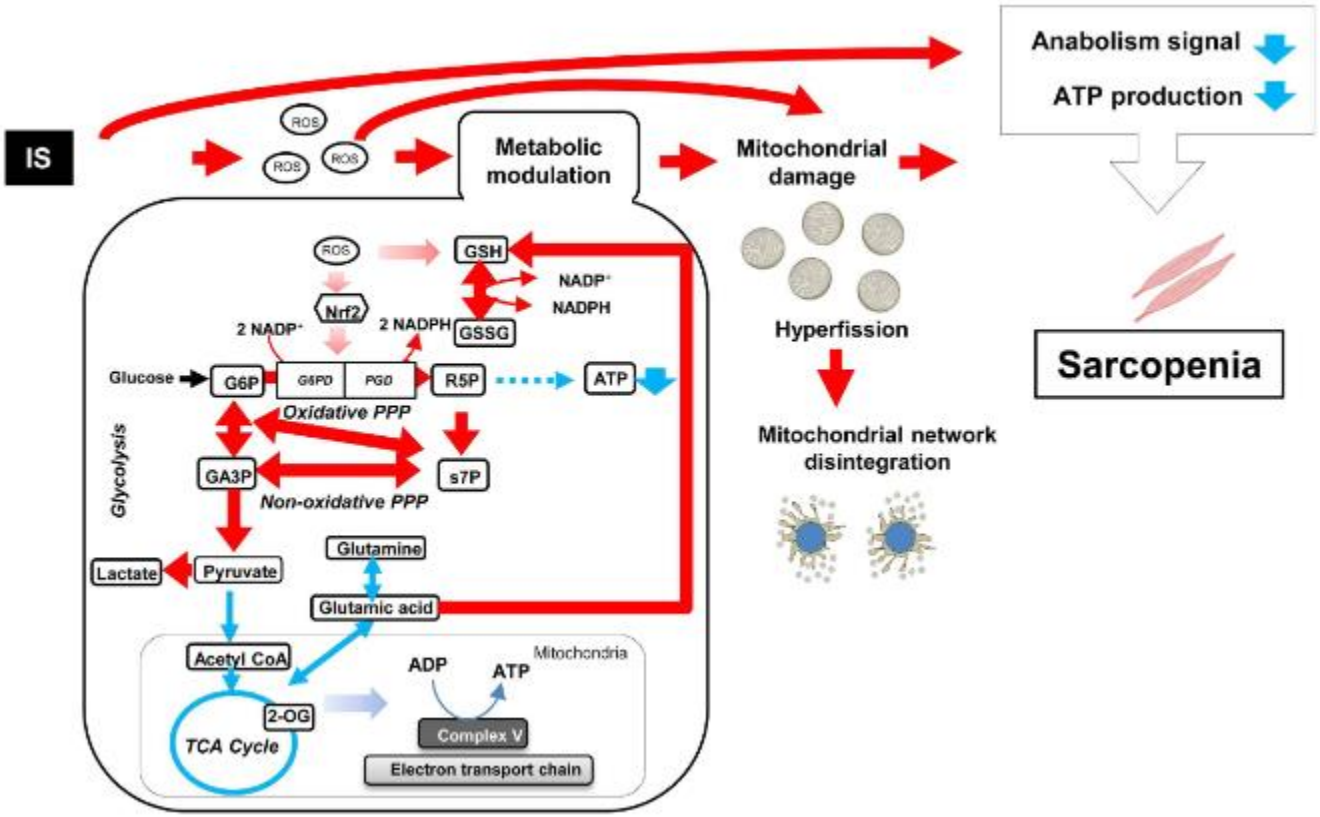
Proc Natl Acad Sci USA 2013;12;110(11):4410-5

Olfactory receptor responding to gut microbiota-derived signals plays a role in renin secretion and blood pressure regulation



Proc Natl Acad Sci USA 2013;12;110(11):4410-5

Metabolic alterations by indoxyl sulfate in skeletal muscle induce uremic sarcopenia in chronic kidney disease



Sci Rep. 2016;6:36618

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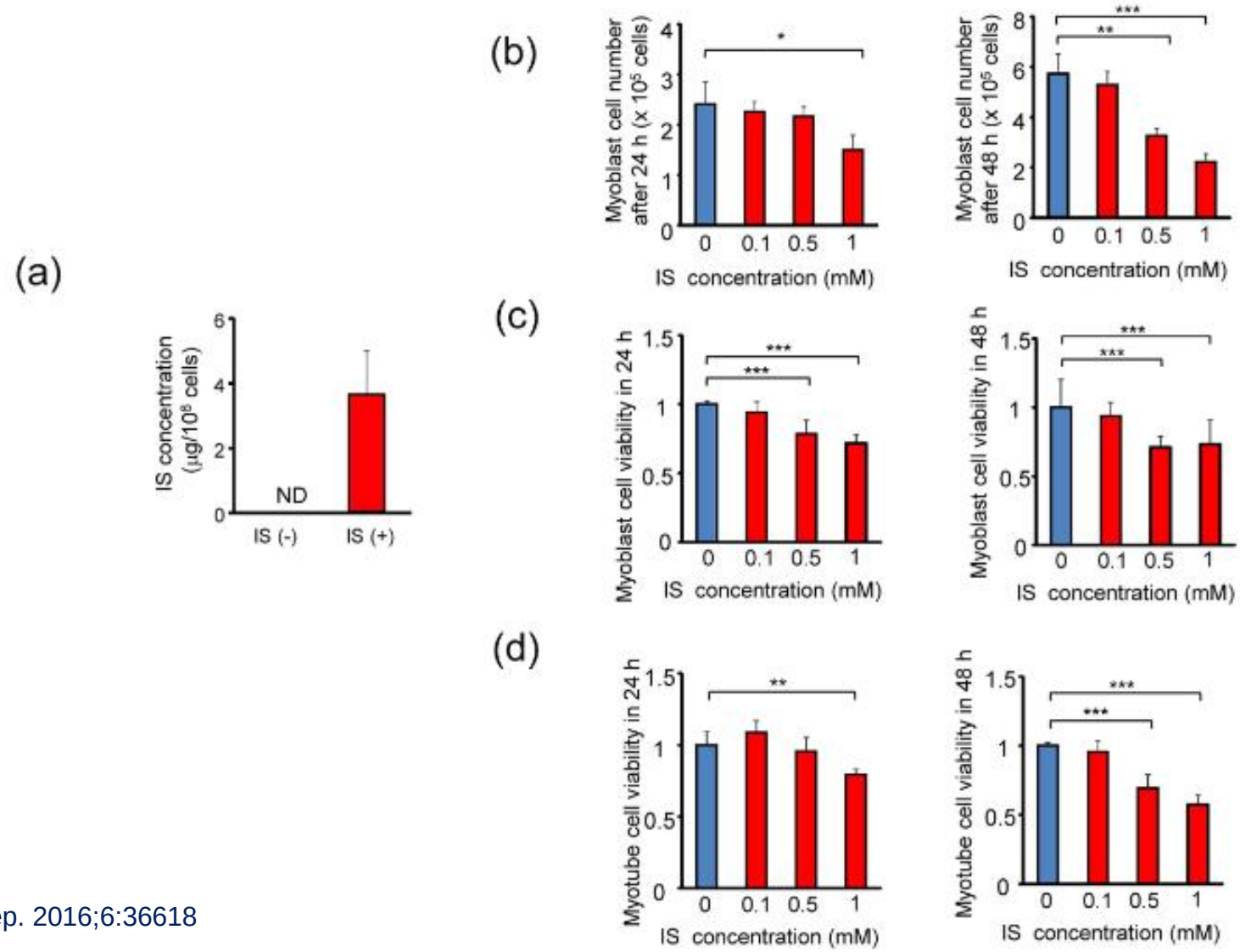

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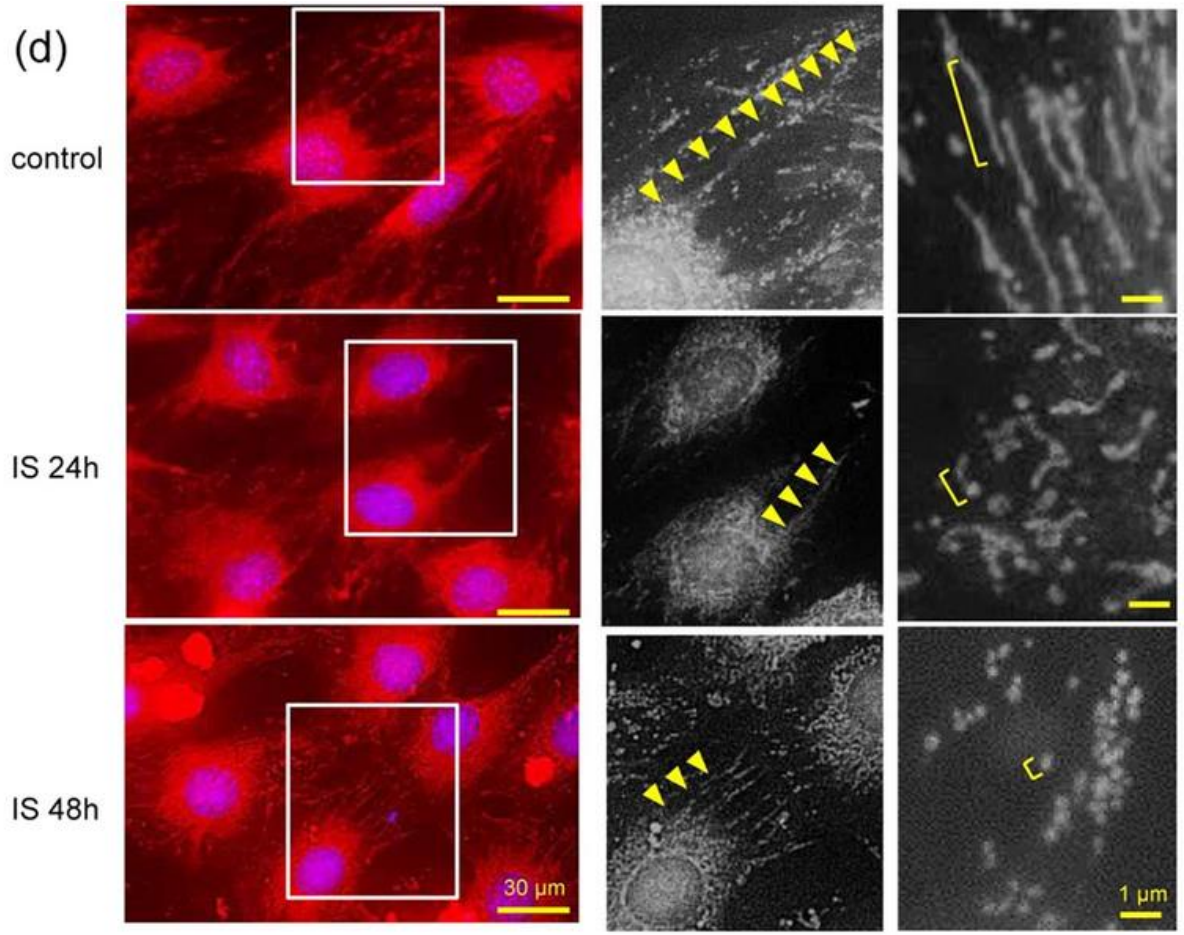
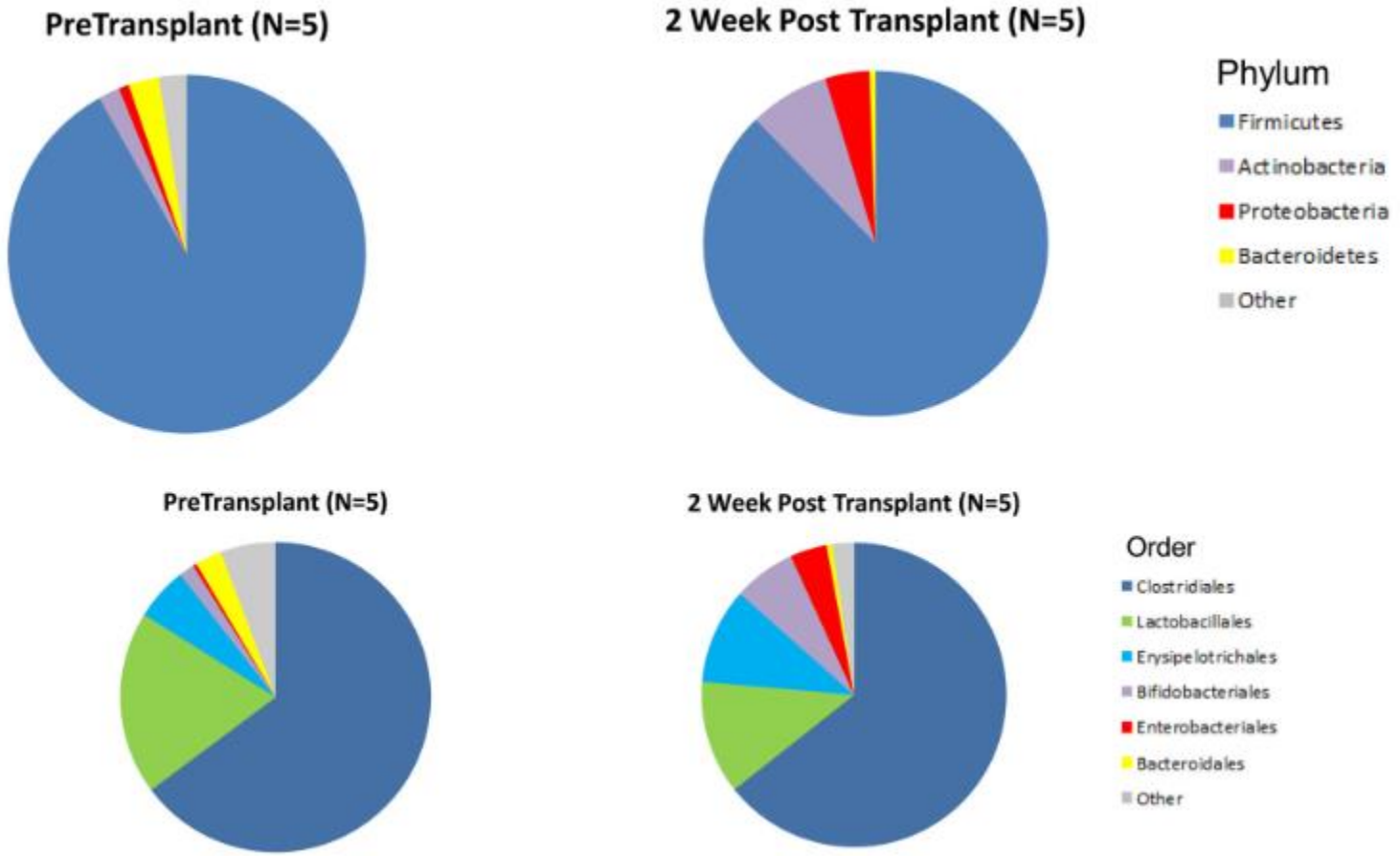
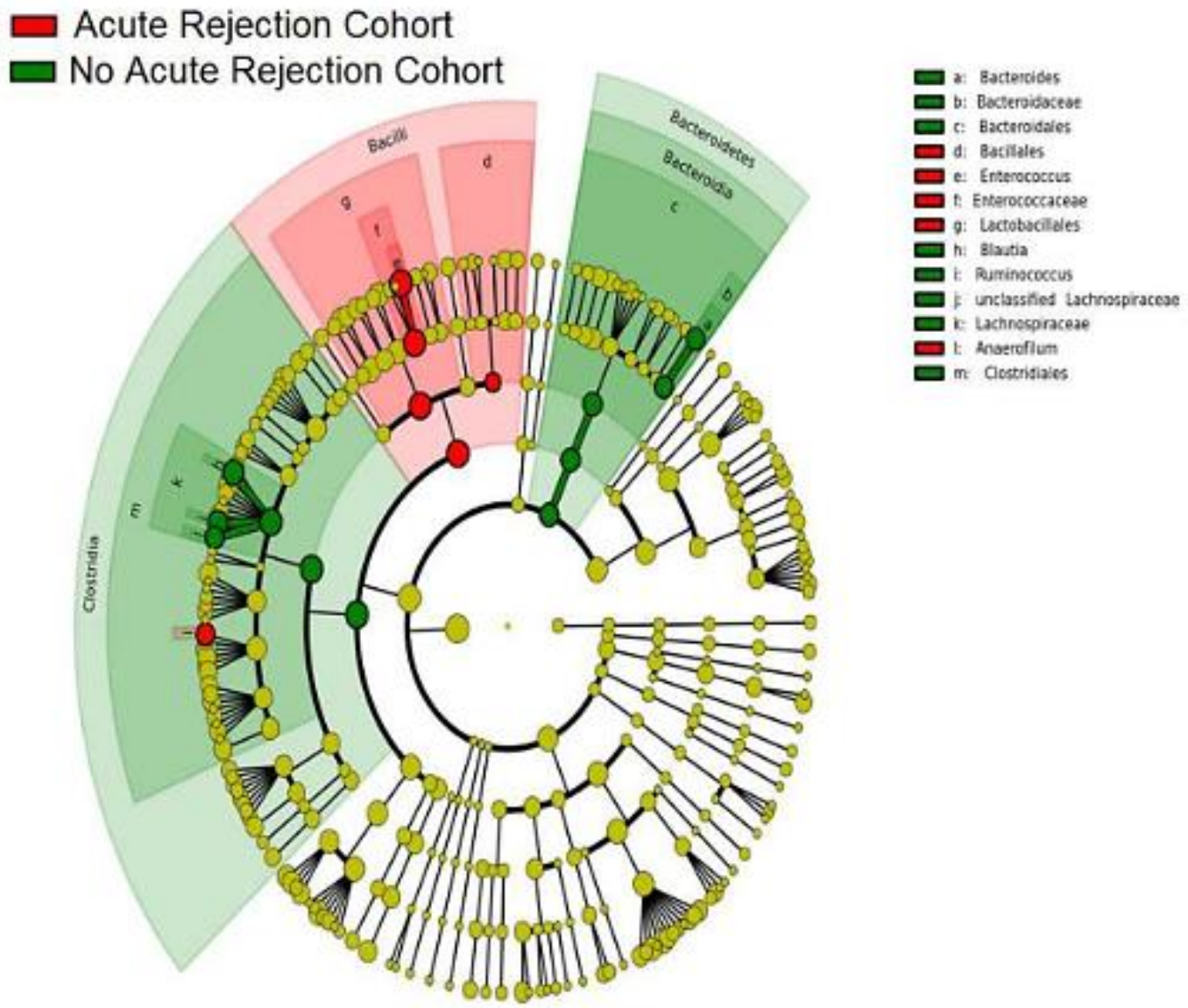


Sci Rep. 2016;6:36618

Gut Microbial Community Structure Following Kidney Transplantation

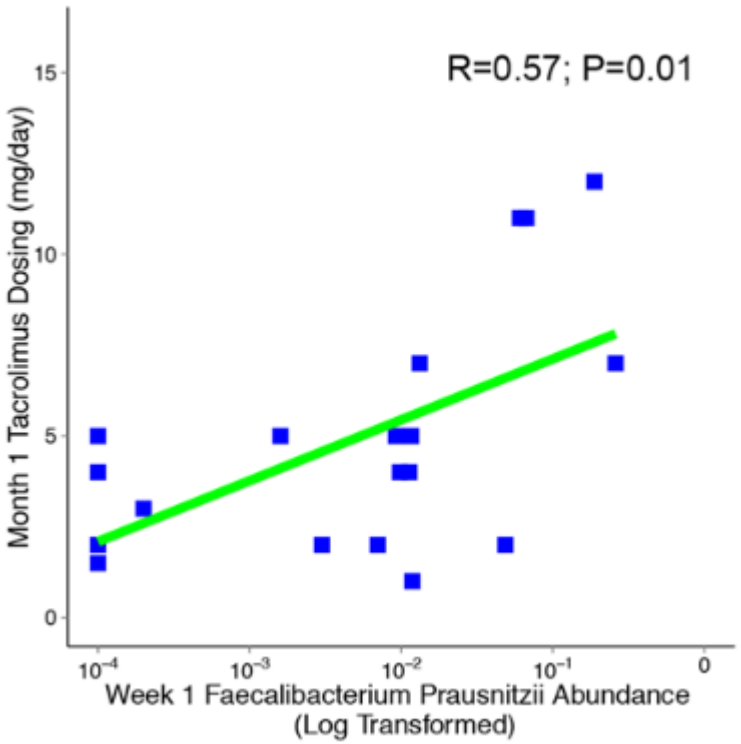


Transplantation 2014;98(7):697–705



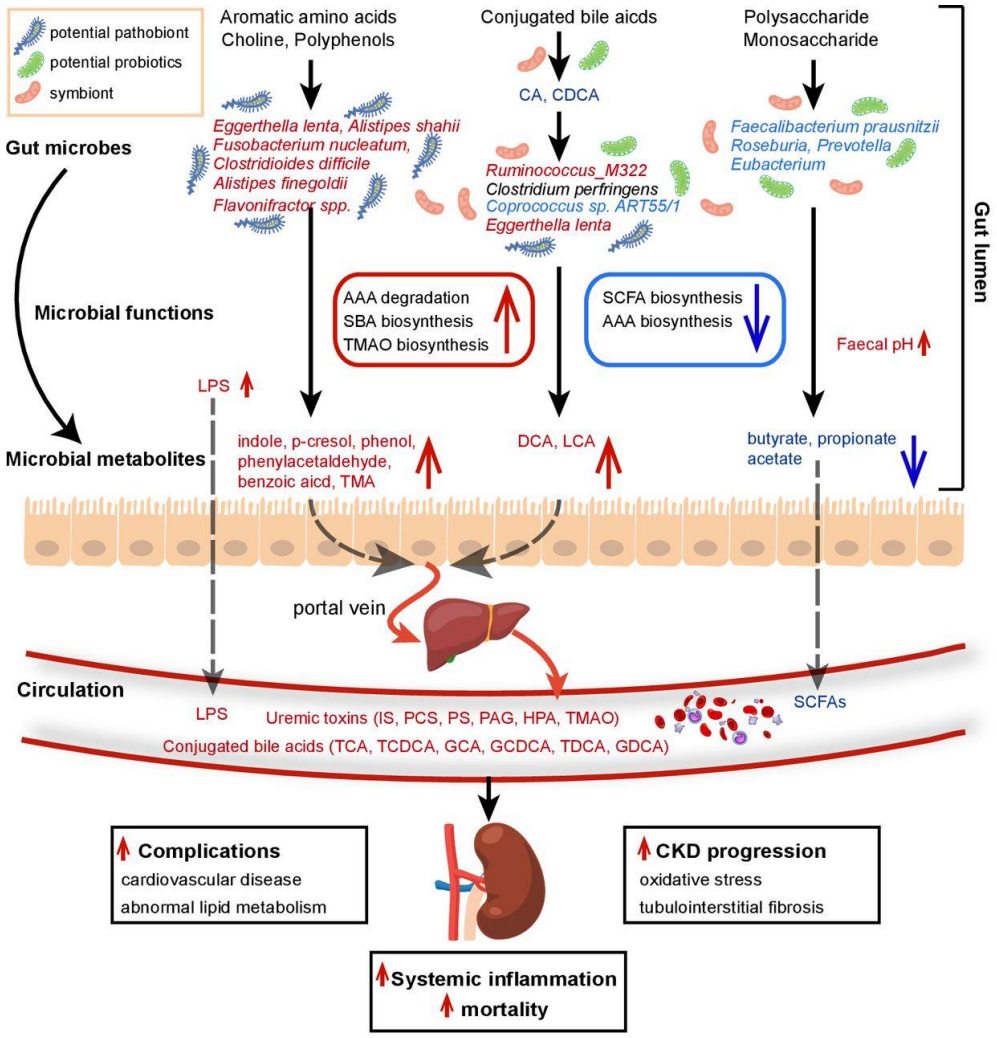
Transplantation 2014;98(7):697–705

Gut Microbiota and Tacrolimus Dosing in Kidney Transplantation



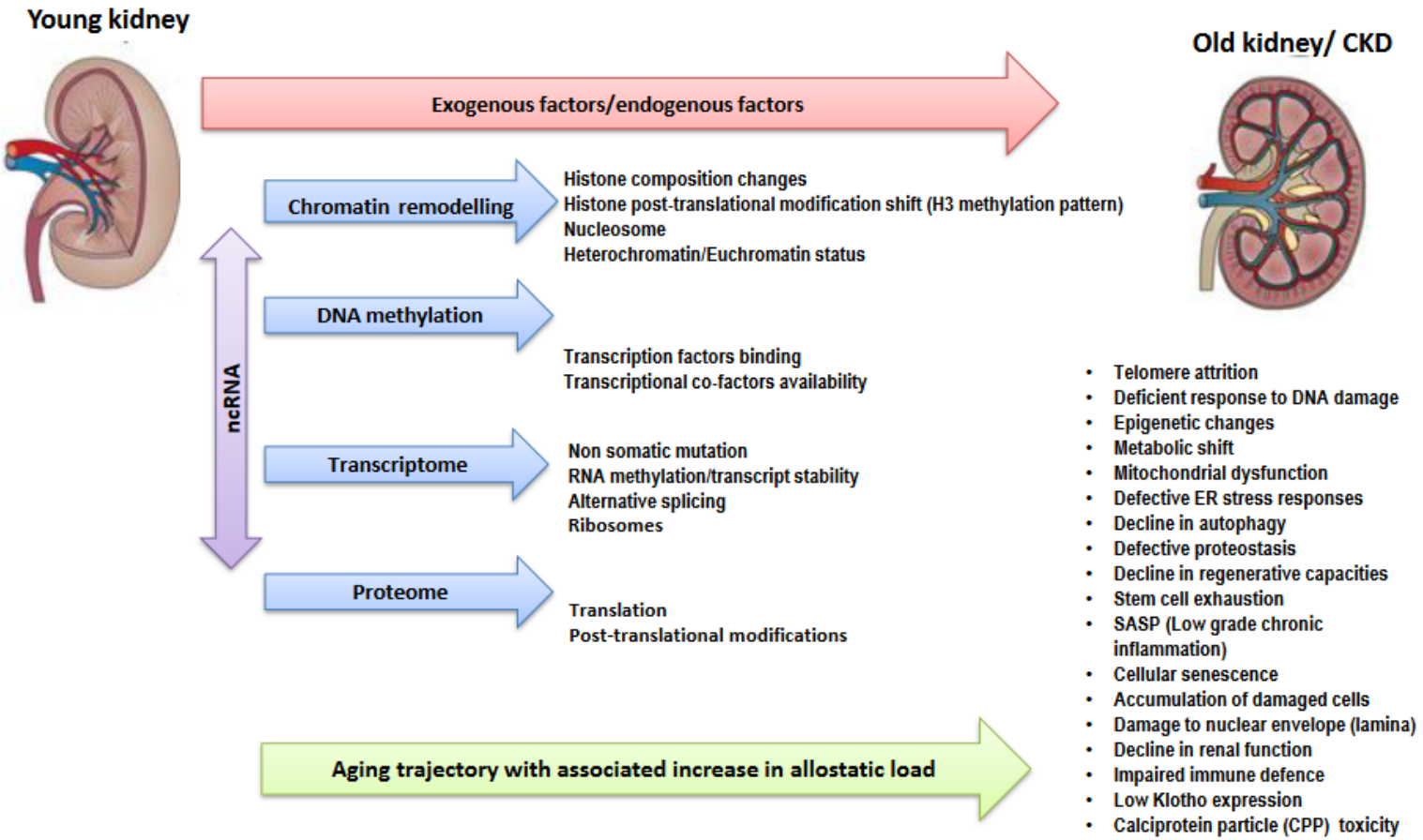
PLoS One 2015;10(3):e0122399

ESRD-gut microbiome

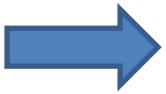


Gut 2020;69:2131-2142

The role of epigenetics in renal ageing



Nat Rev Nephrol. 2017;13(8):471-482

- Gut-Kidney axis
- Inflammation –Immune dysregulation
- Fibrosis
- Oxidative stress
- Hypertension
- Macro- and microvascular disease
- Dysbiosis  Mortality

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INSIDE STORY

Results from the Integrative Human Microbiome Project

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The path to better journal metrics

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GOING SUPERSONIC

Hawking radiation from analogue black holes

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ELECTRONICS

HUMAN TOUCH

A tactile glove that senses how a hand grasps

PAGES 638 & 698

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