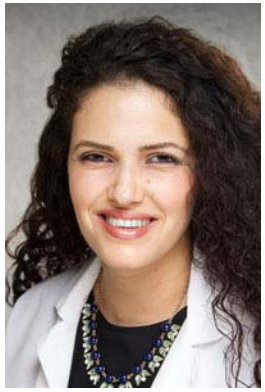
PKD Program in UIHC

with support from Hills family donation



Noureddine

Armstrong

Thomas

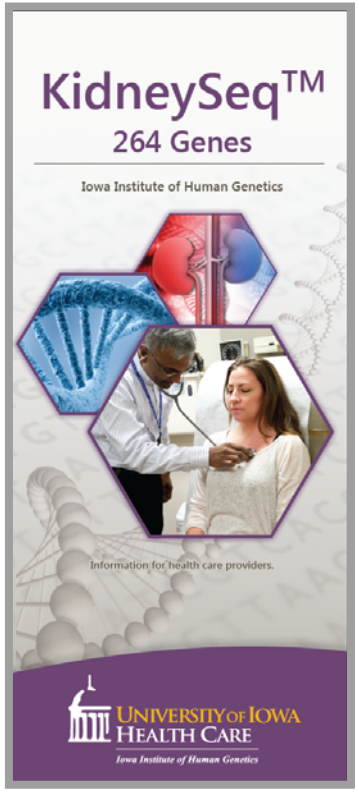
Attanasio

Huang

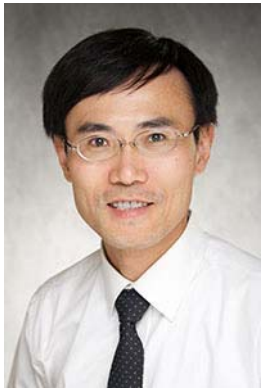
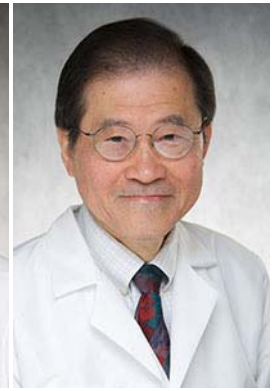
- Specialized PKD clinics for better care and clinical trial (PKD registry)
- Innovative genetic diagnosis for PKD and cystic diseases
- Investigate pathogenesis of cystogenesis
- Develop innovative gene therapy strategy

Renal Genetics Program - Thomas

- Renal Genetics Clinic with dedicated genetics counselor
- First ever comprehensive renal genetics plan (~264 genes)
- Research projects
  - Performance of genetic test - Kidneyseq™
  - Outcome of living kidney donor genetic screening
  - Outcome of genetic screening in atypical cystic diseases
  - Genetic heterogeneity of Alport disease
  - APOL1 gene screening in BKV nephropathy
  - Assessing usefulness of dedicated genetics clinic
  - Case series – Gitelman, Genetic FSGS, PKD, Alport



Research in Huang Lab

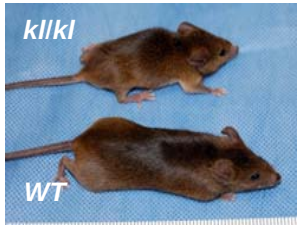



Xie *Huang*

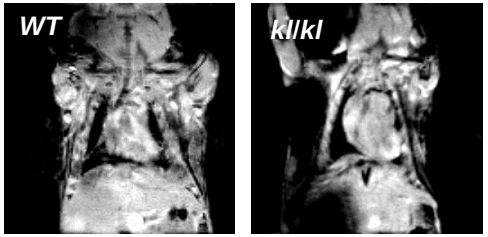
ADPKD

- Investigate pathogenesis of cystogenesis
- Develop innovative gene therapy strategy

Cardiac dysfunction in CKD



- Klotho is an aging suppression protein hormone produced in kidney, is cardioprotective
- Loss of klotho production in CKD contributes to cardiomyopathy
- Mechanism and potential therapeutic of klotho in heart failure



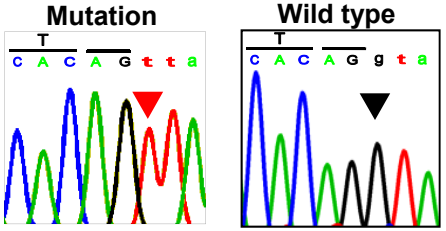
Fluid and electrolyte transport

- Physiology and disease mechanism of ion transport disorder
- Brain-Kidney cross-talk

Research in Attanasio Lab

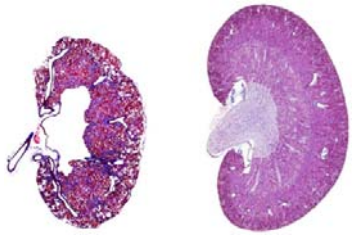
- **Human and mouse genetics of kidney diseases**

  We identify mutations in genes causing human diseases and study their function using gene modified mice



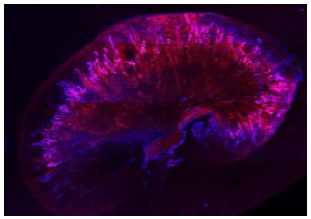
- **Cystic kidney disease and fibrosis**

  Kidney section of a 3 months *Glis2* knockout mouse compared to a normal mouse of the same age. *Glis2* knockout kidneys are cystic and fibrotic and lose function over time



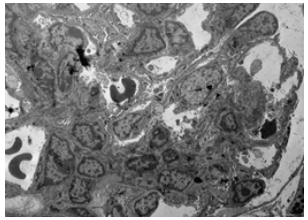
- **Mechanisms of kidney injury, repair and fibrosis**

  After acute kidney injury the cells of the tubules undergo cell cycle arrest (red in the kidney of this transgenic mouse) and cause progressive fibrosis and loss of kidney function



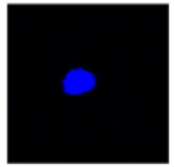
- **Glomerular thrombotic microangiopathy**

  Occluded glomerular capillaries in *Dgke* knockout kidneys, visualized by electron microscopy

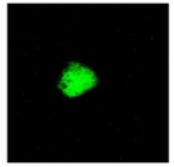


Jalal Research: Vascular Disease in CKD

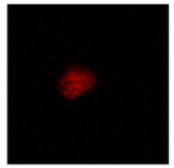
EC biopsy and IF



DAPI



VE Cadherin



Primary antibody of interest

1. Vascular Lab

– Endothelial function (brachial artery flow-mediated dilatation)
– Large artery stiffness (pulse wave velocity)
– Endothelial cell (EC) biopsy and immunofluorescence (IF)
– Cell culture experiments

2. Clinical trials

3. Epidemiological and health sciences research

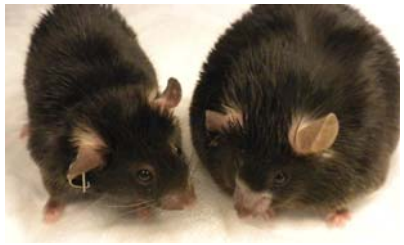
Lowering uric acid in CKD: randomized placebo-controlled study

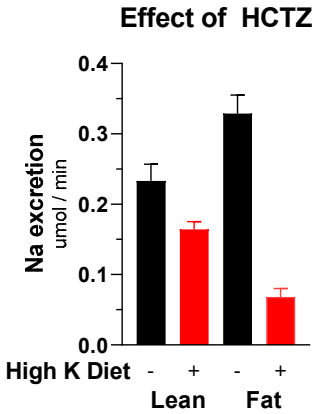
Variable	Placebo N=41	Allopurinol N=39	P -value
Serum urate (mg/dL)	0.05 ± 1.54	-3.24 ± 1.35	<0.0001
FMD % Δ	0.16 ± 4.05	0.91 ± 3.9	0.47
NTG-dilation % Δ	-1.29 ± 5.33	0.93 ± 6.05	0.14

Nizar Lab: Renal Physiology in Hypertension

- Dietary Electrolyte and Fat effects on Na retention and blood pressure

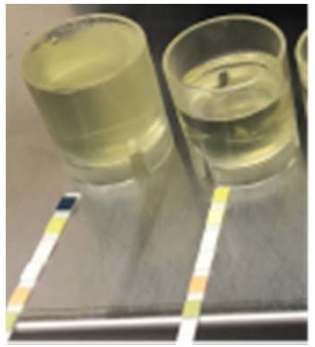
Obesity enhances sensitivity to Thiazide diuretics





- Renal Tubule Insulin receptor regulation of electrolyte reabsorption

Renal Tubule Insulin Receptor knockout causes renal glucose wasting and lower blood pressure

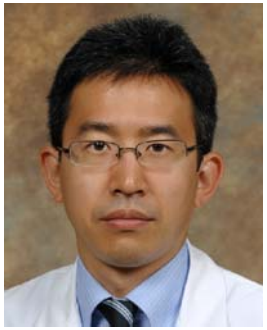


VA CADRE Program: Health Sciences Research


Dixon


Jalal


Swee


Yamada


Griffin

- CADRE (Comprehensive Access & Delivery Research & Evaluation)- multi-discipline team using the nation largest EMR database at Iowa City VA led by Dr. Eli Perencevich
- Renal Investigators: Bradley Dixon, Diana Jalal, Melissa Swee, Masaaki Yamada, Benjamin Griffin
- Excellent track record in career development
- Funding opportunities from VA, NIH, FDA, etc

Examples of Clinical Trials

Bradley Dixon	• ASCEND CKD & ASCEND DIALYSIS • PROTEON 32 • Finerenone Fidelio & Finerenone Figaro
Diana Jalal	• AZ Dapagliflozin • Corvidia
Manish Suneja	• ANCA vasculitis, AKI associated with cardiopulmonary bypass, muscle atrophy
Mony Fraer	• PDOPPS & CKDOPPS • Artemis IGAN
Christie Thomas	• Shire Cinryze for AMR • Apollo
Sarat Kuppachi	• ALTOLD
Lama Noureddine	• CALISTA • SAVE-PKD • Aurinia

Research in Laboratories of Jointly Appointed/Affiliated Faculty

- Richard Smith-

  Professor of Otolaryngology, Internal Medicine, Pediatrics

  Renal Research: Genetics of complement-mediated renal diseases; renal manifestations of complement dysregulation

- Carla Nester-

  Associate Professor of Pediatrics and Internal Medicine (Pediatric Nephrology)

  Renal Research: Natural history of and complement dysregulation in C3 Glomerulopathy

- Peter Snyder-

  Professor of Internal Medicine (Cardiology)

  Renal Research: Epithelial ion transport, hypertension, and salt taste

- Dao-Fu Dai-

  Assistant Professor of Pathology (Renal Pathology)

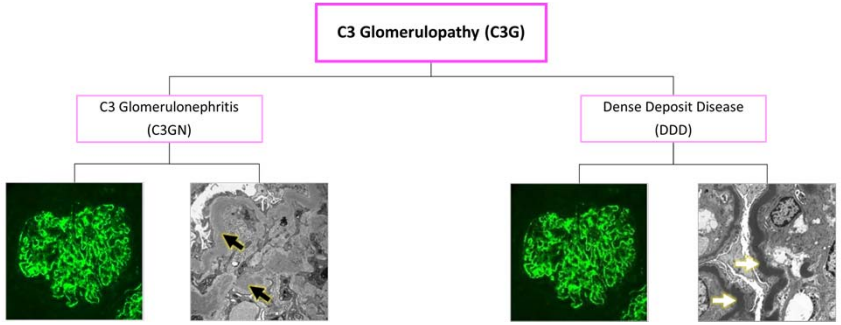
  Renal Research: kidney aging, myeloma-associated kidney diseases and fibrillary glomerulonephritis

Molecular Otolaryngology and Renal Research Laboratories

Smith

Nester

- **Basic Research Division**
  - C3 Glomerulopathy (Dense Deposit Disease and C3 Glomerulonephritis)
    - Study the complex role of genetics in pathogenesis
    - Develop new tests as an index of complement activity and function
    - Collaborate with pharma to develop and validate new treatments
    - Maintain the largest database of C3G patients in the world
    - Sponsor annual Family Outreach and Educational Conferences for families living with C3G

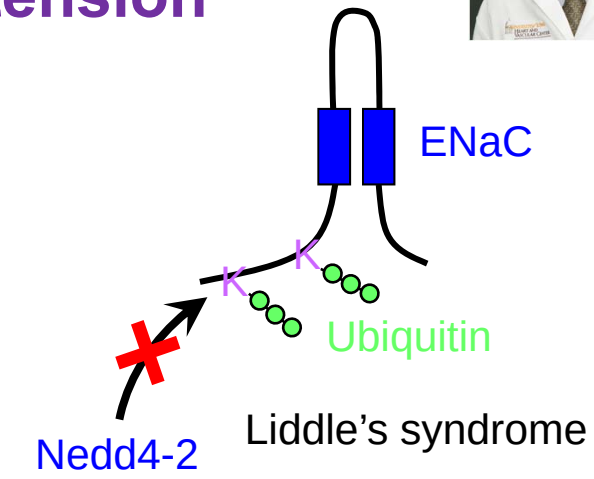


  - Atypical Hemolytic Uremic Syndrome (aHUS)
    - Identify and characterize novel genetic causes for aHUS or aHUS mimics
    - Develop and validate new tests to measure on-going disease activity
    - Maintain the largest database of aHUS patients in North American
    - Sponsor biennial Family Outreach and Educational Conferences for families living with aHUS
- **Clinical Diagnostics Services**
  - Provide genetic testing of all validated disease-associated genes for patients with C3G and aHUS
  - Offer comprehensive biomarker profiling of complement proteins and quantitation of complement activity as a guide to diagnosis and treatment
  - Provide consultative services for clinicians world-wide by reviewing renal biopsies and clinical history
  - Offer opportunities to participate in research studies

Research in Snyder Lab

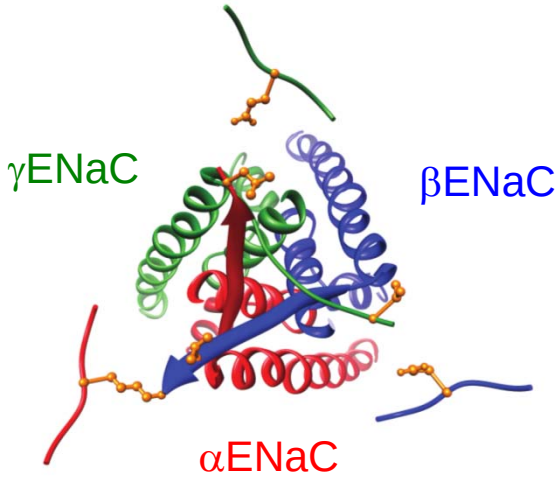
Renal sodium homeostasis and hypertension

- Investigate mechanisms of ENaC trafficking regulation and dysregulation in Liddle's syndrome and other forms of hypertension
- Effect of ENaC SNPs on regulation



ENaC as an extracellular ion sensor

- Investigate mechanisms by which extracellular Na, Cl, and H modulate ENaC gating



Salt taste

- Investigate role of ENaC in controlling salt taste and sodium intake

Research in Dai Lab

One of the long-term goals of my laboratory is to elucidate the roles of mitochondrial and metabolic signaling in aging, heart and kidney diseases, including hypertensive and diabetic nephropathy, polycystic kidney disease, myeloma-associated kidney diseases and fibrillary glomerulonephritis.

We are particularly interested in using mitochondrial antioxidants, mitoprotective strategies, anti-aging and senolytic therapy in preventing AKI and the progression of CKD.