KPMP
Kidney Precision Medicine Project

Tissue Interrogation Site Webinar - September 19, 2016

1. KPMP Overview– Rob Star
2. KPMP Structure – Chris Ketchum
3. Tissue Interrogation Site Specifics – Krystyna Rys-Sikora
4. Questions – KUH Staff

Please visit the KPMP website for full details and FAQs

https://www.niddk.nih.gov/research-funding/research-programs/Pages/kidneyprecisionmedicine.aspx

Or Google "NIDDK Kidney Precision Medicine Project"

KIDNEY

Precision Medicine Meeting

May 2016

Kidney Precision Medicine Project

Goals

- **Understand** human kidney disease
- Ethically **obtain** and **evaluate human kidney biopsies** from participants with AKI or CKD
- Find disease **pathways** in key **cells**
- Find disease **subgroups** to **stratify** patients
- Devise **individualized treatments**
- Improve scientific **knowledge** base
- Improve **pipeline**

KPMP
Kidney Precision Medicine Project

Summary of Process

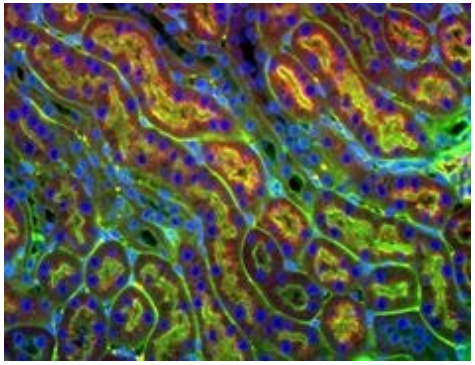
Obtain research kidney biopsy

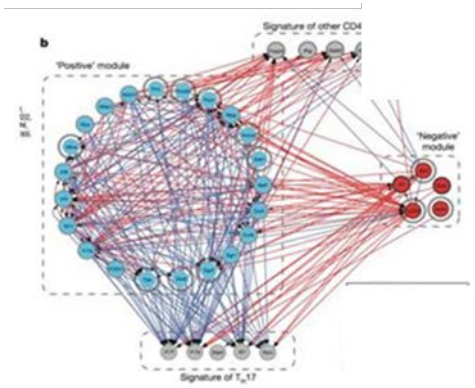
Interrogate biopsy using visualization/omics/etc.

Curate and visualize data

Create Kidney Tissue Atlas

- Phenotype critical compartments with ~40 RNA-protein-lipid-epigenetic markers
- Identify cell, cell fate (healthy, injured, repair), activated pathways
- Determine **diagnosis, sub-group, prognosis**





Ensure quality at every step

KPMP Structure

The NIDDK Kidney Precision Medicine Project aims to ethically obtain and evaluate human kidney biopsies from participants with AKI or CKD, create a kidney tissue atlas, define disease subgroups, and identify critical cells, pathways, and targets for novel therapies. It will have three distinct, but highly interactive activities.

Recruitment Sites (RS)

RFA-16-026 UG3/UH3 = 12 pages

- About 4 awards to recruit either AKI or CKD patients for longitudinal cohort studies with research kidney biopsies
- 2 year UG3 phase to establish common protocols and enroll small numbers of patients
- 3 year UH3 phase to expand longitudinal cohort studies in initial AKI or CKD populations

Tissue Interrogation Sites (TIS)

RFA-16-027 UG3/UH3 = 12 pages

- About 5 awards to support agnostic discovery on human kidney tissue
- 2 year UG3 phase to use or adapt current "state-of-the-art" methods to interrogate existing samples and small numbers of biopsies; to develop and optimize "next generation" tissue interrogation methods
- 3 year UH3 phase to implement next generation methods

Central Hub (CH)

RFA-16-028

Multicomponent U2C (Overall = 6 pages; DCC = 12 pages; DVC = 12 pages; AC = 6 pages)

Data and sample Coordinating Center (DCC)

- Support clinical protocol development and statistical calculations
- Perform standard clinical assessments (e.g., patient data reports, recruitment tables)
- Collect, curate, aggregate, store, distribute, and ensure quality control of all data and samples

Data Visualization Center (DVC)

- Perform digital pathology
- Create a kidney tissue atlas to classify and locate different cell types and interstitial components in health and disease
- Develop and manage a website for internal and external communication, analysis, and discovery

Administrative Core (AC)

- Provide administrative and meeting support
- Establish working groups
- Solicit patient input and feedback
- Administer an Opportunity Pool to form new partnerships

Goals of Tissue Interrogation Sites

- Investigate kidney cell and disease **heterogeneity** in tissue sections and/or dissociated cells
- Facilitate the structural, histological and molecular **assessment of cell states** (healthy function, activation, injury, recovery and repair)
- Develop methods to **distinguish diseased from non-diseased** areas of the kidney
- Identify robust structural, histological and **molecular signatures and pathways** that can be used to accurately (sub) **phenotype individuals with AKI or CKD**
- Generate high quality-data and images for a **kidney tissue atlas**

Tissue Interrogation Site Specifics

- Utilizes the UG3/UH3 mechanism--cooperative, milestone-driven, phased award
- Request $200,000 - $300,000 direct costs per year for the UG3 phase (2 years)
- Request $400,000 - $600,000 direct costs per year for the UH3 phase (3 years)
- No guarantee that any given UG3 award will successfully transition to a UH3 award or that the requested budget escalation will occur
- Applications must address both the UG3 and UH3 phases

Applying

- Domestic and foreign institutions may apply
- Foreign sites must be able to transfer tissue and other specimens across their borders
- Institutions may submit multiple applications
- PI must commit a minimum of 2.4 CM (20%)
  - If a multi-PI, combined effort must meet this minimum
- Letter of intent appreciated, not required
- Limited to 12 pages total
- Only human studies
- Address requirements outlined in Section IV
- Propose specific milestones

Cooperative Responsibilities

- Resource and data sharing plans
  - Expectation that all resources and data are broadly available in an open access format upon validation
  - Address long-term availability upon completion or termination
- Review Cooperative Agreement Terms and Conditions—become part of the Notice of Award
  - Steering Committee, Project Scientists, Project Officers
- Oversight by an OSMB and an EEP
- **Due December 6th, 2016**

Tissue Sources

- For optimization, discovery and validation efforts, TIS **must supply other existing "healthy" (normal) and diseased tissue**
  - Example sources of healthy tissue:
    - Transplant
    - Nephrectomy
    - Autopsy
  - Can include archived tissue
- Unused tissue must go to the Central Hub
- TIS will interrogate a small number of new biopsies in the UG3 phase and scale-up and interrogate additional new biopsies from AKI and CKD cohort studies in the UH3 phase

UG3 Phase

- **Use state-of-the art methods** (already working on kidney tissue and/or dissociated cells) to interrogate human kidney tissue
  - Use liquid- or slide-based methods; 2-D or 3-D methods
  - Promote agnostic (unbiased) discovery
  - Approach hurdles including tissue processing, imaging, and analysis
  - Optimize and validate quality control (QC) methods
  - Submit data and images to the CH for development of the kidney tissue atlas
- Interrogate a **small number of new biopsies**
- **Develop next generation technologies** to better interrogate human kidney biopsies

UH3 Phase

- Scale-up tissue interrogation throughput
- Interrogate human biopsies from individuals with AKI and CKD
- Enrich the kidney tissue atlas
- Contribute standard operating procedures, tissue, and data to the CH
- Implement next generation technologies

Senior Scientific Advisor for KPMP

The NIDDK is seeking a Senior Scientific Advisor for the KPMP. This person will oversee working groups, initiate activities, provide advice on current and future precision medicine projects, manage multi-center clinical studies, and administer a portfolio of basic, translational, and clinical research grants that focus on precision medicine and genetics of AKI and CKD, including clinical diabetic nephropathy and glomerular disease.

Please contact Paul Kimmel for more information

Questions?

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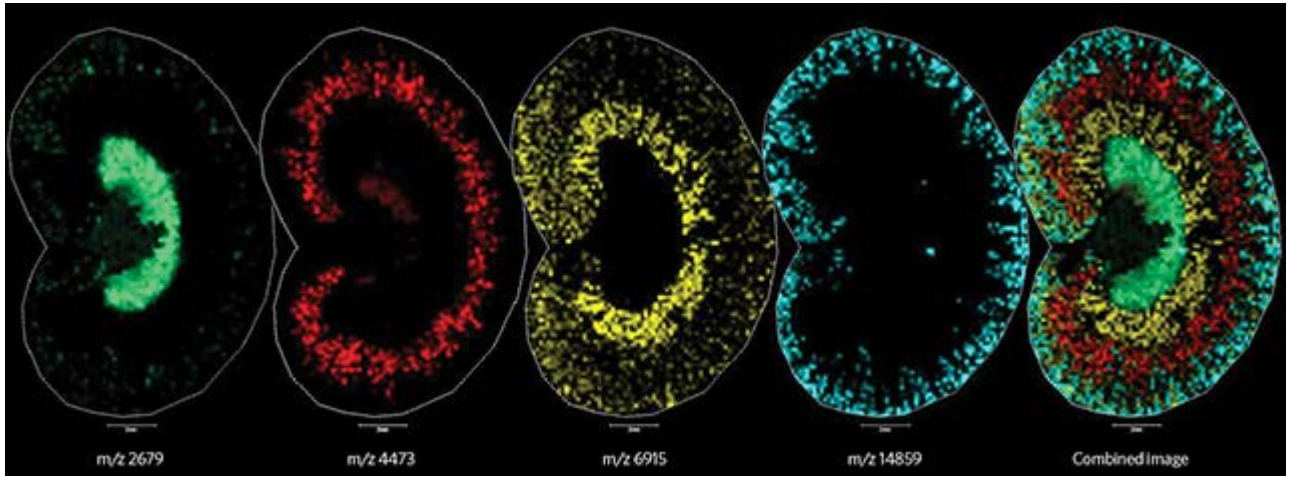
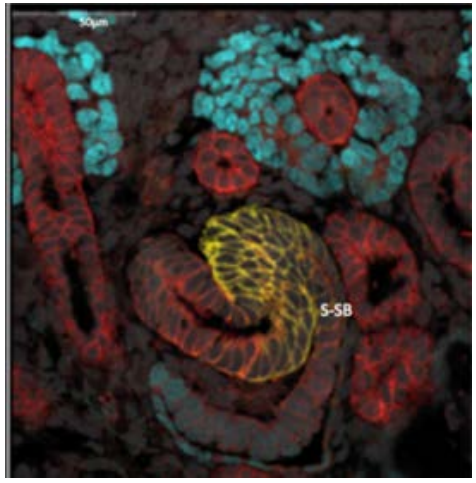
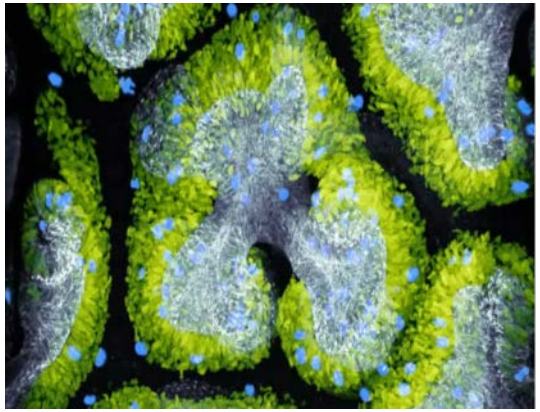
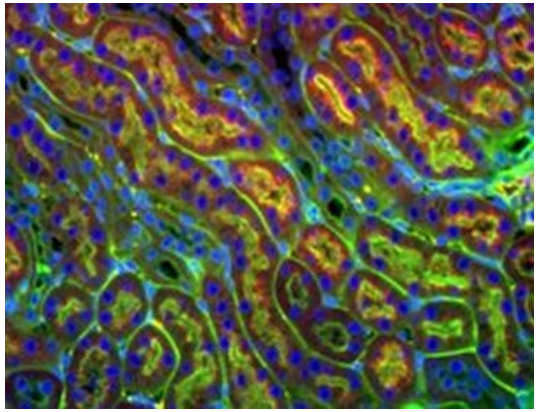
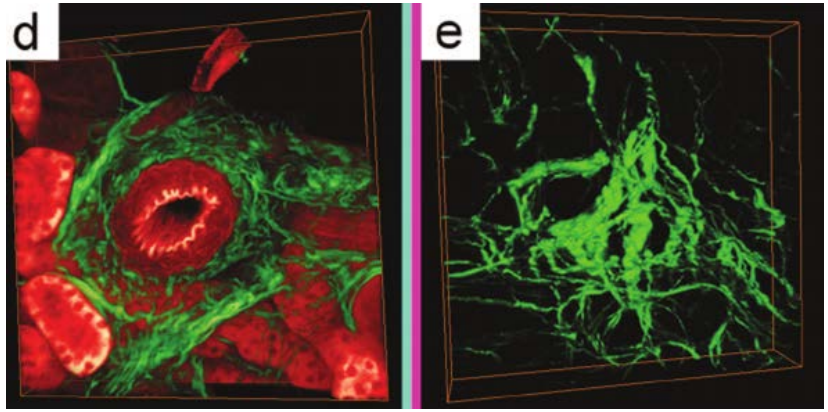
Kidney Tissue Atlas: Pathology of the Future











Find tissue (cells, and interstitial areas between cells) markers to identify (paint) cells, structures, cell trajectory (healthy, injured, repair, regeneration), activated pathways

Understand heterogeneity between regions, neighboring cells

Even better, use 3D imaging to better see interstitium, glomerulus

KPMP Stages

The KPMP aims to ethically obtain and evaluate human kidney biopsies from participants with AKI or CKD, create a kidney tissue atlas, define disease subgroups, and identify critical cells, pathways and targets for novel therapies. It is anticipated that the KPMP will be conducted in stages:

Stage 1 (years 1-2)

- Optimize and validate tissue processing and interrogation methods
- Establish common clinical protocols and cohort studies enrolling a small number of AKI or CKD participants
- Assess quality of phenotype data and biopsy protocols at each site
- Begin work on kidney tissue atlas. Optimize next generation assays

Stage 2 (years 3-5)

- Small scale proof of concept studies to determine if clinical and analytic pipelines are robust
- Implement next generation tissue interrogation assays
- Enrich the kidney tissue atlas.
- Expand longitudinal cohort studies in initial AKI or CKD populations

Stage 3 (years 6+)

- Expand to larger cohort studies
- Expected to occur in the next 5 year funding cycle of the KPMP