Obtain healthy reference tissue to help build the KPMP kidney tissue atlas

Kidney Precision Medicine Project (KPMP)

Recent advances in multi-scale interrogation of human tissue and single cells have set the stage for precision medicine to be applied to kidney disease. The objectives of the Kidney Precision Medicine Project are to ethically and safely obtain and evaluate human kidney biopsies from participants with Acute Kidney Injury (AKI) or Chronic Kidney Disease (CKD), create a kidney tissue atlas, define disease subgroups, and identify critical cells, pathways and targets for novel therapies. Specifically, the KPMP aims to develop or facilitate:

1. **Public resource**. Establish a publicly available data hub with clinical, imaging, cellular and molecular data. Anonymized data will be available to the research community upon validation.
2. **Kidney tissue atlas**. Create a set of maps used to classify and locate different cell types and interstitial components. The atlas will help define disease subgroups and identify cells, pathways and targets for novel therapies.
3. **State/transition markers**. Identify a set of cellular and molecular markers that classify cells as healthy, injured, activated, or undergoing recovery via adaptive or maladaptive repair.
4. **Disease subgroups**. Use all available data, including the kidney tissue atlas, to define patient subgroups and allow for clinical stratification into distinct endophenotypes.
5. **Molecular pathways**. Use data to identify and understand healthy and disease pathways that are activated in a particular cell type in a particular subgroup of patients.
6. **Biomarkers**. Discover a set of subgroup and pathway biomarkers. Ideally plasma or urine protein/antibody pairs, but could be urinary exosomes, miRNA, epigenetic marks, etc.

Kidney Tissue Atlas

A major objective of the KPMP is to create a kidney tissue atlas. The atlas is expected to contain a set of 2- and 3-D maps representing health (e.g., healthy living donor, healthy volunteer) and disease (e.g., KPMP AKI and CKD biopsies) across a diverse population (accounting for sex, age, race, and ethnicity). Maps will be used to classify and locate ('paint') different cell types, cell states (healthy, injured, dying, recovering, undergoing adaptive/maladaptive repair, etc.) and interstitial components (collagens, proteoglycans, signaling molecules, etc.). The maps are expected to include specific genes, proteins, RNAs, metabolites, and/or epigenetic landmarks that are visualized by advanced imaging. The maps are expected to facilitate identification of cell, structural, and regional heterogeneity throughout the kidney, and allow for interrogation of compartments that are currently difficult to visualize (interstitium, glomerulus, etc). The atlas will ultimately be used to improve the diagnosis, staging, grading, prognosis, subgroup stratification, and drug effect prediction in AKI and CKD.

KPMP Opportunity Pool

The KPMP recognizes that it must collaborate with the broader research community to fully achieve these objectives. Thus, the KPMP Central Hub will administer an "Opportunity Pool" to facilitate the formation of new partnerships.

Funding Opportunity Announcement

There is a critical need to obtain human healthy reference tissue, including but not limited to, tissue from healthy living donors or healthy volunteers to develop the KPMP kidney tissue atlas. This solicitation aims to form new collaborative partnerships by providing KPMP opportunity pool funds to applicants proposing to ethically and safely obtain, share, and harmonize human healthy reference kidney tissue with the KPMP. Strong applications will provide non-degraded ("pristine") tissue with the necessary diversity (sex, age, race, and ethnicity) and metadata (including relevant longitudinal clinical data) to meet the objectives of the KPMP. Ideally, it is expected that applicants will employ current KPMP protocols to obtain, share, and harmonize (using associated metadata) at least 20 healthy reference tissue samples per year. Deceased donor and tumor nephrectomy tissue are not eligible for this funding opportunity.

Applicants are encouraged to provide a written commitment from their local IRB to obtain consent for people to participate in the KPMP and for the collection, use, and sharing of human samples and appropriate affiliated metadata for research purposes. Award is contingent on IRB approval.

Awardees will become full members of the KPMP and have the same responsibilities and access to data and results as other KPMP awardees. As such, all awardees must adhere to the KPMP Publications and Presentations (P&P) language and the participating **Institution(s)** must sign the KPMP Confidential Disclosure Agreement (CDA) and Material Transfer Agreement (MTA) documents.

Foreign Institutions are eligible to apply.

Application

Five (5) page applications requesting up to **$100,000 total costs per year for three years** are due **June 28, 2019**.

- The application is the standard PHS 398 form including face page, abstract, detailed budget, biosketches (up to 5 pages each), and research plan. The research plan is limited to 5 pages and should include a discussion of tissue availability, all proposed protocols, preliminary data demonstrating that you can ethically and safely obtain human healthy reference kidney tissue (linked to appropriate metadata), an assessment of tissue quality, and plans for harmonization and integration with the KPMP.
- All applications must be milestone-driven and include a detailed list of expected deliverables and a well-defined timeline.
- Applicants are encouraged to provide a written commitment from their local IRB to obtain consent for people to participate in the KPMP and for the collection, use, and sharing of human samples and appropriate affiliated metadata for research purposes.

- Applicants must state a willingness to travel key personnel two times a year to the Bethesda, MD area for KPMP meetings.
- Applicants must state a willingness to adhere to all KPMP practices, protocols, and policies.
- All applications must be submitted via the KPMP website (PDF format only please).

Budget

- Applications of 5 pages may request up to $100,000 (direct + indirect costs) total costs per year for three years. These costs must include travel of travel key personnel two times a year to the Bethesda area for KPMP meetings.
- A written summary of progress is due annually and following the completion of the funding period. Outyear funding is contingent on prior year progress.
- Awards will be made as subcontracts from the KPMP Central Hub (CH) at the University of Washington and not directly by the NIDDK.
- The number of awards will depend upon the number, quality, duration, and cost of the applications received.
- Funded awards are not allowed to submit a competitive renewal application and unfunded applications are not allowed to revise and resubmit an amended application.

Peer Review

- Each application will receive a primary review by multiple external referees and be given scores for Significance, Investigator, Innovation, Approach, and Environment and an Overall Score based on the NIH Scoring System. Scores will range from 1 to 9, where a score of 1-3 indicates an application addressing a problem of high importance/interest in the field and may have some or no weaknesses. A score of 4-6 may be addressing a problem of high importance in the field, but weaknesses in the criteria bring down the overall impact to medium. A score of 7-9 may be addressing a problem of moderate/high importance in the field, but weaknesses in the criteria bring down the overall impact to low. A score of 5 is considered an average score. Please note that the Overall Score is NOT an average of the other scores.
- Reviewers will also strongly consider the following review criteria:
    - Does the application propose to form a new partnership that will add significant value to the KPMP?
    - Does the application propose a rigorous assessment of tissue availability and quality?
    - Does the application adequately address all ethical and safety considerations for participant recruitment and tissue collection?
    - Does the applicant provide convincing preliminary data that they can obtain and share at least 20 samples per year of high quality (non-degraded) human kidney tissue linked to appropriate metadata?
    - Does the application adequately consider the current KPMP tissue processing protocols and analytic pipelines?
    - Are the proposed milestones, deliverables and timeline appropriate and feasible?
    - Does the applicant(s) state a willingness to travel key personnel two times a year to the Bethesda, MD area for KPMP meetings?

    - Does the applicant(s) state a willingness to adhere to all KPMP practices, protocols, and policies?
- Applications that are incomplete, non-compliant and/or nonresponsive will not be reviewed.
- No additional materials may be submitted after the receipt date.
- Scientists from the applicant institution are in conflict and excluded from review.
- Written comments will be provided for all reviewed applications.
- Reviewed applications will be considered by the KPMP Steering Committee (SC) and approved the KPMP External Expert Panel (EEP). Final funding decisions will be made by the NIDDK.
- All decisions are final, and appeals will not be accepted for applications submitted in response to this solicitation.

Timetable

Five (5) page applications requesting up to **$100,000 total costs per year for three years** are due **June 28, 2019 by 5 p.m. Pacific**.

Peer review: July 2019

Projected award date: August 2019

Attend first KPMP Meeting: Sept 24-25, 2019

Eligible Project Directors/Principal Investigators

- Applicants can NOT be currently supported by the KPMP.
- Current KPMP investigators are eligible to serve as unpaid consultants IF the application has identified a NEW source of human kidney tissue and is proposing to form a NEW collaborative partnership. Overlap with existing funded activities is NOT allowed.
- Individuals with the skills, knowledge, and resources necessary to carry out the proposed research are invited to work with their institution to develop an application for support.
- Individuals from underrepresented racial and ethnic groups as well as individuals with disabilities are always encouraged to apply for NIH support.
- Early Stage Investigators are encouraged to apply, but they must have a full-time faculty position or an equivalent position at non-academic institutions.

Eligible Organizations

Higher Education Institutions

- Public/State Controlled Institution of Higher Education
- Private Institution of Higher Education

The following types of Higher Education Institutions are encouraged to apply for support as Public or Private Institutions of Higher Education:

- Hispanic-serving Institution; Historically Black Colleges and Universities (HBCUs);
- Tribally Controlled Colleges and Universities (TCCUs)
- Alaska Native and Native Hawaiian Serving Institutions; Nonprofit with 501(c)(3) IRS Status (Other than Institution of Higher Education)

Nonprofits Other Than Institutions of Higher Education

- Nonprofits with 501(c)(3) IRS Status (Other than Institutions of Higher Education)
- Nonprofits without 501(c)(3) IRS Status (Other than Institution of Higher Education)

For-Profit Organizations

- Small Businesses
- For-Profit Organization (Other than Small Businesses)

Foreign Institutions

- Non-domestic (non-U.S.) Entities (Foreign Institutions) are eligible to apply.
- Non-domestic (non-U.S.) components of U.S. Organizations are eligible to apply.
- Foreign components, as defined in the NIH Grants Policy Statement, are allowed.

Policies

Human Subjects. Prior to award, all applicants must have approval from their local IRB to obtain consent for people to participate in the KPMP and for the collection, use, and sharing of human samples and appropriate affiliated metadata for research purposes.

Progress Reports. A written summary of progress of funded projects is due annually and following the completion of the funding period.

Sharing. Awardees must comply with the Public Health Service (PHS) policies relating to distribution of unique research resources produced with PHS funding and sharing of all research protocols, data, samples, and other research resources. Appropriate agreements must be executed prior to resource and data sharing. For further information, see the NIH Data Sharing Policy at https://grants.nih.gov/grants/policy/data_sharing/.

- The NIDDK intends the resource sharing plans for the data and samples generated under the KPMP to follow the policy and objectives stated in the original KPMP FOAs. Specifically, consistent with achieving the objectives of the KPMP, all study data (including, but not limited to, raw data, metadata, digital pathology images, and computational data sets), protocols (including analytical methods), technologies, biological samples (including but not limited to biopsies, nephrectomy tissue, tissue blocks, all slides in any form, blood, urine and stool) and other research resources are to be shared immediately across the consortium, and made publicly available to the larger community as soon as quality control procedures have been completed, and in accordance with KPMP Steering Committee (SC) policies, subject to approval by the NIDDK. Data derived from participant clinical records linked to biological data will only be made publicly available once risk of explicit or inferred identification has been mitigated in consultation with the KPMP Community Engagement Working Group and the Data and Safety Monitoring Board. Limited exceptions to the requirement for community dissemination may be

identified by the KPMP SC and are subject to approval by the NIDDK. The NIDDK, in consultation with the SC for this project, will make all final decisions concerning data and sample deposition and data access policies, and all policies are subject to change by the NIDDK as deemed necessary to sustain program principles and priorities, or to ensure the highest standards for responsible research conduct within the project.

- Awardees will comply with and implement the recommendations and decisions of the SC with respect to the sharing of information, data, biosamples, protocols, resources, methods and analyses developed by the KPMP investigators under the KPMP.

Acknowledgment. Awardees must acknowledge the KPMP in all posters, manuscripts or scientific materials generated in part or whole using funds from the KPMP using the following text: "Research reported in this [poster/manuscript] was supported by the National Institute of Diabetes and Digestive and the Kidney Diseases (NIDDK) Kidney Precision Medicine Project (KPMP) Opportunity Pool, (www.kpmp.org), under award number U2CDK114886."

Contact Information

For questions, contact: KPMP Administrator at kpmp@uw.edu