

George M. O'Brien Kidney Resource Alliance Opportunity Pool Program
Round 1 Funding Opportunity Announcement (Clinical trials not allowed)

(Distributed January 2024)

National Institute of Diabetes and Digestive and Kidney Diseases
and the University of Alabama at Birmingham

Background	<p>The George M. O'Brien Kidney Resource Alliance (OKRA) is a consortium of National Resource Centers (NRCs) whose primary purpose is to provide kidney researchers with specialized resources, tools, technologies, services, and expertise beyond those typically available in an individual lab or institutional core. The consortium includes seven NRCs and a National Coordinating Center. The overarching goal of the OKRA Opportunity Pool Program (OKRA OPP) is to prioritize support for early-stage investigators or investigators new to kidney research who are engaged in utilizing existing OKRA resources or developing novel tools or resources that will address scientific and technological gaps in kidney research and promote new collaborations. Although priority will be given to early-stage investigators and investigators new to kidney research, established kidney disease researchers are also welcome to apply.</p>
Overview	<p>The program welcomes small and larger pilot applications to provide one year of support to fund small and large projects broadly related to kidney research. During this funding cycle, multiple projects will be awarded. Justified total costs (including direct and indirect costs) ranging from \$5,000 (for small catalyst awards) up to a maximum of \$75,000 (for a full OPP project) for the one-year project period are allowed.</p> <p>Applications may address a broad array of topics, but must address one of the following areas/emphasis:</p> <ul style="list-style-type: none"> • Use of existing OKRA NRC resources to address basic and/or clinical questions in kidney research. • Innovative measures, techniques and approaches that may either expand the utility of currently existing OKRA resources or add a novel resource to existing array of OKRA resources. <p>A listing of all OKRA NRCs and their resources is attached as an Appendix to this funding announcement. The applicant should contact the NRC leadership that manages the NRC resource the applicant proposes to utilize and obtain a letter of feasibility and support (contact information is listed at the end of this announcement).</p> <p>Clinical trials, as defined by the NIH (https://grants.nih.gov/policy/clinical-trials/definition.htm), are beyond the scope of this program. Awards are expected to prepare the applicant(s) to submit a future investigator-initiated project (e.g., NIH R01).</p>
Eligibility Criteria	<ul style="list-style-type: none"> • Although priority will be given to ESIs and established investigators new to kidney research, established kidney disease researchers may also apply • Applicants must have a faculty position at the time of the application. • Investigators at non-domestic (non-U.S.) entities (foreign institutions) are not eligible to apply. • NRC key personnel are not eligible to apply as PI. • Individuals from underrepresented racial and ethnic groups as well as individuals with disabilities are encouraged to apply. <p><u>Additional notes for ESIs regarding eligibility and priority:</u></p> <ul style="list-style-type: none"> • Early-stage investigators (ESI), as defined by the NIH

	<p>https://grants.nih.gov/policy/early-investigators/index.htm), and researchers new to kidney disease research will receive priority for OKRA OPP funding</p> <ul style="list-style-type: none"> • ESIs are expected to identify an experienced kidney researcher to function as mentor during the project • The NCC will confirm the applicant’s ESI status. Applications that are non-compliant will be administratively withdrawn.
<p>Letter of Intent: Deadline February 19, 2024</p>	<p>A letter of intent must be submitted no later than February 19, 2024. It should be a maximum of one page in length (no smaller than 11 pt Times New Roman font, single line-spacing) and include:</p> <ol style="list-style-type: none"> 1. The study title and aims, significance, and brief rationale 2. A brief description of intended methods/study design and/or key measurements 3. List details of OKRA NRC resource(s) that will be utilized or developed 4. An explanation of the novelty/innovation and potential impact of the proposed approach or topic area 5. Separate from the letter of intent, please: <ol style="list-style-type: none"> a. Identify all members of the study team and their anticipated roles. Include the PIs NIH-style biosketch. 6. Specific instructions for ESIs: <ol style="list-style-type: none"> a. If the principal investigator (PI) is an early-stage investigator, please identify one or more mentors for the project and include an NIH-style biosketch for the mentor as well. b. In addition, we would like to connect you with peers and near peers to help form a network of knowledge exchange (e.g., share scientific resources, ideas, career experiences). Please indicate in your letter of intent if you would like to participate in this opportunity regardless of the outcome of funding.
<p>Full Application Instructions</p>	<p>Letters of intent will be reviewed, and selected applicants will be invited to submit a full application that will include the following elements: Abstract, Research Plan, Reference List, Protection of Human Subjects/IACUC protocol (as appropriate), NIH-style Biosketches, Budget and Justification, and a Letter of Support from the participating OKRA NRC.</p> <p>The Abstract should be a succinct summary of the project that includes the significance of the proposed study, the hypothesis or aim, and the innovative potential of the study. The Abstract should not exceed 200 words in length.</p> <p>The Research Plan should not exceed three pages (no smaller than 11 pt Times New Roman font, single line-spacing, with 0.5” margins). Other aspects of the Full Application (i.e., Abstract, Reference List, Protection of Human Subjects/IACUC protocol, NIH-style Biosketches, and Budget and Justification) are not included within these page limitations. No appendices may be submitted. The research plan will include:</p> <ol style="list-style-type: none"> 1. Specific Aim(s) 2. Research Strategy: <ol style="list-style-type: none"> a. Background and significance b. Innovation c. A detailed description of intended Methods/Study Design, a Statistical Analysis Plan including assessment of study power, Plans for Implementation, and Logistical Considerations d. Key Measurements and Data to be generated, including, where relevant, indication of whether a new OKRA NRC resource will be developed.

	<p>Include a Reference List.</p> <p>Protection of Human Subjects or an IACUC protocol should be addressed in a separate document, as appropriate. Indicate whether or not the project involves human subjects or animal research. If yes, please use the relevant attachment for research involving either human subjects or animals.</p> <p>Please include an NIH Biosketch for each team member.</p> <p>Please also include a detailed Budget and Justification using the NIH SF424 (R&R) Budget form.</p> <p>Include a signed Letter of Feasibility and Support from the participating OKRA NRC for the proposed study.</p>
<p>Key Dates</p>	<p>Letter of intent due date: February 19, 2024 (by 5:00pm local time of the applicant’s organization)</p> <p>Applicants will be notified of invitation to submit a full application on or about March 19, 2024.</p> <p>Full applications will be due six weeks after receipt of the invitation for submission.</p> <p>Notifications to awardees will be distributed in summer 2024.</p>
<p>Budget</p>	<p>Applicants may request justified total costs (direct + indirect costs) ranging from \$5,000 (for a small catalyst award) up to a maximum of \$75,000 (for a full OPP project). A narrative justification should be provided for key personnel and any major equipment (cost greater than \$5,000) deemed to be necessary for the proposed project. This is a federal grant, so federally negotiated F&A rates apply. Budgets should be well-justified and account for all study costs, including costs to OKRA NRC(s), if applicable. Salary effort is an allowable expense and should be limited to the scope of the proposed project.</p> <p>Please contact the participating NRC for resource budget and include that component in the budget section of the grant. Additional instructions to complete the participating NRC portion of the budget will be sent to applicants selected to submit a full application.</p>
<p>Application Submission Instructions</p>	<p>Letters of Intent must be submitted via email to Okrancc@uab.edu</p> <p>Applications will be reviewed by peer reviewers using a standardized review form. Scientific merit will be assessed based on the programmatic priority areas listed above and the NIH criteria of significance, innovation, approach, investigators, environment, use of NRC resources, and the potential to contribute to the applicant’s success in obtaining future independent funding.</p> <p>Invited applicants should submit full applications per the instructions which will be provided by email from the OKRA Opportunity Pool Program.</p>
<p>Requirements of Awardees</p>	<p>Awardees are required to submit a progress report twelve months after receiving funding. Awardees will present their findings to the OKRA Steering Committee at the conclusion of the study. It is expected that each study will culminate in publication(s) or other independent awards such as K or R01 awards. Published work must cite OKRA as a funding source. Awardees will become members of the OKRA Consortium and will be expected to participate in reviews for subsequent OPP application rounds.</p>
<p>Contact Information</p>	<p>For questions, please contact:</p> <p>George M. O’Brien Kidney Resource Alliance National Coordinating Center The University of Alabama at Birmingham Okrancc@uab.edu</p>

APPENDIX

OKRA National Resource Center (NRC) Resource Summaries

Summary

The Indiana University George M. O'Brien Center for Advanced Microscopic Analysis has a unique, highly interactive, integrated and synergistic team of physicians, basic scientists, computer scientists, engineers and a highly trained and committed technical support team to provide local, national and international users cutting edge intravital optical microscopy and 3-dimensional quantitative digital image analysis of the kidney. They have two cores (Molecular Imaging and Intravital Microscopy) that offer a novel set of research methods, quantitative analysis tools and fluorescent biosensors or probes not available elsewhere to facilitate biomedical research, drug discovery and therapeutic approaches to kidney disease.

Molecular Imaging Resource Core

The Molecular Imaging Resource Core provides quantitative, large-scale microscopy of the kidney as a service to kidney and urologic investigators. Services include:

- 3-dimensional confocal tissue cytometry of kidney tissue
- CODEX multiplexed cytometry of mouse and human kidney tissue
- Spatial Transcriptomics of mouse and human kidney tissue (Visium)
- In situ sequencing of mouse and human kidney tissue

Intravital Microscopy Resource Core

The Intravital Microscopy Resource Core provides quantitative intravital microscopy of rodent animal models customized to the specific needs of individual kidney and urologic investigators. Assays and techniques include:

- Glomerular Permeability
- Proximal tubule endocytosis
- Microvascular flow
- Microvascular permeability
- Mitochondrial function
- Cellular oxidative stress
- Apoptosis and necrosis
- Characterization of in vivo fluorescent probe delivery to the kidney
- Characterization of transgenic rodents expressing fluorescently tagged proteins in the kidney

- Fluorescence lifetime imaging of endogenous and exogenous fluorophores in the kidney

Contact Information

If you would like more information regarding services provided by Indiana O'Brien Center for Advanced Microscopic Analysis, please contact:

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[Indiana O'Brien Center for Advanced Microscopic Analysis](#)



The Johns Hopkins O'Brien Center to Advance Kidney Health Equity

Summary

The overarching goal of the Johns Hopkins O'Brien Center to Advance Kidney Health Equity is to serve as a national resource for investigators conducting pre-clinical (basic), clinical or population health research addressing or related to kidney health disparities, and to make recommendations to inform strategies, interventions, and approaches aimed at achieving kidney health equity. The resources and services available from the Johns Hopkins O'Brien Center (JHOC) support this overarching goal.

Biomedical Resource Core (BRC)

The Biomedical Resource Core (BRC) provides a portfolio of research services, resources, and tools to understand and ameliorate disparities in kidney disease, with a focus on dietary and social stressors that drive kidney health disparities. The BRC is comprised of two laboratories, detailed below, which provide services and resources for the conduct of pre-clinical, clinical and population research relevant to advancing kidney health equity,

- Clinical Science Dietary and Social Stressor Laboratory (C-DSSL) Services
 - Through a health equity lens, the C-DSSL will provide consultative services, validated protocols with well-established quality assurance/quality control procedures, and access to materials and equipment, with appropriate external resources. The C-DSSL will execute pilot studies or larger research projects and potential access to our community-based clinical research unit. Resources and services include the following:
 - Clinical study design
 - Dietary assessment and Dietary data
 - Feeding studies modeled on the DASH trials
 - Archived and Completed studies
 - Large longitudinal cohort study data from racially and socioeconomically diverse populations
 - Publicly available datasets
 - EMR registries
 - Datasets with Deep phenotyping
 - Genomics
 - Proteomics
 - Metabolomics
 - Images
 - Samples
 - Stored biospecimens from completed studies
 - Healthy Volunteers for Reference Range
 - Prospective Remnant Sample collection
 - Behavioral intervention studies
 - Translational studies in the community
 - Biostatistical support
 - Biomarker measurement
 - Immunoassays
 - Clinical Chemistry

- Biorepository support
 - Processing aliquoting, short- and long-term sample storage
- Basic Science Dietary and Social Stressor Laboratory (B-DSSL)
 - The B-DSSL will provide investigators with comprehensive services and resources for preclinical research to determine the mechanistic underpinnings of human health disparity stressors, using mice as a model system. Resources and services include the following:
 - Study design
 - Humanized mouse diet protocols
 - Comprehensive mouse kidney phenotyping for diet and stress mechanisms
 - Metabolic Cage and Clearance Studies
 - GFR measurements
 - Telemetric Blood pressure Monitoring
 - Optical Clearing
 - Isolated Nephron segment Ex Vivo Analysis
 - Small Sample RNAseq in Isolated Nephron Segments
 - Indirect calorimetry and Lipid and carbohydrate metabolism phenotyping
 - Oxymax and CLAMS metabolic cages to monitor food intake, water intake, physical activity, metabolic rate (VO₂), respiratory exchange ratio (carbohydrate vs fat oxidation), and energy expenditure
 - Immunological manifestations of dietary and social stressors in the kidney
 - protocols, training, and service to isolate and characterize kidney immune cells by flow cytometric analysis (FACS).
 - Microbiome; germ-free sample banks
 - Mouse biobank of dietary and social stress models

Contact Information

If you would like more information regarding services provided by Johns Hopkins O'Brien Center to Advance Kidney Health Equity, please contact:

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Summary

The George M. O'Brien Michigan Kidney Translational Core Center (MKTC) was established to assist investigators and clinicians worldwide in kidney disease research. Their core objective is to enable multi-omic multi-scalar data integration. MKTC consists of two Biomedical Cores: The Applied Systems Biology Core (ASBC) and Data Analytics Services Core (DASC). They provide specialized core services as well as user-friendly tools to enable kidney researchers and trainees to apply to their work.

Applied Systems Biology Core (ASBC)

The Applied Systems Biology Core (ASBC) primary role is to empower national kidney researchers to analyze, integrate and extract pertinent knowledge from multi-omic datasets (genetic, transcriptomic, epigenomic, metabolomic, proteomic data) from model systems and human studies in support of their individual research needs.

- Interactive, shared data mining services
 - ASBC will provide initial study design consultation and assist with developing customized workflow for integrative analysis for projects of individual investigators
 - Clinical and molecular interactions in investigators' data sets
 - Quantitative morphometric analyses of kidney biopsy samples
 - Model systems studies to identify pathways shared cross-species
 - Structured RNA-DNA sequence data integration
- Standardized workflows of recurrent service elements
 - Transcript driven data-mining workflow
 - Single cell RNA Sequencing analysis pipeline
 - Streamlined self-organizing map (SOM) to identify functional subgroups
 - Weighted Correlation Network Analysis (WGCNA) to identify co-expressed molecular elements within datasets
 - Metabolomics driven analysis workflow
 - Platform specific data processing, data normalization, identification of differentially expressed metabolites
 - Multi-scalar data analysis and integration
 - Integration of different combinations of available clinical phenotype, morphology, genetic, epigenomic, transcriptomic, proteomic, metabolomic datasets.
 - Building models for classification or statistical association purposes
 - pathway mapping and enrichment analysis
 - clinical and molecular interactions in investigators' data sets
 - Multi-omic data integration to identify biomarkers and regulatory networks
 - Metscape applications

Data Analytic Services Core (DASC)

The Data Analytic Services Core (DASC) provides access to unique sets of data through distinct data analysis platforms. The database is updated quarterly to provide investigators with quick and easy access to all the data

being generated as part of the Center and their web portals include sophisticated and user-friendly analytic tools that allow for mining of these datasets.

- Access, training, and support for data exploration with user-friendly web-based analysis tools
 - Nephroseq
 - A fully automated web-based systems biology search engine for context specific renal disease gene expression and data mining
 - TranSMART
 - An open-source platform that allows user-specified exploration of cohort study datasets to researchers
 - A new tranSMART custom configuration for the CPROBE and multiple other cohort studies, including NEPTUNE, H3Africa, M2C2, CPROBE, CRIC and CureGN networks
 - CELLxGENE and Vitessee
 - Single cell and spatial data mining instances for murine and human kidney disease data sets adapted by the DASC for the kidney investigative community
- Investigating biomarker association (gene, protein, metabolite level) in clinical existing cohorts such as C-PROBE through TranSMART instance (in collaboration with the primary study investigators)
- Developing generalized workflow for integrative web-based analysis

Contact Information

If you would like more information regarding services provided by MKTC, please contact:

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[George M. O'Brien Michigan Kidney Translational Core Center](#)

Summary

The Northwestern University National Resource Center (NUGoKidney) aims to revolutionize kidney research by integrating physical science advances, such as nanotechnology, proteomics, and bioelectronics, into kidney disease study and treatment. Its core objectives include developing new methods for kidney research, providing widespread access to innovative physical science tools, and fostering community-wide innovation. The center comprises a Biomedical Resources Core for nanotechnology applications and a Resource Development Core for emerging physical science technologies. This integration of physical sciences and kidney research positions the NU-NRC as a leading institution in advancing kidney health and therapy.

Biomedical Resource Core (BRC)

Services provide precision targeting of desired payloads to specific cells or sub-regions within the kidney through:

- Guidance in Molecular and Cell Target Selection:
 - Our Core co-directors will assist in identifying specific molecular targets for precise drug and payload delivery in the kidney.
 - Application Supported: Therapy Delivery, Diagnostics/ Molecular Imaging
- Nanoparticle Carrier Selection Assistance
 - Co-directors will aid in choosing suitable nanocarriers that align with molecular targets for specific kidney sub-regions.
 - Cargos supported: siRNA, microRNA, Hydrophobic small molecule drug, Hydrophilic small molecule drug, Peptides.
- Synthesis and Attachment of Targeting Moieties
 - After selecting ligands and appropriate nanocarriers, the Core will oversee the synthesis of targeting moieties, leveraging the capabilities of the Peptide Synthesis Core for varied-scale production.
 - Kidney Cell Types or Structures for Nanoparticle-Enhanced Delivery: Proximal Tubule, Consultation with the Core Director (if unsure), Podocyte, Collecting Duct, Glomerulus
 - Cell types we can do later if needed: Endothelium, Monocytes, Renal Interstitium, Renal Lymphatics
- Gene Therapy and Drug Loading into Nanocarriers
 - The Core will facilitate the incorporation of therapeutic payloads into nanoparticles, utilizing various strategies based on the cargo and application.
 - Nanoparticle Types Supported: Liposomes, Lipid nanoparticles, gold nanoparticles, Polymeric nanoparticles, Peptide micelles.
- Evaluating Targeting Fidelity In Vitro and In Vivo
 - Core co-directors will provide expertise in assessing the targeting accuracy of nanotherapeutics both in lab settings and live subjects.

- Main Priorities for NanoCore Assistance: In vitro binding, In vitro biocompatibility, in vitro therapeutic efficacy; design of In vivo pharmacokinetics, In vivo targeting, in vivo therapeutic efficacy studies

Resource Development Core (RDC)

The Resource Development Core (RDC) offers a range of services including:

- Development of New Research Resources
 - The RDC is committed to creating and improving research tools and technologies that can be utilized by the Biomedical Resource Core. This is done through 3 main projects:
 - **Advancing RNA Delivery to Kidney Using Nanotechnology:** This project focuses on the development and optimization of methods for delivering short RNAs (siRNAs and miRNAs) to the kidney.
 - **High Throughput Single-Cell Profiling for Drug Target Identification:** Leveraging the LeaPFroG (Large-Scale Phenotypic Functional Genomics at Scale) platform developed by Shana Kelley in the Chemistry department at Northwestern University, this project aims to identify new drug targets and modifiers of kidney disease progression. A proof-of-concept study will be conducted to find modifiers of IgA binding/interaction with mesangial cells, a key mechanism in the renal injury associated with IgA nephropathy.
 - **Proteoform Imaging Mass Spectrometry (PiMS) Optimization:** Proteoform Imaging Mass Spectrometry (PiMS) technology will be optimized to identify and map proteoforms in kidney thin sections. This project represents a significant step forward in understanding the complexity of kidney protein structures and functions at the molecular level. (In years 3-5)
- Innovative Technology Incubation:
 - The RDC is dedicated to fostering the development and validation of emerging physical science technologies in kidney research, ensuring their applicability, quality, and potential impact through meticulous evaluation.
 - **Community Engagement:** Engages with leading scientists to incubate and integrate new technologies, nurturing a collaborative atmosphere for the exchange of ideas and technological improvement.
 - **Validation and Quality Control:** Implements standardized evaluation protocols to assess and ensure the performance and reliability of new technologies within research settings.
 - **Impact Assessment:** Dedicates efforts to gauge the potential contributions of innovative technologies to kidney research and their role in enhancing established research methodologies.
 - **Technology Integration Support:** Offers robust infrastructure and support for seamlessly incorporating new technologies into current research, aiding researchers in effective technology adoption and utilization.
 - **Educational Outreach:** Conducts workshops and seminars aimed at educating the kidney research community on emerging technologies, ensuring the widespread dissemination of knowledge regarding the latest advances.
- Interdisciplinary Collaboration
 - The RDC leverages Northwestern University's strong base of physical scientists in nanomedicine, bioengineering, and chemistry, all committed to kidney research, fostering a robust interdisciplinary approach.

Contact Information

If you would like more information regarding services provided by NUGoKidney, please contact:

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Northwestern University George M. O'Brien Kidney Resource Center



Summary

The O'Brien Kidney Research Center at the University of Pittsburgh and Icahn School of Medicine at Mount Sinai seeks to enhance the efficiency and productivity of a large number of kidney-related research projects currently in progress; facilitate acquisition of data for new projects; promote collaborations among center investigators; and provide tools to facilitate translational research. These functions depend on the Center's Biomedical Cores: Physiology Core, Model Systems Core, and KIDNIT (Kidney Imaging) Resource Development Core. Our Cores provide physiological, cell biological, genetic, analytical, molecular biological, and drug discovery tools, as well as model organisms.

Physiology Core

The overall goal of the Physiology Core is to elucidate, at a molecular and cellular level, the function and regulation of key proteins involved in kidney health and disease. The Core provides *in vitro* and *in vivo* technologies to explore the function and regulation of membrane transporters, channels, and other resident proteins using single molecule approaches, model organisms, and native epithelia. Services provided are listed below:

- Available Resources
 - Isolation of single nephron segments for immunofluorescence, enzyme assays, RNA and protein isolation
 - *In vitro* microperfusion of isolated tubules for measurement of transepithelial ion and solute transport
 - *In vitro* microperfusion of isolated tubules for functional fluorescence assays of single cell function
 - Isolation of *Xenopus laevis* oocytes
 - Oocyte two-electrode voltage clamp
 - Quantification of surface protein expression
 - Patch-clamp analyses
 - Epithelial transport in Ussing chambers
 - Functional imaging analyses
 - Other procedures

- Hands-on Training
 - *Xenopus laevis* technologies
 - use of microinjectors
 - use of micropipette pullers and microforges to craft micropipettes for patch-clamp and *in vitro* microperfusion
 - Two-electrode voltage clamp
 - Ussing chamber systems
 - Patch-clamp
 - Nephron segment microdissection/isolation and microperfusion

Model Systems Core

The overall goal of the Model Systems Core is to provide a diverse array of innovative model systems ranging from yeast, to cultured kidney cells and organoids, to whole animal rodent models to understand and explore kidney development, function, and systemic physiology in normal and disease states. Core directors will facilitate integration between these model systems, enabling investigators to test hypotheses at multiple resolutions from molecules to cells to tubules to whole animals. Services provided are listed below:

- Yeast Models Subcore
 - Protein quality control (degradation, ubiquitylation) assays
 - Protein trafficking assays (immunofluorescence, density centrifugation)
 - Positive genetic selection assays
 - Computational identification of functional variants
 - Bioinformatic analysis of genotype-phenotype correlations (TopMed, Clinvar, UK BioBank)

- Epithelial Models Subcore
 - Mammalian cell culture models (proximal tubule, collecting duct, polarized epithelia)
 - Organoid models to study nephron development
 - Organoid models to study kidney physiology
 - Organoid models to study kidney injury

- Animal Models Subcore
 - Measurement of GFR and RBF
 - Metabolic cage studies, urine metabolites
 - Blood pressure telemetry
 - Cardiac Function (pressure-time parameters)
 - Real-time super-resolution ultrasound of kidney microvasculature
 - Purine metabolomics
 - Mitochondrial / Bioenergetics (Seahorse)
 - Injury biomarker assessment
 - Disease Models: AKI (ischemia-reperfusion injury)
 - Disease Models: AKI (cisplatin nephrotoxicity)
 - Disease Models: AKI (gentamicin nephrotoxicity)
 - Disease Models: AKI (cecal ligation and puncture)
 - Disease Models: AKI (sickle cell crisis)
 - Disease Models: CKD (genetic models)
 - Disease Models: CKD (FSGS)
 - Disease Models: CKD (unilateral ureteral obstruction)
 - Disease Models: CKD (two kidney one clip hypertension)
 - Disease Models: CKD (chronic angiotensin II infusion)
 - Special Rodent Diets (low and high Na⁺ and K⁺)

Kidney Imaging: Developing Novel and Innovative Tools (KIDNIT) Development Core

The KIDNIT Resource Development Core provides a national resource for investigators who require detailed and quantitative morphological analysis of kidney-associated cells and tissues, particularly those that are epithelial in nature, as well as whole organs. Services include:

- Consultation and Training opportunities
 - Consultation for development of new approaches to study the kidney and lower urinary tract using morphological tools.
 - Training in sample preparation of kidney and bladder tissues for light and electron microscopic analysis.

- Training in specialized sample preparation to perform labeling and analysis of cleared organs and tissues.
- Training in quantitative image analysis.
- Training in live-cell and intravital approaches to study the biology/pathobiology of kidney and bladder tissues.
- Standard light microscopy
 - Brightfield, darkfield, epifluorescence, DIC
 - Macro (stereo) imaging microscopy
- Confocal microscopy
 - Laser scanning confocal microscopy
 - Spinning disk confocal microscopy
 - Ribbon scanning confocal microscopy for cleared organs/tissues
 - Fluorescent lifetime imaging
 - Fluorescent recovery after photobleaching
- Multiphoton microscopy
 - Multiphoton confocal microscopy
 - Fluorescent lifetime imaging
 - Fluorescent recovery after photobleaching
 - Intravital imaging
- TIRF microscopy
 - TIRF imaging acquisition and analysis
- Super-resolution microscopy
 - STED
 - CREST
 - STORM
 - AX/NSPARC
- Live-cell microscopy
 - Spinning disk confocal microscopy
 - Fluorescent lifetime imaging
 - Fluorescent recovery after photobleaching
 - Lattice light sheet microscopy
 - Incubator microscopy
 - Microinjection
- Large Volume Light-Sheet microscopy
 - Meso-Spim light sheet microscopy
- Additional imaging modalities
 - Whole slide scanning - brightfield and epifluorescence
 - iPOL imaging
- Electron microscopy
 - Scanning electron microscopy (field-emission)
 - Transmission electron microscopy
 - Freeze fracture microscopy

- Platinum replica electron microscopy
- Negative staining
- Freeze substitution
- Ultramicrotomy
- Ultrathin cryo EM
- CLEM
- Immuno-Electron microscopy

- Image analysis
 - Photoshop
 - Imaris
 - Metamorph
 - NIS elements
 - Leica LASX
 - NIH image/FIJI

Contact Information

If you would like more information regarding services provided by Pittsburgh Center for Kidney Research, please contact:

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or

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Pittsburgh Center for Kidney Research



UAB-UCSD O'Brien Center for Acute Kidney Injury Research

Summary

The University of Alabama at Birmingham – University of California at San Diego (UAB-UCSD) O'Brien Center for Acute Kidney Injury (AKI) Research is an interdisciplinary center of excellence in AKI-related research. The overall mission of the UAB-UCSD O'Brien Center for AKI Research is to improve the health of patients by fostering research specifically targeted to the prevention and treatment of AKI and its complications. The two Biomedical Research Cores (a Clinical Core and a Pre-clinical Core) and Resource Development Core integrate existing intellectual and technological resources to provide the Consortium a set of services/resources for innovative investigation in AKI-related research.

Clinical Core

The Clinical Core catalyzes the translation of bench discoveries to applications that impact human AKI. They achieve this through providing access to curated clinical data from prior clinical studies and new harmonized real world multimodal data from electronic health records (EHR) to support epidemiological studies of AKI and clinical research, including AKI risk-classification, sub-phenotyping, and simulated trials. They also have access to biospecimens from prior studies hosted by the core. Below is a list of detailed services provided by this core:

- Study Planning and Design
- Study Initiation and Conduct
- Study Analysis and Interpretation
- Biological Sample Repository
- Cloud-based multimodal databases for AKI and critical care nephrology research studies
- Biostatistics and Bioinformatics Support Services
 - Analysis of pilot data
 - Design of epidemiological, clinical studies or clinical trials
 - Sample size and/or power analysis
 - Analyses of study results
 - Database development
 - Forms, manual of operations, and/or instrument development
 - Data Safety and Monitoring
 - Big data transformation & pipeline development
 - Methodologies and Applications of Artificial Intelligence and Digital Health

Pre-Clinical Core

The Pre-Clinical Core provides the facilities and requisite skills (Animal Models Resource) to generate and study murine models of AKI and provides unique facilities and requisite skills (Renal Physiology Resource) to determine renal physiological changes in AKI. Pre-Clinical s Core services include:

- Kidney ischemia/reperfusion (IRI)

- Unilateral Ureteral Obstruction
- Orthotopic kidney transplantation
- Tail vein injection or venipuncture (per animal)
- GFR (transcutaneous FITC-sinistrin) in rodents
- Cannulation (indwelling with injection port)
- Use of a microsurgical workstation (per hour)
- Training (per hour/per day)
- Misc. surgical services involving body wall penetration (per hour)
- 5/6th nephrectomy (both steps)
- Radio-telemetry determination of blood pressure:
 - 8-day exp. each animal
 - 10-day exp. each animal
 - 15-day exp. each animal
 - 30-day exp. each animal
- LC-MS/MS Creatinine determination (per test)
- Functional renal imaging (tracer dependent, per hour)
- Structural and metabolic imaging (US, MRI, microCT) (per hour)
- Nuclear imaging (Gamma camera, SPECT/CT, PET/CT) (per hour)
- Optical Imaging (Bioluminescence, Fluorescence) (per hour)
- Image Analysis
- Whole kidney clearance/oxygen consumption studies
- Tissue oxygen partial pressure determination in kidney
- Determination of GFR in awake rodents
- In vitro assessment of oxygen consumption in tubules
- Micropuncture for nephron function and TG feedback
- Metabolic cage experiments in mice (per animal and week)
- Automated tail-cuff blood pressure determination (each, 6 days)

- Videometric flow velocitometry (VMFV)
- Laser Capture Microdissection from frozen tissue (~70 pieces individually collected per sample; sample quality and amount appropriate for RNA-Seq or potentially proteomics)
 - for glomeruli
 - for antibody-guided dissection of tubular segments

Resource Development Core

With both the clinical and pre-clinical cores, the Resource Development Core will provide a dynamic resource and platform to develop, test and refine innovations that will accelerate pre-clinical and clinical research. In the pre-clinical area, new analytical approaches in metabolomics as well as functional in vivo imaging will be incubated to probe unique biological characteristics of disease development. In the clinical area, tools for federated machine learning using big EHR data will be developed.

- Development of novel microfluidic methods aimed at high resolution molecular cartography in kidney tissue and molecular and functional kidney-specific imaging approaches in pre-clinical AKI.
- Development of a federated learning platform using a collaborative digital workspace to support big EHR data analyses across multiple institutions.

Contact Information

If you would like more information regarding services provided by UAB-UCSD O'Brien Center for AKI Research, please contact:

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Summary

The Washington University Kidney O'Brien Center for Chronic Kidney Disease Research (WUCKD-NRC) primary goals are to develop and disseminate tools and new technologies for the investigation of chronic kidney disease and fibrosis. The WUCKD-NRC achieves these goals through two Biomedical Cores – the Metabolism Core (Meta-Core) and the Variant Validation Core.

Metabolism Core (Meta-Core)

The aim of the Metabolism Core (Meta-Core) is to facilitate the use of metabolic assays in pre-clinical models of chronic kidney disease (CKD) for the kidney community by providing the following services following consultation with core faculty:

- Seahorse bioflux analyzer (XF24/XF96)
 - Measures metabolism and define metabolic substrate preferences ideally on adherent cells but also on freshly isolated tubules.
- High resolution respirometry (Oroboros)
 - Measures mitochondrial function in tissues ex vivo, and this is facilitated through the Nutrition Obesity Research Center (NORC).
- Substrate oxidation assays
 - Utilizes radioactive-labeled substrates (e.g. 3H-palmitate) to measure oxidation in tissue ex vivo.
- Untargeted metabolomics
 - Performed on cells or tissues using the mass spectrometry resources of the Metabolomics Core through the lab of Gary Patti.
- Stable isotope flux studies
 - Used to look at specific pathway activity and flux in both cell culture systems and whole animals using mass spectrometry.

Variant Validation Core

The widespread and increasing use of whole exome sequencing (WES) and whole genome sequencing (WGS) to investigate the genetic bases for CKD and other kidney disorders has led to a much better understanding of the etiology of monogenic diseases. The aim of the Variant Validation Core (VVC) is to investigate variants of uncertain significance (VUS) discovered in patients with kidney disease or a kidney developmental disorder for potential pathogenicity. The VVC will use experimental approaches in cultured cells and in mice. The experimental approach for each VUS will be tailored for 1) the particular gene and protein that are potentially involved; and 2) the particular disease or disorder that would likely develop if the VUS is indeed pathogenic. Immediate services and resources that are being offered include:

- COL4A3/A4/A5 VUS (missense) analysis by split nano-Luciferase collagen IV assembly and secretion assays using transfected cells

- COL4A3/A4/A5 VUS (intronic) analysis by RNA splicing assays using transfected cells
- COL4A3/A4/A5 VUS analysis by high resolution quantitative immunofluorescence imaging in paraffin sections of kidney biopsies
- COL4A3/A4/A5 VUS analysis in vivo by mouse gene editing
- Analysis of VUS in other genes through design and implementation of tailored laboratory assays

Contact Information

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