Grant Number: 5U24DK110791-04
FAIN: U24DK110791

Principal Investigator(s):
RAJIV DHIR, MD

Project Title: University of Pittsburgh as the GUDMAP Tissue Hub and Collection Site

(b)(6)

University of Pittsburgh
123 University Place, B21
Grants and Contracts Officer
Pittsburgh, PA 152132303

Award e-mailed to: ornih@offres.pitt.edu

Period Of Performance:
Budget Period: 06/01/2019 – 05/31/2020
Project Period: 09/15/2016 – 05/31/2021

Dear Business Official:

The National Institutes of Health hereby awards a grant in the amount of $0 (see "Award Calculation" in Section I and "Terms and Conditions" in Section III) to UNIVERSITY OF PITTSBURGH AT PITTSBURGH in support of the above referenced project. This award is pursuant to the authority of 42 USC 241 31 USC 6305 42 CFR 52 and is subject to the requirements of this statute and regulation and of other referenced, incorporated or attached terms and conditions.

Acceptance of this award including the "Terms and Conditions" is acknowledged by the grantee when funds are drawn down or otherwise obtained from the grant payment system.

Each publication, press release, or other document about research supported by an NIH award must include an acknowledgment of NIH award support and a disclaimer such as "Research reported in this publication was supported by the National Institute Of Diabetes And Digestive And Kidney Diseases of the National Institutes of Health under Award Number U24DK110791. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health." Prior to issuing a press release concerning the outcome of this research, please notify the NIH awarding IC in advance to allow for coordination.

Award recipients must promote objectivity in research by establishing standards that provide a reasonable expectation that the design, conduct and reporting of research funded under NIH awards will be free from bias resulting from an Investigator's Financial Conflict of Interest (FCOI), in accordance with the 2011 revised regulation at 42 CFR Part 50 Subpart F. The Institution shall submit all FCOI reports to the NIH through the eRA Commons FCOI Module. The regulation does not apply to Phase I Small Business Innovative Research (SBIR) and Small Business Technology Transfer (STTR) awards. Consult the NIH website http://grants.nih.gov/grants/policy/coi/ for a link to the regulation and additional important information.

If you have any questions about this award, please contact the individual(s) referenced in Section IV.

Sincerely yours,

(b)(6)

Grants Management Officer
NATIONAL INSTITUTE OF DIABETES AND DIGESTIVE AND KIDNEY DISEASES

Additional information follows

SECTION I – AWARD DATA – 5U24DK110791-04

Award Calculation (U.S. Dollars)

Salaries and Wages	$39,353
Fringe Benefits	$12,354
Personnel Costs (Subtotal)	$51,707
Materials & Supplies	$4,497
Travel	$1,697
Other	$7,528
Federal Direct Costs	$65,429
Federal F&A Costs	$34,571
Approved Budget	$100,000
Total Amount of Federal Funds Obligated (Federal Share)	$100,000
Less Unobligated Balance	$100,000
TOTAL FEDERAL AWARD AMOUNT	$0
AMOUNT OF THIS ACTION (FEDERAL SHARE)	$0

SUMMARY TOTALS FOR ALL YEARS		
YR	**THIS AWARD**	**CUMULATIVE TOTALS**
4	$0	$0
5	$613,000	$613,000

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

Fiscal Information:

CFDA Name:	Diabetes, Digestive, and Kidney Diseases Extramural Research
CFDA Number:	93.847
EIN:	1250965591A1
Document Number:	UDK110791A
PMS Account Type:	P (Subaccount)
Fiscal Year:	2019

IC	CAN	2019	2020
DK	8472288	$0	$613,000

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

NIH Administrative Data:
PCC: KDH KDB / **OC**: 414P / **Released**: (b)(6) 06/04/2019
Award Processed: 06/05/2019 12:08:14 AM

SECTION II – PAYMENT/HOTLINE INFORMATION – 5U24DK110791-04

For payment and HHS Office of Inspector General Hotline information, see the NIH Home Page at http://grants.nih.gov/grants/policy/awardconditions.htm

SECTION III – TERMS AND CONDITIONS – 5U24DK110791-04

This award is based on the application submitted to, and as approved by, NIH on the above-titled project and is subject to the terms and conditions incorporated either directly or by reference in the following:

a. The grant program legislation and program regulation cited in this Notice of Award.
b. Conditions on activities and expenditure of funds in other statutory requirements, such as those included in appropriations acts.
c. 45 CFR Part 75.
d. National Policy Requirements and all other requirements described in the NIH Grants Policy Statement, including addenda in effect as of the beginning date of the budget

period.

e. Federal Award Performance Goals: As required by the periodic report in the RPPR or in the final progress report when applicable.
f. This award notice, INCLUDING THE TERMS AND CONDITIONS CITED BELOW.

(See NIH Home Page at http://grants.nih.gov/grants/policy/awardconditions.htm for certain references cited above.)

Research and Development (R&D): All awards issued by the National Institutes of Health (NIH) meet the definition of "Research and Development" at 45 CFR Part§ 75.2**.** As such, auditees should identify NIH awards as part of the R&D cluster on the Schedule of Expenditures of Federal Awards (SEFA). The auditor should test NIH awards for compliance as instructed in Part V, Clusters of Programs. NIH recognizes that some awards may have another classification for purposes of indirect costs. The auditor is not required to report the disconnect (i.e., the award is classified as R&D for Federal Audit Requirement purposes but non-research for indirect cost rate purposes), unless the auditee is charging indirect costs at a rate other than the rate(s) specified in the award document(s).

Carry over of an unobligated balance into the next budget period requires Grants Management Officer prior approval.

This award is subject to the requirements of 2 CFR Part 25 for institutions to receive a Dun & Bradstreet Universal Numbering System (DUNS) number and maintain an active registration in the System for Award Management (SAM). Should a consortium/subaward be issued under this award, a DUNS requirement must be included. See http://grants.nih.gov/grants/policy/awardconditions.htm for the full NIH award term implementing this requirement and other additional information.

This award has been assigned the Federal Award Identification Number (FAIN) U24DK110791. Recipients must document the assigned FAIN on each consortium/subaward issued under this award.

Based on the project period start date of this project, this award is likely subject to the Transparency Act subaward and executive compensation reporting requirement of 2 CFR Part 170. There are conditions that may exclude this award; see http://grants.nih.gov/grants/policy/awardconditions.htm for additional award applicability information.

In accordance with P.L. 110-161, compliance with the NIH Public Access Policy is now mandatory. For more information, see NOT-OD-08-033 and the Public Access website: http://publicaccess.nih.gov/.

In accordance with the regulatory requirements provided at 45 CFR 75.113 and Appendix XII to 45 CFR Part 75, recipients that have currently active Federal grants, cooperative agreements, and procurement contracts with cumulative total value greater than $10,000,000 must report and maintain information in the System for Award Management (SAM) about civil, criminal, and administrative proceedings in connection with the award or performance of a Federal award that reached final disposition within the most recent five-year period. The recipient must also make semiannual disclosures regarding such proceedings. Proceedings information will be made publicly available in the designated integrity and performance system (currently the Federal Awardee Performance and Integrity Information System (FAPIIS)). Full reporting requirements and procedures are found in Appendix XII to 45 CFR Part 75. This term does not apply to NIH fellowships.

Treatment of Program Income:
Other Research (Add/Deduct Option)

Clinical Trial Indicator: No
This award does not support any NIH-defined Clinical Trials. See the NIH Grants Policy Statement Section 1.2 for NIH definition of Clinical Trial.

RESTRICTION: Funds may only be used to pay for the cost of processing, shipping and handling tissue samples from external sources to the GUDMAP atlas projects.

Notice: Under governing regulations, Federal funds administered by the Department of Health and Human Services shall not be expended for research involving human subjects, and individuals shall not be enrolled in such research, without prior approval by the Office of Human Research Protections (OHRP) of an assurance to comply with the requirements of 45 CFR 46 to protect human research subjects. This restriction applies to all collaborating sites without OHRP-approved assurances, whether domestic or foreign, and compliance must be ensured by the awardee.

Notice: Under governing policy, federal funds administered by the Public Health Service (PHS) shall not be expended for research involving live vertebrate animals without prior approval by the Office of Laboratory Animal Welfare (OLAW) of an assurance to comply with the PHS policy on humane care and use of laboratory animals. This restriction applies to all performance sites (e.g., collaborating institutions, subcontractors, subgrantees) without OLAW-approved assurances, whether domestic or foreign.

The issuance of this award has been delayed due to administrative funding considerations. According to NIH policy, if pre-award costs are necessary, they may be approved by the authorized Institution
Official(s).

This award uses as an offset the unobligated balance ($100,000) from the -02 year Federal Financial Report.

In addition to the PI, the following individuals are named as key personnel:

(b)(6)

Written prior approval is required if any of the individual(s) named above withdraws from the project entirely, is absent from the project during any continuous period of 3 months or more, or reduces time devoted to the project by 25 percent or more from the level that was approved at the time of award.

This grant is in response to RFA/PA DK15-016. Acceptance of this award requires compliance with this solicitation. See the NIH Guide at http://grants.nih.gov/grants/guide/index.html for copy of the RFA/PA that includes administrative and programmatic requirements specific to this award.

In accordance with the Salary Limitation in NIH Guide Notice NOT-OD-19-031, Notice of Fiscal Policies in Effect for FY2019, none of the funds in this award shall be used to pay the salary of an individual at a rate in excess of Executive Level II. Therefore, this award and/or future years are adjusted accordingly, if applicable. See the Salary Cap Summary for a historical record of the salary cap, including effective dates.

Grantees can determine which progress reports are due through the website located at https://public.era.nih.gov/chl/public/search/index.jsp and should periodically check the site, which is updated on or around the 30th of each month. Progress report due dates are also available in the eRA Commons Status system. In addition, automatic e-mail notifications are sent to the PD/PI prior to due date.

As of October 17, 2014, the National Institutes of Health (NIH) requires grantees to submit all type 5 progress reports using the eRA Research Performance Progress Report (RPPR) module. Annual progress reports submitted in any format other than the RPPR will not be processed by the NIH and will require resubmission through the RPPR module in accordance with NIH Guide Notice NOT-OD-15-014 released October 16, 2014.

The following special terms of award are in addition to, and not in lieu of, otherwise applicable U.S. Office of Management and Budget (OMB) administrative guidelines, U.S. Department of Health and Human Services (DHHS) grant administration regulations at 45 CFR Parts 74 and 92 (Part 92 is applicable when State and local Governments are eligible to apply), and other HHS, PHS, and NIH grant administration policies.

The administrative and funding instrument used for this program will be the cooperative agreement, an "assistance" mechanism (rather than an "acquisition" mechanism), in which substantial NIH programmatic involvement with the awardees is anticipated during the performance of the activities.

Under the cooperative agreement, the NIH purpose is to support and stimulate the recipients' activities by involvement in and otherwise working jointly with the award recipients in a partnership role; it is not to assume direction, prime responsibility, or a dominant role in the activities. Consistent with this concept, the dominant role and prime responsibility resides with the awardees for the project as a whole, although specific tasks and activities may be shared among the awardees and the NIH as defined below.

The PD(s)/PI(s) will have the primary responsibility for:

- All aspects of the scientific activities, including defining the objectives and approaches, planning, conduct, analysis, and publication of results, interpretations, and conclusions of studies conducted under the terms and conditions of the cooperative agreement award.
- Collaborating with other investigators in the program for protocol development, sample, reagents and data sharing as appropriate, data quality control, and data organization
- Accountability towards the applicant organization officials and to the NIDDK for the performance and proper conduct of the research supported by the project in accordance with the terms and conditions of the award.
- Serving as a voting member of the Steering Committee and will attend the Planning Meeting and a Steering Committee meeting in the first year, two Steering Committee meetings a year in subsequent years and monthly teleconference calls.
- Accepting and implementing the goals, priorities, procedures, protocols, and policies agreed upon by the Steering Committee and subcommittees, and be responsible for close coordination and cooperation with the components of the GUDMAP consortium and with NIDDK staff.
- Adhering to PHS policy for the distribution of unique research resources produced with PHS funding as described under Special Requirements.
- Establishing written milestones for the project, in negotiation with NIDDK Project Staff prior to funding.
- Release all study design materials and procedure manuals into the public domain and/or make them available to other investigators, according to the approved plan for making data and materials available to the scientific community and the NIDDK, for the conduct of research at no charge other than the costs of reproduction and distribution, consistent with achieving the goals of this program initiative.
- Awardees will retain custody of and have primary rights to the data and software developed under these awards, subject to Government rights of access consistent with current DHHS, PHS, and NIH policies.

NIH staff will have substantial programmatic involvement that is above and beyond the normal stewardship role in awards, as described below:

- An NIH Project Scientist will have substantial programmatic involvement that is above and beyond the normal stewardship role in awards, as described below. However, the dominant role and prime responsibility for the project as a whole resides with the awardees, although specific tasks and activities in carrying out the studies will be shared by awardees and the NIDDK.
- NIDDK will designate a Project Officer and a Grants Management Specialist to provide normal program stewardship and administrative oversight of the cooperative agreement.
- NIDDK will form an External Advisory Committee (EAC), comprised of the NIDDK Project Scientist and other NIH extramural staff with relevant scientific expertise or who manage research grant programs that relate scientifically to the goals of the GUDMAP projects, and outside advisors selected by the NIDDK. The EAC will meet annually with the GUDMAP Steering Committee to review and assess GUDMAP and to advise NIDDK of

scientific developments and opportunities that may enhance the achievement of the GUDMAP goals.

- The NIDDK Project Scientist will attend and participate as a voting member in all meetings of the Steering Committee, and provide liaison between the Steering Committee and the External Advisory Committee.
- The NIDDK Project Scientist will help the Steering Committee develop and draft operating policies.
- The NIDDK Project Officer will review the scientific progress of the individual GUDMAP components, for compliance with operating policies developed by the Steering Committee, and may recommend to the NIDDK to withhold support, suspend, or terminate an award for lack of scientific progress or failure to adhere to policies established by the Steering Committee.
- An agency program official or IC program director will be responsible for the normal scientific and programmatic stewardship of the award and will be named in the award notice. The assigned Program Officer may also serve as an NIDDK Project Scientist.

Areas of Joint Responsibility include:

- Steering Committee - The NIDDK Project Scientist, PIs from the project funded through this FOA and RFA-DK-15-014, and RFA-DK-15-015 and voluntary representatives from the previously funded GUDMAP atlas projects funded under RFA-DK-11-001 will be responsible for forming a Steering Committee as defined below. An arbitration system, as detailed below, will be available to resolve disagreements among members of the Steering Committee. The Steering Committee will be the main governing board of the GUDMAP consortium. It will develop collaborative protocols, identify technological impediments to success and strategies to overcome them, develop shared software tools for disseminating information about the projects, and identify opportunities for sharing techniques and tools that might be developed in future GUDMAP atlas projects.
- The Steering Committee will be composed of the PIs from the project funded through this FOA, RFA-DK-15-014, and RFA-DK-15-015, representatives from the previously funded GUDMAP projects, and the NIDDK Project Scientist. The representatives and the PIs will each have one vote. The NIDDK Project Scientist for this project will have one vote. The Steering Committee will select a chairperson who will be someone other than an NIH staff member.
- The Steering Committee may, as it deems necessary, invite additional, non-voting scientific advisors to meetings at which research priorities and opportunities are discussed. The NIH reserves the right to augment the scientific or consumer expertise of the Steering Committee when necessary.
- There will be two Steering Committee meetings annually. The first meeting will be a Planning Meeting to be held in the Washington, DC area on **June 20-21, 2016**. At the Planning Meeting, the Steering Committee will be formed and a chairperson selected from among the members. At the Planning Meeting, the Steering Committee may: (a) draft a charter to detail policies and procedures, a process for monitoring compliance with the policies and procedures, and a process for recommending that the NIDDK Project Administrators act on evidence of non-compliance of any Consortium component with Steering Committee policies; (b) agree upon the terms of the charter; and (c) devise a plan for working with the GUDMAP database developers to provide ongoing input into database and website design.
- At the second and subsequent meetings, the Steering Committee will refine the GUDMAP scientific objectives and implementation as necessary, consistent with data produced by former and possible future GUDMAP atlas projects and from other laboratories.
- The Steering Committee will plan workshops, to which non-GUDMAP participants will also be invited, to inform the research community of the progress made toward development of the atlas, and to inform the research community of any technological advances related to the implementation of the GUDMAP website/database. The NIDDK Project Scientist, the External Advisory Committee, and other NIH staff as appropriate will provide the Steering Committee with advice on participants for the workshops and symposia.
- The Steering Committee may establish subcommittees as it deems appropriate.
- Awardee members of the Steering Committee will be required to accept and implement policies approved by the Steering Committee.

- The EAC will meet annually with the GUDMAP Steering Committee to review and assess the progress of the GUDMAP consortium and to advise NIDDK of scientific developments and opportunities that may enhance the achievement of the GUDMAP goals.

Dispute Resolution
Any disagreements that may arise in scientific or programmatic matters (within the scope of the award) between award recipients and the NIH may be brought to Dispute Resolution. A Dispute Resolution Panel will have three members: a designee of the Steering Committee chosen without NIH staff voting, one NIH designee, and a third designee with expertise in the relevant area who is chosen by the other two; in the case of individual disagreement, the first member may be chosen by the individual awardee. This special dispute resolution procedure does not alter the awardee's right to appeal an adverse action that is otherwise appealable in accordance with PHS regulation 42 CFR Part 50, Subpart D and DHHS regulation 45 CFR Part 16.

STAFF CONTACTS

The Grants Management Specialist is responsible for the negotiation, award and administration of this project and for interpretation of Grants Administration policies and provisions. The Program Official is responsible for the scientific, programmatic and technical aspects of this project. These individuals work together in overall project administration. Prior approval requests (signed by an Authorized Organizational Representative) should be submitted in writing to the Grants Management Specialist. Requests may be made via e-mail.

Grants Management Specialist: (b)(6)
Email: (b)(6) @extra.niddk.nih.gov **Phone**: (b)(6) **Fax**: (b)(6)

Program Official: (b)(6)
Email: (b)(6) @niddk.nih.gov **Phone**: (b)(6)

SPREADSHEET SUMMARY
GRANT NUMBER: 5U24DK110791-04

INSTITUTION: UNIVERSITY OF PITTSBURGH AT PITTSBURGH

Budget	Year 4	Year 5
Salaries and Wages	$39,353	$236,510
Fringe Benefits	$12,354	$74,246
Personnel Costs (Subtotal)	$51,707	$310,756
Materials & Supplies	$4,497	$27,027
Travel	$1,697	$10,200
Other	$7,528	$45,242
TOTAL FEDERAL DC	$65,429	$393,225
TOTAL FEDERAL F&A	$34,571	$219,775
TOTAL COST	$0	$613,000

Facilities and Administrative Costs	Year 4	Year 5
F&A Cost Rate 1	56.5%	56.5%
F&A Cost Base 1	$61,187	$388,983
F&A Costs 1	$34,571	$219,775

A. COVER PAGE

Project Title: University of Pittsburgh as the GUDMAP Tissue Hub and Collection Site	
Grant Number: 5U24DK110791-04	**Project/Grant Period:** 09/15/2016 - 05/31/2021
Reporting Period: 06/01/2018 - 05/31/2019	**Requested Budget Period:** 06/01/2019 - 05/31/2020
Report Term Frequency: Annual	**Date Submitted:** 04/02/2019
Program Director/Principal Investigator Information: RAJIV DHIR , MD **Phone number:** (412) 623-1321 **Email:** dhirr@upmc.edu	**Recipient Organization:** UNIVERSITY OF PITTSBURGH AT PITTSBURGH UNIVERSITY OF PITTSBURGH OFFICE OF RESEARCH PITTSBURGH, PA 152132303 **DUNS:** 004514360 **EIN:** 1250965591A1 **RECIPIENT ID:**
Change of Contact PD/PI: N/A	
Administrative Official: (b)(6) UNIVERSITY OF PITTSBURGH 123 University Place Room B21 PITTSBURGH, PA 15213 **Phone number:** (b)(6) **Email:** (b)(6) @pitt.edu	**Signing Official:** (b)(6) 123 University Place B21 University Club Pittsburgh, PA 15213 **Phone number:** (b)(6) **Email:** (b)(6) @pitt.edu
Human Subjects: Yes HS Exempt: No Exemption Number: Phase III Clinical Trial:	**Vertebrate Animals:** No
hESC: No	**Inventions/Patents:** No

B. ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

Aim 1: To generate an inventory of genitourinary tissue throughout normal human development The main goal of this aim is to develop a pipeline for the acquisition, quality control and distribution of human genitourinary samples obtained throughout development (6-42 weeks gestation). We currently have access to 6-24 week samples through the HSTB. However, for later gestational stages (25-42 weeks gestation) we have partnered with the International institute for the Advancement of Medicine. This will provide access to a novel resource for neonatal donation. We aim to collect and store a minimum of 5 samples per developmental week. Each of these samples will have histology, immunohistochemistry and in situ hybridization performed to assess tissue quality, protein and RNA integrity. Furthermore, we will obtain maternal blood, urine and amniotic fluid; based on the clinical situation and ability to procure. Based on our current experience, we get these biological
materials in most cases. Anonymized demographic information of each specimen will also be provided.

Aim 2: To provide fresh genitourinary tissue and biological research specimens This aim will generate an ongoing resource to distribute fresh developmental human genitourinary samples
from various stages (6-42 weeks) to the GUDMAP Atlas projects. The samples will be procured by a pathologist and inspected for mechanical damage. Samples will be collected from all qualified cases. The samples will then be subdivided based on the demand for fresh/frozen aliquots; the validation laboratory for quality control will keep a portion of each sample. The tissue samples will be immediately sent out for live cell use or immediately separated into distinct cellular populations before shipping based on researcher demands. Permissible annotating information; including demographics of each specimen, will also be provided.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: ACCOMPLISHMENTS_2019 FINAL.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

For this reporting period, is there one or more Revision/Supplement associated with this award for which reporting is required?

No

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

NOTHING TO REPORT

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

There is very active e-mail and phone communication between the GUDMAP investigators, the Data Hub and the Tissue Hub. In addition, the Tissue Hub activities account for approximately 50% of the 90 minute long monthly consortium video conference calls.

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

Continue providing materials to requesting investigators within the consortia. We will be performing extensive analyses on collected specimens both from a quality assessment perspective as well as to potentially assist GUDMAP investigators with specific pathology needs related to either localization studies and/or imaging.

ACCOMPLISHMENTS

Summary

The goal of this project is to provide human genitourinary tissues (kidneys, ureters, bladders and genital structures) to research projects funded in the GenitoUrinary Development Molecular Anatomy Project (GUDMAP), as part of a consortium to build a molecular atlas of human genitourinary development.

Biospecimen Collection/Quality Control:

The Tissue Hub has been shipping biospecimens to GUDMAP consortium members since June 2017. The Tissue Hub participates in monthly GUDMAP consortium phone calls for updates regarding the provision of tissue provided to GUDMAP Atlas projects, which provide a mechanism for feedback from consortium members about current tissue specimens, and to ascertain specific biospecimen and processing needs as projects evolve. The interface between the Tissue Hub and the Atlas projects remains collaborative in nature, and the Tissue Hub continues to strive to facilitate individual projects in this manner.

As part of the quality control process, the Validation Laboratory has been performing PCR-based genotyping on all biospecimens to document gender, in addition to an anatomical assessment performed by pathology since June 2018, in response to feedback from an investigator who had received one specimen of the incorrect gender in the prior grant year. Since that time, all PCR genotypes have corresponded to the gender determined by anatomical assessment. The Validation Laboratory has also performed pilot studies in collaboration with project PIs to identify optimal means of sample processing for the downstream applications for individual organs. For example, the validation laboratory performed tests of RNA quality following biospecimen collection in RPMI, storage and RNA isolation, compared to placing biospecimens in OCT, isolation of a subset of the tissue and RNA isolation. We recently received interest from the Cohn lab for additional biospecimens that can be provided by the Tissue Hub for single cell RNA sequencing, and engaged in technical discussions regarding the best way to generate viable single cell suspensions for single cell RNA sequencing from these tissues. The monthly feedback from GUDMAP investigators has been consistently positive regarding the tissue quality that has been received.

PRODUCTS

With the appropriate regulatory approvals and MTAs in place, the Tissue Hub is actively providing biospecimens to the GUDMAP investigators, with the current numbers from this funding year outlined in Table 1.

Table 1. Biospecimen disbursements from Tissue Hub to GUDMAP investigators.

GUDMAP Investigator	Fresh Tissue Disbursements June 1, 2018- March 1, 2019	
(b)(6)		(b)(4)
Totals		

In the prior grant funding year, the GUDMAP investigators identified a research need for biospecimens that could not be provided through the Health Sciences Tissue Bank at the University of Pittsburgh given how the biospecimens are collected. Given this, the Tissue Hub

developed a mechanism by which GUDMAP investigators can obtain these tissues through the Human Developmental Biology Resource (HDBR), and currently covers all the costs to the GUDMAP investigators for these shipments. The current numbers for this funding year are provided in Table 2.

Table 2. Shipments from Human Developmental Biology Resource (HDBR) to GUDMAP investigators.

GUDMAP Investigator	June 1, 2018- March 1, 2019	
(b)(6)		(b)(4)
Totals		

CHANGES/PROBLEMS

(b)(6); who was the (b)(6) Dr. (b)(6) was recruited by the Unviersity of Pittsburgh as (b)(6) replacement; and as the (b)(6) (b)(6) is replacing (b)(6) on the GUDMAP grant. This transition has been smooth and uneventful.

The Health Sciences Tissue Bank has been re-named the Pittsburgh Biospecimen Core in the past year. We do not anticipate that this will impact the function of the Tissue Hub in the GUDMAP consortium in any way.

For unclear reasons, the numbers of consents (N=29) from normal cases (N=81) in the last year has decreased significantly, which has impacted the number of specimens shipped from the Tissue Hub.

Due to the nature of the consenting process that is ethically and legally required for this type of tissue, we cannot be actively engaged in consenting. We have maintained active communication with our clinical partners in Obstetrics, and have not identified any significant changes that have occurred regarding the consenting process. Internally, we have reviewed our data monthly to evaluate other potential remediable factors, but the barrier is at the time of consent.

Our source for the younger time points is HDBR, which has been working hard with the investigators to provide the necessary samples. The quality of the specimens is sometimes not ideal for all groups and purposes, but the tissue shipments have in general increased. We act as a liason for this interaction and continue to work closely with HDBR.

BUDGETARY INFORMATION

The budget for Year 4 has minor adjustments in % effort and supplies; to maintain the total direct costs of the grant.

C. PRODUCTS

C.1 PUBLICATIONS

Are there publications or manuscripts accepted for publication in a journal or other publication (e.g., book, one-time publication, monograph) during the reporting period resulting directly from this award?

No

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Nothing to report

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Have inventions, patent applications and/or licenses resulted from the award during the reporting period? No

If yes, has this information been previously provided to the PHS or to the official responsible for patent matters at the grantee organization?

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Category	Explanation
Research Material	The Tissue Hub will collect specimens as per the needs of the GUDMAP investigators. The biospecimens will be both from surgical pathology specimens (products of conception) as well as autopsy material (still-births). In addition, additional specimens may be collected depending on investigator and programmatic needs and direction. The specimen types that can be accrued, and possible specimen accrual limitations, have been discussed with consortia members. Collection protocols will continue to be modified and fine-tuned to reflect the needs and the reality of human biospecimen collections; since diagnostic assessment is the primary purpose.
Data or Databases	The data collected and provided by the Hub will be in two broad categories. Firstly, we will provide annotation information related to the specimens collected for the GUDMAP investigators. The data elements to be collected have been defined by the consortium. The data will be securely provided to the Data Hub, which will host this information. The second major data component will be imaging data generated from the specimens and slides etc. In addition, molecular data will also be generated from select specimens.

D. PARTICIPANTS

D.1 WHAT INDIVIDUALS HAVE WORKED ON THE PROJECT?

Commons ID	S/K	Name	Degree(s)	Role	Cal	Aca	Sum	Foreign Org	Country	SS
(b)(6)	Y	DHIR, RAJIV	MD	PD/PI	(b)(6)					NA
	N	(b)(6)		QC Manager						NA
	N			HSTB Supervisor						NA
	N			Project Manager						NA
	N			Data Coordinator						NA
(b)(6)	N			Co-Investigator						NA
	N			Technician						NA
	N			Technician						NA
(b)(6)	N		BS,OTH,PHD	Co-Investigator						NA
	N		BS,MS,MD	Co-Investigator						NA
	N			Co-Investigator						NA
	N			Student						NA
	N			Technician						NA

Glossary of acronyms:
S/K - Senior/Key
DOB - Date of Birth
Cal - Person Months (Calendar)
Aca - Person Months (Academic)
Sum - Person Months (Summer)
Foreign Org - Foreign Organization Affiliation
SS - Supplement Support
RE - Reentry Supplement
DI - Diversity Supplement
OT - Other
NA - Not Applicable

D.2 PERSONNEL UPDATES

D.2.a Level of Effort

Will there be, in the next budget period, either (1) a reduction of 25% or more in the level of effort from what was approved by the agency for the PD/PI(s) or other senior/key personnel designated in the Notice of Award, or (2) a reduction in the level of effort below the minimum amount of effort required by the Notice of Award?

No

D.2.b New Senior/Key Personnel

Are there, or will there be, new senior/key personnel?

Yes

File uploaded: New_Investigator_(b)(6) pdf

D.2.c Changes in Other Support

Has there been a change in the active other support of senior/key personnel since the last reporting period?

Yes

File uploaded: Other Support RPPR.pdf

D.2.d New Other Significant Contributors

Are there, or will there be, new other significant contributors?

No

D.2.e Multi-PI (MPI) Leadership Plan

Will there be a change in the MPI Leadership Plan for the next budget period?

NA

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Withheld pursuant to exemption

(b)(6)

of the Freedom of Information and Privacy Act

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Withheld pursuant to exemption

(b)(6)

of the Freedom of Information and Privacy Act

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Withheld pursuant to exemption

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of the Freedom of Information and Privacy Act

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Withheld pursuant to exemption

(b)(6)

of the Freedom of Information and Privacy Act

For New and Renewal Applications (PHS 398) – DO NOT SUBMIT UNLESS REQUESTED

PHS 398 OTHER SUPPORT

Provide active and pending support for all senior/key personnel. **Other Support includes all financial resources, whether Federal, non-Federal, commercial or institutional, available in direct support of an individual's research endeavors, including but not limited to research grants, cooperative agreements, contracts, and/or institutional awards.** Training awards, prizes, or gifts do not need to be included.

There is no "form page" for other support. Information on other support should be provided in the *format* shown below, using continuation pages as necessary. ***Include the principal investigator's name at the top and number consecutively with the rest of the application.*** The sample below is intended to provide guidance regarding the type and extent of information requested.
For instructions and information pertaining to the use of and policy for other support, see Other Support in the Supplemental Instructions, Part III, Policies, Assurances, Definitions, and Other Information.
Effort devoted to projects must be measured using person months. Indicate calendar, academic, and/or summer months associated with each project.

Format

NAME OF INDIVIDUAL **Rajiv Dhir, MD, MBA**
ACTIVE/PENDING

ACTIVE

U19 OH009077-08 (Becich) 09/01/2006–08/31/2021 (b)(6)
CDC $35,688
National Mesothelioma Virtual Bank for Translational Research
The proposed Mesothelioma Virtual Bank (MVB) for Translational Research will create and maintain infrastructure to support a national virtual patient registry and tissue bank. MVB proposes to create and maintain a set of resources through a cooperative working group that will make available their independent stores of mesothelioma tissue for public access.

P30CA047904 (Ferris) 08/01/2015-07/31/2020 (b)(6)
NIH $84,621
Cancer Center Support Grant
Dr. Dhir directs the Tissue and Research Pathology Services (TARPS) portion of the UPCI Cancer Center Support Grant

UM1CA18669003 (Chu) 03/01/2018-2/28/2020 (b)(6)
NIH $24,283
NCI ET-CTN with Phase 1 Emphasis at UPCI
Our institution is working to transform the NCI-sponsored cooperative experimental therapeutics clinical trials program from a series of separate institutions conducting early-phase cancer treatment trials to a new consolidated, integrated Program, referred to as the NCI Experimental Therapeutics-Clinical Trials Network (ET-CTN).

U01HL12895403 (Wisniewski/Sciurba) 08/01/2015-07/31/2020 (b)(6)
NIH $11,897
Network Management Core (NEMO) for the Pulmonary Trials Cooperative (PTC)
The NEMO will have primary responsibility for organizing and operating this multi-center cooperative which conducts multiple simple clinical trials in both inpatient and outpatient settings in adults with a variety of chronic pulmonary diseases, including but not limited to interstitial lung disease (ILD), pulmonary hypertension (PH), chronic obstructive pulmonary disease (COPD), sarcoidosis, and obstructive sleep apnea, but excluding asthma and acute lung injury and critical care.

Federal Contract (Sciurba) 03/01/2016-2/28/2020 (b)(6)
NIH $30,131
Lung Tissue Research Consortium (LTRC): Clinical Centers
Contribute to the lung tissue Research consortium by meeting necessary subject recruitment goals, Providing high quality specimens and offering expertise in innovative Techniques in subject characterization, metagenomic characterization of The microbiome and gene expression analysis.

16X018 Federal Contract (Dhir) 09/30/2015-8/30/2019 (b)(6)
Leidos $561,606
Clinical Proteomic Tumor Analysis Consortium Phase III Tissue Source Site
These analyses will serve to clarify how the molecular biology facilitates refinement of driver genes, enhances understanding of the pathogenesis through proteomic subtyping, and illuminates dynamic alterations in post translational modifications responsible for the disregulation of cancer signaling networks and pathways; in essence, providing novel information for regarding the molecular biology of cancer.

1U54DK112079 - 02 (Wang) 09/22/2016-06/30/2021 (b)(6)
NIH $70,587
University of Pittsburgh OBrien Cooperative Research Center Program
Success of the proposed multidisciplinary research will elucidate the molecular mechanisms of BPH and related LUTS, which may lead to new targets for developing novel preventive and/or therapeutic approaches for this disease.

1U24 DK110791-02 (Dhir) 09/15/2016 – 06/30/2021 (b)(6)
NIH $125,176
University of Pittsburgh as the GUDMAP Tissue Hub and Collection Site An understanding of human genitourinary development is critical to tackling the growing number of developmental diseases affecting these tissues. This grant proposes to leverage the significant infrastructure of the University of Pittsburgh to provide high quality fetal tissue to the GUDMAP atlas projects.

1UG3 DK114861-01 (Kellum) 09/15/2017-06/30/2019 (b)(6)
National Institutes of Health $11,678
PReCISE AKI (Phenotyping REnal Cases in Sepsis and surgery for Early Acute Kidney Injury)
This project seeks to enroll patients with Early Acute Kidney Injury (AKI) as well as to contribute to enrollment of patients with established AKI as part of the UG3/UH3 consortium.

PENDING

NONE

OVERLAP: No Overlap

OTHER SUPPORT

(b)(6)

ACTIVE

(b)(6)

PENDING

None

OVERLAP

None

E. IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

NOTHING TO REPORT

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

Not Applicable

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

NOTHING TO REPORT

F. CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

NOTHING TO REPORT

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

Yes

Is the research exempt from Federal regulations?

No

Does this project involve a clinical trial?

No

G.4.b Inclusion Enrollment Data

Report Attached: Research on tissue from an elective or spontaneous abortion < 24 weeks gestation

G.4.c ClinicalTrials.gov

Does this project include one or more applicable clinical trials that must be registered in ClinicalTrials.gov under FDAAA?

No

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Are there personnel on this project who are newly involved in the design or conduct of human subjects research?

No

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Does this project involve vertebrate animals?

No

G.8 PROJECT/PERFORMANCE SITES

Organization Name:	DUNS	Congressional	Address

		District	
Primary: University of Pittsburgh	004514360	PA-018	UPMC Shadyside 5230 Centre Avenue Pittsburgh PA 152320000
University of Pittsburgh	004514360	PA-018	Children's Hospital of UPMC 4401 Penn Avenue Pittsburgh PA 152240000
University of Pittsburgh	004514360	PA-018	Magee Womens Hospital of UPMC 300 Halket Street Pittsburgh PA 152130000
UNIVERSITY OF PITTSBURGH AT PITTSBURGH	004514360	PA-018	UNIVERSITY OF PITTSBURGH OFFICE OF RESEARCH PITTSBURGH PA 152132303
UNIVERSITY OF PITTSBURGH AT PITTSBURGH	004514360		UNIVERSITY OF PITTSBURGH OFFICE OF RESEARCH PITTSBURGH PA 152132303
University of Pittsburgh	004514360	PA-014	UPMC Shadyside 5230 Centre Avenue Pittsburgh PA 152320000
University of Pittsburgh	004514360	PA-014	Children's Hospital of UPMC 4401 Penn Avenue Pittsburgh PA 152240000
University of Pittsburgh	004514360	PA-014	Magee Womens Hospital of UPMC 300 Halket Street Pittsburgh PA 152130000
UNIVERSITY OF PITTSBURGH AT PITTSBURGH	004514360		UNIVERSITY OF PITTSBURGH OFFICE OF RESEARCH PITTSBURGH PA 152132303

G.9 FOREIGN COMPONENT

No foreign component

G.10 ESTIMATED UNOBLIGATED BALANCE

G.10.a Is it anticipated that an estimated unobligated balance (including prior year carryover) will be greater than 25% of the current year's total approved budget?

No

G.11 PROGRAM INCOME

Is program income anticipated during the next budget period?

No

G.12 F&A COSTS

Is there a change in performance sites that will affect F&A costs?

No

Inclusion Enrollment Report

Inclusion Data Record (IDR) #: 132193

Using an Existing Dataset or Resource: No

Delayed Onset Study ?: No

Clinical Trial: No

Enrollment Location: Domestic

NIH Defined Phase III Clinical Trial: No

Study Title: Research on tissue from an elective or spontaneous abortion < 24 weeks gestation

Planned Enrollment

Racial Categories	Ethnic Categories									Total
	Not Hispanic or Latino			Hispanic or Latino			Unknown/Not Reported Ethnicity			
	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	
American Indian/Alaska Native	0	0		0	0					0
Asian	50	0		0	0					50
Native Hawaiian or Other Pacific Islander	0	0		0	0					0
Black or African American	100	0		10	0					110
White	200	0		20	0					220
More than One Race	0	0		20	0					20
Unknown or Not Reported										
Total	**350**	**0**		**50**	**0**					**400**

Cumulative Enrollment

Racial Categories	Ethnic Categories									Total
	Not Hispanic or Latino			Hispanic or Latino			Unknown/Not Reported Ethnicity			
	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	
American Indian/Alaska Native	0	0	0	0	0	0	0	0	0	0
Asian	0	50	0	0	0	0	0	0	0	50
Native Hawaiian or Other Pacific Islander	0	0	0	0	0	0	0	0	0	0
Black or African American	0	100	0	10	0	0	0	0	0	110
White	0	200	0	20	0	0	0	0	0	220
More than One Race	0	0	0	20	0	0	0	0	0	20
Unknown or Not Reported	0	0	0	0	0	0	0	0	0	0
Total	**0**	**350**	**0**	**50**	**0**	**0**	**0**	**0**	**0**	**400**

RESEARCH & RELATED BUDGET - SECTION A & B

ORGANIZATIONAL DUNS*: 004514360

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF PITTSBURGH AT PITTSBURGH

Start Date*: 06-01-2019 **End Date*:** 05-31-2020

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1.		Rajiv		Dhir		Project Lead	(b)(6)				37,920.00	9,809.00	47,729.00
2.		(b)(6)				Co-Investigator					3,083.00	797.00	3,880.00
3.						Co-Investigator					6,165.00	1,595.00	7,760.00
4.						Co-Investigator					30,956.00	8,007.00	38,963.00
5.						Co-Investigator					23,540.00	6,089.00	29,629.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name:

Total Senior/Key Person **127,961.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
9	Supervisors, Techs, and Data Coordinator	(b)(6)			134,846.00	47,949.00	182,795.00
9	**Total Number Other Personnel**					**Total Other Personnel**	**182,795.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**310,756.00**

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E

ORGANIZATIONAL DUNS*: 004514360

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF PITTSBURGH AT PITTSBURGH

Start Date*: 06-01-2019 **End Date*:** 05-31-2020

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	**0.00**
Total Equipment	**0.00**

Additional Equipment: File Name:

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	10,200.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**10,200.00**

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		0.00
2. Stipends		0.00
3. Travel		0.00
4. Subsistence		0.00
5. Other:		
0 Number of Participants/Trainees	**Total Participant Trainee Support Costs**	**0.00**

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K

ORGANIZATIONAL DUNS*: 004514360

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF PITTSBURGH AT PITTSBURGH

Start Date*: 06-01-2019 **End Date*:** 05-31-2020

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	27,027.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. PBC Tissue embedding/processing, storage and disbursement	4,242.00
9. Website maintenance, project management tool, BIOS	8,000.00
10. New Castle Shipping costs	33,000.00
Total Other Direct Costs	**72,269.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**393,225.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. MTDC	56.5	388,983.00	219,776.00
		Total Indirect Costs	**219,776.00**

Cognizant Federal Agency U.S. Department of Health and Human Services, (b)(6)

(Agency Name, POC Name, and POC Phone Number) (b)(6)

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**613,001.00**

J. Fee	Funds Requested ($)*
	0.00

K. Budget Justification* File Name: Budget Justification Final Year 4.pdf

(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

BUDGET JUSTIFICATION – Year 4

Personnel

Rajiv Dhir, MD, MBA: PI, Effort = (b)(6) Dr. Dhir is the medical director of the Pitt Biospecimen Core (PBC) of the University of Pittsburgh and a practicing pathologist with subspecialty training in Genitourinary Pathology. He will be responsible for the oversight of the project. This will include interfacing and working with internal collaborators to ensure accrual and annotation of the appropriate specimens. He will also interact with the external collaborators and clients to ensure appropriate specimen aggregation and disbursement. He will work closely with NIDDK to ensure successful execution of the project, meeting the mission and goals of the Tissue Core. Annual effort of (b)(6) is requested.

(b)(6) Effort = (b)(6) This (b)(6) will be responsible for coordination and management of day to day operations. She supervises PBC staff members and will manage the overall efforts of the PBC and set operational standards related to the PBC scope of work. She will assure proper communication and resolution conflicts and issues.

1. **Tissue Hub Infrastructure Support**

A crucial component of this application is the infrastructure for the Tissue Hub, which will include personnel for the development and maintenance of a secure web-based interface for GUDMAP investigators, assurance of regulatory compliance, data collection and record-keeping, and management of the quality assurance program associated with this project.

(b)(6) Co-I, Effort = (b)(6) is the (b)(6) and will be the director of the Tissue hub Infrastructure. He also serves as the faculty in-charge of the informatics requirements of PBC. He provides direction and advice related to the different Information systems and tools used by PBC. He is also the director of the Imaging core; a subsidiary of PBC. The imaging core will perform whole slide image acquisition and provide access to these images for the Tissue Core clients. Annual effort of (b)(6) is requested.

(b)(6) Effort = (b)(6) This (b)(6) will be responsible for project intake, tracking and recording keeping. She will coordinate the GUDMAP investigator requests to the GUDMAP-Human Tissue Repository including documenting the needs of the investigator, assuring regulatory compliance, coordinating with tissue and data collection staff members and assuring proper completion and shipping of requests. Annual effort of (b)(6) is requested.

(b)(6) Effort = (b)(6) This (b)(6) will be responsible for the quality program. He will manage all aspects of quality management including record keeping, training of staff members to standard operating procedures (SOPs), data entry practices and audits, and quality related events. He will coordinate the overall record keeping and management of the quality metrics from the tissue collection and data entry processes with the quality measurements performed through the Department of Pediatrics team.

(b)(6) Effort = (b)(6) This (b)(6) will be responsible for overall management of the Biospecimen Inventory and Operations System with regard to the this project. He will manage the specimen search process, control the data entry lexicon as needed, and provide reports of collection activity for investigators who request samples and as needed for other purposes. He will maintain the data integrity and make corrections and amendments based on the quality control activities. In the case that new fields and library elements are required he will manage that process in conjunction with the Project Manager and Quality Manager. He will be required to produce final sample pick lists as specimens are disbursed.

(b)(6) Effort = (b)(6) is the technician responsible for processing tissues, immunohistochemistry and immunofluorescence needs of the project. He is also the supervisor of the Research Histology core facility and is responsible for the development of specialized techniques required by the program and for processes not included in the fee-for-service activity.

(b)(6) Effort = (b)(6) The (b)(6) will be responsible for aggregating information from the different information systems on the specimens offered as part of the Tissue Core. This will include pathology information as well as more specialized information (like cytogenetics); if applicable. The data coordinator will work with the Project manager on cohort identification for

the different requests. In addition the data coordinator will also be responsible for providing data to the clients of the Tissue Core.

2. Fetal Tissue Procurement Laboratory (Magee Women's Hospital)

All of the fetal tissue will be collected at Magee Women's Hospital, undergo a gross examination, and then be transported to the validation laboratory for further assessment prior to distribution.

(b)(6) **:** Co-I, Effort = (b)(6) is the (b)(6) He will be responsible for evaluating appropriate surgical pathology and autopsy specimens, and overseeing collection of the biological materials for the Tissue Core and will act as the director of the tissue procurement laboratory. He will perform the clinical evaluation of the gross genitourinary specimen and ensure quality control of the dissection to minimize mechanical disruption. He will train the staff to obtain early gestational age genitourinary specimens, and work closely with (b)(6) to perform routine and specialized histological assessment of the appropriate specimens. Annual effort of (b)(6) s requested.

Kindly note that (b)(6) retired and (b)(6) was recruited by the Unviersity of Pittsburgh as (b)(6) replacement. (b)(6) is replacing (b)(6) on the GUDMAP grant.

(b)(6) **:** Effort = (b)(6) This PBC tissue bank technician and will perform the day-to-day tasks associated with the collection of specimens. This includes maintaining a working knowledge of all SOPs related to the ongoing collections that are requested by the GUDMAP investigators. She will coordinate with the clinical departments within Magee Women's Hospital of UPMC, interface with the Pathology and other hospital staff members as required to obtain the requested specimens and enter data related to each case in the BIOS.

(b)(6) Effort = (b)(6) This (b)(6) and technician will perform the day-to-day tasks associated with the collection of specimens. This includes maintaining a working knowledge of all SOPs related to the ongoing collections that are requested by the GUDMAP investigators. She will coordinate with the clinical departments within Magee Women's Hospital of UPMC, interface with the Pathology and other hospital staff members as required to obtain the requested specimens and enter data related to each case in the BIOS.

3. Validation Laboratory (Children's Hospital of Pittsburgh)

The validation laboratory will perform quality assurance measures, as per GUDMAP project needs (eg. histological assessment, *in situ* hybridization and RNA isolation).

(b)(6) Co-I, Effort = (b)(6) is a kidney developmental biologist with over (b)(6) studying the genitourinary tract and will act as the director of the validation laboratory. Furthermore, he is also a classically trained human anatomist, histologist and embryologist. The quality assurance of the specimens will be performed by at least two independent evaluations (b)(6) for GUDMAP project needs. (b)(6) will work closely with (b)(6) to train staff to perform the gross dissection for early gestational age genitourinary tissues, and tissues not currently being obtained by the Tissue Bank, as per GUDMAP project needs. He will also oversee the training of (b)(6) (tissue hub technician) in all aspects of dissection, histology and molecular evaluation of the fetal tissues.

(b)(6) **:** Co-I, Effort = (b)(6) is a clinician scientist (Pediatric Nephrologist) with a research program related to kidney development and will act as the co-director of the validation laboratory. She has a thorough understanding of genitourinary development. She will participate in quality assurance of specimens as noted above. Furthermore, (b)(6) will provide direction and advice regarding the clinical parameters that will be used to screen fetal and neonatal tissues to exclude pathological specimens, and will evaluate individual cases as needed.

(b)(6) **:** Effort = (b)(6) This grant will fund (b)(6) of the technicians salary. This technician will perform all the required validation of the specimens including: histology, immunohistochemistry, in situ hybridization, cell isolation and real time PCR.

Supplies

PBC Consumable Laboratory Supplies: (b)(4) is requested for sample collections, integrity, maintenance, and transport including sample and shipping containers, dry ice, and other basic supplies.

Shipping: Funds are requested for the shipment of tissue from New Castle, UK to the participating GUDMAP investigators, $33,000 is requested in year 4.

Validation Laboratory Consumable Laboratory Supplies: (b)(4) monthly will be required to purchase reagents for staining, immunohistochemistry and in situ reagents as well as cell, culture medium and consumable plastics related to these processes. These processes will be performed in response to the needs of the GUDMAP investigators.

Travel

Pathology: The Project PI and PBC staff will need to travel to GUDMAP consortia meetings, to be held twice a year. A total of $4,200 is allocated for this travel in year 4.

Validation Laboratories: The Project co-investigators will need to travel to GUDMAP consortia meetings, to be held twice a year. (b)(6) will also attend the American Society of Nephrology meeting where GUDMAP typically has a booth. A total of $6,000 is allocated for this travel in year 4.

Other Expenses

Tissue embedding/processing, storage, and disbursement: $4,242 for year 4. These are billable services based on the fiscal parameters in place within the University of Pittsburgh for the PBC. Tissue embedding and processing will be required at all levels for quality management and to provide product to GUDMAP investigators. Storage costs are based on the partial cost of a freezer with a 10 year life span plus projected maintenance and certification costs. The cost for disbursement of samples to GUDMAP investigators will be charged to the account award for this project.

Website maintenance, project management tool, BIOS, image acquisition: $8,000. Resources will be required to maintain and update our internally developed inventory management system (BIOS). The project management tool is internally developed and is the mechanism for starting and following the progress of the request from the client. The clients will be provided access to the contents of the resource via a Sharepoint link that will be password protected. Whole slide image acquisition will be done to offer clients access to high quality images of the specimens in the resource. These images will be from routine and specialized histologic and immunohistochemical/ in-situ protocols. We also have capabilities for image analysis and will offer, if required.

Notice of Award

RESOURCE-RELATED COOPERATIVE AGREEMENT PROJECTS **Federal Award Date:** 01/15/2020

Department of Health and Human Services
National Institutes of Health
NATIONAL INSTITUTE OF DIABETES AND DIGESTIVE AND KIDNEY DISEASES

Grant Number: 5U24DK110791-03 REVISED
FAIN: U24DK110791

Principal Investigator(s):
RAJIV DHIR, MD

Project Title: University of Pittsburgh as the GUDMAP Tissue Hub and Collection Site

(b)(6)
University of Pittsburgh
123 University Place, B21
Grants and Contracts Officer
Pittsburgh, PA 152132303

Award e-mailed to: ornih@offres.pitt.edu

Period Of Performance:
Budget Period: 06/01/2018 – 05/31/2019
Project Period: 09/15/2016 – 05/31/2021

Dear Business Official:

The National Institutes of Health hereby revises this award (see "Award Calculation" in Section I and "Terms and Conditions" in Section III) to UNIVERSITY OF PITTSBURGH AT PITTSBURGH in support of the above referenced project. This award is pursuant to the authority of 42 USC 241 31 USC 6305 42 CFR 52 and is subject to the requirements of this statute and regulation and of other referenced, incorporated or attached terms and conditions.

Acceptance of this award including the "Terms and Conditions" is acknowledged by the grantee when funds are drawn down or otherwise obtained from the grant payment system.

Each publication, press release, or other document about research supported by an NIH award must include an acknowledgment of NIH award support and a disclaimer such as "Research reported in this publication was supported by the National Institute Of Diabetes And Digestive And Kidney Diseases of the National Institutes of Health under Award Number U24DK110791. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health." Prior to issuing a press release concerning the outcome of this research, please notify the NIH awarding IC in advance to allow for coordination.

Award recipients must promote objectivity in research by establishing standards that provide a reasonable expectation that the design, conduct and reporting of research funded under NIH awards will be free from bias resulting from an Investigator's Financial Conflict of Interest (FCOI), in accordance with the 2011 revised regulation at 42 CFR Part 50 Subpart F. The Institution shall submit all FCOI reports to the NIH through the eRA Commons FCOI Module. The regulation does not apply to Phase I Small Business Innovative Research (SBIR) and Small Business Technology Transfer (STTR) awards. Consult the NIH website http://grants.nih.gov/grants/policy/coi/ for a link to the regulation and additional important information.

If you have any questions about this award, please contact the individual(s) referenced in Section IV.

Sincerely yours,

(b)(6)

Grants Management Officer
NATIONAL INSTITUTE OF DIABETES AND DIGESTIVE AND KIDNEY DISEASES

Additional information follows

SECTION I – AWARD DATA – 5U24DK110791-03 REVISED

Award Calculation (U.S. Dollars)

Salaries and Wages	$208,341
Fringe Benefits	$65,717
Personnel Costs (Subtotal)	$274,058
Materials & Supplies	$18,980
Travel	$7,451
Other	$32,729
ADP/Computer Services	$5,499
Federal Direct Costs	$338,717
Federal F&A Costs	$188,668
Approved Budget	$527,385
Total Amount of Federal Funds Obligated (Federal Share)	$527,385
Less Unobligated Balance	$106,761
TOTAL FEDERAL AWARD AMOUNT	$420,624
AMOUNT OF THIS ACTION (FEDERAL SHARE)	$0

SUMMARY TOTALS FOR ALL YEARS		
YR	**THIS AWARD**	**CUMULATIVE TOTALS**
3	$420,624	$420,624
4	$613,001	$613,001
5	$613,001	$613,001

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

Fiscal Information:

CFDA Name:	Diabetes, Digestive, and Kidney Diseases Extramural Research
CFDA Number:	93.847
EIN:	1250965591A1
Document Number:	UDK110791A
PMS Account Type:	P (Subaccount)
Fiscal Year:	2018

IC	CAN	2018	2019	2020
DK	8472288	$420,624	$613,001	$613,001

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

NIH Administrative Data:
PCC: KDH KDB / **OC**: 41029 / **Released**: (b)(6) 01/15/2020
Award Processed: 01/15/2020 07:00:54 PM

SECTION II – PAYMENT/HOTLINE INFORMATION – 5U24DK110791-03 REVISED

For payment and HHS Office of Inspector General Hotline information, see the NIH Home Page at http://grants.nih.gov/grants/policy/awardconditions.htm

SECTION III – TERMS AND CONDITIONS – 5U24DK110791-03 REVISED

This award is based on the application submitted to, and as approved by, NIH on the above-titled project and is subject to the terms and conditions incorporated either directly or by reference in the following:

a. The grant program legislation and program regulation cited in this Notice of Award.
b. Conditions on activities and expenditure of funds in other statutory requirements, such as those included in appropriations acts.
c. 45 CFR Part 75.

d. National Policy Requirements and all other requirements described in the NIH Grants Policy Statement, including addenda in effect as of the beginning date of the budget period.
e. Federal Award Performance Goals: As required by the periodic report in the RPPR or in the final progress report when applicable.
f. This award notice, INCLUDING THE TERMS AND CONDITIONS CITED BELOW.

(See NIH Home Page at http://grants.nih.gov/grants/policy/awardconditions.htm for certain references cited above.)

Research and Development (R&D): All awards issued by the National Institutes of Health (NIH) meet the definition of "Research and Development" at 45 CFR Part§ 75.2**.** As such, auditees should identify NIH awards as part of the R&D cluster on the Schedule of Expenditures of Federal Awards (SEFA). The auditor should test NIH awards for compliance as instructed in Part V, Clusters of Programs. NIH recognizes that some awards may have another classification for purposes of indirect costs. The auditor is not required to report the disconnect (i.e., the award is classified as R&D for Federal Audit Requirement purposes but non-research for indirect cost rate purposes), unless the auditee is charging indirect costs at a rate other than the rate(s) specified in the award document(s).

Carry over of an unobligated balance into the next budget period requires Grants Management Officer prior approval.

This award is subject to the requirements of 2 CFR Part 25 for institutions to receive a Dun & Bradstreet Universal Numbering System (DUNS) number and maintain an active registration in the System for Award Management (SAM). Should a consortium/subaward be issued under this award, a DUNS requirement must be included. See http://grants.nih.gov/grants/policy/awardconditions.htm for the full NIH award term implementing this requirement and other additional information.

This award has been assigned the Federal Award Identification Number (FAIN) U24DK110791. Recipients must document the assigned FAIN on each consortium/subaward issued under this award.

Based on the project period start date of this project, this award is likely subject to the Transparency Act subaward and executive compensation reporting requirement of 2 CFR Part 170. There are conditions that may exclude this award; see http://grants.nih.gov/grants/policy/awardconditions.htm for additional award applicability information.

In accordance with P.L. 110-161, compliance with the NIH Public Access Policy is now mandatory. For more information, see NOT-OD-08-033 and the Public Access website: http://publicaccess.nih.gov/.

In accordance with the regulatory requirements provided at 45 CFR 75.113 and Appendix XII to 45 CFR Part 75, recipients that have currently active Federal grants, cooperative agreements, and procurement contracts with cumulative total value greater than $10,000,000 must report and maintain information in the System for Award Management (SAM) about civil, criminal, and administrative proceedings in connection with the award or performance of a Federal award that reached final disposition within the most recent five-year period. The recipient must also make semiannual disclosures regarding such proceedings. Proceedings information will be made publicly available in the designated integrity and performance system (currently the Federal Awardee Performance and Integrity Information System (FAPIIS)). Full reporting requirements and procedures are found in Appendix XII to 45 CFR Part 75. This term does not apply to NIH fellowships.

Treatment of Program Income:
Other Research (Add/Deduct Option)

Clinical Trial Indicator: No
This award does not support any NIH-defined Clinical Trials. See the NIH Grants Policy Statement Section 1.2 for NIH definition of Clinical Trial.

This revision reflects an authorized carryover of $106,761 ($68,275 direct costs and $38,486 F&A costs) from the -02 year as requested on and may be used for the stated purpose only.

The following terms from the previous Notice of Award also apply to this award:

RESTRICTION: Funds may only be used to pay for the cost of acquiring, processing and shipping tissue samples to the GUDMAP atlas projects. This includes covering the cost of processing and shipping tissue from external sources.

Notice: Under governing regulations, Federal funds administered by the Department of Health and Human Services shall not be expended for research involving human subjects, and individuals shall not be enrolled in such research, without prior approval by the Office of Human Research Protections (OHRP) of an assurance to comply with the requirements of 45 CFR 46 to protect human research subjects. This restriction applies to all collaborating sites without OHRP-approved assurances, whether domestic or foreign, and compliance must be ensured by the awardee.

Notice: Under governing policy, federal funds administered by the Public Health Service (PHS) shall not be expended for research involving live vertebrate animals without prior approval by the Office of Laboratory Animal Welfare (OLAW) of an assurance to comply with the PHS policy on humane care and use of laboratory animals. This restriction applies to all performance sites (e.g., collaborating institutions, subcontractors, subgrantees) without OLAW-approved assurances, whether domestic or foreign.

The issuance of this award has been delayed due to administrative funding considerations. According to NIH policy, if pre-award costs are necessary, they may be approved by the authorized Institution Official(s).

In addition to the PI, the following individuals are named as key personnel:

(b)(6)

Written prior approval is required if any of the individual(s) named above withdraws from the project entirely, is absent from the project during any continuous period of 3 months or more, or reduces time devoted to the project by 25 percent or more from the level that was approved at the time of award.

This grant is in response to RFA/PA DK15-016. Acceptance of this award requires compliance with this solicitation. See the NIH Guide at http://grants.nih.gov/grants/guide/index.html for copy of the RFA/PA that includes administrative and programmatic requirements specific to this award.

In accordance with NIH Guide Notice NOT-OD-18-137, Notice of Salary Limitation on Grants, Cooperative Agreements, and Contracts, none of the funds in this award shall be used to pay the salary of an individual at a rate in excess of the applicable salary cap. Therefore, this award and/or future years are adjusted accordingly, if applicable. See the Salary Cap Summary for a historical record of the salary cap, including effective dates.

Grantees can determine which progress reports are due through the website located at https://public.era.nih.gov/chl/public/search/index.jsp and should periodically check the site, which is updated on or around the 30th of each month. Progress report due dates are also available in the eRA Commons Status system. In addition, automatic e-mail notifications are sent to the PD/PI prior to due date.

As of October 17, 2014, the National Institutes of Health (NIH) requires grantees to submit all type 5 progress reports using the eRA Research Performance Progress Report (RPPR) module. Annual progress reports submitted in any format other than the RPPR will not be

processed by the NIH and will require resubmission through the RPPR module in accordance with NIH Guide Notice NOT-OD-15-014 released October 16, 2014.

The following special terms of award are in addition to, and not in lieu of, otherwise applicable U.S. Office of Management and Budget (OMB) administrative guidelines, U.S. Department of Health and Human Services (DHHS) grant administration regulations at 45 CFR Parts 74 and 92 (Part 92 is applicable when State and local Governments are eligible to apply), and other HHS, PHS, and NIH grant administration policies.

The administrative and funding instrument used for this program will be the cooperative agreement, an "assistance" mechanism (rather than an "acquisition" mechanism), in which substantial NIH programmatic involvement with the awardees is anticipated during the performance of the activities.

Under the cooperative agreement, the NIH purpose is to support and stimulate the recipients' activities by involvement in and otherwise working jointly with the award recipients in a partnership role; it is not to assume direction, prime responsibility, or a dominant role in the activities. Consistent with this concept, the dominant role and prime responsibility resides with the awardees for the project as a whole, although specific tasks and activities may be shared among the awardees and the NIH as defined below.

The PD(s)/PI(s) will have the primary responsibility for:

- All aspects of the scientific activities, including defining the objectives and approaches, planning, conduct, analysis, and publication of results, interpretations, and conclusions of studies conducted under the terms and conditions of the cooperative agreement award.
- Collaborating with other investigators in the program for protocol development, sample, reagents and data sharing as appropriate, data quality control, and data organization
- Accountability towards the applicant organization officials and to the NIDDK for the performance and proper conduct of the research supported by the project in accordance with the terms and conditions of the award.
- Serving as a voting member of the Steering Committee and will attend the Planning Meeting and a Steering Committee meeting in the first year, two Steering Committee meetings a year in subsequent years and monthly teleconference calls.
- Accepting and implementing the goals, priorities, procedures, protocols, and policies agreed upon by the Steering Committee and subcommittees, and be responsible for close coordination and cooperation with the components of the GUDMAP consortium and with NIDDK staff.
- Adhering to PHS policy for the distribution of unique research resources produced with PHS funding as described under Special Requirements.
- Establishing written milestones for the project, in negotiation with NIDDK Project Staff prior to funding.
- Release all study design materials and procedure manuals into the public domain and/or make them available to other investigators, according to the approved plan for making data and materials available to the scientific community and the NIDDK, for the conduct of research at no charge other than the costs of reproduction and distribution, consistent with achieving the goals of this program initiative.
- Awardees will retain custody of and have primary rights to the data and software developed under these awards, subject to Government rights of access consistent with current DHHS, PHS, and NIH policies.

NIH staff will have substantial programmatic involvement that is above and beyond the normal stewardship role in awards, as described below:

- An NIH Project Scientist will have substantial programmatic involvement that is above and beyond the normal stewardship role in awards, as described below. However, the dominant role and prime responsibility for the project as a whole resides with the awardees, although specific tasks and activities in carrying out the studies will be shared by awardees and the NIDDK.
- NIDDK will designate a Project Officer and a Grants Management Specialist to provide normal program stewardship and administrative oversight of the cooperative agreement.
- NIDDK will form an External Advisory Committee (EAC), comprised of the NIDDK Project Scientist and other NIH extramural staff with relevant scientific expertise or who manage research grant programs that relate scientifically to the goals of the GUDMAP projects,

and outside advisors selected by the NIDDK. The EAC will meet annually with the GUDMAP Steering Committee to review and assess GUDMAP and to advise NIDDK of scientific developments and opportunities that may enhance the achievement of the GUDMAP goals.

- The NIDDK Project Scientist will attend and participate as a voting member in all meetings of the Steering Committee, and provide liaison between the Steering Committee and the External Advisory Committee.
- The NIDDK Project Scientist will help the Steering Committee develop and draft operating policies.
- The NIDDK Project Officer will review the scientific progress of the individual GUDMAP components, for compliance with operating policies developed by the Steering Committee, and may recommend to the NIDDK to withhold support, suspend, or terminate an award for lack of scientific progress or failure to adhere to policies established by the Steering Committee.
- An agency program official or IC program director will be responsible for the normal scientific and programmatic stewardship of the award and will be named in the award notice. The assigned Program Officer may also serve as an NIDDK Project Scientist.

Areas of Joint Responsibility include:

- Steering Committee - The NIDDK Project Scientist, PIs from the project funded through this FOA and RFA-DK-15-014, and RFA-DK-15-015 and voluntary representatives from the previously funded GUDMAP atlas projects funded under RFA-DK-11-001 will be responsible for forming a Steering Committee as defined below. An arbitration system, as detailed below, will be available to resolve disagreements among members of the Steering Committee. The Steering Committee will be the main governing board of the GUDMAP consortium. It will develop collaborative protocols, identify technological impediments to success and strategies to overcome them, develop shared software tools for disseminating information about the projects, and identify opportunities for sharing techniques and tools that might be developed in future GUDMAP atlas projects.
- The Steering Committee will be composed of the PIs from the project funded through this FOA, RFA-DK-15-014, and RFA-DK-15-015, representatives from the previously funded GUDMAP projects, and the NIDDK Project Scientist. The representatives and the PIs will each have one vote. The NIDDK Project Scientist for this project will have one vote. The Steering Committee will select a chairperson who will be someone other than an NIH staff member.
- The Steering Committee may, as it deems necessary, invite additional, non-voting scientific advisors to meetings at which research priorities and opportunities are discussed. The NIH reserves the right to augment the scientific or consumer expertise of the Steering Committee when necessary.
- There will be two Steering Committee meetings annually. The first meeting will be a Planning Meeting to be held in the Washington, DC area on **June 20-21, 2016**. At the Planning Meeting, the Steering Committee will be formed and a chairperson selected from among the members. At the Planning Meeting, the Steering Committee may: (a) draft a charter to detail policies and procedures, a process for monitoring compliance with the policies and procedures, and a process for recommending that the NIDDK Project Administrators act on evidence of non-compliance of any Consortium component with Steering Committee policies; (b) agree upon the terms of the charter; and (c) devise a plan for working with the GUDMAP database developers to provide ongoing input into database and website design.
- At the second and subsequent meetings, the Steering Committee will refine the GUDMAP scientific objectives and implementation as necessary, consistent with data produced by former and possible future GUDMAP atlas projects and from other laboratories.
- The Steering Committee will plan workshops, to which non-GUDMAP participants will also be invited, to inform the research community of the progress made toward development of the atlas, and to inform the research community of any technological advances related to the implementation of the GUDMAP website/database. The NIDDK Project Scientist, the External Advisory Committee, and other NIH staff as appropriate will provide the Steering Committee with advice on participants for the workshops and symposia.
- The Steering Committee may establish subcommittees as it deems appropriate.
- Awardee members of the Steering Committee will be required to accept and implement policies approved by the Steering Committee.

- The EAC will meet annually with the GUDMAP Steering Committee to review and assess the progress of the GUDMAP consortium and to advise NIDDK of scientific developments and opportunities that may enhance the achievement of the GUDMAP goals.

Dispute Resolution
Any disagreements that may arise in scientific or programmatic matters (within the scope of the award) between award recipients and the NIH may be brought to Dispute Resolution. A Dispute Resolution Panel will have three members: a designee of the Steering Committee chosen without NIH staff voting, one NIH designee, and a third designee with expertise in the relevant area who is chosen by the other two; in the case of individual disagreement, the first member may be chosen by the individual awardee. This special dispute resolution procedure does not alter the awardee's right to appeal an adverse action that is otherwise appealable in accordance with PHS regulation 42 CFR Part 50, Subpart D and DHHS regulation 45 CFR Part 16.
- See more at: http://grants.nih.gov/grants/guide/rfa-files/RFA-DK-15-016.html#sthash.UY9M5nfL.dpuf

STAFF CONTACTS

The Grants Management Specialist is responsible for the negotiation, award and administration of this project and for interpretation of Grants Administration policies and provisions. The Program Official is responsible for the scientific, programmatic and technical aspects of this project. These individuals work together in overall project administration. Prior approval requests (signed by an Authorized Organizational Representative) should be submitted in writing to the Grants Management Specialist. Requests may be made via e-mail.

Grants Management Specialist: (b)(6)
Email: (b)(6) @extra.niddk.nih.gov **Phone**: (b)(6) **Fax**: (b)(6)

Program Official: (b)(6)
Email: (b)(6) @niddk.nih.gov **Phone**: (b)(6)

SPREADSHEET SUMMARY
GRANT NUMBER: 5U24DK110791-03 REVISED

INSTITUTION: UNIVERSITY OF PITTSBURGH AT PITTSBURGH

Budget	Year 3	Year 4	Year 5
Salaries and Wages	$208,341	$226,544	$226,544
Fringe Benefits	$65,717	$71,911	$71,911
Personnel Costs (Subtotal)	$274,058	$298,455	$298,455
Materials & Supplies	$18,980	$27,490	$27,490
Travel	$7,451	$10,792	$10,792
Other	$32,729	$46,992	$46,992
ADP/Computer Services	$5,499	$7,965	$7,965
TOTAL FEDERAL DC	$338,717	$391,694	$391,694
TOTAL FEDERAL F&A	$188,668	$221,307	$221,307
TOTAL COST	$420,624	$613,001	$613,001

Facilities and Administrative Costs	Year 3	Year 4	Year 5
F&A Cost Rate 1	55.5%	56.5%	56.5%
F&A Cost Base 1	$31,095	$391,694	$391,694
F&A Costs 1	$17,258	$221,307	$221,307
F&A Cost Rate 2	56.5%		
F&A Cost Base 2	$303,380		
F&A Costs 2	$171,410		

A. OVERALL COVER PAGE

Project Title: University of Pittsburgh as the GUDMAP Tissue Hub and Collection Site	
Grant Number: 5U24DK110791-03	**Project/Grant Period:** 09/15/2016 - 05/31/2021
Reporting Period: 06/01/2017 - 05/31/2018	**Requested Budget Period:** 06/01/2018 - 05/31/2019
Report Term Frequency: Annual	**Date Submitted:** 04/02/2018
Program Director/Principal Investigator Information: RAJIV DHIR , MD **Phone number:** (412) 623-1321 **Email:** dhirr@upmc.edu	**Recipient Organization:** UNIVERSITY OF PITTSBURGH AT PITTSBURGH UNIVERSITY OF PITTSBURGH OFFICE OF RESEARCH PITTSBURGH, PA 152132303 **DUNS:** 004514360 **EIN:** 1250965591A1 **RECIPIENT ID:**
Change of Contact PD/PI: N/A	
Administrative Official: (b)(6) UNIVERSITY OF PITTSBURGH 123 University Place Room B21 PITTSBURGH, PA 15213 **Phone number:** (b)(6) **Email:** (b)(6) @pitt.edu	**Signing Official:** (b)(6) UNIVERSITY OF PITTSBURGH 123 University Place Room B21 PITTSBURGH, PA 15213 **Phone number:** (b)(6) **Email:** (b)(6) @pitt.edu
Human Subjects: Yes HS Exempt: No Exemption Number: Phase III Clinical Trial:	**Vertebrate Animals:** No
hESC: No	**Inventions/Patents:** No

B. OVERALL ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

Aim 1: To generate an inventory of genitourinary tissue throughout normal human development The main goal of this aim is to develop a pipeline for the acquisition, quality control and distribution of human genitourinary samples obtained throughout development (6-42 weeks gestation). We currently have access to 6-24 week samples through the HSTB. However, for later gestational stages (25-42 weeks gestation) we have partnered with the International institute for the Advancement of Medicine. This will provide access to a novel resource for neonatal donation. We aim to collect and store a minimum of 5 samples per developmental week. Each of these samples will have histology, immunohistochemistry and in situ hybridization performed to assess tissue quality, protein and RNA integrity. Furthermore, we will obtain maternal blood, urine and amniotic fluid; based on the clinical situation and ability to procure. Based on our current experience, we get these biological
materials in most cases. Anonymized demographic information of each specimen will also be provided.

Aim 2: To provide fresh genitourinary tissue and biological research specimens This aim will generate an ongoing resource to distribute fresh developmental human genitourinary samples
from various stages (6-42 weeks) to the GUDMAP Atlas projects. The samples will be procured by a pathologist and inspected for mechanical damage. Samples will be collected from all qualified cases. The samples will then be subdivided based on the demand for fresh/frozen aliquots; the validation laboratory for quality control will keep a portion of each sample. The tissue samples will be immediately sent out for live cell use or immediately separated into distinct cellular populations before shipping based on researcher demands. Permissible annotating information; including demographics of each specimen, will also be provided.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

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B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

For this reporting period, is there one or more Revision/Supplement associated with this award for which reporting is required?

No

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

NOTHING TO REPORT

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

There is very active e-mail and phone communication between the GUDMAP investigators, the Data Hub and the Tissue Hub. In addition, the Tissue Hub activities account for approximately 50% of the 90 minute long monthly consortium video conference calls.

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

Continue providing materials to requesting investigators within the consortia. We will be performing extensive analyses on collected specimens both from a quality assessment perspective as well as to potentially assist GUDMAP investigators with specific pathology needs related to either localization studies and/or imaging.

ACCOMPLISHMENTS

Summary

The goal of this project is to provide human genitourinary tissues (kidneys, ureters, bladders and genital structures) to research projects funded in the GenitoUrinary Development Molecular Anatomy Project (GUDMAP), as part of a consortium to build a molecular atlas of human genitourinary development.

Institutional Review Board (IRB) and Material Transfer Agreement (MTA):

The IRB for the Health Sciences Tissue Bank at the University of Pittsburgh for the collection of biospecimens from products of conception has been approved with the following modifications: (1) to allow for sharing with external investigators, (2) to include verbiage related to genomic and molecular testing in the consents; and (3) to include a new consent form for specimens from autopsy materials/ stillbirths. As per regulations, the autopsy material needed appropriate Committee for Oversight of Research and Clinical Training Involving Decedents (CORID) vetting. The IRB for the GUDMAP consortium was an expedited submission working off the biospecimen collection IRB and is approved. The MTAs for sharing biospecimens with GUDMAP consortium members are in place.

Biospecimen Collection/Quality Control:

The Tissue Hub has been actively shipping biospecimens to GUDMAP consortium members since June 2017. The Tissue Hub maintains active monthly communications with the consortium members to ascertain specific biospecimen and processing needs. These have typically comprised monthly emails or phone calls between Health Sciences Tissue Bank staff, GUDMAP PIs, and (b)(6) The interface between the Tissue Hub and the tissue projects is very collaborative in nature and decisions in the best interest of the individual investigators is easily facilitated in this manner. (b)(6) has been overseeing the collection and dissection of the specimens to accrue genitourinary specimens.

As part of the quality control process, the Validation Laboratory performs genotyping on all biospecimens to document gender, in addition to an anatomical assessment. The Validation Laboratory has also performed pilot studies in collaboration with project PIs to identify optimal means of sample processing for the downstream applications for individual organs. For example, the validation laboratory performed tests of RNA quality following biospecimen collection in RPMI, storage and RNA isolation, compared to placing biospecimens in OCT, isolation of a subset of the tissue and RNA isolation. (b)(6) and his lab have been receiving and utilizing specimens and assessing different modalities to ensure the highest quality specimens for the consortium members for their respective needs. The monthly feedback from GUDMAP investigators has been consistently positive regarding the tissue quality that has been received. With the appropriate regulatory approvals and MTAs in place, the Tissue Hub is actively providing biospecimens to the GUDMAP investigators as outlined in Table 1.

Table 1. Biospecimen disbursements from Tissue Hub to GUDMAP investigators.

GUDMAP Investigator	Fresh Tissue Disbursements June 1, 2017- March 1, 2018	Frozen Tissue Disbursements June 1, 2017- March 1, 2018
(b)(6)	(b)(4)	

(b)(6)	(b)(4)
Totals	

The GUDMAP investigators identified a research need for biospecimens that could not be provided through the Health Sciences Tissue Bank at the University of Pittsburgh given how the biospecimens are collected. Given this, the Tissue Hub developed a mechanism by which GUDMAP investigators can obtain these tissues through the Human Developmental Biology Resource (HDBR), and currently covers all the costs to the GUDMAP investigators for these shipments. The current numbers are provided in Table 2. The volume of shipments from HDBR to GUDMAP investigators is expected to increase significantly in the next funding cycle, as GUDMAP investigators have requested that they receive shipments of individual fresh biospecimens in culture media, as opposed to shipments of frozen tissue that can be grouped together. In pilot data, this method of tissue preservation and shipping has been most robust for downstream applications, particularly as it pertains to highthroughput RNA sequencing.

Table 2. Shipments from Human Developmental Biology Resource (HDBR) to GUDMAP investigators.

GUDMAP Investigator	June 1, 2017- March 1, 2018
(b)(6)	(b)(4)
Totals	

Information Technology Initiatives:
The Tissue Hub has developed inventory and data management tools internally to appropriately annotate the GUDMAP tissue collections. The Tissue Hub, in concert with the PIs of the GUDMAP projects, have defined de-identified clinical information that is collected for each of the biospecimens. Biospecimens are linked to barcodes, and provided to GUDMAP PIs, which allows for access to de-identified clinical information should it be required for the individual projects.

C. OVERALL PRODUCTS

C.1 PUBLICATIONS

Are there publications or manuscripts accepted for publication in a journal or other publication (e.g., book, one-time publication, monograph) during the reporting period resulting directly from this award?

No

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Nothing to report

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Have inventions, patent applications and/or licenses resulted from the award during the reporting period? No

If yes, has this information been previously provided to the PHS or to the official responsible for patent matters at the grantee organization?

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Category	Explanation
Data or Databases	The data collected and provided by the Hub will be in two broad categories. Firstly, we will provide annotation information related to the specimens collected for the GUDMAP investigators. The data elements to be collected have been defined by the consortium. The data will be securely provided to the Data Hub, which will host this information. The second major data component will be imaging data generated from the specimens and slides etc. In addition, molecular data will also be generated from select specimens.
Research Material	The Tissue Hub will collect specimens as per the needs of the GUDMAP investigators. The biospecimens will be both from surgical pathology specimens (products of conception) as well as autopsy material (still-births). In addition, additional specimens may be collected depending on investigator and programmatic needs and direction. The specimen types that can be accrued, and possible specimen accrual limitations, have been discussed with consortia members. Collection protocols will continue to be modified and fine-tuned to reflect the needs and the reality of human biospecimen collections; since diagnostic assessment is the primary purpose.

D. OVERALL PARTICIPANTS

D.1 WHAT INDIVIDUALS HAVE WORKED ON THE PROJECT?

Commons ID	S/K	Name	Degree(s)	Role	Cal	Aca	Sum	Foreign Org	Country	SS
(b)(6)	Y	DHIR, RAJIV	MD	PD/PI	(b)(6)					NA
	N	(b)(6)		Technician						NA
	N			Technician						NA
	N			Technician						NA
(b)(6)	N		BS,MS,MD	Co-Investigator						NA
	N			QC Manager						NA
(b)(6)	Y		BS,OTH,PHD	Co-Investigator						NA
	N			Data Coordinator						NA
	N			HSTB Supervisor						NA
	N			Project Manager						NA
	N			Co-Investigator						NA
(b)(6)	N			Co-Investigator						NA

Glossary of acronyms:
S/K - Senior/Key
DOB - Date of Birth
Cal - Person Months (Calendar)
Aca - Person Months (Academic)
Sum - Person Months (Summer)
Foreign Org - Foreign Organization Affiliation
SS - Supplement Support
RE - Reentry Supplement
DI - Diversity Supplement
OT - Other
NA - Not Applicable

D.2 PERSONNEL UPDATES

D.2.a Level of Effort

Will there be, in the next budget period, either (1) a reduction of 25% or more in the level of effort from what was approved by the agency for the PD/PI(s) or other senior/key personnel designated in the Notice of Award, or (2) a reduction in the level of effort below the minimum amount of effort required by the Notice of Award?

No

D.2.b New Senior/Key Personnel

Are there, or will there be, new senior/key personnel?

No

D.2.c Changes in Other Support

Has there been a change in the active other support of senior/key personnel since the last reporting period?

Yes

File uploaded: Other Support.pdf

D.2.d New Other Significant Contributors

Are there, or will there be, new other significant contributors?

No

D.2.e Multi-PI (MPI) Leadership Plan

Will there be a change in the MPI Leadership Plan for the next budget period?

NA

For New and Renewal Applications (PHS 398) – DO NOT SUBMIT UNLESS REQUESTED

PHS 398 OTHER SUPPORT

Provide active and pending support for all senior/key personnel. **Other Support includes all financial resources, whether Federal, non-Federal, commercial or institutional, available in direct support of an individual's research endeavors, including but not limited to research grants, cooperative agreements, contracts, and/or institutional awards.** Training awards, prizes, or gifts do not need to be included.

There is no "form page" for other support. Information on other support should be provided in the *format* shown below, using continuation pages as necessary. ***Include the principal investigator's name at the top and number consecutively with the rest of the application.*** The sample below is intended to provide guidance regarding the type and extent of information requested.
For instructions and information pertaining to the use of and policy for other support, see Other Support in the Supplemental Instructions, Part III, Policies, Assurances, Definitions, and Other Information.
Effort devoted to projects must be measured using person months. Indicate calendar, academic, and/or summer months associated with each project.

Format

NAME OF INDIVIDUAL **Rajiv Dhir, MD, MBA**
ACTIVE/PENDING

ACTIVE

U19 OH009077-08 (Becich) 09/01/2006–08/31/2021 (b)(6)
CDC $35,688
National Mesothelioma Virtual Bank for Translational Research
The proposed Mesothelioma Virtual Bank (MVB) for Translational Research will create and maintain infrastructure to support a national virtual patient registry and tissue bank. MVB proposes to create and maintain a set of resources through a cooperative working group that will make available their independent stores of mesothelioma tissue for public access.

P30CA047904 (Chu) 08/01/2015-07/31/2020 (b)(6)
NIH $84,621
Cancer Center Support Grant
Dr. Dhir directs the Tissue and Research Pathology Services (TARPS) portion of the UPCI Cancer Center Support Grant

UM1CA18669003 (Chu) 03/01/2016-2/28/2017 (b)(6)
NIH $24,283
NCI ET-CTN with Phase 1 Emphasis at UPCI
Our institution is working to transform the NCI-sponsored cooperative experimental therapeutics clinical trials program from a series of separate institutions conducting early-phase cancer treatment trials to a new consolidated, integrated Program, referred to as the NCI Experimental Therapeutics-Clinical Trials Network (ET-CTN).

U01HL12895403 (Wisniewski/Sciurba) 08/01/2015-07/31/2020 (b)(6)
NIH $11,678
Network Management Core (NEMO) for the Pulmonary Trials Cooperative (PTC)
The NEMO will have primary responsibility for organizing and operating this multi-center cooperative which conducts multiple simple clinical trials in both inpatient and outpatient settings in adults with a variety of chronic pulmonary diseases, including but not limited to interstitial lung disease (ILD), pulmonary hypertension (PH), chronic obstructive pulmonary disease (COPD), sarcoidosis, and obstructive sleep apnea, but excluding asthma and acute lung injury and critical care.

Federal Contract (Sciurba) 03/01/2016-2/28/2019 (b)(6)
NIH $30,131
Lung Tissue Research Consortium (LTRC): Clinical Centers
Contribute to the lung tissue Research consortium by meeting necessary subject recruitment goals, Providing high quality specimens and offering expertise in innovative Techniques in subject characterization, metagenomic characterization of The microbiome and gene expression analysis.

16X018 Federal Contract (Dhir) 09/30/2015-9/29/2018 (b)(6)
Leidos $399,895
Clinical Proteomic Tumor Analysis Consortium Phase III Tissue Source Site
These analyses will serve to clarify how the molecular biology facilitates refinement of driver genes, enhances understanding of the pathogenesis through proteomic subtyping, and illuminates dynamic alterations in post translational modifications responsible for the disregulation of cancer signaling networks and pathways; in essence, providing novel information for regarding the molecular biology of cancer.

1U54DK112079 - 02 (Wang) 09/22/2016-06/30/2021 (b)(6)
NIH $70,587
University of Pittsburgh OBrien Cooperative Research Center Program
Success of the proposed multidisciplinary research will elucidate the molecular mechanisms of BPH and related LUTS, which may lead to new targets for developing novel preventive and/or therapeutic approaches for this disease.

1U24 DK110791-02 (Dhir) 09/15/2016 – 06/30/2021 (b)(6)
NIH $309,928
University of Pittsburgh as the GUDMAP Tissue Hub and Collection Site An understanding of human genitourinary development is critical to tackling the growing number of developmental diseases affecting these tissues. This grant proposes to leverage the significant infrastructure of the University of Pittsburgh to provide high quality fetal tissue to the GUDMAP atlas projects.

(b)(4) (b)(6) 08/16/2017 – 08/15/2018 (b)(6)
Corporate Contract $9,363
Effect of androgen deprivation on Bcl-2 expression in human benign prostatic hyperplasia (BPH)
In this project, we are proposing to perform immunostaining of Bcl-2 and Bcl-XL on tissues from patients treated with ADT prior to radical prostatectomy.

1UG3 DK114861-01 (Kellum) 09/15/2017-06/30/2019 (b)(6)
National Institutes of Health $11,678
PReCISE AKI (Phenotyping REnal Cases in Sepsis and surgery for Early Acute Kidney Injury)
This project seeks to enroll patients with Early Acute Kidney Injury (AKI) as well as to contribute to enrollment of patients with established AKI as part of the UG3/UH3 consortium.

PENDING

(b)(4); (b)(6)

OVERLAP: No Overlap

Other Support

(b)(6)

ACTIVE

(b)(4); (b)(6)

E. OVERALL IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

NOTHING TO REPORT

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

Not Applicable

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

NOTHING TO REPORT

F. OVERALL CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. OVERALL SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

NOTHING TO REPORT

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

Yes

Is the research exempt from Federal regulations?

No

Does this project involve a clinical trial?

No

G.4.b Inclusion Enrollment Data

Report Attached: Research on tissue from an elective or spontaneous abortion < 24 weeks gestation

G.4.c ClinicalTrials.gov

Does this project include one or more applicable clinical trials that must be registered in ClinicalTrials.gov under FDAAA?

No

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Are there personnel on this project who are newly involved in the design or conduct of human subjects research?

No

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Does this project involve vertebrate animals?

No

G.8 PROJECT/PERFORMANCE SITES

Organization Name:	DUNS	Congressional District	Address

Primary: University of Pittsburgh	004514360	PA-014	UPMC Shadyside 5230 Centre Avenue Pittsburgh PA 152320000
University of Pittsburgh	004514360	PA-014	Children's Hospital of UPMC 4401 Penn Avenue Pittsburgh PA 152240000
University of Pittsburgh	004514360	PA-014	Magee Womens Hospital of UPMC 300 Halket Street Pittsburgh PA 152130000
UNIVERSITY OF PITTSBURGH AT PITTSBURGH	004514360		UNIVERSITY OF PITTSBURGH OFFICE OF RESEARCH PITTSBURGH PA 152132303

G.9 FOREIGN COMPONENT

No foreign component

G.10 ESTIMATED UNOBLIGATED BALANCE

G.10.a Is it anticipated that an estimated unobligated balance (including prior year carryover) will be greater than 25% of the current year's total approved budget?

No

G.11 PROGRAM INCOME

Is program income anticipated during the next budget period?

No

G.12 F&A COSTS

Not Applicable

Inclusion Enrollment Report

Inclusion Data Record (IDR) #: 1078054

Using an Existing Dataset or Resource: No

Delayed Onset Study ?: No

Clinical Trial: No

Enrollment Location: Domestic

NIH Defined Phase III Clinical Trial: No

Study Title: Research on tissue from an elective or spontaneous abortion < 24 weeks gestation

Planned Enrollment

Racial Categories	Ethnic Categories									Total
	Not Hispanic or Latino			Hispanic or Latino			Unknown/Not Reported Ethnicity			
	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	
American Indian/Alaska Native	0	0		0	0					**0**
Asian	50	0		0	0					**50**
Native Hawaiian or Other Pacific Islander	0	0		0	0					**0**
Black or African American	100	0		10	0					**110**
White	200	0		20	0					**220**
More than One Race	0	0		20	0					**20**
Unknown or Not Reported										
Total	**350**	**0**		**50**	**0**					**400**

Cumulative Enrollment

Only planned enrollment data exists for this data record. The PD/PI did not enter cumulative inclusion enrollment data.

RESEARCH & RELATED BUDGET - SECTION A & B

ORGANIZATIONAL DUNS*: 004514360

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF PITTSBURGH AT PITTSBURGH

Start Date*: 06-01-2018 **End Date*:** 05-31-2019

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1.		Rajiv		Dhir		Project Lead	(b)(6)				37,920.00	9,651.00	47,571.00
2.		(b)(6)				Co-investigator					3,000.00	764.00	3,764.00
3.						Co-investigator					26,846.00	6,832.00	33,678.00
4.						Co-investigator					6,000.00	1,527.00	7,527.00
5.						Co-investigator					21,012.00	5,348.00	26,360.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name:

Total Senior/Key Person **118,900.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
9	Supervisors, Techs, and Data Coord	(b)(6)			132,773.00	48,108.00	180,881.00
9	**Total Number Other Personnel**					**Total Other Personnel**	**180,881.00**

Total Salary, Wages and Fringe Benefits (A+B) **299,781.00**

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E

ORGANIZATIONAL DUNS*: 004514360

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF PITTSBURGH AT PITTSBURGH

Start Date*: 06-01-2018 **End Date*:** 05-31-2019

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	**0.00**
Total Equipment	**0.00**

Additional Equipment: File Name:

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	10,840.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**10,840.00**

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		0.00
2. Stipends		0.00
3. Travel		0.00
4. Subsistence		0.00
5. Other:		
0 Number of Participants/Trainees	**Total Participant Trainee Support Costs**	**0.00**

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K

ORGANIZATIONAL DUNS*: 004514360

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF PITTSBURGH AT PITTSBURGH

Start Date*: 06-01-2018 **End Date*:** 05-31-2019

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	27,612.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	8,000.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. HSTB Services	4,242.00
9. New Castle, UK Shipping Costs to consortium sites	42,959.00
Total Other Direct Costs	**82,813.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**393,434.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. MTDC	0.0	389,192.00	219,569.00
		Total Indirect Costs	**219,569.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number): U.S. Department of Health and Human Services (b)(6) (b)(6)

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**613,003.00**

J. Fee	Funds Requested ($)*
	0.00

K. Budget Justification* File Name: budget justification _yr 3.pdf

(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

BUDGET JUSTIFICATION – Year 3

Personnel

Rajiv Dhir, MD, MBA: PI, Effort = (b)(6) Dr. Dhir is the medical director of the Health Sciences Tissue Bank (HSTB) of the University of Pittsburgh and a practicing pathologist with subspecialty training in Genitourinary Pathology. He will be responsible for the oversight of the project. This will include interfacing and working with internal collaborators to ensure accrual and annotation of the appropriate specimens. He will also interact with the external collaborators and clients to ensure appropriate specimen aggregation and disbursement. He will work closely with NIDDK to ensure successful execution of the project, meeting the mission and goals of the Tissue Core. Annual effort of (b)(6) is requested.

(b)(6) : Effort = (b)(6) This (b)(6) will be responsible for coordination and management of day to day operations. She supervises HSTB staff members and will manage the overall efforts of the HSTB and set operational standards related to the HSTB scope of work. She will assure proper communication and resolution conflicts and issues.

1. Tissue Hub Infrastructure Support

A crucial component of this application is the infrastructure for the Tissue Hub, which will include personnel for the development and maintenance of a secure web-based interface for GUDMAP investigators, assurance of regulatory compliance, data collection and record-keeping, and management of the quality assurance program associated with this project.

(b)(6) : Co-I, Effort = (b)(6) is the (b)(6) (b)(6) and will be the director of the Tissue hub Infrastructure. He also serves as the faculty in-charge of the informatics requirements of HSTB. He provides direction and advice related to the different Information systems and tools used by HSTB. He is also the director of the Imaging core; a subsidiary of HSTB. The imaging core will perform whole slide image acquisition and provide access to these images for the Tissue Core clients. Annual effort of (b)(6) is requested.

(b)(6) Effort = (b)(6) This (b)(6) will be responsible for project intake, tracking and recording keeping. She will coordinate the GUDMAP investigator requests to the GUDMAP-Human Tissue Repository including documenting the needs of the investigator, assuring regulatory compliance, coordinating with tissue and data collection staff members and assuring proper completion and shipping of requests. Annual effort of (b)(6) is requested.

(b)(6) Effort = (b)(6) This (b)(6) will be responsible for the quality program. He will manage all aspects of quality management including record keeping, training of staff members to standard operating procedures (SOPs), data entry practices and audits, and quality related events. He will coordinate the overall record keeping and management of the quality metrics from the tissue collection and data entry processes with the quality measurements performed through the Department of Pediatrics team.

(b)(6) Effort = (b)(6) This (b)(6) specialist will be responsible for overall management of the Biospecimen Inventory and Operations System with regard to the this project. He will manage the specimen search process, control the data entry lexicon as needed, and provide reports of collection activity for investigators who request samples and as needed for other purposes. He will maintain the data integrity and make corrections and amendments based on the quality control activities. In the case that new fields and library elements are required he will manage that process in conjunction with the Project Manager and Quality Manager. He will be required to produce final sample pick lists as specimens are disbursed.

(b)(6) Effort = (b)(6) is the technician responsible for processing tissues, immunohistochemistry and immunofluorescence needs of the project. He is also the supervisor of the Research Histology core facility and is responsible for the development of specialized techniques required by the program and for processes not included in the fee-for-service activity.

(b)(6) : Effort = (b)(6) The (b)(6) will be responsible for aggregating information from the different information systems on the specimens offered as part of the Tissue Core. This will include pathology information as well as more specialized information (like cytogenetics); if applicable. The data coordinator will work with the Project manager on cohort identification for

the different requests. In addition the data coordinator will also be responsible for providing data to the clients of the Tissue Core.

2. Fetal Tissue Procurement Laboratory (Magee Women's Hospital)

All of the fetal tissue will be collected at Magee Women's Hospital, undergo a gross examination, and then be transported to the validation laboratory for further assessment prior to distribution.

(b)(6): Co-I, Effort = (b)(6) is the (b)(6) (b)(6) He will be responsible for evaluating appropriate surgical pathology and autopsy specimens, and overseeing collection of the biological materials for the Tissue Core and will act as the director of the tissue procurement laboratory. He will perform the clinical evaluation of the gross genitourinary specimen and ensure quality control of the dissection to minimize mechanical disruption. He will train the staff to obtain early gestational age genitourinary specimens, and work closely with (b)(6) to perform routine and specialized histological assessment of the appropriate specimens. Annual effort of (b)(6) is requested.

(b)(6): Effort = (b)(6) This HSTB tissue bank technician and will perform the day-to-day tasks associated with the collection of specimens. This includes maintaining a working knowledge of all SOPs related to the ongoing collections that are requested by the GUDMAP investigators. She will coordinate with the clinical departments within Magee Women's Hospital of UPMC, interface with the Pathology and other hospital staff members as required to obtain the requested specimens and enter data related to each case in the BIOS.

(b)(6) Effort = (b)(6) This (b)(6) and technician will perform the day-to-day tasks associated with the collection of specimens. This includes maintaining a working knowledge of all SOPs related to the ongoing collections that are requested by the GUDMAP investigators. She will coordinate with the clinical departments within Magee Women's Hospital of UPMC, interface with the Pathology and other hospital staff members as required to obtain the requested specimens and enter data related to each case in the BIOS.

3. Validation Laboratory (Children's Hospital of Pittsburgh)

The validation laboratory will perform quality assurance measures, as per GUDMAP project needs (eg. histological assessment, *in situ* hybridization and RNA isolation).

(b)(6) Co-I, Effort = (b)(6) is a kidney developmental biologist with over (b)(6) studying the genitourinary tract and will act as the director of the validation laboratory. Furthermore, he is also a classically trained human anatomist, histologist and embryologist. The quality assurance of the specimens will be performed by at least two independent evaluations (b)(6) for GUDMAP project needs. (b)(6) will work closely with (b)(6) to train staff to perform the gross dissection for early gestational age genitourinary tissues, and tissues not currently being obtained by the Tissue Bank, as per GUDMAP project needs. He will also oversee the training of (b)(6) (tissue hub technician) in all aspects of dissection, histology and molecular evaluation of the fetal tissues.

(b)(6): Co-I, Effort = (b)(6) is a clinician scientist (Pediatric Nephrologist) with a research program related to kidney development and will act as the co-director of the validation laboratory. She has a thorough understanding of genitourinary development. She will participate in quality assurance of specimens as noted above. Furthermore, (b)(6) will provide direction and advice regarding the clinical parameters that will be used to screen fetal and neonatal tissues to exclude pathological specimens, and will evaluate individual cases as needed.

(b)(6) Effort = (b)(6) This grant will fund (b)(6) of the technicians salary. This technician will perform all the required validation of the specimens including: histology, immunohistochemistry, in situ hybridization, cell isolation and real time PCR.

Supplies

HSTB Consumable Laboratory Supplies: (b)(4) is requested for sample collections, integrity, maintenance, and transport including sample and shipping containers, dry ice, and other basic supplies.

Shipping: Funds are requested for the shipment of tissue from New Castle, UK to the participating GUDMAP investigators, $42,959 is requested in year 3.

Validation Laboratory Consumable Laboratory Supplies: (b)(4) monthly will be required to purchase reagents for staining, immunohistochemistry and in situ reagents as well as cell, culture medium and consumable plastics related to these processes. These processes will be performed in response to the needs of the GUDMAP investigators.

Travel

Pathology: The Project PI and HSTB staff will need to travel to GUDMAP consortia meetings, to be held twice a year. A total of $4,840 is allocated for this travel in year 3.

Validation Laboratories: The Project co-investigators will need to travel to GUDMAP consortia meetings, to be held twice a year. (b)(6) will also attend the American Society of Nephrology meeting where GUDMAP typically has a booth. A total of $6,000 is allocated for this travel in year 3.

(b)(6) will also attend the International Meeting on Development Nephrology to be held in 2018, where GUDMAP will hold workshops.

Other Expenses

Tissue embedding/processing, storage, and disbursement: $4,242 for year 3. These are billable services based on the fiscal parameters in place within the University of Pittsburgh for the HSTB. Tissue embedding and processing will be required at all levels for quality management and to provide product to GUDMAP investigators. Storage costs are based on the partial cost of a freezer with a 10 year life span plus projected maintenance and certification costs. The cost for disbursement of samples to GUDMAP investigators will be charged to the account award for this project.

Website maintenance, project management tool, BIOS, image acquisition: $8,000. Resources will be required to maintain and update our internally developed inventory management system (BIOS). The project management tool is internally developed and is the mechanism for starting and following the progress of the request from the client. The clients will be provided access to the contents of the resource via a Sharepoint link that will be password protected. Whole slide image acquisition will be done to offer clients access to high quality images of the specimens in the resource. These images will be from routine and specialized histologic and immunohistochemical/ in-situ protocols. We also have capabilities for image analysis and will offer, if required.

Notice of Award

RESOURCE-RELATED COOPERATIVE AGREEMENT PROJECTS **Federal Award Date:** 07/03/2017

Department of Health and Human Services
National Institutes of Health
NATIONAL INSTITUTE OF DIABETES AND DIGESTIVE AND KIDNEY DISEASES

Grant Number: 5U24DK110791-02
FAIN: U24DK110791

Principal Investigator(s):
RAJIV DHIR, MD

Project Title: University of Pittsburgh as the GUDMAP Tissue Hub and Collection Site

(b)(6)
University of Pittsburgh
123 University Place, B21
Grants and Contracts Officer
Pittsburgh, PA 152132303

Award e-mailed to: ornih@offres.pitt.edu

Period Of Performance:
Budget Period: 06/01/2017 – 05/31/2018
Project Period: 09/15/2016 – 05/31/2021

Dear Business Official:

The National Institutes of Health hereby awards a grant in the amount of $479,336 (see "Award Calculation" in Section I and "Terms and Conditions" in Section III) to UNIVERSITY OF PITTSBURGH AT PITTSBURGH in support of the above referenced project. This award is pursuant to the authority of 42 USC 241 31 USC 6305 42 CFR 52 and is subject to the requirements of this statute and regulation and of other referenced, incorporated or attached terms and conditions.

Acceptance of this award including the "Terms and Conditions" is acknowledged by the grantee when funds are drawn down or otherwise obtained from the grant payment system.

Each publication, press release, or other document about research supported by an NIH award must include an acknowledgment of NIH award support and a disclaimer such as "Research reported in this publication was supported by the National Institute Of Diabetes And Digestive And Kidney Diseases of the National Institutes of Health under Award Number U24DK110791. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health." Prior to issuing a press release concerning the outcome of this research, please notify the NIH awarding IC in advance to allow for coordination.

Award recipients must promote objectivity in research by establishing standards that provide a reasonable expectation that the design, conduct and reporting of research funded under NIH awards will be free from bias resulting from an Investigator's Financial Conflict of Interest (FCOI), in accordance with the 2011 revised regulation at 42 CFR Part 50 Subpart F. The Institution shall submit all FCOI reports to the NIH through the eRA Commons FCOI Module. The regulation does not apply to Phase I Small Business Innovative Research (SBIR) and Small Business Technology Transfer (STTR) awards. Consult the NIH website http://grants.nih.gov/grants/policy/coi/ for a link to the regulation and additional important information.

If you have any questions about this award, please contact the individual(s) referenced in Section IV.

Sincerely yours,

(b)(6)

Grants Management Officer
NATIONAL INSTITUTE OF DIABETES AND DIGESTIVE AND KIDNEY DISEASES

Additional information follows

SECTION I – AWARD DATA – 5U24DK110791-02

Award Calculation (U.S. Dollars)

Salaries and Wages	$178,322
Fringe Benefits	$56,043
Personnel Costs (Subtotal)	$234,365
Materials & Supplies	$39,960
Travel	$9,798
Other	$27,300
Federal Direct Costs	$311,423
Federal F&A Costs	$167,913
Approved Budget	$479,336
Total Amount of Federal Funds Obligated (Federal Share)	$479,336
TOTAL FEDERAL AWARD AMOUNT	$479,336
AMOUNT OF THIS ACTION (FEDERAL SHARE)	$479,336

SUMMARY TOTALS FOR ALL YEARS		
YR	**THIS AWARD**	**CUMULATIVE TOTALS**
2	$479,336	$479,336
3	$613,002	$613,002
4	$613,001	$613,001
5	$613,001	$613,001

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

Fiscal Information:

CFDA Name: Diabetes, Digestive, and Kidney Diseases Extramural Research
CFDA Number: 93.847
EIN: 1250965591A1
Document Number: UDK110791A
PMS Account Type: P (Subaccount)
Fiscal Year: 2017

IC	CAN	2017	2018	2019	2020
DK	8472288	$479,336	$613,002	$613,001	$613,001

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

NIH Administrative Data:
PCC: KDH KDB / **OC**: 414P / **Released**: (b)(6) 06/30/2017
Award Processed: 07/03/2017 11:21:15 AM

SECTION II – PAYMENT/HOTLINE INFORMATION – 5U24DK110791-02

For payment and HHS Office of Inspector General Hotline information, see the NIH Home Page at http://grants.nih.gov/grants/policy/awardconditions.htm

SECTION III – TERMS AND CONDITIONS – 5U24DK110791-02

This award is based on the application submitted to, and as approved by, NIH on the above-titled project and is subject to the terms and conditions incorporated either directly or by reference in the following:

a. The grant program legislation and program regulation cited in this Notice of Award.
b. Conditions on activities and expenditure of funds in other statutory requirements, such as those included in appropriations acts.
c. 45 CFR Part 75.
d. National Policy Requirements and all other requirements described in the NIH Grants

Policy Statement, including addenda in effect as of the beginning date of the budget period.

e. Federal Award Performance Goals: As required by the periodic report in the RPPR or in the final progress report when applicable.
f. This award notice, INCLUDING THE TERMS AND CONDITIONS CITED BELOW.

(See NIH Home Page at http://grants.nih.gov/grants/policy/awardconditions.htm for certain references cited above.)

Research and Development (R&D): All awards issued by the National Institutes of Health (NIH) meet the definition of "Research and Development" at 45 CFR Part§ 75.2**.** As such, auditees should identify NIH awards as part of the R&D cluster on the Schedule of Expenditures of Federal Awards (SEFA). The auditor should test NIH awards for compliance as instructed in Part V, Clusters of Programs. NIH recognizes that some awards may have another classification for purposes of indirect costs. The auditor is not required to report the disconnect (i.e., the award is classified as R&D for Federal Audit Requirement purposes but non-research for indirect cost rate purposes), unless the auditee is charging indirect costs at a rate other than the rate(s) specified in the award document(s).

Carry over of an unobligated balance into the next budget period requires Grants Management Officer prior approval.

This award is subject to the requirements of 2 CFR Part 25 for institutions to receive a Dun & Bradstreet Universal Numbering System (DUNS) number and maintain an active registration in the System for Award Management (SAM). Should a consortium/subaward be issued under this award, a DUNS requirement must be included. See http://grants.nih.gov/grants/policy/awardconditions.htm for the full NIH award term implementing this requirement and other additional information.

This award has been assigned the Federal Award Identification Number (FAIN) U24DK110791. Recipients must document the assigned FAIN on each consortium/subaward issued under this award.

Based on the project period start date of this project, this award is likely subject to the Transparency Act subaward and executive compensation reporting requirement of 2 CFR Part 170. There are conditions that may exclude this award; see http://grants.nih.gov/grants/policy/awardconditions.htm for additional award applicability information.

In accordance with P.L. 110-161, compliance with the NIH Public Access Policy is now mandatory. For more information, see NOT-OD-08-033 and the Public Access website: http://publicaccess.nih.gov/.

In accordance with the regulatory requirements provided at 45 CFR 75.113 and Appendix XII to 45 CFR Part 75, recipients that have currently active Federal grants, cooperative agreements, and procurement contracts with cumulative total value greater than $10,000,000 must report and maintain information in the System for Award Management (SAM) about civil, criminal, and administrative proceedings in connection with the award or performance of a Federal award that reached final disposition within the most recent five-year period. The recipient must also make semiannual disclosures regarding such proceedings. Proceedings information will be made publicly available in the designated integrity and performance system (currently the Federal Awardee Performance and Integrity Information System (FAPIIS)). Full reporting requirements and procedures are found in Appendix XII to 45 CFR Part 75. This term does not apply to NIH fellowships.

Treatment of Program Income:
Other Research (Add/Deduct Option)

RESTRICTION: Funds may only be used to offset the cost of acquiring, processing and shipping tissue samples to the GUDMAP atlas projects. This includes covering the cost of processing and shipping tissue from external sources.

Notice: Under governing regulations, Federal funds administered by the Department of Health and Human Services shall not be expended for research involving human subjects, and individuals shall not be enrolled in such research, without prior approval by the Office of Human Research Protections (OHRP) of an assurance to comply with the requirements of 45 CFR 46 to protect human research subjects. This restriction applies to all collaborating sites without OHRP-approved assurances, whether domestic or foreign, and compliance must be ensured by the awardee.

Notice: Under governing policy, federal funds administered by the Public Health Service (PHS) shall not be expended for research involving live vertebrate animals without prior approval by the Office of Laboratory Animal Welfare (OLAW) of an assurance to comply with the PHS policy on humane care and use of laboratory animals. This restriction applies to all performance sites (e.g., collaborating institutions, subcontractors, subgrantees) without OLAW-approved assurances, whether domestic or foreign.

The issuance of this award has been delayed due to administrative funding considerations. According to NIH policy, if pre-award costs are necessary, they may be approved by the authorized Institution Official(s).

In addition to the PI, the following individuals are named as key personnel:

(b)(6)

Written prior approval is required if any of the individual(s) named above withdraws from the project entirely, is absent from the project during any continuous period of 3 months or more, or reduces time devoted to the project by 25 percent or more from the level that was approved at the time of award.

This grant is in response to RFA/PA DK15-016. Acceptance of this award requires compliance with this solicitation. See the NIH Guide at http://grants.nih.gov/grants/guide/index.html for copy of the RFA/PA that includes administrative and programmatic requirements specific to this award.

The following special terms of award are in addition to, and not in lieu of, otherwise applicable U.S. Office of Management and Budget (OMB) administrative guidelines, U.S. Department of Health and Human Services (DHHS) grant administration regulations at 45 CFR Parts 74 and 92 (Part 92 is applicable when State and local Governments are eligible to apply), and other HHS, PHS, and NIH grant administration policies.

The administrative and funding instrument used for this program will be the cooperative agreement, an "assistance" mechanism (rather than an "acquisition" mechanism), in which substantial NIH programmatic involvement with the awardees is anticipated during the performance of the activities.

Under the cooperative agreement, the NIH purpose is to support and stimulate the recipients' activities by involvement in and otherwise working jointly with the award recipients in a partnership role; it is not to assume direction, prime responsibility, or a dominant role in the activities. Consistent with this concept, the dominant role and prime responsibility resides with the awardees for the project as a whole, although specific tasks and activities may be shared among the awardees and the NIH as defined below.

The PD(s)/PI(s) will have the primary responsibility for:

- All aspects of the scientific activities, including defining the objectives and approaches, planning, conduct, analysis, and publication of results, interpretations, and conclusions of studies conducted under the terms and conditions of the cooperative agreement award.
- Collaborating with other investigators in the program for protocol development, sample, reagents and data sharing as appropriate, data quality control, and data organization

- Accountability towards the applicant organization officials and to the NIDDK for the performance and proper conduct of the research supported by the project in accordance with the terms and conditions of the award.
- Serving as a voting member of the Steering Committee and will attend the Planning Meeting and a Steering Committee meeting in the first year, two Steering Committee meetings a year in subsequent years and monthly teleconference calls.
- Accepting and implementing the goals, priorities, procedures, protocols, and policies agreed upon by the Steering Committee and subcommittees, and be responsible for close coordination and cooperation with the components of the GUDMAP consortium and with NIDDK staff.
- Adhering to PHS policy for the distribution of unique research resources produced with PHS funding as described under Special Requirements.
- Establishing written milestones for the project, in negotiation with NIDDK Project Staff prior to funding.
- Release all study design materials and procedure manuals into the public domain and/or make them available to other investigators, according to the approved plan for making data and materials available to the scientific community and the NIDDK, for the conduct of research at no charge other than the costs of reproduction and distribution, consistent with achieving the goals of this program initiative.
- Awardees will retain custody of and have primary rights to the data and software developed under these awards, subject to Government rights of access consistent with current DHHS, PHS, and NIH policies.

NIH staff will have substantial programmatic involvement that is above and beyond the normal stewardship role in awards, as described below:

- An NIH Project Scientist will have substantial programmatic involvement that is above and beyond the normal stewardship role in awards, as described below. However, the dominant role and prime responsibility for the project as a whole resides with the awardees, although specific tasks and activities in carrying out the studies will be shared by awardees and the NIDDK.
- NIDDK will designate a Project Officer and a Grants Management Specialist to provide normal program stewardship and administrative oversight of the cooperative agreement.
- NIDDK will form an External Advisory Committee (EAC), comprised of the NIDDK Project Scientist and other NIH extramural staff with relevant scientific expertise or who manage research grant programs that relate scientifically to the goals of the GUDMAP projects, and outside advisors selected by the NIDDK. The EAC will meet annually with the GUDMAP Steering Committee to review and assess GUDMAP and to advise NIDDK of scientific developments and opportunities that may enhance the achievement of the GUDMAP goals.
- The NIDDK Project Scientist will attend and participate as a voting member in all meetings of the Steering Committee, and provide liaison between the Steering Committee and the External Advisory Committee.
- The NIDDK Project Scientist will help the Steering Committee develop and draft operating policies.
- The NIDDK Project Officer will review the scientific progress of the individual GUDMAP components, for compliance with operating policies developed by the Steering Committee, and may recommend to the NIDDK to withhold support, suspend, or terminate an award for lack of scientific progress or failure to adhere to policies established by the Steering Committee.
- An agency program official or IC program director will be responsible for the normal scientific and programmatic stewardship of the award and will be named in the award notice. The assigned Program Officer may also serve as an NIDDK Project Scientist.

Areas of Joint Responsibility include:

- Steering Committee - The NIDDK Project Scientist, PIs from the project funded through this FOA and RFA-DK-15-014, and RFA-DK-15-015 and voluntary representatives from the previously funded GUDMAP atlas projects funded under RFA-DK-11-001 will be responsible for forming a Steering Committee as defined below. An arbitration system, as detailed below, will be available to resolve disagreements among members of the Steering Committee. The Steering Committee will be the main governing board of the GUDMAP consortium. It will develop collaborative protocols, identify technological impediments to success and strategies to overcome them, develop shared software tools

for disseminating information about the projects, and identify opportunities for sharing techniques and tools that might be developed in future GUDMAP atlas projects.

- The Steering Committee will be composed of the PIs from the project funded through this FOA, RFA-DK-15-014, and RFA-DK-15-015, representatives from the previously funded GUDMAP projects, and the NIDDK Project Scientist. The representatives and the PIs will each have one vote. The NIDDK Project Scientist for this project will have one vote. The Steering Committee will select a chairperson who will be someone other than an NIH staff member.
- The Steering Committee may, as it deems necessary, invite additional, non-voting scientific advisors to meetings at which research priorities and opportunities are discussed. The NIH reserves the right to augment the scientific or consumer expertise of the Steering Committee when necessary.
- There will be two Steering Committee meetings annually. The first meeting will be a Planning Meeting to be held in the Washington, DC area on **June 20-21, 2016**. At the Planning Meeting, the Steering Committee will be formed and a chairperson selected from among the members. At the Planning Meeting, the Steering Committee may: (a) draft a charter to detail policies and procedures, a process for monitoring compliance with the policies and procedures, and a process for recommending that the NIDDK Project Administrators act on evidence of non-compliance of any Consortium component with Steering Committee policies; (b) agree upon the terms of the charter; and (c) devise a plan for working with the GUDMAP database developers to provide ongoing input into database and website design.
- At the second and subsequent meetings, the Steering Committee will refine the GUDMAP scientific objectives and implementation as necessary, consistent with data produced by former and possible future GUDMAP atlas projects and from other laboratories.
- The Steering Committee will plan workshops, to which non-GUDMAP participants will also be invited, to inform the research community of the progress made toward development of the atlas, and to inform the research community of any technological advances related to the implementation of the GUDMAP website/database. The NIDDK Project Scientist, the External Advisory Committee, and other NIH staff as appropriate will provide the Steering Committee with advice on participants for the workshops and symposia.
- The Steering Committee may establish subcommittees as it deems appropriate.
- Awardee members of the Steering Committee will be required to accept and implement policies approved by the Steering Committee.
- The EAC will meet annually with the GUDMAP Steering Committee to review and assess the progress of the GUDMAP consortium and to advise NIDDK of scientific developments and opportunities that may enhance the achievement of the GUDMAP goals.

Dispute Resolution

Any disagreements that may arise in scientific or programmatic matters (within the scope of the award) between award recipients and the NIH may be brought to Dispute Resolution. A Dispute Resolution Panel will have three members: a designee of the Steering Committee chosen without NIH staff voting, one NIH designee, and a third designee with expertise in the relevant area who is chosen by the other two; in the case of individual disagreement, the first member may be chosen by the individual awardee. This special dispute resolution procedure does not alter the awardee's right to appeal an adverse action that is otherwise appealable in accordance with PHS regulation 42 CFR Part 50, Subpart D and DHHS regulation 45 CFR Part 16.
- See more at: http://grants.nih.gov/grants/guide/rfa-files/RFA-DK-15-016.html#sthash.UY9M5nfL.dpuf

STAFF CONTACTS

The Grants Management Specialist is responsible for the negotiation, award and administration of this project and for interpretation of Grants Administration policies and provisions. The Program Official is responsible for the scientific, programmatic and technical aspects of this project. These individuals work together in overall project administration. Prior approval requests (signed by an Authorized Organizational Representative) should be submitted in writing to the Grants Management Specialist. Requests may be made via e-mail.

Grants Management Specialist: (b)(6)
Email: (b)(6) @extra.niddk.nih.gov **Phone**: (b)(6) **Fax**: (b)(6)

Program Official: (b)(6)
Email: (b)(6)@niddk.nih.gov **Phone:** (b)(6)

SPREADSHEET SUMMARY
GRANT NUMBER: 5U24DK110791-02

INSTITUTION: UNIVERSITY OF PITTSBURGH AT PITTSBURGH

Budget	Year 2	Year 3	Year 4	Year 5
Salaries and Wages	$178,322	$224,405	$224,284	$224,284
Fringe Benefits	$56,043	$70,527	$70,489	$70,489
Personnel Costs (Subtotal)	$234,365	$294,932	$294,773	$294,773
Materials & Supplies	$39,960	$50,288	$50,261	$50,261
Travel	$9,798	$12,331	$12,324	$12,324
Other	$27,300	$34,355	$34,336	$34,336
TOTAL FEDERAL DC	$311,423	$391,906	$391,694	$391,694
TOTAL FEDERAL F&A	$167,913	$221,096	$221,307	$221,307
TOTAL COST	$479,336	$613,002	$613,001	$613,001

Facilities and Administrative Costs	Year 2	Year 3	Year 4	Year 5
F&A Cost Rate 1	54%	55.5%	56.5%	56.5%
F&A Cost Base 1	$32,448	$33,115	$391,694	$391,694
F&A Costs 1	$17,522	$18,379	$221,307	$221,307
F&A Cost Rate 2	55.5%	56.5%		
F&A Cost Base 2	$270,975	$358,791		
F&A Costs 2	$150,391	$202,717		

A. OVERALL COVER PAGE

Project Title: University of Pittsburgh as the GUDMAP Tissue Hub and Collection Site	
Grant Number: 5U24DK110791-02	**Project/Grant Period:** 09/15/2016 - 05/31/2021
Reporting Period: 09/15/2016 - 05/31/2017	**Requested Budget Period:** 06/01/2017 - 05/31/2018
Report Term Frequency: Annual	**Date Submitted:** 04/03/2017
Program Director/Principal Investigator Information: RAJIV DHIR , MD **Phone number:** (412) 623-1321 **Email:** dhirr@upmc.edu	**Recipient Organization:** UNIVERSITY OF PITTSBURGH AT PITTSBURGH UNIVERSITY OF PITTSBURGH OFFICE OF RESEARCH 123 UNIVERSITY PL, B21 PITTSBURGH, PA 152132303 **DUNS:** 004514360 **EIN:** 1250965591A1 **RECIPIENT ID:**
Change of Contact PD/PI: N/A	
Administrative Official: (b)(6) University of Pittsburgh 123 University Place Pittsburgh, PA 15213 **Phone number:** (b)(6) **Email:** (b)(6) @pitt.edu	**Signing Official:** (b)(6) University of Pittsburgh 123 University Place Pittsburgh, PA 15213 **Phone number:** (b)(6) **Email:** (b)(6) @pitt.edu
Human Subjects: Yes HS Exempt: No Exemption Number: Phase III Clinical Trial:	**Vertebrate Animals:** No
hESC: No	**Inventions/Patents:** No

B. OVERALL ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

Aim 1: To generate an inventory of genitourinary tissue throughout normal human development The main goal of this aim is to develop a pipeline for the acquisition, quality control and distribution of human genitourinary samples obtained throughout development (6-42 weeks gestation). We currently have access to 6-24 week samples through the HSTB. However, for later gestational stages (25-42 weeks gestation) we have partnered with the International institute for the Advancement of Medicine. This will provide access to a novel resource for neonatal donation. We aim to collect and store a minimum of 5 samples per developmental week. Each of these samples will have histology, immunohistochemistry and in situ hybridization performed to assess tissue quality, protein and RNA integrity. Furthermore, we will obtain maternal blood, urine and amniotic fluid; based on the clinical situation and ability to procure. Based on our current experience, we get these biological
materials in most cases. Anonymized demographic information of each specimen will also be provided.

Aim 2: To provide fresh genitourinary tissue and biological research specimens This aim will generate an ongoing resource to distribute fresh developmental human genitourinary samples
from various stages (6-42 weeks) to the GUDMAP Atlas projects. The samples will be procured by a pathologist and inspected for mechanical damage. Samples will be collected from all qualified cases. The samples will then be subdivided based on the demand for fresh/frozen aliquots; the validation laboratory for quality control will keep a portion of each sample. The tissue samples will be immediately sent out for live cell use or immediately separated into distinct cellular populations before shipping based on researcher demands. Permissible annotating information; including demographics of each specimen, will also be provided.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

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B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

For this reporting period, is there one or more Revision/Supplement associated with this award for which reporting is required?

No

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

NOTHING TO REPORT

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

There is very active e-mail and phone communication between the GUDMAP investigators, the Data Hub and the Tissue Hub. In addition, the Tissue Hub activities account for approximately 50% of the 90 minute long monthly consortium video conference calls.

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

With the IRB and MTA processes accomplished, the Tissue Hub will start providing materials to the investigators. In addition, we are engaged in developing appropriate protocols to specifically address the needs of different projects. Finally, we will be performing extensive analyses on collected specimens both from a quality assessment perspective as well as to potentially assist GUDMAP investigators with specific pathology needs related to either localization studies and/or imaging.

ACCOMPLISHMENTS

Summary
The goal of this project is to provide human genitourinary tissues (kidneys, ureters, bladders and genital structures) to research projects funded in the GenitoUrinary Development Molecular Anatomy Project (GUDMAP), as part of a consortium to build a molecular atlas of human genitourinary development.

Institutional Review Board (IRB) and Material Transfer Agreement (MTA):
The existing IRB for the Health Sciences Tissue Bank at the University of Pittsburgh for the collection of biospecimens from products of conception required significant modifications to allow for sharing with external investigators. In addition, the verbiage related to genomic and molecular testing in the consents was updated. Finally, since there is an anticipated need for specimens from autopsy materials/ stillbirths; a new consent form was created to address tissue accrual from those specific clinical encounters rather than products of gestation. As per regulations, the autopsy material needed appropriate Committee for Oversight of Research and Clinical Training Involving Decedents (CORID) vetting. This IRB has been approved. The IRB for the GUDMAP consortium is an expedited submission working off the biospecimen collection IRB. This GUDMAP IRB is now in the final stages of institutional vetting and approval.

The draft MTA for sharing biospecimens with consortium members was sent out to the NIDDK and the GUDMAP funded investigators for review, and subsequent processing. The MTA documents should be in place in the near future. We anticipate that the legal and IRB processes should be accomplished in the next few weeks. Following that, the GUDMAP Tissue Hub and Collection site will be ready to start sharing biospecimens.

Biospecimen Collection/Quality Control:
The Tissue Hub has been in active communication with the consortium members to ascertain specific biospecimen and processing needs. We have been engaging in pilot studies internally, both from a collection as well as a quality control/quality assurance perspective. With the approval of the collection IRB, the collection of biospecimens that can be shared with GUDMAP consortia members is happening with the new consent forms in place. (b)(6) has been overseeing the collection and dissection of the specimens to accrue genitourinary specimens. (b)(6) and his lab have been receiving and utilizing specimens and assessing different modalities to ensure the highest quality specimens for the consortium members.

Information Technology Initiatives:
The Tissue Hub has been engaged in creating inventory and data management tools internally to appropriately annotate the GUDMAP tissue collections. In addition, local efforts have also focused on imaging of slides/ specimens to provide data and analysis. The Tissue Hub has been actively working with (b)(6) and the University of Southern California, as the GUDMAP Data Hub, to set up a portal and data transfer mechanism for collection and data annotation information to be securely transferred and available to GUDMAP investigators.

C. OVERALL PRODUCTS

C.1 PUBLICATIONS

Are there publications or manuscripts accepted for publication in a journal or other publication (e.g., book, one-time publication, monograph) during the reporting period resulting directly from this award?

No

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Nothing to report

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Have inventions, patent applications and/or licenses resulted from the award during the reporting period?

No

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Category	Explanation
Data or Databases	The data collected and provided by the Hub will be in two broad categories. Firstly, we will provide annotation information related to the specimens collected for the GUDMAP investigators. The data elements to be collected have been defined by the consortium. The data will be securely provided to the Data Hub, which will host this information. The second major data component will be imaging data generated from the specimens and slides etc. In addition, molecular data will also be generated from select specimens.
Research Material	The Tissue Hub will collect specimens as per the needs of the GUDMAP investigators. The biospecimens will be both from surgical pathology specimens (products of conception) as well as autopsy material (still-births). In addition, additional specimens may be collected depending on investigator and programmatic needs and direction. The specimen types that can be accrued, and possible specimen accrual limitations, have been discussed with consortia members. Collection protocols will continue to be modified and fine-tuned to reflect the needs and the reality of human biospecimen collections; since diagnostic assessment is the primary purpose.

D. OVERALL PARTICIPANTS

D.1 WHAT INDIVIDUALS HAVE WORKED ON THE PROJECT?

Commons ID	S/K	Name	Degree(s)	Role	Cal	Aca	Sum	Foreign Org	Country	SS
(b)(6)	Y	DHIR, RAJIV	MD	PD/PI	(b)(6)					NA
	N	(b)(6)		Technician						NA
	N			Technician						NA
	N			Technician						NA
	N			QC Manager						NA
(b)(6)	N			Co-Investigator						NA
	Y		BS,OTH,PHD	Co-Investigator						NA
	N			HSTB Supervisor						NA
	N			Project Manager						NA
	N			Co-Investigator						NA
(b)(6)	N		BS,MS,MD	Co-Investigator						NA

Glossary of acronyms:
S/K - Senior/Key
DOB - Date of Birth
Cal - Person Months (Calendar)
Aca - Person Months (Academic)
Sum - Person Months (Summer)
Foreign Org - Foreign Organization Affiliation
SS - Supplement Support
RE - Reentry Supplement
DI - Diversity Supplement
OT - Other
NA - Not Applicable

D.2 PERSONNEL UPDATES

D.2.a Level of Effort

Will there be, in the next budget period, either (1) a reduction of 25% or more in the level of effort from what was approved by the agency for the PD/PI(s) or other senior/key personnel designated in the Notice of Award, or (2) a reduction in the level of effort below the minimum amount of effort required by the Notice of Award?

No

D.2.b New Senior/Key Personnel

Are there, or will there be, new senior/key personnel?

No

D.2.c Changes in Other Support

Has there been a change in the active other support of senior/key personnel since the last reporting period?

Yes

File uploaded: Dhir Other Support Feb 2017.pdf

D.2.d New Other Significant Contributors

Are there, or will there be, new other significant contributors?

No

D.2.e Multi-PI (MPI) Leadership Plan

Will there be a change in the MPI Leadership Plan for the next budget period?

NA

For New and Renewal Applications (PHS 398) – DO NOT SUBMIT UNLESS REQUESTED

PHS 398 OTHER SUPPORT

Provide active and pending support for all senior/key personnel. **Other Support includes all financial resources, whether Federal, non-Federal, commercial or institutional, available in direct support of an individual's research endeavors, including but not limited to research grants, cooperative agreements, contracts, and/or institutional awards.** Training awards, prizes, or gifts do not need to be included.

There is no "form page" for other support. Information on other support should be provided in the *format* shown below, using continuation pages as necessary. ***Include the principal investigator's name at the top and number consecutively with the rest of the application.*** The sample below is intended to provide guidance regarding the type and extent of information requested.
For instructions and information pertaining to the use of and policy for other support, see Other Support in the Supplemental Instructions, Part III, Policies, Assurances, Definitions, and Other Information.
Effort devoted to projects must be measured using person months. Indicate calendar, academic, and/or summer months associated with each project.

Format

NAME OF INDIVIDUAL **Rajiv Dhir, MD, MBA**
ACTIVE/PENDING

ACTIVE

U19AI101196-04 (Buckheit) 06/22/2012-05/31/2017 (b)(6)
Imquest/NIH $26,534
Development and Evaluation of Dual compartment combination Microbicides
We propose to develop and evaluate the first safe, effective and user-acceptable dual compartment microbicide. Given that over 90% of HIV infections occur as a function of unprotected rectal or vaginal intercourse, having a single product that targets both compartments, reduces infections across a range of sexual activities, reduces infections across all at-risk populations, and is usable by same-sex and opposite sex partners will have a significant impact on the HIV pandemic.

P50 CA090440-14, (Siegfried) 06/01/2001-06/30/2017 (NCE) (b)(6)
NIH $81,496
SPORE in Lung Cancer
The goal of this application is to use a multi-disciplinary approach to tackle the problem of poor outcomes in lung cancer, a deadly disease with only a 15% 5-year survival rate. We intend to improve outcomes for lung cancer patients by identifying new ways to treat the disease that are based on the biology of the individual patient's tumor and new ways to predict risk and prevent lung cancer based on an individual's genetics. Dr. Dhir directs the tissue and blood Core.

U19 OH009077-06,CR (Becich) 09/01/2006–08/31/2021 (b)(6)
CDC $26,534
National Mesothelioma Virtual Bank for Translational Research
The proposed Mesothelioma Virtual Bank (MVB) for Translational Research will create and maintain infrastructure to support a national virtual patient registry and tissue bank. MVB proposes to create and maintain a set of resources through a cooperative working group that will make available their independent stores of mesothelioma tissue for public access.

P30CA047904-27 (Davidson) 08/01/2015-07/31/2020 (b)(6)
NIH $84,113
Cancer Center Support Grant
Dr. Dhir directs the Tissue and Research Pathology Services (TARPS) portion of the UPCI Cancer Center Support Grant

UM1CA18669003 (Chu) 03/01/2016-2/28/2017 (b)(6)
NIH $44,518
NCI ET-CTN with Phase 1 Emphasis at UPCI
Our institution is working to transform the NCI-sponsored cooperative experimental therapeutics clinical trials program from a series of separate institutions conducting early-phase cancer treatment trials to a new

consolidated, integrated Program, referred to as the NCI Experimental Therapeutics-Clinical Trials Network (ET-CTN).

U01HL12895401 (Wisniewski/Sciurba) 08/01/2015-07/31/2020 (b)(6)
NIH $11,080
Network Management Core (NEMO) for the Pulmonary Trials Cooperative (PTC)
The NEMO will have primary responsibility for organizing and operating this multi-center cooperative which conducts multiple simple clinical trials in both inpatient and outpatient settings in adults with a variety of chronic pulmonary diseases, including but not limited to interstitial lung disease (ILD), pulmonary hypertension (PH), chronic obstructive pulmonary disease (COPD), sarcoidosis, and obstructive sleep apnea, but excluding asthma and acute lung injury and critical care.

Federal Contract (Sciurba) 03/01/2016-2/28/2019 (b)(6)
NIH $38,243
Lung Tissue Research Consortium (LTRC): Clinical Centers
Contribute to the lung tissue Research consortium by meeting necessary subject recruitment goals, Providing high quality specimens and offering expertise in innovative Techniques in subject characterization, metagenomic characterization of The microbiome and gene expression analysis.

RFPS16-005 Federal Contract (Dhir) 09/30/2015-9/29/2017 (b)(6)
Leidos $123,323
Clinical Proteomic Tumor Analysis Consortium Phase III Tissue Source Site
These analyses will serve to clarify how the molecular biology facilitates refinement of driver genes, enhances understanding of the pathogenesis through proteomic subtyping, and illuminates dynamic alterations in post translational modifications responsible for the disregulation of cancer signaling networks and pathways; in essence, providing novel information for regarding the molecular biology of cancer.

1U54DK112079 - 01 (Wang) 12/01/2016 – 11/30/2021 (b)(6)
NIH $70,474
University of Pittsburgh OBrien Cooperative Research Center Program

U24 (Dhir) 09/15/2016 – 06/30/2021 (b)(6)
NIH 1 U24 DK110791-01 $400,000
University of Pittsburgh as the GUDMAP Tissue Hub and Collection Site An understanding of human genitourinary development is critical to tackling the growing number of developmental diseases affecting these tissues. This grant proposes to leverage the significant infrastructure of the University of Pittsburgh to provide high quality fetal tissue to the GUDMAP atlas projects.

PENDING

(b)(4); (b)(6)

OVERLAP: No Overlap

E. OVERALL IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

NOTHING TO REPORT

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

Not Applicable

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

NOTHING TO REPORT

F. OVERALL CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

The IRB process is almost done for the Tissue Hub. We have worked very closely with the IRB and do not anticipate any issues; as these have already been addressed. The collection IRB has already been extensively revamped; and has been IRB approved for about 6 weeks. The collection of biospecimens, that can be shared with GUDMAP consortia members, are happening with the new consent forms in place. The GUDMAP IRB is going through a final review and should be approved in the next few weeks. The draft MTA has been sent to the NIDDK and to the GUDMAP consortium members. The respective consortia sites could have delays if their legal teams want significant changes to the MTA verbiage. That is the only possible challenge that we anticipate at this point.

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. OVERALL SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

NOTHING TO REPORT

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

Yes

Is the research exempt from Federal regulations?

No

Does this project involve a clinical trial?

No

G.4.b Inclusion Enrollment Data

Report Attached: Research on tissue from an elective or spontaneous abortion < 24 weeks gestation

G.4.c ClinicalTrials.gov

Does this project include one or more applicable clinical trials that must be registered in ClinicalTrials.gov under FDAAA?

No

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Are there personnel on this project who are newly involved in the design or conduct of human subjects research?

Yes

(b)(6) replaced (b)(6) who was a co-investigator on this grant and has left the University of Pittsburgh. (b)(6) completed the Collaborative Institutional Training Initiative (CITI) Biomedical Human Subjects Research on 09/14/2016 This course covers the historical development of human subject protections, as well as current regulatory information and ethical issues.

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Does this project involve vertebrate animals?

No

G.8 PROJECT/PERFORMANCE SITES

Organization Name:	DUNS	Congressional District	Address
Primary: University of Pittsburgh	004514360	PA-014	UPMC Shadyside 5230 Centre Avenue Pittsburgh PA 152320000
University of Pittsburgh	004514360	PA-014	Children's Hospital of UPMC 4401 Penn Avenue Pittsburgh PA 152240000
University of Pittsburgh	004514360	PA-014	Magee Womens Hospital of UPMC 300 Halket Street Pittsburgh PA 152130000
UNIVERSITY OF PITTSBURGH AT PITTSBURGH	004514360		UNIVERSITY OF PITTSBURGH OFFICE OF RESEARCH PITTSBURGH PA 152132303

G.9 FOREIGN COMPONENT

No foreign component

G.10 ESTIMATED UNOBLIGATED BALANCE

G.10.a Is it anticipated that an estimated unobligated balance (including prior year carryover) will be greater than 25% of the current year's total approved budget?

Yes

Estimated unobligated balance: 261812

G.10.b Provide an explanation for unobligated balance:
It is expected we wil have greater than 25% carryover due to the delay in the IRB and MTA as well as pending invoices for IT professional services. Without the IRB and MTA in place, the work to prepare and ship samples could not be completed. We expect that in year 2 of the award, we will address all pending requests for tissue from year 1 as well as those needed in year 2. For this reason, we plan to formally request the carryover funds from year 1 from the NIDDK to ensure we have the funds to address all requests for year 2.

G.10.c If authorized to carryover the balance, provide a general description of how it is anticipated that the funds will be spent

G.11 PROGRAM INCOME

Is program income anticipated during the next budget period?

No

G.12 F&A COSTS

Not Applicable

Inclusion Enrollment Report

Inclusion Data Record (IDR) #: 1078054

Using an Existing Dataset or Resource: No

Delayed Onset Study ?: No

Clinical Trial: No

Enrollment Location: Domestic

NIH Defined Phase III Clinical Trial: No

Study Title: Research on tissue from an elective or spontaneous abortion < 24 weeks gestation

Planned Enrollment

Racial Categories	Ethnic Categories									Total
	Not Hispanic or Latino			Hispanic or Latino			Unknown/Not Reported Ethnicity			
	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	
American Indian/Alaska Native	0	0		0	0					**0**
Asian	50	0		0	0					**50**
Native Hawaiian or Other Pacific Islander	0	0		0	0					**0**
Black or African American	100	0		10	0					**110**
White	200	0		20	0					**220**
More than One Race	0	0		20	0					**20**
Unknown or Not Reported										
Total	**350**	**0**		**50**	**0**					**400**

Cumulative Enrollment

Only planned enrollment data exists for this data record. The PD/PI did not enter cumulative inclusion enrollment data.

RESEARCH & RELATED BUDGET - SECTION A & B

ORGANIZATIONAL DUNS*: 004514360

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF PITTSBURGH AT PITTSBURGH

Start Date*: 06-01-2017 **End Date*:** 05-31-2018

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1.		Rajiv		DHir		Project Lead	(b)(6)				37,400.00	9,278.00	46,678.00
2.		(b)(6)				Co-investigator					20,550.00	5,098.00	25,648.00
3.						Co-investigator					26,846.00	6,660.00	33,506.00
4.						Co-investigator					9,000.00	2,233.00	11,233.00
5.						Co-investigator					6,000.00	1,489.00	7,489.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name:

Total Senior/Key Person **124,554.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
9	Support staff	(b)(6)			127,745.00	46,755.00	174,500.00
9	**Total Number Other Personnel**					**Total Other Personnel**	**174,500.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**299,054.00**

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E

ORGANIZATIONAL DUNS*: 004514360

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF PITTSBURGH AT PITTSBURGH

Start Date*: 06-01-2017 **End Date*:** 05-31-2018

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	**0.00**
Total Equipment	**0.00**

Additional Equipment: File Name:

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	12,502.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**12,502.00**

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		0.00
2. Stipends		0.00
3. Travel		0.00
4. Subsistence		0.00
5. Other:		
0 Number of Participants/Trainees	**Total Participant Trainee Support Costs**	**0.00**

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K

ORGANIZATIONAL DUNS*: 004514360

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF PITTSBURGH AT PITTSBURGH

Start Date*: 06-01-2017 **End Date*:** 05-31-2018

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	50,991.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. HSTB Services	8,000.00
9. Project Management Tool, BIOS (IT Services)	26,335.00
10. Shipping costs	500.00
Total Other Direct Costs	**85,826.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**397,382.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. MTDC	54.0	32,448.00	17,522.00
2. MTDC	55.5	356,933.00	198,098.00
		Total Indirect Costs	**215,620.00**

Cognizant Federal Agency
(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**613,002.00**

J. Fee	Funds Requested ($)*
	0.00

K. Budget Justification*	File Name: Fetal budget justification _yr 2.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

BUDGET JUSTIFICATION

Personnel

Rajiv Dhir, MD, MBA: PI, Effort = (b)(6). Dr. Dhir is the medical director of the Health Sciences Tissue Bank (HSTB) of the University of Pittsburgh and a practicing pathologist with subspecialty training in Genitourinary Pathology. He will be responsible for the oversight of the project. This will include interfacing and working with internal collaborators to ensure accrual and annotation of the appropriate specimens. He will also interact with the external collaborators and clients to ensure appropriate specimen aggregation and disbursement. He will work closely with NIDDK to ensure successful execution of the project, meeting the mission and goals of the Tissue Core (**Figure 1**: Proposed organizational structure of the Tissue Core). Annual effort of (b)(6) is requested.

(b)(6): Effort = (b)(6) will be responsible for coordination and management of day to day operations. She supervises HSTB staff members and will manage the overall efforts of the HSTB and set operational standards related to the HSTB scope of work. She will assure proper communication and resolution conflicts and issues.

1. **Tissue Hub Infrastructure Support**

A crucial component of this application is the infrastructure for the Tissue Hub, which will include personnel for the development and maintenance of a secure web-based interface for GUDMAP investigators, assurance of regulatory compliance, data collection and record-keeping, and management of the quality assurance program associated with this project.

(b)(6) Co-I, Effort = (b)(6) is the Director of (b)(6) and will be the director of the Tissue hub Infrastructure. He also serves as the faculty in-charge of the informatics requirements of HSTB. He provides direction and advice related to the different Information systems and tools used by HSTB. He is also the director of the Imaging core; a subsidiary of HSTB. The imaging core will perform whole slide image acquisition and provide access to these images for the Tissue Core clients. Annual effort of (b)(6) is requested.

(b)(6) Effort = (b)(6) This (b)(6) will be responsible for project intake, tracking and recording keeping. She will coordinate the GUDMAP investigator requests to the GUDMAP-Human Tissue Repository including documenting the needs of the investigator, assuring regulatory compliance, coordinating with tissue and data collection staff members and assuring proper completion and shipping of requests. Annual effort of (b)(6) is requested.

(b)(6): Effort = (b)(6) This (b)(6) will be responsible for the quality program. He will manage all aspects of quality management including record keeping, training of staff members to standard operating procedures (SOPs), data entry practices and audits, and quality related events. He will coordinate the overall record keeping and management of the quality metrics from the tissue collection and data entry processes with the quality measurements performed through the Department of Pediatrics team.

(b)(6): Effort = (b)(6) This (b)(6) specialist will be responsible for overall management of the Biospecimen Inventory and Operations System with regard to the this project. He will manage the specimen search process, control the data entry lexicon as needed, and provide reports of collection activity for investigators who request samples and as needed for other purposes. He will maintain the data integrity and make corrections and amendments based on the quality control activities. In the case that new fields and library elements are required he will manage that process in conjunction with the Project Manager and Quality Manager. He will be required to produce final sample pick lists as specimens are disbursed.

(b)(6): Effort = (b)(6) is the technician responsible for processing tissues, immunohistochemistry and immunofluorescence needs of the project. He is also the supervisor of the Research Histology core facility and is responsible for the development of specialized techniques required by the program and for processes not included in the fee-for-service activity.

(b)(6): Effort = (b)(6) The (b)(6) will be responsible for aggregating information from the different information systems on the specimens offered as part of the Tissue Core. This will include pathology information as well as more specialized information (like

cytogenetics); if applicable. The data coordinator will work with the Project manager on cohort identification for the different requests. In addition the data coordinator will also be responsible for providing data to the clients of the Tissue Core.

2. Fetal Tissue Procurement Laboratory (Magee Women's Hospital)

All of the fetal tissue will be collected at Magee Women's Hospital, undergo a gross examination, and then be transported to the validation laboratory for further assessment prior to distribution.

(b)(6) **:** Co-I, Effort = (b)(6) is the (b)(6) (b)(6) He will be responsible for evaluating appropriate surgical pathology and autopsy specimens, and overseeing collection of the biological materials for the Tissue Core and will act as the director of the tissue procurement laboratory. He will perform the clinical evaluation of the gross genitourinary specimen and ensure quality control of the dissection to minimize mechanical disruption. He will train the staff to obtain early gestational age genitourinary specimens, and work closely with (b)(6) to perform routine and specialized histological assessment of the appropriate specimens. Annual effort of (b)(6) is requested.

(b)(6) Effort = (b)(6) This HSTB tissue bank technician and will perform the day-to-day tasks associated with the collection of specimens. This includes maintaining a working knowledge of all SOPs related to the ongoing collections that are requested by the GUDMAP investigators. She will coordinate with the clinical departments within Magee Women's Hospital of UPMC, interface with the Pathology and other hospital staff members as required to obtain the requested specimens and enter data related to each case in the BIOS.

(b)(6) Effort = (b)(6) This (b)(6) and technician will perform the day-to-day tasks associated with the collection of specimens. This includes maintaining a working knowledge of all SOPs related to the ongoing collections that are requested by the GUDMAP investigators. She will coordinate with the clinical departments within Magee Women's Hospital of UPMC, interface with the Pathology and other hospital staff members as required to obtain the requested specimens and enter data related to each case in the BIOS.

3. Validation Laboratory (Children's Hospital of Pittsburgh)

The validation laboratory will perform quality assurance measures, as per GUDMAP project needs (eg. histological assessment, *in situ* hybridization and RNA isolation).

(b)(6) **:** Co-I, Effort = (b)(6) is a kidney developmental biologist with over (b)(6) studying the genitourinary tract and will act as the director of the validation laboratory. Furthermore, he is also a classically trained human anatomist, histologist and embryologist. The quality assurance of the specimens will be performed by at least two independent evaluations (b)(6) for GUDMAP project needs. (b)(6) will work closely with (b)(6) to train staff to perform the gross dissection for early gestational age genitourinary tissues, and tissues not currently being obtained by the Tissue Bank, as per GUDMAP project needs. He will also oversee the training of (b)(6) (tissue hub technician) in all aspects of dissection, histology and molecular evaluation of the fetal tissues.

(b)(6) **:** Co-I, Effort = (b)(6) is a clinician scientist (Pediatric Nephrologist) with a research program related to kidney development and will act as the co-director of the validation laboratory. She has a thorough understanding of genitourinary development. She will participate in quality assurance of specimens as noted above. Furthermore, (b)(6) will provide direction and advice regarding the clinical parameters that will be used to screen fetal and neonatal tissues to exclude pathological specimens, and will evaluate individual cases as needed.

(b)(6) **:** Effort = (b)(6) This grant will fund (b)(6) of the technicians salary. This technician will perform all the required validation of the specimens including: histology, immunohistochemistry, in situ hybridization, cell isolation and real time PCR.

Supplies

HSTB Consumable Laboratory Supplies: (b)(4) Or about (b)(4) monthly will be used for sample collections, integrity, maintenance, and transport including sample and shipping containers, dry ice, and other basic supplies.

Shipping: Funds are requested for the shipment of tissue, $500 is requested.

Validation Laboratory Consumable Laboratory Supplies: (b)(4) Or about (b)(4) monthly will be required to purchase reagents for staining, immunohistochemistry and in situ reagents as well as cell, culture medium and consumable plastics related to these processes. These processes will be performed in response to the needs of the GUDMAP investigators.

Travel

Pathology: The Project PI and HSTB staff will need to travel to GUDMAP consortia meetings, to be held twice a year. A total of $6,502 is allocated for this travel in year 2.

Validation Laboratories: The Project co-investigators will need to travel to GUDMAP consortia meetings, to be held twice a year. (b)(6) will also attend the American Society of Nephrology meeting where GUDMAP typically has a booth. A total of $6,000 is allocated for this travel in year 2.

(b)(6) will also attend the International Meeting on Development Nephrology to be held in 2018, where GUDMAP will hold workshops.

Other Expenses

Tissue embedding/processing, storage, and disbursement: $8,000 for year 2. These are billable services based on the fiscal parameters in place within the University of Pittsburgh for the HSTB. Tissue embedding and processing will be required at all levels for quality management and to provide product to GUDMAP investigators. Storage costs are based on the partial cost of a freezer with a 10 year life span plus projected maintenance and certification costs. The cost for disbursement of samples to GUDMAP investigators will be charged to the account award for this project.

Website maintenance, project management tool, BIOS, image acquisition: $26,335. Resources will be required to maintain and update our internally developed inventory management system (BIOS). The project management tool is internally developed and is the mechanism for starting and following the progress of the request from the client. The clients will be provided access to the contents of the resource via a Sharepoint link that will be password protected. Whole slide image acquisition will be done to offer clients access to high quality images of the specimens in the resource. These images will be from routine and specialized histologic and immunohistochemical/ in-situ protocols. We also have capabilities for image analysis and will offer, if required.

Notice of Award

RESOURCE-RELATED COOPERATIVE AGREEMENT PROJECTS **Federal Award Date:** 09/12/2016

Department of Health and Human Services
National Institutes of Health
NATIONAL INSTITUTE OF DIABETES AND DIGESTIVE AND KIDNEY DISEASES

Grant Number: 1U24DK110791-01
FAIN: U24DK110791

Principal Investigator(s):
RAJIV DHIR, MD

Project Title: University of Pittsburgh as the GUDMAP Tissue Hub and Collection Site

(b)(6)
University of Pittsburgh
123 University Place, B21
Grants and Contracts Officer
Pittsburgh, PA 152132303

Award e-mailed to: (b)(6) @offres.pitt.edu

Period Of Performance:
Budget Period: 09/15/2016 – 05/31/2017
Project Period: 09/15/2016 – 05/31/2021

Dear Business Official:

The National Institutes of Health hereby awards a grant in the amount of $600,000 (see "Award Calculation" in Section I and "Terms and Conditions" in Section III) to UNIVERSITY OF PITTSBURGH AT PITTSBURGH in support of the above referenced project. This award is pursuant to the authority of 42 USC 241 31 USC 6305 42 CFR 52 and is subject to the requirements of this statute and regulation and of other referenced, incorporated or attached terms and conditions.

Acceptance of this award including the "Terms and Conditions" is acknowledged by the grantee when funds are drawn down or otherwise obtained from the grant payment system.

Each publication, press release, or other document about research supported by an NIH award must include an acknowledgment of NIH award support and a disclaimer such as "Research reported in this publication was supported by the National Institute Of Diabetes And Digestive And Kidney Diseases of the National Institutes of Health under Award Number U24DK110791. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health." Prior to issuing a press release concerning the outcome of this research, please notify the NIH awarding IC in advance to allow for coordination.

Award recipients must promote objectivity in research by establishing standards that provide a reasonable expectation that the design, conduct and reporting of research funded under NIH awards will be free from bias resulting from an Investigator's Financial Conflict of Interest (FCOI), in accordance with the 2011 revised regulation at 42 CFR Part 50 Subpart F. The Institution shall submit all FCOI reports to the NIH through the eRA Commons FCOI Module. The regulation does not apply to Phase I Small Business Innovative Research (SBIR) and Small Business Technology Transfer (STTR) awards. Consult the NIH website http://grants.nih.gov/grants/policy/coi/ for a link to the regulation and additional important information.

If you have any questions about this award, please contact the individual(s) referenced in Section IV.

Sincerely yours,

(b)(6)

Grants Management Officer
NATIONAL INSTITUTE OF DIABETES AND DIGESTIVE AND KIDNEY DISEASES

Additional information follows

SECTION I – AWARD DATA – 1U24DK110791-01

Award Calculation (U.S. Dollars)

Salaries and Wages	$225,631
Fringe Benefits	$68,514
Personnel Costs (Subtotal)	$294,145
Materials & Supplies	$47,891
Travel	$9,914
Other	$44,613
Federal Direct Costs	$396,563
Federal F&A Costs	$203,437
Approved Budget	$600,000
Total Amount of Federal Funds Obligated (Federal Share)	$600,000
TOTAL FEDERAL AWARD AMOUNT	$600,000
AMOUNT OF THIS ACTION (FEDERAL SHARE)	$600,000

SUMMARY TOTALS FOR ALL YEARS		
YR	**THIS AWARD**	**CUMULATIVE TOTALS**
1	$600,000	$600,000
2	$613,002	$613,002
3	$613,002	$613,002
4	$613,002	$613,002
5	$613,002	$613,002

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

Fiscal Information:

CFDA Name:	Diabetes, Digestive, and Kidney Diseases Extramural Research
CFDA Number:	93.847
EIN:	1250965591A1
Document Number:	UDK110791A
PMS Account Type:	P (Subaccount)
Fiscal Year:	2016

IC	CAN	2016	2017	2018	2019	2020
DK	8472288	$600,000	$613,002	$613,002	$613,002	$613,002

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

NIH Administrative Data:
PCC: KDH KDB / **OC**: 414L / **Released**: (b)(6) 09/11/2016
Award Processed: 09/12/2016 07:02:07 PM

SECTION II – PAYMENT/HOTLINE INFORMATION – 1U24DK110791-01

For payment and HHS Office of Inspector General Hotline information, see the NIH Home Page at http://grants.nih.gov/grants/policy/awardconditions.htm

SECTION III – TERMS AND CONDITIONS – 1U24DK110791-01

This award is based on the application submitted to, and as approved by, NIH on the above-titled project and is subject to the terms and conditions incorporated either directly or by reference in the following:

a. The grant program legislation and program regulation cited in this Notice of Award.
b. Conditions on activities and expenditure of funds in other statutory requirements, such as those included in appropriations acts.
c. 45 CFR Part 75.

d. National Policy Requirements and all other requirements described in the NIH Grants Policy Statement, including addenda in effect as of the beginning date of the budget period.
e. Federal Award Performance Goals: As required by the periodic report in the RPPR or in the final progress report when applicable.
f. This award notice, INCLUDING THE TERMS AND CONDITIONS CITED BELOW.

(See NIH Home Page at http://grants.nih.gov/grants/policy/awardconditions.htm for certain references cited above.)

Research and Development (R&D): All awards issued by the National Institutes of Health (NIH) meet the definition of "Research and Development" at 45 CFR Part§ 75.2**.** As such, auditees should identify NIH awards as part of the R&D cluster on the Schedule of Expenditures of Federal Awards (SEFA). The auditor should test NIH awards for compliance as instructed in Part V, Clusters of Programs. NIH recognizes that some awards may have another classification for purposes of indirect costs. The auditor is not required to report the disconnect (i.e., the award is classified as R&D for Federal Audit Requirement purposes but non-research for indirect cost rate purposes), unless the auditee is charging indirect costs at a rate other than the rate(s) specified in the award document(s).

Carry over of an unobligated balance into the next budget period requires Grants Management Officer prior approval.

This award is subject to the requirements of 2 CFR Part 25 for institutions to receive a Dun & Bradstreet Universal Numbering System (DUNS) number and maintain an active registration in the System for Award Management (SAM). Should a consortium/subaward be issued under this award, a DUNS requirement must be included. See http://grants.nih.gov/grants/policy/awardconditions.htm for the full NIH award term implementing this requirement and other additional information.

This award has been assigned the Federal Award Identification Number (FAIN) U24DK110791. Recipients must document the assigned FAIN on each consortium/subaward issued under this award.

Based on the project period start date of this project, this award is likely subject to the Transparency Act subaward and executive compensation reporting requirement of 2 CFR Part 170. There are conditions that may exclude this award; see http://grants.nih.gov/grants/policy/awardconditions.htm for additional award applicability information.

In accordance with P.L. 110-161, compliance with the NIH Public Access Policy is now mandatory. For more information, see NOT-OD-08-033 and the Public Access website: http://publicaccess.nih.gov/.

In accordance with the regulatory requirements provided at 45 CFR 75.113 and Appendix XII to 45 CFR Part 75, recipients that have currently active Federal grants, cooperative agreements, and procurement contracts with cumulative total value greater than $10,000,000 must report and maintain information in the System for Award Management (SAM) about civil, criminal, and administrative proceedings in connection with the award or performance of a Federal award that reached final disposition within the most recent five-year period. The recipient must also make semiannual disclosures regarding such proceedings. Proceedings information will be made publicly available in the designated integrity and performance system (currently the Federal Awardee Performance and Integrity Information System (FAPIIS)). Full reporting requirements and procedures are found in Appendix XII to 45 CFR Part 75. This term does not apply to NIH fellowships.

Treatment of Program Income:
Other Research (Add/Deduct Option)

Notice: Under governing regulations, Federal funds administered by the Department of Health and Human Services shall not be expended for research involving human subjects, and individuals shall not be enrolled in such research, without prior approval by the Office of Human Research Protections (OHRP) of an assurance to comply with the requirements of 45 CFR 46 to protect human research subjects. This restriction applies to all collaborating sites without OHRP-approved assurances, whether domestic or foreign, and compliance must be ensured by the awardee.

Notice: Under governing policy, federal funds administered by the Public Health Service (PHS) shall not be expended for research involving live vertebrate animals without prior approval by the Office of Laboratory Animal Welfare (OLAW) of an assurance to comply with the PHS policy on humane care and use of laboratory animals. This restriction applies to all performance sites (e.g., collaborating institutions, subcontractors, subgrantees) without OLAW-approved assurances, whether domestic or foreign.

The present award is made without an OLAW-approved assurance and/or currently valid verification of IACUC approval for this project with the following restriction: Only activities that do not involve vertebrate animals may be conducted pending acceptance by the NIDDK of verification of IACUC approval. The verification of IACUC approval must be submitted not later than November 3, 2016 to the grants management specialist named below.

Failure to submit the verification of IACUC approval within the required timeframe or to otherwise comply with the above requirements can result in suspension and/or termination of this award, withholding of support, audit disallowances and/or other appropriate action.

The grantee is required to follow the model organism sharing plan included in the application and may not implement any changes in the plan without the written prior approval of the NIDDK.

In addition to the PI, the following individuals are named as key personnel:

(b)(6)

Written prior approval is required if any of the individual(s) named above withdraws from the project entirely, is absent from the project during any continuous period of 3 months or more, or reduces time devoted to the project by 25 percent or more from the level that was approved at the time of award.

This grant is in response to RFA/PA DK15-016. Acceptance of this award requires compliance with this solicitation. See the NIH Guide at http://grants.nih.gov/grants/guide/index.html for copy of the RFA/PA that includes administrative and programmatic requirements specific to this award.

Although the initial budget period for this award is 09/15/2016-05/31/2017, the award includes funds for 12 months of support. Future year budget periods will cycle on 06/01/2017. Allowable preaward costs may be charged to this award in accordance with the conditions outlined in the NIH Grants Policy Statement (revised November 2015) and with institutional requirements for prior approval.

In accordance with NIH Guide Notice NOT-OD-16-045, Notice of Salary Limitation on Grants, Cooperative Agreements, and Contracts, none of the funds in this award shall be used to pay the salary of an individual at a rate in excess of the applicable salary cap. Therefore this award and/or future years are adjusted accordingly, if applicable. See the salary cap summary and the time frames associated with salary caps at http://grants.nih.gov/grants/policy/salcap_summary.htm.

In order to meet current NIDDK objectives and based on the relative scientific merit ranking of this application, the budget for the initial period has been programmatically reduced. Although specific budget adjustments have been made, the Institution and Principal Investigator retain standard rebudgeting authorities for this mechanism of support.

See the budget information below for additional information.

Grantees can determine which progress reports are due through the website located at https://public.era.nih.gov/chl/public/search/index.jsp , and should periodically check the site, which is updated on or around the 30th of each month. Progress report due dates are also available in the eRA Commons Status system. In addition, automatic e-mail notifications are sent to the PD/PI prior to due date.

As of October 17, 2014, the National Institutes of Health (NIH) requires grantees to submit all type 5 progress reports using the eRA Research Performance Progress Report (RPPR) module. Annual progress reports submitted in any format other than the RPPR will not be processed by the NIH and will require resubmission through the RPPR module in accordance with NIH Guide Notice Number NOT-OD-15-014 released October 16, 2014.

The following special terms of award are in addition to, and not in lieu of, otherwise applicable U.S. Office of Management and Budget (OMB) administrative guidelines, U.S. Department of Health and Human Services (DHHS) grant administration regulations at 45 CFR Parts 74 and 92 (Part 92 is applicable when State and local Governments are eligible to apply), and other HHS, PHS, and NIH grant administration policies.
The administrative and funding instrument used for this program will be the cooperative agreement, an "assistance" mechanism (rather than an "acquisition" mechanism), in which substantial NIH programmatic involvement with the awardees is anticipated during the performance of the activities. Under the cooperative agreement, the NIH purpose is to support and stimulate the recipients' activities by involvement in and otherwise working jointly with the award recipients in a partnership role; it is not to assume direction, prime responsibility, or a dominant role in the activities. Consistent with this concept, the dominant role and prime responsibility resides with the awardees for the project as a whole, although specific tasks and activities may be shared among the awardees and the NIH as defined below.

The PD(s)/PI(s) will have the primary responsibility for:

- All aspects of the scientific activities, including defining the objectives and approaches, planning, conduct, analysis, and publication of results, interpretations, and conclusions of studies conducted under the terms and conditions of the cooperative agreement award.
- Collaborating with other investigators in the program for protocol development, sample, reagents and data sharing as appropriate, data quality control, and data organization
- Accountability towards the applicant organization officials and to the NIDDK for the performance and proper conduct of the research supported by the project in accordance with the terms and conditions of the award.
- Serving as a voting member of the Steering Committee and will attend the Planning Meeting and a Steering Committee meeting in the first year, two Steering Committee meetings a year in subsequent years and monthly teleconference calls.
- Accepting and implementing the goals, priorities, procedures, protocols, and policies agreed upon by the Steering Committee and subcommittees, and be responsible for close coordination and cooperation with the components of the GUDMAP consortium and with NIDDK staff.
- Adhering to PHS policy for the distribution of unique research resources produced with PHS funding as described under Special Requirements.
- Establishing written milestones for the project, in negotiation with NIDDK Project Staff prior to funding.
- Release all study design materials and procedure manuals into the public domain and/or make them available to other investigators, according to the approved plan for making data and materials available to the scientific community and the NIDDK, for the conduct of research at no charge other than the costs of reproduction and distribution, consistent with achieving the goals of this program initiative.
- Awardees will retain custody of and have primary rights to the data and software developed under these awards, subject to Government rights of access consistent with current DHHS, PHS, and NIH policies.

NIH staff will have substantial programmatic involvement that is above and beyond the normal stewardship role in awards, as described below:

- An NIH Project Scientist will have substantial programmatic involvement that is above and beyond the normal stewardship role in awards, as described below. However, the dominant role and prime responsibility for the project as a whole resides with the

awardees, although specific tasks and activities in carrying out the studies will be shared by awardees and the NIDDK.

- NIDDK will designate a Project Officer and a Grants Management Specialist to provide normal program stewardship and administrative oversight of the cooperative agreement.
- NIDDK will form an External Advisory Committee (EAC), comprised of the NIDDK Project Scientist and other NIH extramural staff with relevant scientific expertise or who manage research grant programs that relate scientifically to the goals of the GUDMAP projects, and outside advisors selected by the NIDDK. The EAC will meet annually with the GUDMAP Steering Committee to review and assess GUDMAP and to advise NIDDK of scientific developments and opportunities that may enhance the achievement of the GUDMAP goals.
- The NIDDK Project Scientist will attend and participate as a voting member in all meetings of the Steering Committee, and provide liaison between the Steering Committee and the External Advisory Committee.
- The NIDDK Project Scientist will help the Steering Committee develop and draft operating policies.
- The NIDDK Project Officer will review the scientific progress of the individual GUDMAP components, for compliance with operating policies developed by the Steering Committee, and may recommend to the NIDDK to withhold support, suspend, or terminate an award for lack of scientific progress or failure to adhere to policies established by the Steering Committee.
- An agency program official or IC program director will be responsible for the normal scientific and programmatic stewardship of the award and will be named in the award notice. The assigned Program Officer may also serve as an NIDDK Project Scientist.

Areas of Joint Responsibility include:

- Steering Committee - The NIDDK Project Scientist, PIs from the project funded through this FOA and RFA-DK-15-014, and RFA-DK-15-015 and voluntary representatives from the previously funded GUDMAP atlas projects funded under RFA-DK-11-001 will be responsible for forming a Steering Committee as defined below. An arbitration system, as detailed below, will be available to resolve disagreements among members of the Steering Committee. The Steering Committee will be the main governing board of the GUDMAP consortium. It will develop collaborative protocols, identify technological impediments to success and strategies to overcome them, develop shared software tools for disseminating information about the projects, and identify opportunities for sharing techniques and tools that might be developed in future GUDMAP atlas projects.
- The Steering Committee will be composed of the PIs from the project funded through this FOA, RFA-DK-15-014, and RFA-DK-15-015, representatives from the previously funded GUDMAP projects, and the NIDDK Project Scientist. The representatives and the PIs will each have one vote. The NIDDK Project Scientist for this project will have one vote. The Steering Committee will select a chairperson who will be someone other than an NIH staff member.
- The Steering Committee may, as it deems necessary, invite additional, non-voting scientific advisors to meetings at which research priorities and opportunities are discussed. The NIH reserves the right to augment the scientific or consumer expertise of the Steering Committee when necessary.
- There will be two Steering Committee meetings annually. The first meeting will be a Planning Meeting to be held in the Washington, DC area on **June 20-21, 2016**. At the Planning Meeting, the Steering Committee will be formed and a chairperson selected from among the members. At the Planning Meeting, the Steering Committee may: (a) draft a charter to detail policies and procedures, a process for monitoring compliance with the policies and procedures, and a process for recommending that the NIDDK Project Administrators act on evidence of non-compliance of any Consortium component with Steering Committee policies; (b) agree upon the terms of the charter; and (c) devise a plan for working with the GUDMAP database developers to provide ongoing input into database and website design.
- At the second and subsequent meetings, the Steering Committee will refine the GUDMAP scientific objectives and implementation as necessary, consistent with data produced by former and possible future GUDMAP atlas projects and from other laboratories.
- The Steering Committee will plan workshops, to which non-GUDMAP participants will also be invited, to inform the research community of the progress made toward development of the atlas, and to inform the research community of any technological

advances related to the implementation of the GUDMAP website/database. The NIDDK Project Scientist, the External Advisory Committee, and other NIH staff as appropriate will provide the Steering Committee with advice on participants for the workshops and symposia.

- The Steering Committee may establish subcommittees as it deems appropriate.
- Awardee members of the Steering Committee will be required to accept and implement policies approved by the Steering Committee.
- The EAC will meet annually with the GUDMAP Steering Committee to review and assess the progress of the GUDMAP consortium and to advise NIDDK of scientific developments and opportunities that may enhance the achievement of the GUDMAP goals.

Dispute Resolution

Any disagreements that may arise in scientific or programmatic matters (within the scope of the award) between award recipients and the NIH may be brought to Dispute Resolution. A Dispute Resolution Panel will have three members: a designee of the Steering Committee chosen without NIH staff voting, one NIH designee, and a third designee with expertise in the relevant area who is chosen by the other two; in the case of individual disagreement, the first member may be chosen by the individual awardee. This special dispute resolution procedure does not alter the awardee's right to appeal an adverse action that is otherwise appealable in accordance with PHS regulation 42 CFR Part 50, Subpart D and DHHS regulation 45 CFR Part 16.
- See more at: http://grants.nih.gov/grants/guide/rfa-files/RFA-DK-15-016.html#sthash.UY9M5nfL.dpuf

STAFF CONTACTS

The Grants Management Specialist is responsible for the negotiation, award and administration of this project and for interpretation of Grants Administration policies and provisions. The Program Official is responsible for the scientific, programmatic and technical aspects of this project. These individuals work together in overall project administration. Prior approval requests (signed by an Authorized Organizational Representative) should be submitted in writing to the Grants Management Specialist. Requests may be made via e-mail.

Grants Management Specialist: (b)(6)
Email: (b)(6) @extra.niddk.nih.gov **Phone:** (b)(6) **Fax:** (b)(6)

Program Official: (b)(6)
Email: (b)(6) @niddk.nih.gov **Phone:** (b)(6)

SPREADSHEET SUMMARY
GRANT NUMBER: 1U24DK110791-01

INSTITUTION: UNIVERSITY OF PITTSBURGH AT PITTSBURGH

Budget	Year 1	Year 2	Year 3	Year 4	Year 5
Salaries and Wages	$225,631	$224,475	$223,034	$223,034	$223,034
Fringe Benefits	$68,514	$68,163	$67,726	$67,726	$67,726
Personnel Costs (Subtotal)	$294,145	$292,638	$290,760	$290,760	$290,760
Equipment				$1	$1
Materials & Supplies	$47,891	$47,646	$47,340	$47,340	$47,340
Travel	$9,914	$9,863	$9,800	$9,800	$9,800
Other	$44,613	$44,384	$44,003	$43,794	$43,794
TOTAL FEDERAL DC	$396,563	$394,531	$391,903	$391,695	$391,695
TOTAL FEDERAL F&A	$203,437	$218,471	$221,099	$221,307	$221,307
TOTAL COST	$600,000	$613,002	$613,002	$613,002	$613,002

Facilities and Administrative Costs	Year 1	Year 2	Year 3	Year 4	Year 5
F&A Cost Rate 1	54%	54%	55.5%	56.5%	56.5%
F&A Cost Base 1	$376,735	$32,878	$32,659	$391,694	$391,694
F&A Costs 1	$203,437	$17,754	$18,126	$221,307	$221,307

F&A Cost Rate 2		55.5%	56.5%		
F&A Cost Base 2		$361,653	$359,244		
F&A Costs 2		$200,717	$202,973		

PI: **DHIR, RAJIV**	Title: University of Pittsburgh as the GUDMAP Tissue Hub and Collection Site	
Received: 11/06/2015	FOA: DK15-016	Council: 05/2016
Competition ID: FORMS-C	FOA Title: GENITOURINARY DEVELOPMENT MOLECULAR ANATOMY PROJECT (GUDMAP) - HUMAN TISSUE CORE (U24)	
1 U24 DK110791-01	Dual:	Accession Number: 3880427
IPF: 2059802	Organization: UNIVERSITY OF PITTSBURGH AT PITTSBURGH	
Former Number:	Department: Pathology	
IRG/SRG: ZDK1 GRB-2 (M3)S	AIDS: N	Expedited: N
Subtotal Direct Costs (excludes consortium F&A) Year 1: 400,000 Year 2: 409,050 Year 3: 421,354 Year 4: 427,924 Year 5: 437,770	Animals: N Humans: Y Clinical Trial: N Current HS Code: 30 HESC: N	New Investigator: Early Stage Investigator:
Senior/Key Personnel:	*Organization:*	*Role Category:*
(b)(6)	University of Pittsburgh	Co-Investigator
	University of Pittsburgh	Co-Investigator
Rajiv Dhir M.D.	University of Pittsburgh	PD/PI
(b)(6)	University of Pittsburgh	Co-Investigator
	University of Pittsburgh	Co-Investigator

OMB Number: 4040-0001
Expiration Date: 06/30/2016

APPLICATION FOR FEDERAL ASSISTANCE
SF 424 (R&R)

3. DATE RECEIVED BY STATE	**State Application Identifier**

1. TYPE OF SUBMISSION*

❍ Pre-application ❍ Application ● Changed/Corrected Application

4.a. Federal Identifier

b. Agency Routing Number

2. DATE SUBMITTED | **Application Identifier**

c. Previous Grants.gov Tracking Number
GRANT12034213

5. APPLICANT INFORMATION

Organizational DUNS*: 004514360

Legal Name*: University of Pittsburgh
Department: Office of Research
Division:
Street1*: 123 University Place, B21
Street2:
City*: Pittsburgh
County: Allegheny
State*: PA: Pennsylvania
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*: 15213-2303

Person to be contacted on matters involving this application
Prefix: Mr. First Name*: (b)(6) Suffix:
Position/Title:
Street1*: 123 University Place, B21
Street2: Grants and Contracts Officer
City*: Pittsburgh
County: Allegheny
State*: PA: Pennsylvania
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*: 15213-2303
Phone Number*: (b)(6) Fax Number (b)(6) Email: offres@offres.pitt.edu

6. EMPLOYER IDENTIFICATION NUMBER *(EIN) or (TIN)** 25-0965591

7. TYPE OF APPLICANT* X: Other (specify)

Other (Specify): private, non-profit, state-related educational ins

Small Business Organization Type ❍ Women Owned ❍ Socially and Economically Disadvantaged

8. TYPE OF APPLICATION*

● New ❍ Resubmission
❍ Renewal ❍ Continuation ❍ Revision

If Revision, mark appropriate box(es).

❍ A. Increase Award ❍ B. Decrease Award ❍ C. Increase Duration
❍ D. Decrease Duration ❍ E. Other *(specify)* :

Is this application being submitted to other agencies?* ❍Yes ●No What other Agencies?

9. NAME OF FEDERAL AGENCY*
National Institutes of Health

10. CATALOG OF FEDERAL DOMESTIC ASSISTANCE NUMBER
TITLE:

11. DESCRIPTIVE TITLE OF APPLICANT'S PROJECT*
University of Pittsburgh as the GUDMAP Tissue Hub and Collection Site

12. PROPOSED PROJECT

Start Date* Ending Date*
07/01/2016 06/30/2021

13. CONGRESSIONAL DISTRICTS OF APPLICANT
PA-014

SF 424 (R&R) APPLICATION FOR FEDERAL ASSISTANCE

14. PROJECT DIRECTOR/PRINCIPAL INVESTIGATOR CONTACT INFORMATION

Prefix: Dr. First Name*: Rajiv Middle Name: Last Name*: Dhir Suffix: M.D.

Position/Title: Professor
Organization Name*: University of Pittsburgh
Department: Pathology
Division:
Street1*: UPMC Shadyside
Street2: 5230 Centre Avenue,Room WG 02.6
City*: Pittsburgh
County: Allegheny
State*: PA: Pennsylvania
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*: 15213-2303
Phone Number*: 412-623-1321 Fax Number: Email*: dhirr@upmc.edu

15. ESTIMATED PROJECT FUNDING

a. Total Federal Funds Requested*	$3,207,015.00
b. Total Non-Federal Funds*	$0.00
c. Total Federal & Non-Federal Funds*	$3,207,015.00
d. Estimated Program Income*	$0.00

16.IS APPLICATION SUBJECT TO REVIEW BY STATE EXECUTIVE ORDER 12372 PROCESS?*

a. YES ○ THIS PREAPPLICATION/APPLICATION WAS MADE AVAILABLE TO THE STATE EXECUTIVE ORDER 12372 PROCESS FOR REVIEW ON:

DATE:

b. NO ○ PROGRAM IS NOT COVERED BY E.O. 12372; OR

● PROGRAM HAS NOT BEEN SELECTED BY STATE FOR REVIEW

17. By signing this application, I certify (1) to the statements contained in the list of certifications* and (2) that the statements herein are true, complete and accurate to the best of my knowledge. I also provide the required assurances * and agree to comply with any resulting terms if I accept an award. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties. (U.S. Code, Title 18, Section 1001)

● I agree*

** The list of certifications and assurances, or an Internet site where you may obtain this list, is contained in the announcement or agency specific instructions.*

18. SFLLL or OTHER EXPLANATORY DOCUMENTATION File Name:

19. AUTHORIZED REPRESENTATIVE

Prefix: Dr. First Name*: (b)(6) Suffix: Ph.D

Position/Title*: (b)(6)
Organization Name*: University of Pittsburgh
Department: Office of Research
Division:
Street1*: 123 University Place, B21
Street2:
City*: Pittsburgh
County: Allegheny
State*: PA: Pennsylvania
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*: 15213-2303
Phone Number*: (b)(6) Fax Number: (b)(6) Email*: offres@offres.pitt.edu

Signature of Authorized Representative*

(b)(6)

Date Signed*

11/06/2015

20. PRE-APPLICATION File Name:

21. COVER LETTER ATTACHMENT File Name:1235-Cover letter.pdf

424 R&R and PHS-398 Specific Table Of Contents

OMB Number: 4040-0010
Expiration Date: 06/30/2016

Project/Performance Site Location(s)

Project/Performance Site Primary Location

❍ I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name:	University of Pittsburgh
Duns Number:	0045143600000
Street1*:	UPMC Shadyside
Street2:	5230 Centre Avenue
City*:	Pittsburgh
County:	Allegheny
State*:	PA: Pennsylvania
Province:	
Country*:	USA: UNITED STATES
Zip / Postal Code*:	15232-0000
Project/Performance Site Congressional District*:	PA-014

Project/Performance Site Location 1

❍ I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name:	University of Pittsburgh
DUNS Number:	0045143600000
Street1*:	Children's Hospital of UPMC
Street2:	4401 Penn Avenue
City*:	Pittsburgh
County:	Allegheny
State*:	PA: Pennsylvania
Province:	
Country*:	USA: UNITED STATES
Zip / Postal Code*:	15224-0000
Project/Performance Site Congressional District*:	PA-014

Project/Performance Site Location 2

❍ I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name:	University of Pittsburgh
DUNS Number:	0045143600000
Street1*:	Magee Womens Hospital of UPMC
Street2:	300 Halket Street
City*:	Pittsburgh
County:	Allegheny
State*:	PA: Pennsylvania
Province:	
Country*:	USA: UNITED STATES
Zip / Postal Code*:	15213-0000
Project/Performance Site Congressional District*:	PA-014

Funding Opportunity Number: RFA-DK-15-016. Received Date: 2015-11-06T15:43:10.000-05:00

	File Name
Additional Location(s)	

OMB Number: 4040-0001
Expiration Date: 06/30/2016

RESEARCH & RELATED Other Project Information

1. Are Human Subjects Involved?* ● **Yes** ○ **No**

1.a. If YES to Human Subjects

Is the Project Exempt from Federal regulations? ○ Yes ● No

If YES, check appropriate exemption number: _ 1 _ 2 _ 3 _ 4 _ 5 _ 6

If NO, is the IRB review Pending? ● **Yes** ○ **No**

IRB Approval Date:

Human Subject Assurance Number 00006790

2. Are Vertebrate Animals Used?* ○ **Yes** ● **No**

2.a. If YES to Vertebrate Animals

Is the IACUC review Pending? ○ Yes ○ No

IACUC Approval Date:

Animal Welfare Assurance Number

3. Is proprietary/privileged information included in the application?* ○ **Yes** ● **No**

4.a. Does this project have an actual or potential impact - positive or negative - on the environment?* ○ **Yes** ● **No**

4.b. If yes, please explain:

4.c. If this project has an actual or potential impact on the environment, has an exemption been authorized or an environmental assessment (EA) or environmental impact statement (EIS) been performed? ○ Yes ○ No

4.d. If yes, please explain:

5. Is the research performance site designated, or eligible to be designated, as a historic place?* ○ **Yes** ● **No**

5.a. If yes, please explain:

6. Does this project involve activities outside the United States or partnership with international collaborators?* ○ **Yes** ● **No**

6.a. If yes, identify countries:

6.b. Optional Explanation:

	Filename
7. Project Summary/Abstract*	1236-Abstract Final 20151025.pdf
8. Project Narrative*	1237-Project Narrative.pdf
9. Bibliography & References Cited	1238-References Cited_Final.pdf
10.Facilities & Other Resources	1239-Facilities FINAL GUDMAP 20151030.pdf
11.Equipment	1240-Equipment FINAL GUDMAP 20151030.pdf

Funding Opportunity Number: RFA-DK-15-016. Received Date: 2015-11-06T15:43:10.000-05:00

ABSTRACT

Congenital diseases of the genitourinary tract (kidneys, bladder, ureter, urethra etc.) are a leading cause of organ failure carrying with it an increased risk of death, and are a growing public health burden. At present, the only therapies are dialysis (for the kidneys) and organ transplantation. With the demand for transplants far exceeding supply there is an imminent need for alternate therapies. A comprehensive understanding of how the genitourinary tract develops *in utero* is necessary to effectively develop novel therapies to replace or repair injured tissue. The **GenitoUrinary Development Molecular Anatomy Project (GUDMAP)** has been successful at providing a high-resolution map of gene expression in the mouse GenitoUrinary system. However, a similar description has not been available for the human genitourinary system, nor has it been possible to develop optimized experimental techniques to grow, expand and differentiate human genitourinary progenitor cells *in vitro*. These research efforts by the developmental biology community have been hampered by the lack of a central hub for the procurement, quality control and distribution of human genitourinary samples. The Health Sciences Tissue Bank (HSTB) at the University of Pittsburgh has been involved in human tissue procurement for over 18 years, with a long standing history of collecting, maintaining and disbursing quality samples to research scientists, both in house and outside the University of Pittsburgh. HSTB is embedded within the Department of Pathology of the University of Pittsburgh Health Systems; thus providing rapid access to very high quality tissue and biological specimens. HSTB has established consenting protocols in line with the best practices recommendations from the NIH, a strong informatics backbone to facilitate specimen procurement and annotation, and has in place a robust quality control and quality assurance programs. The HSTB biorepository is fully accredited by the College of American Pathologists (CAP). HSTB has an established program accruing fetal tissues. The fetal tissue IRB has been in place since 2005. HSTB has the infrastructure for dissecting specimens and collecting different tissue types. In this calendar year, we have disbursed over 300 fresh samples collected from 77 cases. The collections can be significantly ramped up as material could have been accrued from as many as 725 cases last year. We have preliminary data showing that we can isolate the human urogenital system (kidneys, ureters and bladders) from various developmental ages (6-24 weeks). We have produced publication quality images of these genitourinary organs (including kidneys and bladder) and have also been able to isolate and expand cells from various genitourinary organs. Further, we have shipped high quality tissue to various GUDMAP investigators and they have verified the quality of the tissue sent. *We propose to act as both the GUDMAP Tissue Hub and Tissue Gathering site to build upon the pre-existing specialized collecting abilities of HSTB and provide high quality genitourinary samples to members of the scientific community including those within GUDMAP.*

Project Narrative:

An understanding of human genitourinary development is critical to tackling the growing number of developmental diseases affecting these tissues. This grant proposes to leverage the significant infrastructure of the University of Pittsburgh to provide high quality fetal tissue to the GUDMAP atlas projects.

Health Sciences Tissue Bank Facilities/Equipment Description

The Health Sciences Tissue Bank (HSTB) provides essential support for University of Pittsburgh research programs needing biological materials from patients seen at UPMC. The main objectives of the HSTB are to provide a mechanism to simplify and streamline the process of research tissue accrual and disbursement, and to provide efficient research pathology support services including histology, immunohistochemistry and paraffin tissue microarrays. The Health Sciences Tissue Bank is part of the University of Pittsburgh Core Research Facilities. Although the tissue bank is under the auspices of The University, we also have a strong working relationship with UPMC and the Department of Pathology. The HSTB has three College of American Pathology (CAP) certified laboratories in the flagship UPMC hospitals: Presbyterian, Shadyside, and Magee Women's Hospital, as well as a collection site in the community hospital (b)(4) In addition, the HSTB extensively interacts with Oncology and Pathology Informatics and has computer and server facilities located in these collaborative facilities. The facilities available to the tissue resource at each of these institutions are detailed below:

Shadyside Hospital (SYS)

Health Sciences Tissue Bank Shadyside Laboratory Space:

The Health Sciences Tissue Bank (HSTB) administrative office is located a short distance from the (b)(4); (b)(6) (b)(4); (b)(6) (b)(4); (b)(6) The HSTB laboratory and freezer room space occupies 3300 square feet. This space includes the tissue banking lab space, research histology lab space, freezer rooms and storage rooms. The space is divided into six rooms. The largest room, measuring 30'x20', is for tissue processing, slide retrieval and storage. This laboratory is equipped with a cryobath, liquid nitrogen tank and dry ice for varied methods of snap freezing tissue, a Thermo cryostat used to cut frozen sections for quality review by a pathologist. Centrifuges, Cytospin, calibrated pipettes, microscopes, and sterile supplies are available for tissue procurement and dissection. The lab space has a refrigerator to store media and other necessary reagents as well as a -80°C freezer for short term sample storage. There are 9 working stations in the lab area all equipped with desktop computers, barcode scanners and hooked up to a network printer. There is a storage area for paraffin embedded tissue blocks and slides. Locked filing cabinets are located in the space for secure storage of documents and files. These facilities provide staff with all the necessary materials to procure quality tissue for tissue collection and disbursement.

The smaller laboratory area, measuring 30'x10' is for research histology. This lab space has the unique equipment necessary for formalin fixed paraffin embedded (FFPE) tissue processing and staining, along with the specific equipment needed for paraffin tissue microarray (TMA) construction. For paraffin processing, a ThermoShandon Excelsior tissue processor and Sakura Tissue Tek embedding center are used. There are 3 Microm microtomes, 2 are equipped with histocollimators. They can be setup for routine sectioning, thick sectioning microtomy and laser capture microdissection (LCM) slides or other protocol specific requests. There is 1 automated stainer for H&E staining and 2 automated Dako stainers used for immunohistochemical (IHC) staining along with calibrated pipettes for serial dilution and titration protocols, which are used to stain tissue based on study design. The tissue microarray portion of the lab contains 2 Beecher Tissue Microarrayers with coring capabilities from 0.6 to 2.0mm. The histology lab also contains its own ThermoShandon cryostat allowing for the capability of providing frozen section slides. Included in the lab is a 2°-8°C walk-in cooler and -20°C freezer for reagent storage. Other available supplies include water baths, glassware, 2 incubator ovens, a fume hood for cover slipping and other tools needed to perform daily tasks. The histology space includes 3 active work stations with desktop computers hooked up to a network printer. One of the work stations has a Slidemate slide writer locally connected to one of the computers used for automated slide labeling.

There are two designated freezer areas. One contains 12 Thermo -80C freezers, while the other room is set up specifically for vapor phase liquid nitrogen freezers, containing 6 vessels. This space has piped liquid nitrogen from the hospital facility. Both freezer rooms also contain additional secure storage space. There are two hallways, measuring 30'x6' and 25'x8', used for filing cabinets for glass slides, paraffin blocks and supplies.

Health Sciences Tissue Bank Shadyside Office Space**:**

Dr. Dhir and the tissue banking staff have offices within the (b)(4); (b)(6) area, which are in near proximity to the (b)(4) . The Director, Dr. Rajiv Dhir, has a 500 sq. ft. office suite which contains a desk space with a desktop computer and multiheaded microscope. This space also contains a conference table with seating for 8. Outside of his suite, there is an anteroom with desk space for his administrative assistant. The Assistant Director has a 110 sq. ft. office within the HSTB at UPMC

Shadyside, along with an 80 sq. ft. shared office space for the Project and Quality Managers. The Research Histology Supervisor has a 130 sq. ft. lab space on the histology side of the main laboratory set up. All office spaces contain desktop computers with dual monitors mapped to network printers, scanners, telephones, locked filing cabinets, and other office supplies necessary for administrative operations. The rooms are also equipped with a dry-erase whiteboard for teaching assistance and microscopes as needed.

UPMC Shadyside (b)(4); (b)(6) This area is approximately 450 sq. ft and includes the main gross room and the frozen section area. It functions as the central processing and sectioning lab for gross pathology at UPMC-Shadyside Hospital. It has 5 grossing stations that have fume hoods for processing non-sterile specimens. Each of the fume hoods is equipped with PCs linked to the hospital mainframe system, sinks, and a DictaPhone Voice Processor for dictation of gross descriptions.
This facility is a fully functional surgical pathology gross room, and contains equipment necessary for this purpose. Such equipment includes: Leica CM1800 CryoStat, H&E staining station, ButcherBoy band saw for sectioning of bone, Cabinet X-Ray System Faxitron Series HP, Polarstar No-frost refrigerator, Revco -70 C upright freezer, Flammable cabinet, Cryobath CB-60 isopentane cryopreservation unit, Aculab GS-2001 Standard Digital Scale, and dissecting equipment, chemicals, glassware, and storage shelves for such purposes. This room also has a two-head American optical microscope for frozen section interpretation.

Health Sciences Tissue Bank - Imaging Services: Imaging services are offered through the Health Sciences Tissue Bank (HSTB). The digital imaging core facility offers clinical and research services. The imaging core has imaging equipment for generating, annotating, interpreting, storing and analyzing digital images. This facility is located at UPMC Shadyside in the Hillman Cancer Pavilion and has about 200 sq. ft. of space for the imaging laboratory. The imaging facility provides pathologist oversight, technical support staff and space for imaging studies, validation, training and conferencing. Images can be securely hosted and made available to investigators for remote viewing or saved locally for investigators on a DVD, USB flash drive or external hard drive.
Equipment: Imaging devices include Nikon digital cameras for macroscopic pathology and Spot insight cameras for microscopic imaging. For virtual microscopy at 20x, 40x and 60x magnification a variety of whole slide scanners (Omnyx, Aperio and Hamamatsu Nanozoomer) are available. The Nanozoomer has z-stack (multiple plane) capability.
Image analysis: The imaging facility offers image algorithm development and image analysis. The Visiopharm platform is primarily used for this work, which allows cellular structures and biomarkers in tissue samples to be detected and quantified, automated alignment of serial tissue sections, and tissue microarray (TMA) image analysis. Quantitative image analysis of immunohistochemistry can also be performed on images using Aperio's nuclear, positive pixel count or membrane algorithms.

Presbyterian University Hospital (PUH)
Health Sciences Tissue Bank Presbyterian Laboratory Space:
The HSTB laboratory and freezer room space occupies 1800 sq. ft in (b)(4); (b)(6) This space includes the tissue banking laboratory and three freezer rooms. The lab space is 100 sq. ft. and is equipped for tissue processing, slide retrieval and storage. This laboratory contains a cryobath and dry ice for varied methods of snap freezing tissue, a Thermo cryostat used to cut frozen sections for quality review by a pathologist. Centrifuges, cryobath, calibrated pipettes, microscopes, and sterile supplies are available for tissue procurement and dissection. The lab space has a refrigerator to store media and other necessary reagents as well as an adjacent 100 sq. ft. freezer room with a -80°C freezer for short term sample storage. There are 4 working stations in the lab area all equipped with desktop computers, barcode scanners and hooked up to a network printer. There is a storage area for paraffin embedded tissue blocks and slides. Locked filing cabinets are located in the space for secure storage of documents and files.
The Presbyterian site has three freezer rooms in (b)(4); (b)(6) one located on the (b)(4) and two located (b)(4) measuring 600 and 300 sq. ft. Combined, the freezer rooms house 14 -80°C freezers and 1 liquid nitrogen storage vessel. The largest of the three rooms located (b)(4) also has 1 desktop computer. The Presbyterian site also has administrative office space located down the hall from the laboratory. The office is 80 sq. ft. and contains a desktop computer and locked filing cabinets. These facilities provide staff with all the necessary materials to procure quality tissue for tissue collection and disbursement.

UPMC Presbyterian Pathology Gross Room:

This area is approximately 1000 sq. ft. in area and includes the main gross room, the imaging room and the frozen section room. The main gross room lab is approximately 750 sq. ft. in area. It functions as the central processing and sectioning lab for gross pathology at Presbyterian University Hospital. There is an additional frozen section room located on the (b)(4) . This frozen section room is equipped with current state-of-the-art informatics and electronics for communication with the operating rooms. This frozen section room measures approximately 400 sq. ft. in area. It has two cryostats and three cutting stations. It also contains two computers connected to the network. The frozen section room has digital video feed to and from the operating rooms. This also allows for instantaneous discussions with the surgeons as well immediate “show and tell” for them. This room serves as the center for procurement of fresh tissue samples for research.

Magee Women’s Hospital (MWH)

Health Sciences Tissue Bank Magee Laboratory Space:

(b)(4); (b)(6)

(b)(4); (b)(6) The Magee site has (b)(4); (b)(6)

(b)(4); (b)(6)

UPMC Magee (b)(4); (b)(6)

Magee-Women’s Hospital (b)(4); (b)(6)

(b)(4); (b)(6)

(b)(4); (b)(6)

UPMC Magee (b)(4); (b)(6)

(b)(4); (b)(6)

UPMC Magee (b)(4); (b)(6)

(b)(4); (b)(6)

The UPMC Magee (b)(4); (b)(6)

(b)(4); (b)(6)

Children's Hospital of Pittsburgh Facilities and Other Resources:

Children's Hospital Laboratory:

(b)(6) has a 450 sq. ft. laboratory (half a bay) on the (b)(4) (b)(4) (b)(6) laboratory is equipped for sophisticated molecular and developmental biological experimentation. The pediatric nephrology division has shared facilities that includes a biosafety hood, - 20°C and -70°C freezers, cell culture incubators, Hypoxia chamber for cell and organ culture, a microtome, 2 dissecting microscopes, an upright fluorescent microscope, a digital camera, electrophoresis and power supplies, 3 thermocyclers, a high quality water purification system, a pH meter, an analytical balance and hybridization ovens. Ample bench top space, desk space and computer access is available. (b)(6) has an office on the (b)(4) that is 140 sq. ft. near (b)(6) laboratory.

(b)(6) laboratory encompasses approximately 900 square feet of laboratory space, adjacent to (b)(6), facilitating access to shared divisional equipment. (b)(6) has an

(b)(4) that is 140 sq. ft. near (b)(6) laboratory.

Animals:
N/A

Computers:
(b)(6) office and laboratory are equipped with iMac desktop computers (1 in the office and 2 in the laboratories) and ample hard drive space. These are connected to an intranet server with additional hard drive space. All computers are connected to the Internet.
(b)(6) office and laboratory are equipped with iMac desktop computers (1 in the office and 3 in the laboratories) and ample hard drive space. These are connected to an intranet server with additional hard drive space. All computers are connected to the Internet.

Clinical:
N/A

Office:
(b)(6) has an office on the (b)(4) that is 140 sq. ft. near (b)(6) laboratory. All staff in the (b)(6) lab has their own individual desk space.
(b)(6) has an office on the (b)(4) that is 140 sq. ft. near (b)(6) laboratory. All staff in the (b)(6) lab has their own individual desk space.

Other:
(b)(4) These cores both consist of a sorter (FACSAriaII) and an analyzer (LSRII), as well as significant expert technical support. This will be available for the project.

Pathology Core:
The Pathology Core is located (b)(4) The Histology core will provide tissue processing, sectioning, general staining, immunohistochemistry, and in situ hybridization. This will be available for the project.

Cell Imaging Core:
The Cell Imaging Core, located (b)(4) has confocal microscopy and live cell imaging as well as technical support. This will be available for the project.

Pittsburgh Center for Kidney Research:
This center facilitates multidisciplinary research related to kidney physiology, cell biology and pathophysiology. The cores include: Core A Cellular Physiology; Core B Single Nephron and Organ Physiology; Core C Urinary Tract Epithelial Imaging; and Core D Use of Model Organisms to Elucidate Novel Aspects of Kidney Function.

Equipment:

Validation laboratories (b)(6)
(b)(6) have a fully equipped laboratory for molecular biology, and flow hoods for cell culture.
Equipment in the lab includes:

- 1 Biosafety hood (Kewaunee)
- 2 Cell culture hoods (Filtech)
- 5 freezers (3 -20 and 2 -80) (Thermo)
- 2 Cell culture incubators (Thermo)
- 1 tissue processor (Leica)
- 1 embedding station (Leica)
- 1 microtome (Thermo)
- 1 Floatation bath (Boekel)
- 3 dissecting microscopes (Leica)
- 1 upright fluorescent microscope (Leica)
- 2 digital cameras (Axio)
- 1 3D reconstructive Imaging equipment (MBF, Zeiss)
- 3 Hybridization ovens (Labnet)
- 3 electrophoresis and power supplies (Fisher)
- 3 thermocyclers (Biorad)
- 1 high quality water purification system (Millipore)
- 1 pH meter (Fisher)
- 1 analytical balance (Denver Instruments)
- 3 hybridization ovens (Fisher)
- 3 water baths (Fisher)

Health Sciences Tissue Bank Laboratories:

(b)(4)

OMB Number: 4040-0001
Expiration Date: 06/30/2016

RESEARCH & RELATED Senior/Key Person Profile (Expanded)

PROFILE - Project Director/Principal Investigator

Prefix: Dr. First Name*: Rajiv Middle Name Last Name*: Dhir Suffix: M.D.

Position/Title*: Professor
Organization Name*: University of Pittsburgh
Department: Pathology
Division:
Street1*: UPMC Shadyside
Street2: 5230 Centre Avenue,Room WG 02.6
City*: Pittsburgh
County: Allegheny
State*: PA: Pennsylvania
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: 15213-2303

Phone Number*: 412-623-1321 Fax Number: E-Mail*: dhirr@upmc.edu

Credential, e.g., agency login: (b)(6)

Project Role*: PD/PI Other Project Role Category:

Degree Type: MD Degree Year: 1989

	File Name
Attach Biographical Sketch*:	1243-Biosketch-RajivDhir 20150825.pdf
Attach Current & Pending Support:	

Tracking Number: GRANT12034939
Funding Opportunity Number: RFA-DK-15-016 . Received Date: 2015-11-06T15:43:10.000-05:00

PROFILE - Senior/Key Person

Prefix: Dr. First Name*: (b)(6) Suffix: M.D.

Position/Title*: (b)(6)
Organization Name*: University of Pittsburgh
Department: Pediatrics
Division: (b)(6)
Street1*:
Street2:
City*: Pittsburgh
County: Allegheny
State*: PA: Pennsylvania
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: 15224-0000

Phone Number*: (b)(6) Fax Number: E-Mail*: (b)(6) @chp.edu

Credential, e.g., agency login: (b)(6)

Project Role*: Co-Investigator Other Project Role Category:

Degree Type: MD Degree Year: 2001

File Name

Attach Biographical Sketch*: 1244(b)(6) biosketch- new.pdf

Attach Current & Pending Support:

PROFILE - Senior/Key Person

Prefix: Dr. First Name*: (b)(6) Suffix: M.D.

Position/Title*: (b)(6)
Organization Name*: University of Pittsburgh
Department: Pathology
Division:
Street1*: UPMC Shadyside Hospital (b)(6)
Street2: 5150 Centre Avenue
City*: Pittsburgh
County: Allegheny
State*: PA: Pennsylvania
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: 15232-0000

Phone Number*: (b)(6) Fax Number (b)(6) E-Mail* (b)(6) @upmc.edu

Credential, e.g., agency login (b)(6)

Project Role*: Co-Investigator Other Project Role Category:

Degree Type: MD Degree Year: 1996

File Name

Attach Biographical Sketch*: 1245(b)(6) NIH Biosketch.pdf

Attach Current & Pending Support:

PROFILE - Senior/Key Person

Prefix: Dr. First Name*: (b)(6) Suffix: M.D.

Position/Title*: (b)(6)
Organization Name*: University of Pittsburgh
Department: Pathology
Division:
Street1*: (b)(6)
Street2:
City*: Pittsburgh
County: Allegheny
State*: PA: Pennsylvania
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: 15213-0000

Phone Number*: (b)(6) Fax Number: E-Mail*: (b)(6)@upmc.edu

Credential, e.g., agency login: (b)(6)

Project Role*: Co-Investigator Other Project Role Category:

Degree Type: MD Degree Year: 1988

Attach Biographical Sketch*: File Name 124(b)(6) Biosketch 102315 Fetal urologic tissue bank.pdf

Attach Current & Pending Support:

PROFILE - Senior/Key Person

Prefix: Dr. First Name*: (b)(6) Suffix: Ph.D

Position/Title*: (b)(6)
Organization Name*: University of Pittsburgh
Department: Pediatrics
Division: (b)(6)
Street1*:
Street2:
City*: Pittsburgh
County: Allegheny
State*: PA: Pennsylvania
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: 15213-0000

Phone Number*: (b)(6) Fax Number: (b)(6) E-Mail*: (b)(6)@chp.edu

Credential, e.g., agency login: (b)(6)

Project Role*: Co-Investigator Other Project Role Category:

Degree Type: PhD Degree Year: 2007

Attach Biographical Sketch*: File Name 1247-(b)(6) NIH Biosketch-GUDMAP.pdf

Attach Current & Pending Support:

OMB No. 0925-0001/0002 (Rev. 08/12 Approved Through 8/31/2015)

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME: Dhir, Rajiv

eRA COMMONS USER NAME (credential, e.g., agency login): RAJIVDHIR

POSITION TITLE: Professor of Pathology in the School of Medicine

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
All-India Institute of Medical Sciences, New Delhi, India	MBBS	1/1984	Pathology
All-India Institute of Medical Sciences, New Delhi, India	M.D.	6/1989	Pathology
University of Pittsburgh Pittsburgh, PA	MBA	4/2012	Business

A. Personal Statement

I am Professor of Pathology at the University of Pittsburgh. I am a practicing pathologist and currently serve as the Chief of Pathology at Shadyside Hospital, one of the flagship hospitals of the University of Pittsburgh. I have has been the Medical Director of the Health Sciences Tissue Bank of the University of Pittsburgh since 1997. I oversee the tissue and biological specimen collection at the 3 flagship hospitals of the University of Pittsburgh Health Systems. This Tissue Resource has developed into a large resource for basic and translational research at the University of Pittsburgh as well collaborative research with investigators outside the University of Pittsburgh. I have been the principal physician involved in developing and implementing an Institutional Honest broker system, incorporating the key data aggregation agencies at the University of Pittsburgh. I have also been involved in the Informatics related initiatives in the Tissue Banking space. I am also one of the participants in the RAND report on Tissue Banking. I have been an invited member of the Marble Arch group, an international consortium of Tissue Bankers.
As a trained Genitourinary Pathologist, I have an active interest in GU diseases; especially BPH. This project represents an opportunity to bring together the Tissue Banking activities and his GU interest.

B. Positions and Honors

Positions and Employment

Positions and Employment:

11/97-12/99	Research Assistant Professor, Pathology, University of Pittsburgh, Pittsburgh, PA
11/97-present	Director, Health Sciences Tissue Bank, University of Pittsburgh Health Systems.
01/00-03/04	Assistant Professor, Pathology, University of Pittsburgh, Pittsburgh, PA
04/00-present	Member, NCI coordination committee, Pathology, IRB and Marketing Subcommittees, Cooperative Prostate Cancer Tissue Resource.
07/00-present	Project Leader, Tissue Resource Core for the Director's Challenge U01 funded for the "Molecular Reclassification of Prostate Cancer".
12/00-present	Project Leader, Tissue Resource Core for program project on Collaborative Urologic Research in Spinal Cord Injury.
06/01-present	Project Leader, Tissue Resource Core for the Lung SPORE.
07/02-present	Division Director, Genito-Urinary Pathology, University of Pittsburgh Health Systems.
09/02-present	Chair, Marketing committee, Co-operative Prostate Cancer Tissue Resource.
11/02-present	Member, NIDDK coordination committee, Pathology and Biomarker Subcommittees, MTOPS consortium.
01/04-present	Medical Director of the Tissue and Research Pathology Services Shared facility for the University of Pittsburgh Cancer Center.
04/04-03/10	Associate Professor, Pathology, University of Pittsburgh, Pittsburgh, PA
01/07-present	Chief of Pathology, University of Pittsburgh, Pittsburgh, PA
03/10-Present	Professor of Pathology, University of Pittsburgh, Pittsburgh, PA
2011-Present	Director, Pathology International Business Development, Pittsburgh, PA

Other Experience and Professional Memberships

American Urological Association	2003-Present
American Association for Cancer Research, Inc.	2003-Present
Association of Pathology Informatics	2001-Present
International Society for Biological and Environmental Repositories	2000-Present
International Association of Pathology	1998-Present
University of Pittsburgh Cancer Institute	1998-Present
International Society of Urologic Pathology	1998-Present
Pittsburgh Pathology Society	1994-Present
College of American Pathologists	1992-Present
American Society of Clinical Pathologists	1992-Present
US and Canadian Academy of Pathology	1992-Present

Honors

Title of Award	**Year**
UPMC ACES (Award for Commitment and Excellence in Service)	2014
Adrianna Selvaggio Dedication to Commitment and Quality Award from the Shadyside Hospital Medical Staff and Administration	2013
Smith Kline Beecham Travel Award from the Society for Basic Urologic Research	1995
Finalist, Pathology Resident Awards, American Society for Clinical Pathology	1995
National Talent Search Scheme Award, given by the National Council for Educational Research and Training, New Delhi, India.	1979
National Award by the Govt. of India	1978
National Award by the Govt. of India	1977

C. Contribution to Science

I have been actively involved in identifying markers on diagnostic, prognostic and therapeutic value in renal cancers.

1. Targeted resequencing of P-arm, chromosome 9 genes associated with Renal Papillary Type 2 Cancer. William A LaFramboise[1], Patricia Petrosko[1], Maureen A Lyons-Weiler[1], Christin M Sciulli[1], Michael A Belsky[1], Michael J Becich[1], J Michael Krill-Burger[1], Clinton J Miller[2], Gavin D Meredith[3], Sheldon I Bastacky[1], Anil V Parwani[1],**Rajiv Dhir[1]**. Accepted; American Journal of Pathology.
2. Amylase α-1A (AMY1A): a novel immunohistochemical marker to differentiate chromophobe renal cell carcinoma from benign oncocytoma. Jain S, Roy S, Amin M, Acquafondata M, Yin M, Laframboise W, Bastacky S, Pantanowitz L, Dhir R, Parwani A. Am J Surg Pathol. 2013 Dec;37(12):1824-30.
3. Renal cell neoplasms contain shared tumor type-specific copy number variations. Krill-Burger JM, Lyons MA, Kelly LA, Sciulli CM, Petrosko P, Chandran UR, Kubal MD, Bastacky SI, Parwani AV, **Dhir R**, Laframboise WA. Am J Pathol. 2012 Jun;180(6):2427-39. Epub 2012 Apr 3.
4. Differential proteomic analysis of renal cell carcinoma tissue interstitial fluid. Teng PN, Hood BL, Sun M, **Dhir R**, Conrads TP. J Proteome Res. 2011 Mar 4;10(3):1333-42.
5. Hagenkord JM, Parwani AV, Lyons-Weiler MA, Alvarez K, Amato R, Gatalia Z, Gonzalez-Berjon JM, Peterson L., **Dhir R**, Monzon FA. Virtual kayotyping with SNP microarrays reduces uncertainty in diagnosis of renal epithelial tumors. Diagn Pathol 2008 Nov;3(1):44.

Working with other colleagues, we have implemented a broad based research support system, including honest broker services for data triage to researchers, tissue and biological specimen acquisition.

6. **Dhir R**. Patel AA, Winters S, Bisceglia M, Swanson D, Aamodt R, Becich MJ. A multi-disciplinary approach to honest broker services for tissue banks and clinical data: a pragmatic and practical model. Cancer 2008 Oct1;113(7):1705-15.

7. **Dhir, R**. Prostate cancer biobanking. Curr Opin Urol 2008 May;18:309-314.

8. Melamed J, Datta MW, Becich MJ, Orenstein JM, **Dhir R**, Silver S, Fidelia-Lambert M, Kadjacsy-Balla A, Macias V, Patel A, Walden PD, Bosland MC, Berman JJ. The cooperative prostate cancer tissue resource: a specimen and data resource cancer researchers. Clin Cancer Res 2004, Jul 15;10(14):4614-21.

As the PI of the contract to the University of Pittsburgh to support the TCGA project, we provided approximately 800 cases and were one of the largest contributors to the TCGA effort.

9. Integrated genomic characterization of papillary thyroid carcinoma. Cancer Genome Atlas Research Network. Electronic address: giordano@umich.edu; Cancer Genome Atlas Research Network. Cell. 2014 Oct 23;159(3):676-90. PMID:25417114.
10. Comprehensive molecular profiling of lung adenocarcinoma. Cancer Genome Atlas Research Network. Nature. 2014 Jul 31; 511(7511):543-50.
11. Comprehensive molecular characterization of gastric adenocarcinoma. Cancer Genome Atlas Research Network. Nature. 2014 Sep 11;513(7517):202-9.
12. Comprehensive molecular characterization of urothelial bladder carcinoma. Cancer Genome Atlas Research Network. Nature. 2014 Mar 20;507(7492):315-22.
13. Comprehensive molecular characterization of clear cell renal cell carcinoma. Cancer Genome Atlas Research Network. Nature. 2013 Jul 4;499(7456):43-9.
14. Integrated genomic characterization of endometrial carcinoma. Cancer Genome Atlas Research Network, Kandoth C, Schultz N, Cherniack AD, Akbani R, Liu Y, Shen H, Robertson AG, Pashtan I, Shen R, Benz CC, Yau C, Laird PW, Ding L, Zhang W, Mills GB, Kucherlapati R, Mardis ER, Levine DA. Nature. 2013 May 2;497(7447):67-73.
15. Comprehensive molecular portraits of human breast tumours. **Cancer Genome Atlas Network**. Nature. 2012 Oct 4;490(7418):61-70.
16. Comprehensive genomic characterization of squamous cell lung cancers. **Cancer Genome Atlas Research Network**, Nature. 2012 Sep 27;489(7417):519-25.
17. Comprehensive molecular characterization of human colon and rectal cancer. Cancer Genome Atlas Network. Nature. 2012 Jul 18;487(7407):330-7.

Complete List of Publications:
http://www.ncbi.nlm.nih.gov/pubmed/?term=dhir+r

D. Research Support

ACTIVE SUPPORT:

P30CA047904-25 (Davidson) NIH Cancer Center Support Grant	08/01/2015-07/31/2020	0.36 Calendar months
U19 OH009077-06, CR (Becich) CDC National Mesothelioma Virtual Bank for Translational Research	9/01/2006-08/31/2016	0.24 Calendar months
P50 CA090440-11,CR (Siegfried) NIH SPORE in Lung Cancer	06/01/2001-06/30/2016	1.2 Calendar months

OVERLAP:
None

OMB No. 0925-0001/0002 (Rev. 08/12 Approved Through 8/31/2015)

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

(b)(6)

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OMB No. 0925-0001/0002 (Rev. 08/12 Approved Through 8/31/2015)

BIOGRAPHICAL SKETCH

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(b)(6)

(b)(6)

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(b)(6)

(b)(6)

(b)(6)

OMB No. 0925-0001/0002 (Rev. 08/12 Approved Through 8/31/2015)

BIOGRAPHICAL SKETCH

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(b)(6)

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(b)(6)

(b)(6)

OMB Number: 4040-0001
Expiration Date: 06/30/2016

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 1

ORGANIZATIONAL DUNS*: 0045143600000

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: University of Pittsburgh

Start Date*: 07-01-2016 **End Date*:** 06-30-2017 **Budget Period: 1**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1 .	Dr.	Rajiv		Dhir	M.D.	PD/PI	(b)(6)				36,660.00	8,358.00	45,018.00
2 .	Dr.	(b)(6)			M.D.	Co-investigator					9,000.00	2,052.00	11,052.00
3 .	Dr.				M.D.	Co-investigator					9,000.00	2,052.00	11,052.00
4 .	Dr.				M.D.	Co-investigator					25,881.00	5,901.00	31,782.00
5 .	Dr.				PhD	Co-investigator					18,540.00	4,227.00	22,767.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name:

Total Senior/Key Person **121,671.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	HSTB Manager	(b)(6)			4,159.00	1,506.00	5,665.00
1	Project Coordinator				20,563.00	7,444.00	28,007.00
3	Research Techincian				75,407.00	27,297.00	102,704.00
1	QA Coordinator				13,028.00	4,716.00	17,744.00
1	IT Coordinator				7,783.00	2,817.00	10,600.00
1	Data Coordinator				7,565.00	2,738.00	10,303.00
8	**Total Number Other Personnel**					**Total Other Personnel**	**175,023.00**

Total Salary, Wages and Fringe Benefits (A+B) **296,694.00**

RESEARCH & RELATED Budget {A-B} (Funds Requested)

Funding Opportunity Number: RFA-DK-15-016 . Received Date: 2015-11-06T15:43:10.000-05:00

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 1

ORGANIZATIONAL DUNS*: 0045143600000
Budget Type*: ● Project ❍ Subaward/Consortium
Organization: University of Pittsburgh

Start Date*: 07-01-2016 **End Date*:** 06-30-2017 **Budget Period: 1**

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	
Total Equipment	
Additional Equipment: File Name:	

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	10,000.00
2. Foreign Travel Costs	
Total Travel Cost	**10,000.00**

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

Funding Opportunity Number: RFA-DK-15-016 . Received Date: 2015-11-06T15:43:10.000-05:00

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 1

ORGANIZATIONAL DUNS*: 0045143600000
Budget Type*: ● Project ○ Subaward/Consortium
Organization: University of Pittsburgh

Start Date*: 07-01-2016 **End Date*:** 06-30-2017 **Budget Period: 1**

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	48,306.00
2. Publication Costs	
3. Consultant Services	
4. ADP/Computer Services	
5. Subawards/Consortium/Contractual Costs	
6. Equipment or Facility Rental/User Fees	
7. Alterations and Renovations	
8 . HSTB Services	20,000.00
9 . Project Management Tool, BIOS	25,000.00
Total Other Direct Costs	**93,306.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**400,000.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . MTDC	54.00	380,000.00	205,200.00
		Total Indirect Costs	**205,200.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number) U.S. Department of Health and Human Services, (b)(6) (b)(6)

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**605,200.00**

J. Fee	Funds Requested ($)*

K. Budget Justification* File Name: 1234-(b)(6) budget justification 10.30.2015.pdf
(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

OMB Number: 4040-0001
Expiration Date: 06/30/2016

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 2

ORGANIZATIONAL DUNS*: 0045143600000

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: University of Pittsburgh

Start Date*: 07-01-2017 **End Date*:** 06-30-2018 **Budget Period: 2**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1 .	Dr.	Rajiv		Dhir	M.D.	PD/PI		(b)(6)			36,660.00	8,358.00	45,018.00
2 .	Dr.	(b)(6)			M.D.	Co-investigator					9,270.00	2,114.00	11,384.00
3 .	Dr.				M.D.	Co-investigator					9,270.00	2,114.00	11,384.00
4 .	Dr.				M.D.	Co-investigator					26,658.00	6,078.00	32,736.00
5 .	Dr.				PhD	Co-investigator					19,096.00	4,354.00	23,450.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name:

Total Senior/Key Person **123,972.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	HSTB Manager	(b)(6)			4,263.00	1,543.00	5,806.00
1	Project Coordinator				21,077.00	7,630.00	28,707.00
3	Research Techincian				77,492.00	28,052.00	105,544.00
1	QA Coordinator				13,353.00	4,834.00	18,187.00
1	IT Coordinator				7,978.00	2,888.00	10,866.00
1	Data Coordinator				7,792.00	2,821.00	10,613.00
8	**Total Number Other Personnel**					**Total Other Personnel**	**179,723.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**303,695.00**

RESEARCH & RELATED Budget {A-B} (Funds Requested)

Funding Opportunity Number: RFA-DK-15-016 . Received Date: 2015-11-06T15:43:10.000-05:00

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 2

ORGANIZATIONAL DUNS*: 0045143600000
Budget Type*: ● Project ❍ Subaward/Consortium
Organization: University of Pittsburgh

Start Date*: 07-01-2017 **End Date*:** 06-30-2018 **Budget Period: 2**

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	
Total Equipment	
Additional Equipment: File Name:	

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	10,000.00
2. Foreign Travel Costs	
Total Travel Cost	**10,000.00**

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 2

ORGANIZATIONAL DUNS*: 0045143600000
Budget Type*: ● Project ○ Subaward/Consortium
Organization: University of Pittsburgh

Start Date*: 07-01-2017 **End Date*:** 06-30-2018 **Budget Period: 2**

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	49,755.00
2. Publication Costs	
3. Consultant Services	
4. ADP/Computer Services	
5. Subawards/Consortium/Contractual Costs	
6. Equipment or Facility Rental/User Fees	
7. Alterations and Renovations	
8 . HSTB Services	20,600.00
9 . Project Management Tool, BIOS	25,000.00
Total Other Direct Costs	**95,355.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**409,050.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . MTDC	55.50	388,448.00	215,589.00
		Total Indirect Costs	**215,589.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number): U.S. Department of Health and Human Services, (b)(6) (b)(6)

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**624,639.00**

J. Fee	Funds Requested ($)*

K. Budget Justification* File Name: 1234-Fetal budget justification 10.30.2015.pdf
(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

OMB Number: 4040-0001
Expiration Date: 06/30/2016

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 3

ORGANIZATIONAL DUNS*: 0045143600000

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: University of Pittsburgh

Start Date*: 07-01-2018 **End Date*:** 06-30-2019 **Budget Period: 3**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1 .	Dr.	Rajiv		Dhir	M.D.	PD/PI		(b)(6)			36,660.00	8,358.00	45,018.00
2 .	Dr.	(b)(6)			M.D.	Co-investigator					9,548.00	2,177.00	11,725.00
3 .	Dr.				M.D.	Co-investigator					9,548.00	2,177.00	11,725.00
4 .	Dr.				M.D.	Co-investigator					27,458.00	6,260.00	33,718.00
5 .	Dr.				PhD	Co-investigator					19,669.00	4,485.00	24,154.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name:

Total Senior/Key Person **126,340.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	HSTB Manager	(b)(6)			4,370.00	1,582.00	5,952.00
1	Project Coordinator				21,604.00	7,821.00	29,425.00
3	Research Techincian				79,635.00	28,828.00	108,463.00
1	QA Coordinator				13,687.00	4,955.00	18,642.00
1	IT Coordinator				8,177.00	2,960.00	11,137.00
1	Data Coordinator				8,025.00	2,905.00	10,930.00
8	**Total Number Other Personnel**					**Total Other Personnel**	**184,549.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**310,889.00**

RESEARCH & RELATED Budget {A-B} (Funds Requested)

Funding Opportunity Number: RFA-DK-15-016 . Received Date: 2015-11-06T15:43:10.000-05:00

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 3

ORGANIZATIONAL DUNS*: 0045143600000
Budget Type*: ● Project ❍ Subaward/Consortium
Organization: University of Pittsburgh

Start Date*: 07-01-2018 **End Date*:** 06-30-2019 **Budget Period: 3**

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	
Total Equipment	
Additional Equipment: File Name:	

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	10,000.00
2. Foreign Travel Costs	3,000.00
Total Travel Cost	**13,000.00**

E. Participant/Trainee Support Costs	**Funds Requested ($)***
1. Tuition/Fees/Health Insurance	
2. Stipends	
3. Travel	
4. Subsistence	
5. Other:	
Number of Participants/Trainees **Total Participant Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 3

ORGANIZATIONAL DUNS*: 0045143600000
Budget Type*: ● Project ○ Subaward/Consortium
Organization: University of Pittsburgh

Start Date*: 07-01-2018 **End Date*:** 06-30-2019 **Budget Period: 3**

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	51,247.00
2. Publication Costs	
3. Consultant Services	
4. ADP/Computer Services	
5. Subawards/Consortium/Contractual Costs	
6. Equipment or Facility Rental/User Fees	
7. Alterations and Renovations	
8 . HSTB Services	21,218.00
9 . Project Management Tool, BIOS	25,000.00
Total Other Direct Costs	**97,465.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**421,354.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . MTDC	56.50	400,136.00	226,077.00
		Total Indirect Costs	**226,077.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number): U.S. Department of Health and Human Services, (b)(6) (b)(6)

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**647,431.00**

J. Fee	Funds Requested ($)*

K. Budget Justification* File Name: 1234-Fetal budget justification 10.30.2015.pdf
(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

Tracking Number: GRANT12034939 Funding Opportunity Number: RFA-DK-15-016 . Received Date: 2015-11-06T15:43:10.000-05:00

OMB Number: 4040-0001
Expiration Date: 06/30/2016

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 4

ORGANIZATIONAL DUNS*: 0045143600000

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: University of Pittsburgh

Start Date*: 07-01-2019 **End Date*:** 06-30-2020 **Budget Period: 4**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1 .	Dr.	Rajiv		Dhir	M.D.	PD/PI		(b)(6)			36,660.00	8,358.00	45,018.00
2 .	Dr.	(b)(6)			M.D.	Co-investigator					9,835.00	2,242.00	12,077.00
3 .	Dr.				M.D.	Co-investigator					9,835.00	2,242.00	12,077.00
4 .	Dr.				M.D.	Co-investigator					28,281.00	6,448.00	34,729.00
5 .	Dr.				PhD	Co-investigator					20,259.00	4,619.00	24,878.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name:

Total Senior/Key Person **128,779.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical	(b)(6)					
1	HSTB Manager				4,479.00	1,621.00	6,100.00
1	Project Coordinator				22,144.00	8,016.00	30,160.00
3	Research Techincian				81,838.00	29,625.00	111,463.00
1	QA Coordinator				14,029.00	5,079.00	19,108.00
1	IT Coordinator				8,381.00	3,034.00	11,415.00
1	Data Coordinator				8,266.00	2,992.00	11,258.00
8	**Total Number Other Personnel**					**Total Other Personnel**	**189,504.00**

Total Salary, Wages and Fringe Benefits (A+B) **318,283.00**

RESEARCH & RELATED Budget {A-B} (Funds Requested)

Funding Opportunity Number: RFA-DK-15-016 . Received Date: 2015-11-06T15:43:10.000-05:00

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 4

ORGANIZATIONAL DUNS*: 0045143600000
Budget Type*: ● Project ❍ Subaward/Consortium
Organization: University of Pittsburgh

Start Date*: 07-01-2019 **End Date*:** 06-30-2020 **Budget Period: 4**

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	
Total Equipment	
Additional Equipment: File Name:	

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	10,000.00
2. Foreign Travel Costs	
Total Travel Cost	**10,000.00**

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 4

ORGANIZATIONAL DUNS*: 0045143600000
Budget Type*: ● Project ○ Subaward/Consortium
Organization: University of Pittsburgh

Start Date*: 07-01-2019 **End Date*:** 06-30-2020 **Budget Period: 4**

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	52,786.00
2. Publication Costs	
3. Consultant Services	
4. ADP/Computer Services	
5. Subawards/Consortium/Contractual Costs	
6. Equipment or Facility Rental/User Fees	
7. Alterations and Renovations	
8 . HSTB Services	21,855.00
9 . Project Management Tool, BIOS	25,000.00
Total Other Direct Costs	**99,641.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**427,924.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . MTDC	56.50	406,071.00	229,430.00
		Total Indirect Costs	**229,430.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number) U.S. Department of Health and Human Services, (b)(6) (b)(6)

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**657,354.00**

J. Fee	Funds Requested ($)*

K. Budget Justification* File Name: 1234-Fetal budget justification 10.30.2015.pdf
(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

OMB Number: 4040-0001
Expiration Date: 06/30/2016

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 5

ORGANIZATIONAL DUNS*: 0045143600000

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: University of Pittsburgh

Start Date*: 07-01-2020 **End Date*:** 06-30-2021 **Budget Period: 5**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1 .	Dr.	Rajiv		Dhir	M.D.	PD/PI		(b)(6)			36,660.00	8,358.00	45,018.00
2 .	Dr.	(b)(6)			M.D.	Co-investigator					10,130.00	2,310.00	12,440.00
3 .	Dr.				M.D.	Co-investigator					10,130.00	2,310.00	12,440.00
4 .	Dr.				M.D.	Co-investigator					29,130.00	6,642.00	35,772.00
5 .	Dr.				PhD	Co-investigator					20,867.00	4,758.00	25,625.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name:

Total Senior/Key Person **131,295.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	HSTB Manager	(b)(6)			4,591.00	1,662.00	6,253.00
1	Project Coordinator				22,697.00	8,216.00	30,913.00
3	Research Techincian				84,103.00	30,445.00	114,548.00
1	QA Coordinator				14,380.00	5,206.00	19,586.00
1	IT Coordinator				8,591.00	3,110.00	11,701.00
1	Data Coordinator				8,514.00	3,082.00	11,596.00
8	**Total Number Other Personnel**					**Total Other Personnel**	**194,597.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**325,892.00**

RESEARCH & RELATED Budget {A-B} (Funds Requested)

Funding Opportunity Number: RFA-DK-15-016 . Received Date: 2015-11-06T15:43:10.000-05:00

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 5

ORGANIZATIONAL DUNS*: 0045143600000
Budget Type*: ● Project ❍ Subaward/Consortium
Organization: University of Pittsburgh

Start Date*: 07-01-2020 **End Date*:** 06-30-2021 **Budget Period: 5**

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	
Total Equipment	
Additional Equipment: File Name:	

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	10,000.00
2. Foreign Travel Costs	
Total Travel Cost	**10,000.00**

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

Funding Opportunity Number: RFA-DK-15-016 . Received Date: 2015-11-06T15:43:10.000-05:00

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 5

ORGANIZATIONAL DUNS*: 0045143600000
Budget Type*: ● Project ○ Subaward/Consortium
Organization: University of Pittsburgh

Start Date*: 07-01-2020 **End Date*:** 06-30-2021 **Budget Period: 5**

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	54,368.00
2. Publication Costs	
3. Consultant Services	
4. ADP/Computer Services	
5. Subawards/Consortium/Contractual Costs	
6. Equipment or Facility Rental/User Fees	
7. Alterations and Renovations	
8 . HSTB Services	22,510.00
9 . Project Management Tool, BIOS	25,000.00
Total Other Direct Costs	**101,878.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**437,770.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . MTDC	56.50	415,259.00	234,621.00
		Total Indirect Costs	**234,621.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number): U.S. Department of Health and Human Services, (b)(6) (b)(6)

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**672,391.00**

J. Fee	Funds Requested ($)*

K. Budget Justification* File Name: 1234-Fetal budget justification 10.30.2015.pdf
(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

Tracking Number: GRANT12034939 Funding Opportunity Number: RFA-DK-15-016 . Received Date: 2015-11-06T15:43:10.000-05:00

BUDGET JUSTIFICATION

Personnel

Rajiv Dhir, MD, MBA: PI, Effort = (b)(6) Dr. Dhir is the medical director of the Health Sciences Tissue Bank (HSTB) of the University of Pittsburgh and a practicing pathologist with subspecialty training in Genitourinary Pathology. He will be responsible for the oversight of the project. This will include interfacing and working with internal collaborators to ensure accrual and annotation of the appropriate specimens. He will also interact with the external collaborators and clients to ensure appropriate specimen aggregation and disbursement. He will work closely with NIDDK to ensure successful execution of the project, meeting the mission and goals of the Tissue Core.

(b)(6) Co-I, Effort = (b)(6) is the (b)(6) (b)(6) He also serves as the (b)(6) He provides direction and advice related to the different Information systems and tools used by HSTB. He is also the director of the Imaging core; a subsidiary of HSTB. The imaging core will perform whole slide image acquisition and provide access to these images for the Tissue Core clients.

(b)(6) Co-I, Effort = (b)(6) is the (b)(6) (b)(6) He will be responsible for evaluating appropriate surgical pathology and autopsy specimens and overseeing collection of the biological materials for the Tissue Core. He will work closely with (b)(6) (b)(6) to perform routine and specialized histological assessment of the appropriate specimens.

(b)(6) Co-I, Effort = (b)(6) is a clinician scientist (b)(6) (b)(6) with a flourishing research program related to kidney development. She has a thorough understanding of genitourinary development and is ideally suited to act as co-coordinator of the validation lab for this project.

(b)(6) Co-I, Effort = (b)(6) is a kidney developmental biologist with over (b)(6) studying the genitourinary tract. Furthermore, he is also a classically trained human anatomist and embryologist which make him ideally suited to act as a coordinator of the validation lab of the proposed tissue hub and collection site.

(b)(6) **:** Effort = (b)(6) This (b)(6) will be responsible coordination management of day to day operations. She supervises HSTB staff members and will manage the overall efforts of the HSTB and set operational standards related to the HSTB scope of work. She will assure proper communication and resolution conflicts and issues.

(b)(6) **:** Effort = (b)(6) This (b)(6) will be responsible for project intake, tracking and recording keeping. She will coordinate the GUDMAP investigator requests to the GUDMAP-Human Tissue Repository including documenting the needs of the investigator, assuring regulatory compliance, coordinating with tissue and data collection staff members and assuring proper completion and shipping of requests. (b)(6) is also a cytotechnologist and smaller portion of her effort will be applied to oversight and performance of this function.

TBN (Technician CHP validation lab): Effort = 12.0 Calendar months (100%). This grant will fund 100% of the technicians salary. This technician will perform all the required validation of the specimens including: histology, immunohistochemistry, in situ hybridization, cell isolation and real time PCR.

(b)(6) Effort = (b)(6) This HSTB tissue bank technician and will perform the day-to-day tasks associated with the collection of specimens. This includes maintaining a working knowledge of all SOPs related to the ongoing collections that are requested by the GUDMAP investigators. She will coordinate with the clinical departments within Magee Women's Hospital of UPMC, interface with the Pathology and other hospital staff members as required to obtain the requested specimens and enter data related to each case in the BIOS.

(b)(6) Effort = (b)(6) This (b)(6) and technician will perform the day-to-day tasks associated with the collection of specimens. This includes maintaining a working knowledge of all SOPs related to the ongoing collections that are requested by the GUDMAP investigators. She will coordinate with the clinical departments within Magee Women's Hospital, interface with the Pathology and other hospital staff members as required to obtain the requested specimens and enter data related to each case in the BIOS.

(b)(6) This (b)(6) will be responsible for the quality program. He will manage all aspects of quality management including record keeping, training of staff members to standard operating procedures (SOPs), data entry practices and audits, and quality related events. He will coordinate the overall record keeping and management of the quality metrics from the tissue collection and data entry processes with the quality measurements performed through the Department of Pediatrics team.

(b)(6) Effort = (b)(6) This (b)(6) specialist will be responsible for overall management of the Biospecimen Inventory and Operations System with regard to this project. He will manage the specimen search process, control the data entry lexicon as needed, and provide reports of collection activity for investigators who request samples and as needed for other purposes. He will maintain the data integrity and make corrections and amendments based on the quality control activities. In the case that new fields and library elements are required he will manage that process in conjunction with the Project Manager and Quality Manager. He will be required to produce final sample pick lists as specimens are disbursed.

(b)(6) Effort = (b)(6) The (b)(6) will be responsible for aggregating information from the different information systems on the specimens offered as part of the Tissue Core. This will include pathology information as well as more specialized information (like cytogenetics); if applicable. The data coordinator will work with the Project manager on cohort identification for the different requests. In addition the data coordinator will also be responsible for providing data to the clients of the Tissue Core.

Supplies

HSTB Consumable Laboratory Supplies: (b)(4) annually. Or about (b)(4) monthly will be used for sample collections, integrity, maintenance, and transport including sample and shipping containers, dry ice, and other basic supplies. (b)(4)

International Institute for the Advancement of Medicine (IIAM): (b)(4) annually. IIAM will be used to source specimens from later developmental ages (24-42 weeks) that are not available through internal sources. IIAM has indicated that they are able to provide samples for approximately (b)(4) per year in this category at a cost of (b)(4)

Validation Laboratory Consumable Laboratory Supplies: (b)(4) annually. Or about (b)(4) monthly will be required to purchase reagents for staining, immunohistochemistry and in situ reagents as well as cell, culture medium and consumable plastics related to these processes. These processes will be performed in response to the needs of the GUDMAP investigators.

Travel

Pathology: The Project PI and a co-investigator will need to travel to GUDMAP consortia meetings, to be held twice a year. A total of $4,000 is allocated for this travel in year 1.

Validation Laboratories: The Project co-investigators will need to travel to consortia meetings, to be held twice a year. (b)(6) will also attend the American Society of Nephrology meeting where GUDMAP typically has a booth. A total of $6,000 is allocated for this travel in year 1.

(b)(6) will also attend the International Meeting on Development Nephrology to be held in 2018, where GUDMAP will hold workshops. In year 3, $3,000 is allocated for this travel.

Other Expenses

Tissue embedding/processing, storage, and disbursement: (b)(4) year 1 with 3% escalation each year in years 2-5. These are billable services based on the fiscal parameters in place within the University of Pittsburgh for the HSTB. Tissue embedding and processing will be required at all levels for quality management and to provide product to GUDMAP investigators and (b)(4) is requested annually. Storage costs are based on the partial cost of a freezer with a 10 year life span plus projected maintenance and certification costs; (b)(4) is requested annually. The cost for disbursement of samples to GUDMAP investigators will be charged to the account award for this project. We estimate that approximately 30 disbursements will be made at a billable cost of (b)(4) each for a total annual cost of (b)(4)

Website maintenance, project management tool, BIOS, image acquisition: $25,000 annually. Resources will be required to maintain and update our internally developed inventory management system (BIOS). The project management tool is internally developed and is the mechanism for starting and following the progress of the request from the client. The clients will be provided access to the contents of the resource via a Sharepoint link that will be password protected. Whole slide image acquisition will be done to offer clients access to high quality images of the specimens in the resource. These images will be from routine and specialized histologic and immunohistochemical/ in-situ protocols. We also have capabilities for image analysis and will offer, if required. We estimate these endeavors will require a total annual support of $25,000.

RESEARCH & RELATED BUDGET - Cumulative Budget

	Totals ($)	
Section A, Senior/Key Person		632,057.00
Section B, Other Personnel		923,396.00
Total Number Other Personnel	40	
Total Salary, Wages and Fringe Benefits (A+B)		1,555,453.00
Section C, Equipment		
Section D, Travel		53,000.00
1. Domestic	50,000.00	
2. Foreign	3,000.00	
Section E, Participant/Trainee Support Costs		
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other		
6. Number of Participants/Trainees		
Section F, Other Direct Costs		487,645.00
1. Materials and Supplies	256,462.00	
2. Publication Costs		
3. Consultant Services		
4. ADP/Computer Services		
5. Subawards/Consortium/Contractual Costs		
6. Equipment or Facility Rental/User Fees		
7. Alterations and Renovations		
8. Other 1	106,183.00	
9. Other 2	125,000.00	
10. Other 3		
Section G, Direct Costs (A thru F)		2,096,098.00
Section H, Indirect Costs		1,110,917.00
Section I, Total Direct and Indirect Costs (G + H)		3,207,015.00
Section J, Fee		

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OMB Number: 0925-0001

1. Project Director / Principal Investigator (PD/PI)

Prefix:	Dr.
First Name*:	Rajiv
Middle Name:	
Last Name*:	Dhir
Suffix:	M.D.

2. Human Subjects

Clinical Trial?	● No	○ Yes
Agency-Defined Phase III Clinical Trial?*	○ No	○ Yes

3. Permission Statement*

If this application does not result in an award, is the Government permitted to disclose the title of your proposed project, and the name, address, telephone number and e-mail address of the official signing for the applicant organization, to organizations that may be interested in contacting you for further information (e.g., possible collaborations, investment)?

● Yes ○ No

4. Program Income*

Is program income anticipated during the periods for which the grant support is requested? ○ Yes ● No

If you checked "yes" above (indicating that program income is anticipated), then use the format below to reflect the amount and source(s). Otherwise, leave this section blank.

Budget Period*	Anticipated Amount ($)*	Source(s)*

Funding Opportunity Number: RFA-DK-15-016. Received Date: 2015-11-06T15:43:10.000-05:00

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5. Human Embryonic Stem Cells

Does the proposed project involve human embryonic stem cells?* ● No ○ Yes

If the proposed project involves human embryonic stem cells, list below the registration number of the specific cell line(s) from the following list: http://grants.nih.gov/stem_cells/registry/current.htm. Or, if a specific stem cell line cannot be referenced at this time, please check the box indicating that one from the registry will be used:

Cell Line(s): Specific stem cell line cannot be referenced at this time. One from the registry will be used.

6. Inventions and Patents (For renewal applications only)

Inventions and Patents*: ○ Yes ○ No

If the answer is "Yes" then please answer the following:

Previously Reported*: ○ Yes ○ No

7. Change of Investigator / Change of Institution Questions

❑ Change of principal investigator / program director

Name of former principal investigator / program director:

Prefix:

First Name*:

Middle Name:

Last Name*:

Suffix:

❑ Change of Grantee Institution

Name of former institution*:

PHS 398 Research Plan

Please attach applicable sections of the research plan, below.

OMB Number: 0925-0001

1. Introduction to Application (for RESUBMISSION or REVISION only)	
2. Specific Aims	1241-Specific Aims_Final.pdf
3. Research Strategy*	1242-FINAL Research Strategy.pdf
4. Progress Report Publication List	
Human Subjects Sections	
5. Protection of Human Subjects	1248-Final Human subjects 20151024.pdf
6. Inclusion of Women and Minorities	1249-Inclusion of Women and Minorities.pdf
7. Inclusion of Children	1250-Inclusion of Children.pdf
Other Research Plan Sections	
8. Vertebrate Animals	
9. Select Agent Research	
10. Multiple PD/PI Leadership Plan	
11. Consortium/Contractual Arrangements	
12. Letters of Support	1251-All LOS.pdf
13. Resource Sharing Plan(s)	1252-ResourceSharing.pdf
Appendix (if applicable)	
14. Appendix	

SPECIFIC AIMS

Congenital malformations of the genitourinary tract carry with them significant morbidity and increased risk of mortality for individual patients, and is a growing public health burden. At present, there are limited therapies available to ameliorate the progressive loss of genitourinary tissue. A comprehensive understanding of how the genitourinary organs (including kidney and urinary tract) develop *in utero* is necessary to effectively develop novel therapies to replace or repair injured tissue. The **GenitoUrinary Development Molecular Anatomy Project (GUDMAP)** has been extraordinarily successful at providing a high-resolution map of gene expression in the murine genitourinary system [1-8]. However, a similar description has not been available for the developing human genitourinary system, nor has it been possible to develop optimized experimental techniques to grow, expand and differentiate human genitourinary progenitor cells *in vitro*. These research efforts by the developmental community have been hampered by the lack of a central hub for the procurement, and distribution of high quality human genitourinary samples.

The Health Sciences Tissue Bank (HSTB) at the University of Pittsburgh has been involved in research human tissue procurement for over 18 years: collecting, maintaining and disbursing quality samples to research scientists, both in (b)(4). HSTB is embedded within the Department of Pathology of the University of Pittsburgh Health Systems; thus providing rapid access to very high quality tissue and biological specimens. HSTB has established consenting protocols in line with the best practices recommendations from the NIH, a strong informatics backbone to facilitate specimen procurement and annotation, and has in place robust quality control and quality assurance programs. The HSTB biorepository is fully accredited by the College of American Pathologists (CAP). HSTB has an established program accruing fetal tissues that has been IRB approved since 2005. In this calendar year, we have disbursed over 300 fresh samples collected from 77 cases. The collections can be significantly ramped up as material could have been accrued from as many as 725 cases last year.

We have preliminary data that we can isolate human genitourinary tissues (kidneys, ureters and bladders) from various developmental ages (6-24 weeks). We have produced publication quality histological images of the developing urogenital organs (including kidneys and bladder), and have immunostained kidneys for endothelium, nephron progenitors and early-differentiated nephron structures and bladders for the urothelium and muscle layers. We have utilized Dynabeads® to separate distinct cellular subpopulations in the kidney including: nephron progenitors, ureteric epithelium, podocytes and endothelium, and have confirmed that we can produce high quality material that is appropriate for RNA sequencing. *We propose to act as both the GUDMAP Tissue Hub and Tissue Gathering site to build upon the pre-existing HSTB and provide top quality genitourinary samples to members of the scientific community including those within GUDMAP*.

Aim 1: To generate an inventory of genitourinary tissue throughout normal human development

The main goal of this aim is to develop a pipeline for the acquisition, quality control and distribution of human genitourinary samples obtained throughout development (6-42 weeks gestation). We currently have access to 6-24 week samples through the HSTB. However, for later gestational stages (25-42 weeks gestation) we have partnered with the International institute for the Advancement of Medicine. This will provide access to a novel resource for neonatal donation. We aim to collect and store a minimum of (b)(4) per developmental week. Each of these samples will have histology, immunohistochemistry and *in situ* hybridization performed to assess tissue quality, protein and RNA integrity. Furthermore, we will obtain maternal blood, urine and amniotic fluid; based on the clinical situation and ability to procure. Based on our current experience, we get these biological materials in most cases. Anonymized demographic information of each specimen will also be provided.

Aim 2: To provide fresh genitourinary tissue and biological research specimens

This aim will generate an ongoing resource to distribute fresh developmental human genitourinary samples from various stages (6-42 weeks) to the GUDMAP Atlas projects. The samples will be procured by a pathologist and inspected for mechanical damage. Samples will be collected from all qualified cases. The samples will then be subdivided based on the demand for fresh/frozen aliquots; the validation laboratory for quality control will keep a portion of each sample. The tissue samples will be immediately sent out for live cell use or immediately separated into distinct cellular populations before shipping based on researcher demands. Permissible annotating information; including demographics of each specimen, will also be provided.

A. BACKGROUND AND SIGNIFICANCE

1. The University of Pittsburgh Health Science Tissue Bank (HSTB) is an established fetal tissue core

Biological research specimen collection at the University of Pittsburgh is centralized through the Health Sciences Tissue Bank (HSTB). The workflow and expertise that is already in place will be leveraged to generate the GUDMAP Tissue Hub and we will also act as the primary tissue collection site. The HSTB has over 18 years of experience of prospectively procuring tissues and biological materials for researchers. The HSTB has a tissue procurement site at Magee-Women's Hospital of the University of Pittsburgh Medical Center (UPMC), which is part of a multi-hospital chain, consisting of 4 flagship hospitals, and 2 large community hospitals. We have been collecting fetal tissue for over 10 years with an established IRB ((b)(6) (b)(6) co-I). Currently the HSTB has numerous researchers acquiring fetal tissue for various projects from 6-24 weeks of gestation. The tissue collections include liver, heart, gonads, legs, brain, genitourinary, and placenta. (b)(6) (co-I) has been utilizing the HSTB to procure genitourinary tissues including kidneys, ureters and bladders.

2. The HSTB has a strict consenting protocol

We have an established consenting protocol in line with the best practices recommendations from the NIH. All patients who present to obstetrics and family planning who wish to undergo an elective abortion, or have experienced a spontaneous abortion, are asked by a registered nurse (not involved with the procurement) to give consent for tissue procurement and banking. There is a 24-hour waiting period after the consent process and the initial registered nurse is not involved with the tissue procurement. This consent form also gives permission for tracking of patient progression, gathering of patient demographics and collection of clinically relevant information to be included in the database as well as an option for the donation of maternal blood, urine and amniotic fluid. The consent form related to research on tissue from an elective abortion (less than 24 weeks gestation) has been designed with extensive input from clinical colleagues and the Institutional Review Board of the University of Pittsburgh to ensure compliance with all Pennsylvania state and federal laws.

3. The proposed GUDMAP Tissue Hub (HUB) and collection site has significant infrastructure

The proposed HUB will leverage the resources of the current HSTB, which has a physical footprint in 4 hospitals of UPMC, which includes space and technical staff. The current organization consists of 16 staff members, which includes: a Medical Director (Dr. Rajiv Dhir, PI), an Assistant Director (b)(6), a Project Manager (b)(6), Quality Assurance Manager (b)(6), lead technicians, supervisors, and technical staff. In addition the HUB will include a fetal pathologist (b)(6) co-I), a pediatric clinician (b)(6) co-I) and a classically trained human anatomist (b)(6) co-I). Dr. Dhir will spearhead this initiative. He is a clinician scientist with intimate knowledge of tissue banks [9-16] and the genitourinary system [17-19]. (b)(6) is a perinatal pathologist who has extensive knowledge and experience related to identification and quality control of fetal specimens [20-22]. Both (b)(6) are developmental biologists with successful research programs related to development of the genitourinary system [23-28]. This team is uniquely qualified to run, quality control and distribute samples to the successful GUDMAP Atlas projects. The HSTB has approximately 1000 sq. ft. of space at each of the flagship hospitals. This reflects significant institutional commitment and support to this research support facility (**see letters from** (b)(6) (b)(6) We have a strong Informatics backbone with our flagship and community hospitals linked through a common laboratory information system. In addition we have a variety of web-based tools to streamline the biological specimen procurement activities and extensively annotate the accrued specimens.

4. The proposed HUB and collection site has protocols for rigorous quality control

To keep up to date with the needs of the ever-growing area of tissue banking, the University of Pittsburgh is an institutional member of the International Society for Biological and Environmental Repositories (ISBER; http://www.isber.org). This is the organization responsible for establishing and disseminating best practices for biorepositories. ISBER works very closely with the National Cancer Institute (NCI) and the NCI's Biorepositories and Biospecimen Research Branch. A unique attribute of ISBER is that it represents repository organizations, users, as well as companies that develop the myriad collection of items and services that sustain repositories. In 2005, the organization published the "best practices for repositories" (ISBER, 2005) [29], a document containing a thorough and comprehensive treatise on repository management and

operations. This was followed by another set of standards developed by the NCI in 2007 (National Cancer Institute best practices for biospecimen resources: http://biospecimens.cancer.gov/global/pdfs/nci_best_practices_060507.pdf). The HSTB repository has maintained these documents as reference material and follows these practices in its daily operations. These practices would be continued, extrapolated, refined and implemented for the HUB efforts.

5. Ischemia time is minimized
We record the warm ischemic time on our samples and take steps to keep it at a minimum to ensure the highest quality biological specimens [30, 31]. We get feedback from our users and utilize this feedback to tailor our collection processes on a case-by-case basis to maximize the needs of investigators. All warm ischemic times are recorded within Biospecimen Inventory and Operations System (BIOS).

6. The proposed HUB has an established track record of being highly collaborative
The HSTB has been a core facility for the University of Pittsburgh Cancer Center for the past decade, providing biological specimens and research pathology support. We receive some funding from the NCI as a Shared Resource as part of the Cancer Center Support Grant (CCSG) for the University of Pittsburgh Cancer Institute. This is the 27th year of funding for CCSG (Core PI: Dr. Dhir, P30 CA047904). In this capacity, HSTB works closely with a multitude of investigators and handles a variety of biospecimen requests both locally and nationally.

7. HSTB has a track record of very effective engagement in National and International initiatives
A. The Cancer Genome Atlas (TCGA): This is a collaboration between the National Cancer Institute (NCI) and National Human Genome Research Institute (NHGRI). TCGA generated large datasets of genomic changes in major types and subtypes of cancer. TCGA accrued matched tumor and normal tissue specimens from 11,000 patients; from 33 cancer types and subtypes [32], including 10 rare cancers. The University of Pittsburgh was the second largest contributor to the TCGA Project, with over 800 qualified cases.

B. The Clinical Proteomic Tumor Analysis Consortium (CPTAC): This is a comprehensive and coordinated effort to accelerate the understanding of the molecular basis of cancer through the application of robust, quantitative, proteomic technologies and workflows. HSTB was part of the initial pilot and has been selected as a collection site for the ongoing expanded phase targeting 2000 cases spanning 10 tumor types.

C. The Cancer Human Biobank (caHUB**):** This is a biorepository and biospecimens derived program that carried out specialized biospecimens and data procurements to support biospecimens science activities. HSTB participated in the caHUB initiative focused on biopreservation variability [33, 34]. HSTB was the largest contributor to this initiative and provided samples and data from approximately 6000 cases; covering four tumor types.

D. SPORE Initiative: HSTB is the biospecimen and research Pathology services resource for our four funded SPORE initiatives: 1. lung, 2. head and neck, 3. skin, and 4. Gynecologic cancers [10, 15]. We have provided samples and data to many investigators outside of the University of Pittsburgh, as part of SPORE driven multi-institutional efforts.

8. Identification of late gestation procurement sites
We have not previously collected tissues from cases later than 24 weeks gestation. We are in the process of altering our IRB and autopsy consent forms to permit the collection of tissues from these cases and allow for deposition of these tissues in our tissue bank. We have developed a relationship with the International Institute for the Advancement of Medicine (IIAM) (iiam.org) who already provide neonatal tissue samples to the NIH initiative LungMap (LungMap.org). The IIAM contains a national tissue bank that will allow for the acquisition of genitourinary tissue from 25-42 weeks of gestation. This tissue bank receives on average 20 neonatal cases a year (**see letter of support from IIAM**). The neonatal tissue will undergo stringent quality assurance and quality control by HSTB, similar to the quality assurance and control (QA/QC) performed for our in house fetal tissue, before being banked or distributed to the requesting, qualified GUDMAP atlas projects.

B. INNOVATION

This application is innovative on multiple levels including: 1. Team approach, 2. Established collaborative system, 3. High quality collection and validation, 4. Data management and project management tools.

1. Team approach

As mentioned in the significance section we have brought together a unique set of individuals with diverse backgrounds to facilitate the establishment of the HUB and collection site. We have leveraged the already existing tissue and data collection expertise of HSTB at the University of Pittsburgh. To this we will add significant clinical, pathological and anatomical expertise in the genitourinary tract for a novel and diverse research team well equipped to perform all the actions necessary of the HUB.

2. Established collaborative system

Currently, HSTB provides high quality tissue samples to over 100 researchers. This is a novel resource embedded within the Department of Pathology that works closely with individual researchers (b)(4) (b)(4) to satisfy the specific research needs of each laboratory. The proposed HUB and collection site at the University of Pittsburgh will utilize a similar collaborative approach with the successful GUDMAP Atlas projects.

3. High quality collection and validation protocol

HSTB is accredited by the College of American Pathologists (CAP) and certified under the Biorepository Accreditation Program (BAP). As part of BAP, “peer” inspectors perform on-site inspection using CAP accreditation checklists. This is a critical and comprehensive assessment of quality practices covering all aspects of biorepository operations (collecting, processing, storing, disbursing and data annotation of biospecimens). The HUB at the University of Pittsburgh also has specific, pathological, clinical and anatomical expertise that will seamlessly work as part of this Tissue Hub, to ensure the highest quality of specimens for all investigators.

4. Data management and project management tools

A. HSTB has developed in-house an inventory management system (BIOS) that will be utilized for tracking the stored specimens. This inventory management system is linked to Medipac; this clinical patient management interface imports demographic data eliminating manual entry; a source of errors. BIOS also interfaces with the Pathology LIS, CoPath; allowing access to Pathology reports.

B. HSTB also has a project management tool through which requests are initiated via a web interface. The project management tool portal shows the progress of the request and has been very useful to introduce transparency in the functioning of HSTB.

C. We also plan to provide GUDMAP investigators access to data related to the number of cases and pertinent details of the case (gestational age, tissue types, relevant QA/QC information). This access will be through secure password protected mechanisms using software like Sharepoint.

C. APPROACH

1. Preliminary Work and Current Status of the University of Pittsburgh Health Sciences Tissue Bank

This proposal includes five different aspects of work. This portion of the proposal is organized to describe our preliminary work and current status in each of the following areas:

1.1. Accrual of tissues and biological specimens (kidney evaluation team, bladder evaluation team)
1.2. Data Annotation
1.3. Packaging and Shipping
1.4. Consenting and IRB related issues
1.5. Material Transfer Agreement (MTA) issues

1.1. Accrual of tissues and biological specimens

Due to the uniqueness of this tissue type, all of the fetal specimens (excluding the neonatal which will be through IIAM) will be derived from Magee Women’s Hospital of UPMC, which performs on average (b)(4) (b)(4) (**Table 1**).

Table 1: Number of fetal cases seen at Magee Women’s hospital

Fetal age			No. Of cases available/year
First trimester (6-12 weeks)	**Second trimester (13-24 weeks)**	**Autopsy**	
(b)(4)			**725**

The current version of the consent form provides opportunity for the patient to also allow donation of maternal blood and urine to the HSTB. Although all of the tissue will be collected from one hospital site, all of the 18 UPMC hospitals are linked by a common laboratory information system. This vast system allows access to information on the maternal medical record and de-identified information related to the demographics will be available to the successful GUDMAP Atlas projects.

Procedures for Collecting, Processing and Distributing Specimens: All fetal tissue is collected through a collaborative process including Family Planning, Obstetrics and Pathology. All patients are consented for the procedure and tissue donation separately by the Family Planning and Obstetrics staff. Furthermore, patients are consented 24-hours in advance, allowing notice of potential cases for the following day. Once a patient has agreed to donate fetal tissues for research purposes, the HSTB is alerted and subsequently Pathology is involved. The HSTB acts as a courier and delivers the material to Pathology for gross examination and dissection. After pickup from the procedure area, the tissue-banking technician brings the specimen to the surgical pathology gross room area. The clinical pathology staff assigned to that bench performs immediate gross pathology assessment. The pathologist (b)(6) co-I) is involved at this stage in the clinical evaluation and subsequent harvesting of the specimen to ensure quality control at the level of gross evaluation. All specimens are grossly evaluated for mechanical disruption. After appropriate materials have been obtained for histologic evaluation for clinical diagnosis, the genitourinary tissue will then be rapidly triaged for GUDMAP Atlas projects. Pathology has snap freezing capabilities as well as the appropriate materials to preserve specimens via other required methods. In addition, the tissue banking space is in close proximity to the gross room. The samples will then be taken to the validation laboratories (b)(6) for further assessment of the tissue prior to distribution; this transfer system is already established based on the existing collaboration.

We have extensive experience and the requisite staff to ensure adherence to the yet to be defined GUDMAP Atlas projects criteria as proven by successful contributions made to TCGA, caHUB and CPTAC. HSTB has in place the infrastructure to provide adequate support for all the elements needed for the GUDMAP project. The Tissue Resource was the only core facility rated "outstanding" in the NCI review of the Cancer Center in 2010 and again in 2015, with an overall impact score of 20 (core PI: Dr. Dhir, P30 CA047904). We have the infrastructure in place as well as the experience to procure and process the required tissue and biological materials for the various GUDMAP projects. In addition the HSTB has extensive experience in running and maintaining a viable CAP accredited tissue resource. The current facilities consist of 45 ultra-low mechanical freezers and 7 liquid nitrogen storage vessels. The HSTB has adequate space for the long-term storage of specimens collected for the GUDMAP project.

The HSTB has an online request tool in place to streamline investigator driven research projects. This online tool allows researchers to submit all contact information, project specific requirements and necessary regulatory documents to the project manager of HSTB. We are in the process of working with our information technology department to generate a secure link for GUDMAP investigators. Once the Project Manager has reviewed and approved the request, the project is assigned to a staff member for appropriate actions. This electronic request site creates a centralized hub where HSTB staff and the requesting investigator can all access the project, provide appropriate documentation, see relevant information and communicate via project updates and email.

HSTB fetal tissue collection: The Fetal Tissue IRB has been in existence since 2005. Since 2010, the numbers of consents and collections has been steadily increasing (**Table 2**) and we are in an excellent position to expand our services to include the needs of the GUDMAP Atlas projects. Accrual of tissues less than 16 weeks only began in the middle of 2015, and we have already collected over 20 cases. Based on the demand of the Atlas projects we can ramp up the accrual for these early cases, since consent efforts to date are based on current needs and most women were not asked to donate.

Table 2: Number of cases, active projects and disbursements per year for fetal tissues

Year	No. of cases	No. of active projects	No. of disbursements
2010	(b)(4)		
2011			
2012			
2013			
2014			
2015	**77**	(b)(4)	

The anticipated volumes for this project are detailed below (**Table 3**). The projected accrual is less than 15% of our actual clinical volumes. We have been conservative to ensure that we have the capacity to meet projected targets.

Table 3: Anticipated fetal collections for GUDMAP per year

Fetal Age				No. of cases/yr
6-12 weeks	12-18 weeks	18-24 weeks	25-42 weeks	
(b)(4)				

The success rate for obtaining kidney and bladder specimens from our cases 16-24 weeks gestation is typically very high (>90%). We have not consistently looked for ureters; however with our team of sub-specialty experts we will be able to troubleshoot, and successfully implement, the dissection of any genitourinary tissue specimens needed by the GUDMAP Atlas projects.

Furthermore, we are also in the process of expanding our IRB protocol to collect neonatal biological samples from later gestational sudden deaths (between 25-42 weeks). To ensure ability to collect specimens from later gestational ages, we have partnered with the International Institute for the Advancement of Medicine (IIAM) (**see letter from** (b)(6)). We envisage collecting tissue specimens from all eligible cases. In addition maternal biofluids may be collected, as per needs of the GUDMAP projects.

The specimens will undergo a thorough histological assessment by an expert pathologist ((b)(6) co-I) and anatomist ((b)(6) , co-I), before being provided for a GUDMAP Atlas project. Additionally, other quality assurance techniques including immunohistochemistry, *in situ* hybridization and RNA isolation can be performed by the validation team (b)(6) ; as per GUDMAP project needs.

Standard Operating Procedures (SOPs): The SOPs of the HSTB contain extensive details related to Collection/ Handling/ Storage/ Data Entry, Quality Management Plan, disbursement of biological specimens and Education and Training of Technical staff. HSTB is a CAP-certified facility. The proposed HUB collection processes would follow similar SOPs. In addition, the GUDMAP collection would have a quality assurance and control (QA/QC) and validation plan reflective of the specific requirements of GUDMAP; including detailed histologic assessment. Immunohistochemistry, *in situ* hybridization and RNA isolation will be performed as part of the quality assessment and validation, based on the specific needs of the GUDMAP projects.

Data and Safety Monitoring Plan: The HSTB has in place a data and safety monitoring plan for all subjects enrolled in tissue and biological specimen donation. The data and safety monitoring plan is part of the annual submission to the IRB. Similar data and safety monitoring plans function in the clinical trials involvement. The activities of the HSTB, with respect to biological specimen aggregation, as well as data annotation, are in full compliance with United States Federal statues, regulations, and ordinances. We also monitor any changes in rules and regulations concerning tissue and biological specimen aggregation and data degradation. The Institutional Review Board of the University of Pittsburgh insures complete compliance with these procedures and policies.

The highlights of the plan are as follows:

1. The data is stored on password-protected computers.
2. The data is provided to investigators only after the identifiers have been removed. The data is NEVER provided with any identifiers. A linkage code is used. The Tissue Bank retains the key to the code.
3. The biological materials are provided to research studies that are IRB approved or are utilizing the Tissue Bank IRB approved protocol that allows disbursement of biological materials that have been de-identified. No materials are ever given to studies that are not IRB approved.
4. The PI evaluates the data every quarter to assess the specimen volume and variety of accrual.
5. Adverse events, if any, need to be documented and immediately provided to the IRB. The principle adverse events that can be associated with a facility like HSTB pertain to data security. No adverse events have occurred in this facility to date.

1.2. Data Annotation

Annotation of biospecimens: We have developed a variety of informatics tools with institutional support and commitment. This is an endeavor that has taken five plus years of committed informatics support from a variety of sources (NCI, National Center for Research Resources and Department of Defense). These bioinformatics tools will be critical for the GUDMAP Atlas projects as they will allow data entry, facilitate storage, querying for specific needs, retrieval and data annotation for GUDMAP projects, in a legal, ethical and HIPAA compliant

manner, consistent with best practices.

The current systems involved in the annotation of biospecimens at the University of Pittsburgh are as follows:
A. Inventory system and Bar-coding: At the University of Pittsburgh we have developed and implemented a web-based inventory system called **BIOS (Biospecimen Inventory and Operations System).** BIOS is a multi-facility web application designed to facilitate the tracking, banking, and distribution of tissue bank specimens. It unifies the efforts of tissue collection, patient's consent status, billing and data aggregation in one module. BIOS facilitates the logging of received samples/specimens collected, association of specimens with IRB protocols, researcher searching of stored specimens, and dispersal of specimens. Currently, BIOS interfaces with the ePatient system, which is a constantly updated feed of all patient information from UPMC facilities. BIOS uses ePatient to retain certain demographic information about the patients associated with each specimen as well as to retrieve/store CoPath reports associated with surgical visits. Demographic and CoPath report data are visible in the BIOS system upon request from users. BIOS provides a central repository for the tissue bankers for tracking and distribution of biospecimens and for robust querying and reporting of biospecimens and associated data to fulfill the requirements of researchers. By combining the flexible query interface of BIOS with the ability to export the result of queries, custom reports can be prepared. We have a dedicated person who has been extensively trained; he can create a variety of reports such as summaries of bank-wide operations during a specified period or daily work lists for a particular banker etc.
BIOS's web application layer is secured through SSL (Secure Sockets Layer) and the use of groups for restricting user access. All new user requests are vetted by UPMC information technology security. Security is further refined based on user role. Facility managers are able to designate a user's role in the system (IT, admin, technician, researcher, pathologist, researcher annotate, researcher request, microarray technician, and read-only). A system security plan is on file with the UPMC System Security team and is reviewed on an annual basis. The BIOS application is scanned by the UPMC System Security team on an annual basis using tools that predict and isolate risks to the security of the system. The Enterprise Provider Solutions Clinical Programs team of UPMC maintains the BIOS application. All new requests for enhancements, bug fixes, or implementations go through this dedicated resource. Similarly this group also serves as a 24-hours a day, 7 days a week help desk for any BIOS related support issues. The BIOS system has been successfully implemented at our institute and is currently being used for the day-to-day operations of a system-wide tissue bank. We have worked on making BIOS accessible and user-friendly for our researchers. **We will provide a similar and appropriate; secure interface for access and sharing information with the GUDMAP Atlas projects; most likely using a Sharepoint type mechanism.**

B. The Pathology Laboratory Information System: Our institute uses CoPath, a Cerner (Kansas City, MO) product. It supports technical workflow, resulting and patient reporting, charge entry and transmission, management reporting, and QA/QC activities for Anatomic Pathology and related labs (14) throughout the UPMC system. This system also includes PICSPlus (v2.5), an integrated module for Anatomical Pathology imaging, and Synoptic Reporting, a feature for capture and reporting of discrete diagnostic elements. These integrated products will be harnessed and utilized to search for specific tissue samples within the proposed HUB and will be linked with high quality images of histology, immunohistochemistry and *in situ* hybridization as well as commenting on RNA quality. We have also implemented state of the art 2-D bar coding in the gross room and histology, making the storage, archival and retrieval of paraffin specimens more robust and efficient. **The reporting and imaging functions are very important for the GUDMAP project; providing clinical annotation as well as high-resolution images.**

C. Electronic Medical Records: A large percentage of our medical records are now in an electronic form. We have developed in-house software capable of mining these records for key text words. The data can then be identified and ported into electronic databases for research use in a de-identified manner. We will provide required appropriate annotating information for the specimens provided for GUDMAP Atlas projects.

D. Web based Tissue Requesting tool: The HSTB currently utilizes a web based project request tool. This tool will have a tailored drop down window specific for the GUDMAP Atlas projects and provide them with secure access to the database. The tool has the ability to manage IRB, MTA and other project related documentation. It automates communication between the HSTB and the tissue utilization committees, the researchers and the HSTB technical staff. This tool drives the fast turnaround time, utilization and other project management metrics.

E. Transferring clinical and epidemiologic data to coordination center and outside collaborators: HSTB has been a part of institutional efforts to transfer clinical and epidemiological data to coordination centers for all outside collaborators. HSTB was an integral part of the cooperative prostate cancer tissue resource (CPCTR) an NCI funded resource that was in existence from 1999-2006. As part of this effort de-identified clinical data was provided to the NCI. The University Of Pittsburgh Department Of Biomedical Informatics and the Division of Pathology Informatics both have extensive experience in terms of transmission of data. Additional capabilities for data transmission have been incorporated as part of the Shared Pathology Informatics Network (SPIN) initiative. Our recent broad engagement with TCGA and caHUB has resulted in transfer of data on over 1700 cases. This is done using the website designated by the NCI/SAIC (Open-Clinica) and Comprehensive Data Resource (CDR). We have extensive experience and the infrastructure to seamlessly transfer de-identified information as part of this project. **This will be extremely important to provide this demographic information to the GUDMAP investigators.**

F. Honest broker infrastructure: The honest broker is an individual/organization/system that acts for or on the behalf of the tissue/databank. The role of the honest broker is to collect and provide health information to research investigators in such a manner that it would not be reasonably possible for the investigators or other individuals to identify the patients directly or indirectly. The honest broker provides a firewall between clinical and research activities. Clinical information is stripped of HIPAA denoted personal health identifiers. Research material may have linkage codes, precluding the identification of patients to researchers. University of Pittsburgh has implemented a novel, IRB-approved mechanism to address honest broker functions to meet the specimen and data needs of researchers. The HSTB stores biologic specimens. The clinical data repositories store clinical information and are handled by various clinical staff from different departments; in the case of GUDMAP this will be Pathology and Gynecology and Obstetrics. Pathology and Oncology Informatics have designed software tools for querying availability of specimens, extracting data, and de-identifying specimens and annotating data for clinical and translational research. These entities partnered and submitted a joint IRB proposal to create an institutional honest broker facility. This provides a large group of honest brokers, ensuring availability for projects without any conflict of interest. This honest broker system currently consists of approximately 41 honest brokers (including 15 from HSTB), two supervisors and four medical faculty members. This infrastructure will be harnessed for the HUB at the University of Pittsburgh. The honest broker system is described in detail in a publication from our group [12]. **This system also provides a very robust system for data aggregation across a variety of different platforms and to the various Atlas projects of GUDMAP.**

G. Anticipated workflow for tissue and data transfer related to GUDMAP Atlas projects: The specimens will be anonymized with patient identifiers stripped from the specimens. The specimens will be annotated with appropriate annotating data. The specimens will be tagged using randomly generated numbers (either provided by NIDDK or generated in-house). The linkage codes are maintained by HSTB in a secure environment. This is a standard approach for biological specimens and data transfer from HSTB to investigators. The data annotation will be provided to the GUDMAP Atlas projects in a HIPAA compliant manner, consistent with the IRB requirements of the University of Pittsburgh. The Honest Broker system plays a critical role in this whole process (as described above). Thus allowing for the information to be provided to each other with identified information as they go through the different steps related to tissue and data accrual, storage, retrieval and disbursement. These are all established practices in routine use within the HSTB.

H. Whole Slide Imaging (WSI): The HSTB has imaging equipment for generating, annotating, interpreting, storing and analyzing digital images. This service is provided with pathologist oversight and appropriate technical support staff. As part of the HUB, we will provide GUDMAP investigators with whole slide images of the various histologic and fluorescence stains performed on the tissues as part of QA/QC. This will help investigators select appropriate specimens and create efficiencies. The WSI capabilities could also be leveraged for sharing of images between projects; enhancing interactions and collaborations.

1.3. Packaging and Shipping: Fetal genitourinary tissues required for research must always be in a condition that will maintain the integrity of the specimen [30, 31, 35]. This also applies to the transport of specimens from one site to another. During transportation, different specimens require maintenance at specific temperatures and this can be achieved by using appropriate packaging material such as dry ice, or gel packs. To maintain temperature at or below -150^{0}C, a liquid nitrogen dry shipper will be used. The HSTB repository has been involved in transporting specimens to and from the repository and has SOPs in place to ensure that tissue integrity is maintained at all times during such activities. The procedures provide details about packaging to

maintain the cold chain (wet ice/dry ice conditions) and other conditions (such as room temperature) for specific tissue types. Currently, there are regulations governing the transportation of potentially infectious materials (US Transportation Regulations- 49 Code of Federal Regulations [CFR]) such as the International Aviation Organization (ICAO) and the International Air Transport Association (IATA) for international transport regulations and information on classifying biospecimens for shipment. Failure to comply with these stipulated rules and regulations could result in delay or refusal of shipment and consequently biospecimen deterioration. All HSTB staff, through University Environmental Health and Safety, are IATA trained and all shipping practices are compliant with IATA regulations which is currently widely accepted as the standard for repository personnel by the NIH. As part of the TCGA and caHUB engagements, we have extensive experience using cryoports shipped to us by the Biospecimen Core Resource (BCR). **Our current level of training for the technical staff ensures awareness related to shipping and packaging related issues and we will utilize this knowledge to ship high quality tissues to the GUDMAP Atlas projects.**

1.4. Consenting and IRB related issues: The HSTB of the University of Pittsburgh has been very cognizant of issues pertaining to the legal and ethical aspects of tissue banking. We are particularly aware of the sensitivity related to human fetal and neonatal tissue that we currently collect and will make available to the GUDMAP Atlas projects. The HSTB and the IRB committee of the University of Pittsburgh have designed a consent form in relation to fetal collection. This form is modeled on the form proposed by the NIH. Since the project needs are no different from internal biospecimen/data needs, we do not anticipate any IRB issues/concerns. This is further emphasized by our longstanding relationship with TCGA and caHUB, which have similar data and biospecimen needs.

1.5. Material Transfer Agreement (MTA) issues: The University of Pittsburgh has experience in drafting and execution of MTAs. Specifically we have experience working with the NCI and the Science Applications International Corporation (SAIC/Leidos). There have been a lot of mutual discussions and work pertaining to MTA language, predominantly as a result of the involvement of HSTB in the Cancer Genome Atlas and caHUB. This experience will be invaluable in the relationship related to this GUDMAP project, if the University of Pittsburgh is invited to participate. The current experience has served to clear the path for future relationships. **To facilitate the transfer of biospecimens to GUDMAP Atlas researchers, a blanket MTA will be set up to encompass all the GUDMAP projects.**

Plan to interface with GUDMAP Atlas projects: As the proposed tissue hub and collection site for the GUDMAP Atlas projects we will interface regularly with all the Atlas projects to ensure that the needs of the individual projects are met. In the beginning this will involve individual phone conference calls with the specific projects, as well as regular coordination committee calls that the NIDDK might schedule. We will have regular calls with the project PIs and sites once the biomaterial and data transfers start occurring. We will work very closely with the projects and with NIDDK to ensure appropriate specimen types and data are provided; as well as perform appropriate quality assessments. We have a track record of being very flexible to ensure researcher satisfaction. We will participate in the monthly conference calls and will also meet in person twice a year at the GUDMAP Atlas project meetings to get updated on all the ground breaking science and personally interact with the PIs and staff from the various projects to create a collaborative environment for high-quality work. In addition, we will attend the annual American Society of Nephrology meeting and the International Workshop on Developmental Nephrology where GUDMAP has a workshop, this is held every 3 years. We have existing relationships with GUDMAP members; and have sought advice to optimize our processes as well as share material; as needed. Kindly see **letters of support from** (b)(6)

(b)(6)

AIM 1: To generate an inventory of genitourinary tissue throughout normal human development

1. General approach and rationale: HSTB has a long-standing relationship with the research community producing high quality tissue, including fetal human tissue, under the strictest consenting procedures. Although there exists significant data related to the molecular characterization of mouse genitourinary development [23-28], the information related to human development is vastly understudied. We propose that we have the knowledge, infrastructure and expertise to acquire, quality control and bank specimens, both snap frozen and paraffin embedded, for use by GUDMAP Atlas projects.

2. Preliminary data:

A. Histology of human fetal kidneys: We have collected embryonic tissues from 6-24 weeks of gestation as previously discussed. Our representative histological data reveals the high quality of the tissue that we are able to collect with well-preserved renal architecture (**Figure 1**). Depicted here is a 21 week old fetal human kidney showing the nephrogenic zone including the developing nephron progenitors, nephron structures (renal vesicles, comma and S-shaped bodies and developing glomeruli) and branching ureteric epithelium. We have had these images evaluated by the Kidney evaluation team including the project pathologist (b)(6) co-I), anatomist (b)(6) co-I) and GUDMAP member (b)(6) **letter of support**).

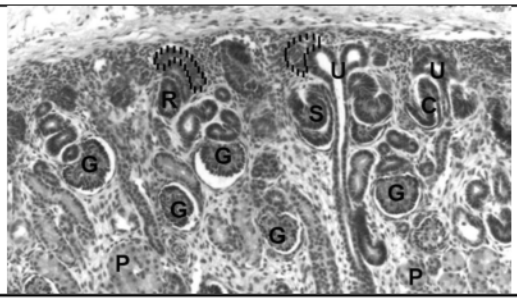

Figure 1: Histological image of human fetal kidney at 21 weeks. This is a representative histological image of the nephrogenic zone from a 21 week-old human fetal kidney. Depicted are many of the developing kidney structures including nephron progenitors (dashed lines), renal vesicles (R), comma (C) and S-shaped bodies (S), glomeruli (G), proximal tubules (P), ureteric epithelium (U).

B. Immunohistochemistry showing the developing renal vasculature: We wanted to determine whether the antigens were preserved and if we could visualize the various vascular components of the developing kidney. We utilized a CD31 antibody (stains all mature endothelial cells). A 19-week-old developing human kidney was utilized; it showed the dense vascular network that exists throughout the nephrogenic zone including the glomerular and peritubular capillary networks (**Figure 2A**). We also demonstrated the highly preserved nature of the intricate glomerular and peritubular capillaries (**Figure 2B**) and large caliber vessels (**Figure 2C**).

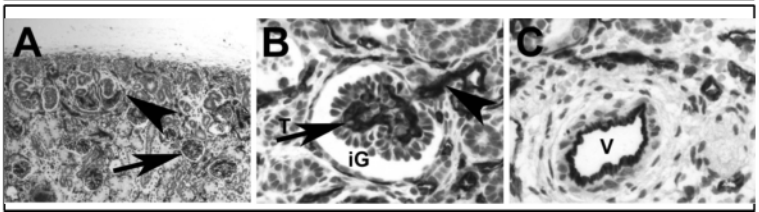

Figure 2: Human fetal kidney at 19 weeks of age stained for endothelium. A. Low power image of the renal cortex stained for CD31 (endothelium) showing numerous immature glomeruli (arrow) with glomerular capillaries (brown), and peritubular capillaries (brown) surrounding the dense renal tubules indicated by the arrowhead. **B.** An immature glomerulus (iG) with the dense capillary loops (arrow) and the accompanying urinary pole (arrowhead) next to a renal tubule (T) associated with peritubular capillaries. **C.** Larger caliber renal vessel (V).

C. Immunofluorescence of the kidney showing the nephron progenitors and early derivatives: We also wanted to determine whether we could use non-amplified immunofluorescence to visualize nephron progenitors and early nephron derivatives. Six2 is a known marker of the nephron progenitors; NCAM is a marker of both the nephron progenitors and the early-differentiated nephron structures [36, 37]. A representative image of a 17-week-old human fetal kidney shows the nephron progenitors stained with Six2 and NCAM (**Figure 3A-C**); the early nephron derivatives are positive for NCAM and have downregulation of Six2 (**Figure 3A-C**). The kidney evaluation team confirmed the staining pattern.

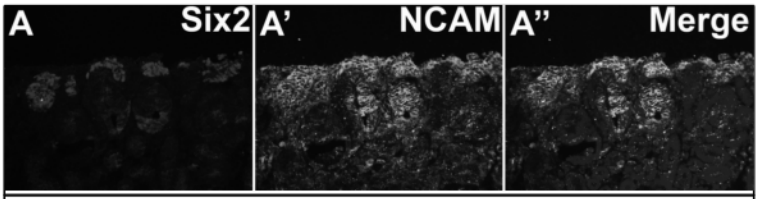

Figure 3: Human fetal kidney at 17 weeks of age stained for nephron progenitors and early derivatives. The nephron progenitors are positive for Six2 (A and A'', red) and NCAM (A' and A'', green). Conversely, the differentiated nephron structures down regulated Six2 but maintained NCAM expression. Dapi = blue

D. Histology of human fetal bladders: We wanted to harvest other urogenital organs to confirm that we could produce high quality tissue samples from other developing genitourinary organs. We focused on the bladder as the urothelium of the bladder is notoriously difficult to fix and stain with high quality due to damage that occurs directly after harvesting. In our first set of samples, we saw a similar urothelial damage phenotype due to post harvesting damage. We consulted (b)(6) (GUDMAP) and (b)(6) (GUDMAP) who advised that immediately post-harvesting the bladders should be bisected and immediately immersed in fixative. This approach has been very successful; please see representative images from a 21-week human fetal bladder, with a continuous urothelium and well-preserved lamina propria (**Figure 4A**) and muscle (**Figure 4B**). These images were evaluated by the Bladder evaluation team including (b)(6) (b)(6) as well as GUDMAP members (b)(6) (**letter of support)** and (b)(6) (**letter of support)**.

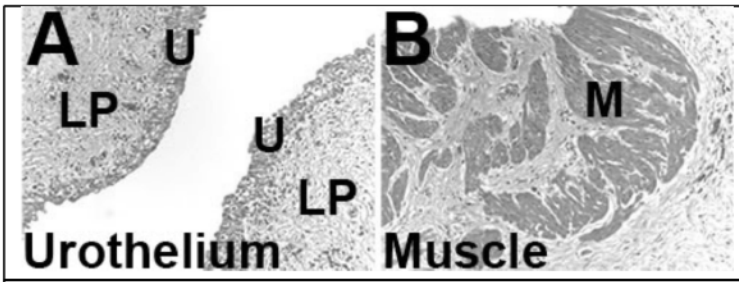

Figure 4: Histological images of human 21-week-old fetal bladders. A. Representative image showing the urothelium (U) and lamina propria (LP). **B.** Image of the bladder muscle (M).

e. Immunostaining of developing bladder urothelium and muscle: As with the kidney tissue we wanted to confirm that the bladder tissue had preserved antigens. We stained for urothelial (Uroplakin 3a and Cadherin 20) and muscle markers (αSMA) [38]. We observed well-preserved urothelium (**Figure 5A-B**), lamina propria (data not shown) and muscle layers (**Figure 5C**). The bladder evaluation team confirmed these findings.

Figure 5: Human fetal bladder at 21 weeks stained for urothelium and muscle. A-B. The urothelium stained for the umbrella (Uroplakin 3a, Upk3a) and superficial (Cadherin, Ck20) cells. **C.** Bladder muscle stained for αSMA (red). Dapi =blue.

3. Experimental Approach:

A. Assessing genitourinary histology: When the genitourinary tissues are received, we will process a third of the tissue into paraffin for histological examination. Sections will be cut at 4μm and stained with hematoxylin and eosin to evaluate basic morphology. Our pathologist and anatomist will evaluate tissue quality. High-resolution images will then be taken and these images will be uploaded and be available for GUDMAP projects and the scientific community. Our target goal is to have available a minimum of 5 cases (tissues and if possible other biologics) per week of gestational age for ages 6-42 weeks.

B. Evaluation of tissue specific antibodies: A subsequent third of the tissue will be embedded into TissueTek optimum cutting temperature (OCT) for immunofluorescence (IF). Based on the needs of GUDMAP projects, we will section at 6μm and perform IF to confirm the presence of antigens. These stained slides will be reviewed to assess for antigen preservation. Similarly, these high-resolution images will be uploaded and made available to the successful Atlas projects and the scientific community.

C. *In situ* hybridization to assess mRNA integrity: The remaining third of the tissue will be embedded into TissueTek optimum cutting temperature (OCT) for *in situ* hybridization (ISH). Based on the needs of GUDMAP projects, we will section at 6μm and perform ISH to confirm preservation of mRNA. These stained slides will be reviewed to assess mRNA degradation. Similarly, these high-resolution images will be uploaded and made available to the successful Atlas projects and the scientific community.

4. Anticipated Results, Pitfalls and Alternatives: We anticipate being able to provide high quality tissue to the successful GUDMAP projects by a combination of the HUB branch of the HSTB and the IIAM (for the later gestation time points). As an alternative for these later gestational time points, we are in the process of updating our IRB protocol at the University of Pittsburgh to include consenting for tissues from neonates of later gestational ages that have undergone sudden death. This would likely produce improved specimen quality and turnaround time since we can immediately harvest the tissue and provide these to the GUDMAP Atlas projects. Furthermore, if in the unlikely event that we are unable to acquire enough tissue from our in house tissue hub and collection site, we will utilize other tissue banks that are known to supply embryonic

tissue including IIAM. We will work closely with the GUDMAP Atlas projects to collect, process and store tissue as per the specific directions of the projects thus ensuring the highest quality of materials. We take great pride in providing to our investigators the highest quality of materials specifically tailored to their scientific needs.

AIM 2: To provide fresh genitourinary tissue and biological research specimens

1. General approach and rationale: As part of Aim 1, we will establish a standard operating procedure to generate a tissue bank of human fetal and neonatal genitourinary tissue, based on the needs of the GUDMAP projects. However, it will also be critical to provide fresh tissues for cell-based experiments to the various projects. Subsequently, in this aim we will work with the individual GUDMAP Atlas projects to collect and send out fresh high quality tissue for cell based experiments.

2. Preliminary data:

A. Isolation of fresh kidney compartments: As mentioned earlier, the HSTB is a well-established tissue core that has a long history of producing high quality fresh tissues for various researchers. The HSTB also has a significant track record of producing high quality fetal tissue and sending this to local researchers (including Dr. (b)(6) for cell based experiments. (b)(6) has developed a unique protocol to isolate various tissue compartments from these developing genitourinary tissues. Here we show that we have isolated from developing kidney proximal tubules, podocytes, ureteric epithelium and nephron progenitors (**Figure 6A**). The nephron progenitors were isolated using an optimized Dynabeads® protocol from the (b)(6) laboratory and grown in the defined expansion media [6]. The human fetal nephron progenitors can also be expanded in culture (**Figure 6B**).

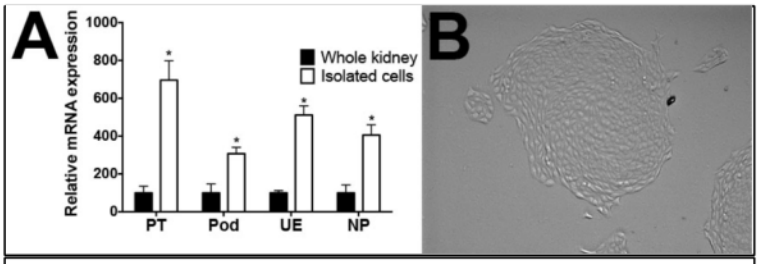

Figure 6: Freshly isolated kidney compartments. A. This histogram represents the isolated kidney compartments and enrichment of proximal tubules (PT), podocytes (Pod), ureteric epithelium (UE) and nephron progenitors (NP). **B.** Representative image of expanded nephron progenitors in culture.

B. Generate high quality RNA from Dynabeads® sorted nephron progenitors: We wanted to determine whether we could generate high quality RNA from these isolated kidney compartments. For these experiments we focused on the nephron progenitors and isolated cells with Dynabeads®. We isolated total RNA with the Qiagen miRNeasy kit, which also includes small RNAs, as these are likely to be of interest to GUDMAP Atlas projects. Here we show a bioanalyzer gel image (**Figure 7A**) and corresponding representative RNA plot depicting the small RNAs and 18S/28S ratio of the mRNAs (**Figure 7B**).

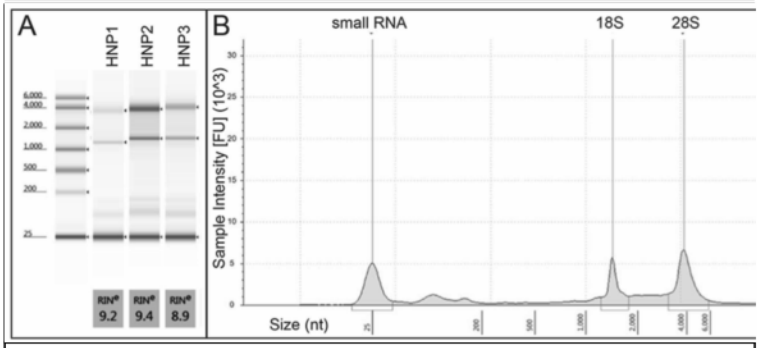

Figure 7: High quality RNA isolated from human fetal nephron progenitors. A. Bioanalyzer plot of 3 separate nephron progenitor (HNP1-3) isolations showing the high quality RNA as shown by the RIN values. **B.** Representitive plot showing the small RNAs and 18S to 28S peaks of mRNAs for the isolated nephron progenitors.

C. Human fetal kidneys can be shipped, nephron progenitors isolated and expanded in culture: We have shown from our preliminary data that we can isolate and culture distinct cell populations from the developing kidney tissues. However, it is critical that we are able to send high quality tissue to outside investigators and maintain tissue viability; and provide samples from which cells can be isolated and grown. To this end we have worked with (b)(6) (**see letter**) and shipped kidneys to his laboratory for cellular isolation and expansion in culture. His laboratory used their standard protocol to isolate nephron progenitors from the human kidney samples. These were then plated and the cells grown under the

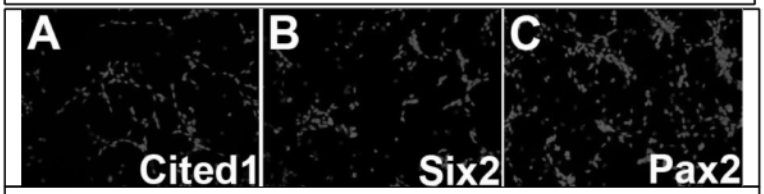

Figure 8: Nephron progenitor expansion *in vitro*. A-C. Isolated nephron progenitors maintain expression of the nephron progenitor markers (red) Cited1 (A), Six2 (B) and Pax2 (B). Dapi = blue.

expansion conditions [6]. They were able to expand the nephron progenitors and maintain nephron progenitor markers (**Figure 8**) without causing nephron progenitor differentiation (data not shown).

3. Experimental Approach:

A. Collection of fresh tissue for immediate shipment: In our preliminary data we show that we can collect genitourinary organs and produce high quality histological images and cell culture material both in house and via shipment to GUDMAP laboratories. In this aim, we will develop a collaborative relationship with the successful GUDMAP projects to provide high quality fresh samples based on individual needs. The tissue will be dissected by (b)(6) and a designated technician, and inspected for mechanical damage. The tissue will then be sent to the validation laboratories for further analysis before shipment. A small piece of the tissue will be used for histological evaluation to confirm tissue integrity. **The remaining tissue will be sent directly to the GUDMAP Atlas project investigators, arriving within 24 hours of acquisition**. The ages and number of samples that are required will be determined via interactions between the HUB and the individual Atlas projects (the current HSTB approach for all projects). We will work with each investigator to ensure they receive the highest quality fresh samples and will adjust collection, based on individual project requirements and feedback.

B. Isolation of distinct cell populations for shipment: We have developed in house techniques for the isolation of distinct cellular populations. Based on consultation with the Atlas projects we will determine the specific needs and cellular compartments that are needed to complete the projects and will isolate these cell types using Dynabeads®. In brief, we will utilize the Dynabeads® FlowComp™ Flexi kit (Invitrogen). This kit contains Dynabeads® that are conjugated to streptavidin. We will then biotinylate with the specific antibody needed to separate the required cell type. We will incubate isolated cells from the required tissues with the specific biotinylated antibody; then incubate these cells with bound antibodies with the streptavidin conjugated Dynabeads®. These will then be placed into a magnet to separate the cells. We will utilize a release buffer to remove the beads from the cells; by placing the cells back into the magnet to remove the beads. We will then verify the purity of these cells prior to shipment to the individual atlas projects.

C. Provide Laser capture and microdissection (LCM) services**:** HSTB provides LCM for specific projects. We have experience using the Leica LMD6000 LCM platform. If a specific GUDMAP project requires micro-dissected samples, the HUB will be glad to work with the PI of that project to provide this service.

4. Anticipated Results, Pitfalls and Alternatives: In this aim we anticipate being able to harvest and distribute high quality tissue and cells from the various fetal organ tissues to the successful Atlas projects. A pathologist and anatomist will evaluate all the tissues before shipment. We will validate each sample by taking a small piece for histology. We do not anticipate any major problems related to the acquisition and distribution of the tissues. Some tissues might need different processing to maintain tissue integrity; e.g. with the bladder urothelium. In these instances we will work with the individual projects to maximize the quality of the material they require. However, if we are unable to meet the demands of the various Atlas projects via the volume of our tissue hub and collection site, we will utilize additional identified tissue collection sites such as IIAM. Secondly, we will harvest isolated cell populations from the various developing genitourinary tissues based on the needs of the Atlas projects. We have extensive experience with this isolation technique and do not anticipate difficulties with this isolation. If we have problems with particular antibodies to bind to cell populations, we will work with the individual Atlas projects to optimize the isolation process for the cell type of interest.

D. Plans for banked tissue beyond grant period: A premise of this proposal is that the University of Pittsburgh HUB would collect and store specimens in addition to those immediately required by the GUDMAP investigators. This includes duplicate and consortium priority specimens; HSTB would retain custody of these residual specimens. In order to sustain the availability of residual specimens after the award period, the costs for ongoing storage, record keeping, and the effort required to disburse the specimens and associated data would be invoiced to the requesting investigator. The utility of sustaining such a valuable resource would depend on charging reasonably affordable rates. HSTB would need to cover the costs to maintain storage of residual specimens and provide sufficient and timely follow-up to requests. Therefore this plan presupposes that some cost to maintain this resource could fall to the HSTB. In addition to residual specimens, GUDMAP investigators may want to request prospective collection after the award period; we would make efforts to fulfill such requests assuming regulatory and financial agreements can be completed.

Human Subjects

1. The protection of human subjects from research risks

All the work that is outlined in this proposal is covered under an Institutional Review Board (IRB) (IRB # 0702050) from the University of Pittsburgh IRB committee and is adherent with all the state and federal laws. Furthermore, the University of Pittsburgh's DHHS Human Subjects Assurance Number is 00006790.

Obtaining tissues from patients undergoing procedures: These are patients who have signed the tissue banking consent form, which is a form separate from the procedure consent form. This tissue banking consent form allows these tissues and biological materials to be banked and stored with appropriate patient identifiers. The signed consent form also gives the Tissue Bank the ability to extract additional information and data from the currently existing medical record archives. The consent form also permits the additional collection of blood and urine, if agreed upon by the patient. The signed consent form also provides the Tissue Bank the ability to obtain follow-up data.
This research consent process is separate from the procedure related consent processes, which are done by the clinician performing the procedure. The separation of the research consent process from the clinical procedure related consent process allows the patient to focus more clearly and definitively on the consent for research. In addition, the research consent can be revoked at any time until the tissue has been disbursed and utilized. To minimize the possibility of coercion or undue influence, no monetary or other considerations will be provided as an inducement to participation. There is also a 24-hour period between the time of consent and the procedure to allow the patient sufficient time to consider and reconsider their decision. Similarly, the consenting research subject will not be allowed to direct the tissue to any specific researcher. The researchers will have no contact with the subjects.

Characteristics of the Subject Population: This proposal aims to provide a tissue resource encompassing all women of childbearing ages. The sole site of collection will be the Magee Women's Hospital that has a robust program for fetal genitourinary tissue specimen collection.

Plans for Recruitment of Subjects and Consent Procedures: The patient must sign the consent form for the procedure that will be used to obtain the tissue (i.e., dilation and curettage, dilation and evacuation, labor induction) or have signed consent for care before she can be approached to sign the fetal tissue research consent. For women having an elective abortion, this rule complies with the Pennsylvania Abortion Control Act. The patient may not designate the recipient of the tissue or organ in consenting to its use for research. The person obtaining consent for fetal tissue procurement must be a clinician involved in the care of the patient to comply with HIPAA. The person obtaining consent for fetal tissue procurement cannot be the surgeon or care provider overseeing the medical evacuation of the uterus nor the person who obtained consent for the elective abortion. For women having an elective abortion, this rule complies with the Pennsylvania Abortion Control Act. The attending physician retains the responsibility for determining the procedure to be used for termination of the pregnancy or treatment of a spontaneous abortion.

Data and safety monitoring plan: The Health Science Tissue Bank has in place a data and safety monitoring plan for all subjects enrolled in tissue and biological specimen donation. The data and safety monitoring plan is part of the annual submission to the IRB. Similar data and safety monitoring plans function in the clinical trials involvement. The activities of the Health Sciences Tissue Bank, with respect to biological specimen aggregation, as well as data annotation, are in full compliance with United States Federal statues, regulations, and ordinances. We also monitor any changes in rules and regulations concerning tissue and biological specimen aggregation and data degradation. The Institutional Review Board of the University of Pittsburgh insures complete compliance with these procedures and policies.
The highlights of the plan are as follows:

1. The data is stored on password-protected computers.
2. The data is provided to investigators only after the identifiers have been removed. The data is NEVER provided with any identifiers. A linkage code is used. The Tissue Bank retains the key to the code.
3. The biological materials are provided to research studies that are IRB approved or are utilizing the Tissue Bank IRB approved protocol that allows disbursement of biological materials that have been de-identified. No materials are ever given to studies that are not IRB approved.
4. The PI evaluates the data every quarter to assess the volume of accrual and the variety of specimens accrued.

5. Adverse events, if any, need to be documented and immediately provided to the IRB. The principle adverse events that can be associated with a facility like HSTB pertain to data security. No adverse events have occurred in this facility till date.

2. Inclusion (or exclusion) of individuals on the basis of sex/gender, race, and ethnicity

Gender: Our research proposal aims to provide genitourinary tissue for research related to the GUDMAP atlas projects. The program will collect both male and female tissue depending on the needs of the successful atlas projects.

Race: Pittsburgh is a racially mixed metropolis and this is reflected in the patient population seen at Magee Women's Hospital. Magee will provide an appropriate racial mix to the tissue specimens procured.

Children: Not Applicable.

Age: The age distribution of patients included in this proposal is representative of the demographics of this region and information related to the age will be provided to the researchers. The fetal tissues collected from Magee will be in the gestational age range of 6-24 weeks. We have an agreement in place with the International institute for the Advancement of Medicine. This agreement will provide us access to neonatal samples who were delivered in the gestational age range of 25-42 weeks. This will provide access to a novel resource for neonatal donation.

Women and female minorities will be included in this project. All federal, state, and local regulations will be followed in the consenting process and collection of the fetal tissues. In particular, we will adhere to 45 CFR 46 Subpart B 46.204.

OMB Number: 0925-0002

Planned Enrollment Report

Study Title: Research on tissue from an elective or spontaneous abortion < 24 weeks gestation

Domestic/Foreign: Domestic

Comments: About half the tissues will be collected under this IRB approved project. Tissues from 25-42 gestational weeks will be obtained from IIAM and will include collections from throughout the US.

Racial Categories	Ethnic Categories				Total
	Not Hispanic or Latino		Hispanic or Latino		
	Female	Male	Female	Male	
American Indian/Alaska Native	0	0	0	0	**0**
Asian	50	0	0	0	**50**
Native Hawaiian or Other Pacific Islander	0	0	0	0	**0**
Black or African American	100	0	10	0	**110**
White	200	0	20	0	**220**
More than One Race	0	0	20	0	**20**
Total	**350**	**0**	**50**	**0**	**400**

Study 1 of 1

Funding Opportunity Number: RFA-DK-15-016. Received Date: 2015-11-06T15:43:10.000-05:00

Children will not be included in this project as the aims are to collect fetal tissues.

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Please note that the letters of support are listed alphabetically first by University of Pittsburgh faculty/UPMC and then by External Collaborators.

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Resource Sharing

This application proposes to establish the GUDMAP human fetal tissue hub and collection site at the University of Pittsburgh. This will be achieved by leveraging the already highly collaborative and successful Health Sciences Tissue Bank. We have a proven track record of collaborative relations with researchers within the University of Pittsburgh and externally through the various national projects we are involved in. All specimens collected by HSTB are de-identified and distributed to the investigators by an honest broker system to protect the identity of the patients. Demographic and other appropriate annotating information will be available and provided for the various specimens. During the validation process we will generate high quality images to verify the tissue quality and usefulness for the successful projects. These images will be made freely available and shared with the greater scientific community through the GUDMAP website. We also plan to provide GUDMAP investigators access to data related to the number of cases and pertinent details of the case (gestational age, tissue types and relevant QA/QC information). This access will be through secure password protected mechanisms using software like Sharepoint. The tissues collected under this project are not patentable and therefore IP rights will not be exercised.