Impact of the *Xenopus* system on the missions of the NIDDK

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Xenopus has played a very important role in the mission of NIDDK for a long time. *Xenopus* oocytes have been and still are an invaluable system to study the conductive properties of many channels and transporters expressed on renal epithelial cells. Many recent technological advances such as antisense morpholino oligomers for gene knockdowns, transgenic GFP lines for imaging and the genome information for *X. tropicalis* have promoted *Xenopus* as a valuable model not only to study early embryonic development, but also to investigate organogenesis. This has been realized by NIDDK and projects exploring the pronephric kidney, the pancreas and the liver are among the currently funded grants.

Electrophysiology using *Xenopus* oocytes: *Xenopus* oocytes express a low number of endogenous membrane transporters and channels because they are virtually independent from exogenous nutrients. As such they have been and are the preferred *in vivo* model to characterize channels, receptors and transporters present on renal epithelial cells that are crucially important for kidney function. Oocytes are used to study electrophysiological properties, stoichiometries and the role of post-translational modification. The system is also very amendable to high-throughput screening approaches. As such it has been a powerful tool to perform functional screens for genes encoding ion channels and transporters. In addition to their basic science component these studies have significant impact in respect to human diseases. For example, studies on hypertension have used *Xenopus* oocytes to demonstrate that defects in With no Lysine kinase 4 (WNK4) causes increased activity of the renal transporter molecules NKCC2 and NCC and thereby directly interferes with blood pressure control.

Kidney Development: *Xenopus* embryos due to their aquatic life develop a functional pronephric kidney within 31 hours post fertilization. Thus, *Xenopus* has been established as a valuable animal model to study kidney development. Over the years, it has become evident that the process of kidney development is evolutionary conserved and findings in *Xenopus* are directly applicable to studies in higher vertebrates such as humans and mouse. One of the most recent advances was the realization that *Xenopus* is a powerful model organism to study the patterning of the nephron along its proximal-distal axis. With the availability of the *Xenopus tropicalis* genome it was possible to identify many structural proteins that are specifically expressed in defined segments of the pronephros. This patterning was highly reminiscent to the one found in individual nephrons of the metanephric kidney. It provided a novel angle to understand how transcription factors actually pattern the kidney along its proximal distal axis as illustrated by the recent study on the Iroquois (Irx) gene family. Similarly, the synchronous development of the *Xenopus* pronephros has also provided many novel insights in how kidney progenitors differentiate into their mature counterparts (e.g. the blood-filtering podocyte) or how microRNAs regulate terminal differentiation of the renal epithelial cells.

In addition to understanding the processes that regulate normal kidney development, the pronephric kidney of *Xenopus* is also a valuable tool to study kidney diseases. Knockdown of genes mutated in human forms of Polycystic Kidney Disease result in a “PKD-like” phenotype in *Xenopus* that is used to better understand the molecular mechanisms leading to kidney cyst formation. In particular, the speed of analysis and the nearly unlimited availability of embryos provide an ideal *in vivo* test system to study aspect of Polycystic Kidney Disease that cannot be performed in mouse as easily.

Finally, the *Xenopus* kidney is a great system to study tissue engineering. *Xenopus* was the first organism, where it could be shown that the combined action of Retinoic Acid and Activin

can convert primitive ectoderm into a functional kidney that can even be transplanted in nephrectomized *Xenopus* embryos. Ongoing work has extended these studies to several cell types in the kidney and has played an important role in identifying novel kidney-specific genes as well as ways to generate kidney epithelial cells *in vitro*.

Pancreas Development: The formation of the pancreas and the control of islet cell differentiation is one of the most coveted models of lineage specification. It is of high clinical importance due to its disturbance during diabetes. While mouse and chick have been the traditional models to study pancreas formation, the *Xenopus* pancreas has been developed as a viable alternative. Even though there are differences at later stages of pancreas development and its reorganization during metamorphosis, the early pancreas development in *Xenopus* is very similar to that of mice and humans. Many results are directly applicable to mammalian systems. In fact, one of the most important genes in pancreatic development, *Pdx1*, was initially discovered in *Xenopus*. The current research in *Xenopus* pancreas development follows similar avenues as outlined for the kidney. However, one particular interest is directed towards developing a transcriptional network of pancreas development in an effort to understand how early endodermal progenitors are specified first to a pancreatic fate, then to an endocrine fate and finally to a beta cell fate. For this approach *Xenopus* is uniquely suited since combinatorial knockdown studies using antisense morpholino oligomers allow analyses that are much more time-effective than compound mouse mutants.

Liver Development: Another organ system that has recently found more attention in *Xenopus* is the liver. The liver is an essential organ, yet the molecular basis of liver development is still poorly understood. Therefore, liver transplantation is often the only option for life threatening liver malfunctions. In an effort to develop alternative treatment options such as tissue replacement therapies from stem cells, the processes involved in hepatic tissue specification and the initial patterning of the foregut domain that will give rise to the liver are of high interest. Using the advantages of *Xenopus* it was recently shown that liver development relies on canonical and noncanonical Wnt signaling. Both pathways are necessary, but their activities have to be coordinated correctly to promote proper outgrowth of the liver bud.

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Xenopus Grants funding by the NIDDK

According to NIH RePORTER Search Tool, in the fiscal year of 2009, the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) **funded 53 grants** for projects involving *Xenopus*. These grants total **$11,307,900**. See appendix for complete list.

2009 *Xenopus* White Paper – Community Needs

Executive Summary

Xenopus - a crucial model organism for biomedical research:

Experiments in model animals are a cornerstone of biomedical research and have a massive impact on our understanding of human health and disease. The frog, *Xenopus,* is a widely used and crucial vertebrate model organism that offers a unique combination of three powerful advantages: strong conservation of essential biological mechanisms, a remarkable experimental repertoire, and unparalleled cost-effectiveness when compared to murine or other mammalian models.

In fact, for many experimental applications, *Xenopus* is the only viable model system. For example, in cell and molecular biology, *Xenopus* extracts allow for individual components of the cell cycle or DNA replication/repair machinery to be analyzed in a manner that cannot be recapitulated *in vivo* or in cell culture. For developmental biology, no other model system allows for high-throughput genomic/proteomic screening and at the same time allows for transplant/explant analysis (i.e. "experimental embryology"). The *Xenopus* oocyte is unique as a system for studying channel physiology using the patch-clamp and as a system for protein expression. Finally, *Xenopus* is the only vertebrate model that readily produces enough biological material for biochemical purification from eggs, intact embryos, or isolated embryonic tissues. The combination of these characteristics offers a wide range of experimental opportunities for studies using the *Xenopus* system in contrast to other vertebrates such as the mouse or zebrafish.

NIH Investment in *Xenopus:*

The NIH has made a substantial and continuing investment in *Xenopus* research. Indeed, a search of the NIH rePORT database for R01's or equivalent grants using the search term "*Xenopus*" returned **427 grants for a total cost of $127,583,776** for FY08 and FY09. Despite this investment in individuals' research, the *Xenopus* community lacks many resources that are considered entirely essential for other model systems, including a complete genome sequence, stock and training centers, and a comprehensive model organism database.

Xenopus as a Model System and Human Disease:

Given the tremendous advantages of the *Xenopus* system, the pace of new biological discovery by the *Xenopus* Community is brisk. Using *Xenopus*, we have significantly improved our understanding of human disease genes and their mechanisms, justifying the NIH's investment in *Xenopus*. Below we provide examples of just a few of the human health discoveries made in the last two years:

Xenopus embryos are used for *in vivo* analysis of gene expression and function:

Nephronophthisis - *Hum Mol Genet.* 2008. 17, 3655-62; *Nat Genet. 2005*. 37, 537-43.
Cutis laxa - *Nat Genet.* 2009. 41, 1016-21.
Meckel-Gruber syndrome - *Am J Hum Genet.* 2008. 82, 959-70.
Colorectal cancer - *Genome Res.* 2009. 19, 987-93.

Xenopus egg extracts are used for *in vitro* biochemical studies:

Fanconi Anemia - *Mol. Cell.* 2009. 35, 704-15; *J Biol Chem.* 2009, 284, 25560-8.
C-myc oncogene - *Nature*. 2007. 448, 445-51.
BRCA1 - *Cell*. 2006. 127, 539-552

Xenopus oocytes are used to study gene expression and channel activity:

Trypanosome transmission - *Nature* 2009. 459, 213-217.
Epilepsy, ataxia, sensorineural deafness - *N Engl J Med.* 360, 1960-70.
Catastrophic cardiac arrhythmia (Long-QT syndrome) - *PNAS* 2009. 106,13082-7.
Megalencephalic leukoencephalopathy - *Hum Mol Genet.* 2008. 17, 3728-39.

Xenopus as a Model System and Basic Biological Processes:

Xenopus also plays a crucial role in elucidating the basic cellular and biochemical mechanisms underlying the entire spectrum of human pathologies. Again only a few of the many discoveries in the last two years are highlighted here:

Xenopus embryos were used for studies of TGF-® signal transduction.
(*Cell*. 2009. 136,123-35; *Science*. 2007. 315, 840-3).

Xenopus egg extracts revealed fundamental aspects of cell division.
(*Nature*. 2008. 453, 1132-6; *Science*. 2008. 319, 469-72).

Xenopus embryos were used for studying mucociliary epithelia.
(*Nat Genet.* 2008. 40, 871-9; *Nature*. 2007. 447, 97-101).

Xenopus embryos were used for studying development of the vasculature.
(*Cell*. 2008.135, 1053-64).

Xenopus egg extracts provided key insight into DNA damage responses.
(*Mol Cell.* 2009. 35,704-15; *Cell.* 2008. 134, 969-80).

Xenopus embryos linked telomerase to Wnt signaling.
(*Nature*. 2009. 460, 66-72).

Xenopus was used for small molecule screens to develop therapeutics.
(Nat Chem Biol. 2008. 4, 119-25; Blood. 2009. 114, 1110-22).

Immediate Needs of the *Xenopus* Community:

It is the consensus of the *Xenopus* community that their biomedical research could be greatly accelerated by the development of key resources that are currently lacking. These resources would be of use to the entire *Xenopus* research community. In this White Paper, the community identifies seven resources in two categories: Three Immediate Needs and four Essential Resources:

The **Immediate Needs** are a common set of key resources that were identified as the most pressing by three committees established to identify needed resources across the broad and diverse *Xenopus* community. There is a broad, community-wide consensus that these resources would have an immediate impact on all *Xenopus* users and should be assigned the highest priority in order to accelerate the pace of biomedical research using *Xenopus* as a model system.

These Immediate Needs and the resulting improvements in biomedical research are as follows:

1. *Establishment of the Xenopus Resource and Training Center at the MBL in Woods Hole.*
   -Will allow rapid distribution of transgenic *Xenopus laevis* lines expressing fluorescent reporters and tagged proteins (for example histone-RFP for visualizing the mitotic spindle or organ specific GFP in embryos)
   -Will allow centralized generation, housing, and distribution of genetically modified *X. tropicalis* lines, including both mutants and transgenics.
   -Will allow both current investigators and the next generation of researchers to get hands-on training in *Xenopus*-based biomedical research methods (including cell, molecular, and developmental methods).
2. *Expansion and improvement of Xenbase, a Xenopus model organism database.*
   -Maintain and curate data for the essential primary database for *Xenopus* researchers.

-Enhance the functionality of *Xenbase* by introducing a phenotypes feature.
-Support new content on *Xenbase*, including proteomics support, a new genome browser, and Wiki for *Xenopus* methods.
-Continue and expand collaborative and service efforts (e.g. provide *Xenopus* data to other databases including NCBI, UniProtK, Mascot and Tornado).

3. *Complete sequencing of the Xenopus laevis genome.*
-Will allow the deconvolution of data in mass-spectrometry-based proteomic studies.
-Will facilitate identification of conserved gene regulatory regions to build gene-regulatory networks.
-Will facilitate site-specifc studies of DNA transaction (repair and replication)
-Will facilitate identification of all ORFs to build an ORFeome for rapid functional characterization of genes
-Will facilitate the design of morpholino oligonucleotides for gene depletion studies
-Will faciliate the analysis of chromatin-immunoprecipitations to identify DNA-bound to transcription factors and DNA modifications.

Essential Resources Needed by the *Xenopus* Community:

In addition to these immediate, community-wide needs, the committees identified four **Essential Resources** that should be developed as soon as possible, so that *Xenopus* biologists can more effectively fulfill the missions of the NIH. The *Xenopus* community considers all four of these additional resources to be essential, but understands that priorities must be set, and ranks these behind the Immediate Needs. These Essential Resources are as follows:

4. *Xenopus ORFeome in recombineering vectors.*
5. *Improvement of the X. tropicalis genome sequence and annotation*
6. *Development of methods for disrupting gene function in Xenopus.*
7. *Generation and Distribution of antibodies for Xenopus research.*

Anticipated Gains for Biomedical Research:

Xenopus is a crucial model organism for biomedical research. With the development of large-scale community-wide resources, *Xenopus* is poised to be become the premier vertebrate model for systems-level approaches to understanding biological mechanisms in cell, molecular, and developmental biology.

The National Research Council and the National Academy of Sciences have recently called on the Unites States “to launch a new multiagency, multiyear, and multidisciplinary initiative to capitalize on the extraordinary advances recently made in biology”. This report (http://www.nap.edu/catalog.php?record_id=12764) recommends the term "new biology" to describe an approach to research where “physicists, chemists, computer scientists, engineers, mathematicians, and other scientists are integrated into the field of biology.” The promise of systems-level analysis in *Xenopus*, combined with its already proven strengths, make *Xenopus* the ideal model organism for pursuing this “new biology.”

Genome improvements will provide *Xenopus* researchers with the ability to perform genome-wide screens for biological activities that will in turn allow the rapid assembly and analysis of gene regulatory networks. The ORFeome will greatly facilitate such genome-wide screening by allowing all ORFs to be rapidly analyzed or large numbers of proteins to be tagged for analysis of protein-protein interaction or for *in vivo* visualization. Using extracts and biochemical purification coupled with mass-spectrometry and genomic sequence, protein interactomes can be rapidly identified and validated. Because *Xenopus* can be so easily manipulated and because vast amounts of biological material can be generated, cell-type specific interactomes can also be identified. Large-scale genetic screens will identify important novel genes in developmental pathways, especially given the relatively simple genome of *X. tropicalis* compared to zebrafish. Finally, the flexibility of both *Xenopus* extracts and embryos make this system ideal for chemical biology screens. Identifying these gene-regulatory networks, interactomes, and novel genes will be only the first steps, of course. The well-

established power of *Xenopus* for rapid analysis of gene function will then allow deeply mechanistic analyses to complement the systems-level approaches described above.

It is the combination of these characteristics that distinguishes *Xenopus* from other vertebrate model systems such as mouse and zebrafish and allows for a systems-level approach to understanding biological mechanisms. The tremendous promise of the *Xenopus* model cannot be realized, however, without the immediate development of community-wide research resources. This White Paper presents the needed resources, and we look to the NIH for guidance in how to best achieve these goals.

For complete details of the 2009 Xenopus White Paper, please visit
http://www.xenbase.org/community/xenopuswhitepaper.do

Appendix

Xenopus Grants funded by the NIDDK

Project Number	Activity	Project Title	Principal Investigator	Organization	FY Total Cost by IC
5R01DK062348-07	R01	CNS ACTION OF APPETITE SUPPRESSANT AMINOSTEROL	AHIMA, REXFORD S	UNIVERSITY OF PENNSYLVANIA	$307,242
3R01DK062348-06S1	R01	CNS ACTION OF APPETITE SUPPRESSANT AMINOSTEROL	AHIMA, REXFORD S	UNIVERSITY OF PENNSYLVANIA	$18,270
5R01DK067214-05	R01	FUNCTIONS OF THE HUMAN OST-ALPHA AND OST-BETA PROTEINS	BALLATORI, NAZZARENO	UNIVERSITY OF ROCHESTER	$281,862
5K08DK078361-03	K08	ROLE OF THE RENAL SODIUM-PHOSPHATE CO-TRANSPORTER NAPI-IIC IN PHOSPHATE HOMEOSTAS	BERGWITZ, CLEMENS	MASSACHUSETTS GENERAL HOSPITAL	$137,970
5K08DK068226-06	K08	SODIUM CHLORIDE COTRANSPORTER REGULATION BY WNK KINASE	CAI, HUI	EMORY UNIVERSITY	$128,250
5P01DK017433-37	P01	CELLULAR AND MOLECULAR STUDIES OF RENAL TRANSPORT	CAPLAN, MICHAEL J	YALE UNIVERSITY	$1,097,195
5R21DK080431-02	R21	ISOLATION AND CHARACTERIZATION OF RAT KIDNEY ACTIVE UREA TRANSPORTER	CHEN, GUANGPING	EMORY UNIVERSITY	$193,750
5R01DK044158-19	R01	MYC ROLE IN HEMATOPOIESIS, VASCULOGENESIS & AGIOGENESIS	CLEVELAND, JOHN L.	SCRIPPS RESEARCH INSTITUTE	$345,824
2R01DK062914-05A2	R01	CELL SIGNALING IN DEVELOPING EPITHELIA	DRESSLER, GREGORY R	UNIVERSITY OF MICHIGAN AT ANN ARBOR	$347,625
5R01DK051496-11	R01	REGULATION OF THIAZIDE-SENSITIVE NACL TRANSPORT	ELLISON, DAVID H.	OREGON HEALTH AND SCIENCE UNIVERSITY	$277,817
5R01DK032753-26	R01	MECHANISMS OF TRANSPORT IN PROXIMAL AND DISTAL TUBULES	GUGGINO, WILLIAM B.	JOHNS HOPKINS UNIVERSITY	$348,500

3R01DK032753-25A1S1	R01	MECHANISMS OF TRANSPORT IN PROXIMAL AND DISTAL TUBULES	GUGGINO, WILLIAM B.	JOHNS HOPKINS UNIVERSITY	$16,400
3P01DK061521-05S1	P01	TISSUE CULTURE CORE	GUNN, ROBERT B	EMORY UNIVERSITY	$2,021
5R01DK059913-09	R01	NONGENOMIC STEROID SIGNALING IN OOCYTES	HAMMES, STEPHEN R	UNIVERSITY OF ROCHESTER	$300,470
5K08DK067245-06	K08	MECHANISMS OF REGULATION OF ANION EXCHANGER SLC26A6	HASSAN, HATIM A	UNIVERSITY OF CHICAGO	$142,020
5K08DK070668-05	K08	REGULATION OF THE SODIUM CHLORIDE COTRANSPORTER	HOOVER, ROBERT S	UNIVERSITY OF CHICAGO	$125,010
5R01DK077197-03	R01	TRANSCRIPTIONAL REGULATORY NETWORKS CONTROLLING XENOPUS PANCREAS DEVELOPMENT	HORB, MARKO E	CLINICAL RESEARCH INSTITUTE OF MONTREAL	$195,804
5R01DK064572-07	R01	MECHANISMS FOR ALTERED GLUCOSE HOMEOSTASIS DURING HAART	HRUZ, PAUL W	WASHINGTON UNIVERSITY	$297,920
3R01DK064572-07S1	R01	MECHANISMS FOR ALTERED GLUCOSE HOMEOSTASIS DURING HAART	HRUZ, PAUL W	WASHINGTON UNIVERSITY	$38,195
5R01DK069403-04	R01	ORIGIN AND REGULATION OF KIDNEY PROGENITOR CELLS	HUKRIEDE, NEIL A	UNIVERSITY OF PITTSBURGH AT PITTSBURGH	$277,004
5F30DK082153-02	F30	FUNCTIONALLY PROBING HSGLT2 IN DIABETES TREATMENT AND GLUCOSE HOMEOSTASIS	HUMMEL, CHARLES STANTON	UNIVERSITY OF CALIFORNIA LOS ANGELES	$30,826
5F32DK083160-02	F32	TRANSCRIPTIONAL REGULATION OF BETA-CELL-SPECIFIC EXPRESSION OF THE MAFA GENE	HUNTER, CHAD S	VANDERBILT UNIVERSITY	$43,020
1R01DK082430-01	R01	HISTONE PROLINE ISOMERIZATION AND GENE REGULATION	KIKYO, NOBUAKI	UNIVERSITY OF MINNESOTA TWIN CITIES	$377,500
5R37DK051391-14	R37	BIOMECHANICAL REGULATION OF RENAL ION TRANSPORTERS	KLEYMAN, THOMAS R.	UNIVERSITY OF PITTSBURGH AT PITTSBURGH	$305,881

1R01DK081594-01A1	R01	IDENTIFICATION, CHARACTERIZATION AND REGULATION OFINTERMEDIATE CONDUCTANCE K CHAN	LENG, QIANG	YALE UNIVERSITY	$400,847
1ZIADK053214-03	ZIA	NOVEL APPROACHES TO OBESITY: MODULATION OF INTESTINAL GLUCOSE ABSORPTION	LEVINE, MARK J		$176,155
5R01DK080047-02	R01	DIVALENT METAL-ION TRANSPORTER DMT1 AND ITS ROLE IN INTESTINAL METAL-ION UPTAKE	MACKENZIE, BRYAN	UNIVERSITY OF CINCINNATI	$273,000
3R01DK080047-02S2	R01	DIVALENT METAL-ION TRANSPORTER DMT1 AND ITS ROLE IN INTESTINAL METAL-ION UPTAKE	MACKENZIE, BRYAN	UNIVERSITY OF CINCINNATI	$35,846
5R01DK030111-27	R01	REGULATION OF HORMONE-SENSITIVE EFFECTOR SYSTEMS	MALBON, CRAIG C	STATE UNIVERSITY NEW YORK STONY BROOK	$374,964
5F32DK082145-02	F32	NON-CANONICAL WNT SIGNALS IN KIDNEY TUBULOGENESIS	MILLER, RACHEL KATHERINE	UNIVERSITY OF TEXAS MD ANDERSON CAN CTR	$50,054
5F32DK082154-02	F32	AN INVESTIGATION OF THE RENAL NA-K-CI COTRANSPORTER	MONETTE, MICHELLE YVONNE	YALE UNIVERSITY	$50,054
2R01DK062277-06	R01	ROLE OF WNT/BETA-CATENIN SIGNALING IN LIVER DEVELOPMENT	MONGA, SATDARSHAN SINGH	UNIVERSITY OF PITTSBURGH AT PITTSBURGH	$442,957
3P01DK070756-03S1	P01	EPITHELIAL OXALATE AND CITRATE TRANSPORT	MOUNT, DAVID BRUCE	BRIGHAM AND WOMEN'S HOSPITAL	$46,596
3P30DK034989-25S1	P30	CORE--MORPHOLOGY CORE	NATHANSON, MICHAEL H	YALE UNIVERSITY	$98,046
5R01DK079784-02	R01	MECHANISM OF FETAL AND NEONATAL HANDLING OF HIV DRUGS	NIGAM, SANJAY K	UNIVERSITY OF CALIFORNIA SAN DIEGO	$328,313
5K08DK073487-05	K08	THE FUNCTIONAL ROLE OF THE PXL DOMAIN OF SGK1 IN EPITHELIAL SODIUM TRANSPORT	PAO, ALAN C	STANFORD UNIVERSITY	$119,530

5R01DK056695-08	R01	SGK REGULATION OF EPITHELIAL SODIUM TRANSPORT	PEARCE, DAVID	UNIVERSITY OF CALIFORNIA SAN FRANCISCO	$301,389
3R01DK056695-08S1	R01	SGK REGULATION OF EPITHELIAL SODIUM TRANSPORT	PEARCE, DAVID	UNIVERSITY OF CALIFORNIA SAN FRANCISCO	$109,574
5R01DK072154-03	R01	INTERPLAY OF RENAL CA AND NA TRANSPORT PATHWAYS	PENG, JI-BIN	UNIVERSITY OF ALABAMA AT BIRMINGHAM	$262,175
5K01DK080194-02	K01	AN EPITHELIAL MODEL FOR V-TYPE H+-ATPASE-DRIVEN ACID-BASE TRANSPORT	PIERMARINI, PETER M	CORNELL UNIVERSITY ITHACA	$105,854
3K01DK080194-02S1	K01	AN EPITHELIAL MODEL FOR V-TYPE H+-ATPASE-DRIVEN ACID-BASE TRANSPORT	PIERMARINI, PETER M	CORNELL UNIVERSITY ITHACA	$54,000
5K99DK081610-02	K99	OLFACTORY PROTEINS IN THE KIDNEY AND REGULATION OF GLOMERULAR FILTRATION RATE	PLUZNICK, JENNIFER L	YALE UNIVERSITY	$88,354
5K08DK069608-05	K08	MOLECULAR BASIS OF BLADDER ORGANOGENESIS	REDDY, PRAMOD P	CHILDREN'S HOSPITAL MED CTR (CINCINNATI)	$125,010
5K01DK078679-03	K01	THE FUNCTIONAL ROLE OF GILZ IN EPITHELIAL SODIUM TRANSPORT	SOUNDARARAJAN, RAMA	UNIVERSITY OF CALIFORNIA SAN FRANCISCO	$124,200
3R21DK077763-02S1	R21	MICRORNAS IN KIDNEY DEVELOPMENT	WESSELY, OLIVER	LOUISIANA STATE UNIV HSC NEW ORLEANS	$3,845
1R01DK080745-01A2	R01	THE ROLE OF BICAUDAL-C IN POLYCYSTIC KIDNEY DISEASE	WESSELY, OLIVER	LOUISIANA STATE UNIV HSC NEW ORLEANS	$340,800
5F30DK082121-02	F30	GENE REGULATORY NETWORK FOR PODOCYTE DEVELOPMENT	WHITE, JEFFREY THOMAS	LOUISIANA STATE UNIV HSC NEW ORLEANS	$28,874
5R01DK068258-05	R01	PURINERGIC NEUROGENIC MUCOSAL SECRETION	WOOD, JACKIE D.	OHIO STATE UNIVERSITY	$277,835
5R01DK077133-02	R01	ROLE OF SGLTS IN GLUCOSE HOMEOSTASIS AND TISSUE METABOLISM	WRIGHT, ERNEST M	UNIVERSITY OF CALIFORNIA LOS ANGELES	$327,250
5R01DK043955-19	R01	MECHANISMS OF WATER FLOW ACROSS BIOLOGICAL MEMBRANES	ZEIDEL, MARK L.	BETH ISRAEL DEACONESS MEDICAL CENTER	$330,216

5R01DK070858-03	R01	MOLECULAR BASIS OF LIVER DEVELOPMENT	ZORN, AARON M	CHILDREN'S HOSPITAL MED CTR (CINCINNATI)	$301,350
1R01DK080823-01A1	R01	MAMMALIAN FOREGUT AND LIVER DEVELOPMENT	WELLS, JAMES M;ZORN, AARON M ;	CHILDREN'S HOSPITAL MED CTR (CINCINNATI)	$394,437
3R01DK080823-01A1S1	R01	MAMMALIAN FOREGUT AND LIVER DEVELOPMENT	WELLS, JAMES M;ZORN, AARON M ;	CHILDREN'S HOSPITAL MED CTR (CINCINNATI)	$99,999
				Total	$11,307,900