

# Developmental Biology

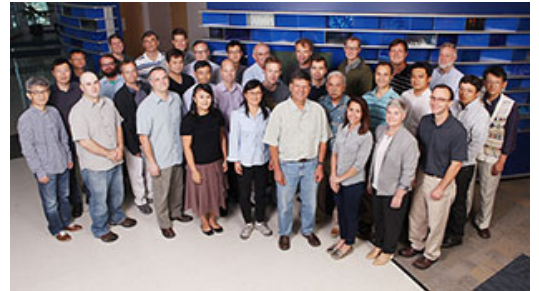
## Division Details

### RESEARCH AND TRAINING DETAILS

Faculty	21
Joint Appointment Faculty	27
Research Fellows and Post Docs	23
Research Graduate Students	59
Total Annual Grant Award Dollars	\$10,264,941
Total Annual Industry Award Dollars	\$129,895
Total Publications	54

### CLINICAL ACTIVITIES AND TRAINING

Clinical Fellows	3
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Row 1: J Park, J Waxman, K Campbell, F Hamada, Y Lan, R Kopan, S Bruggmann, S Huppert, R Waclaw

Row 2: YC Hu, M Weirauch, J Wells, T Nakamura, R Jiang, R Cornwall, D Millay, S Sumanas, SK Dey, T Defalco, S Namekawa, Y Yoshida

Row 3: J Ma, S Crone, V Kalinichenko, R Stottmann, C Mayhew, SW Cha, J Lessard, B Gebelein, A Zorn, M Kofron, S Potter, M Nakafuku

## Research Highlights

### Confocal Imaging Core

In 2015, the [Confocal Imaging Core](#) in the [Cincinnati Children's Research Foundation](#) (CCRF) underwent a number of changes to improve investigator access to equipment and add technical capabilities to the core. We added 3 Nikon A1(R) confocal microscopes with advanced diode-based laser launches in 2015 and early 2016. We also added a new high-speed wide-field inverted microscope with support from the [Perinatal Institute](#) and funds from the [Division of Neurosurgery](#). Finally, an upright wide-field microscope was recently installed. The upright microscope will be in the [Division of Pulmonary Biology](#). The CCRF purchased a new IVIS Spectrum CT managed by the CIC and housed in the veterinary services barrier facility. This system allows luminescence, fluorescence and microCT imaging of whole mice and rats for short and long-term studies. Usage on confocal and multiphoton microscopes exceeded 12,000 hours for calendar year 2015. Users also booked over 5,000 hours of wide-field microscope time and 6,500 hours of image analysis time. The CIC staff also trained 100+ new users on confocal, multi-photon, and wide-field microscopy as well as image analysis.

2015 was the CIC's first full year as a national [Nikon Center of Excellence](#). As part of this partnership, Cincinnati Children's CIC hosted visitors from a variety of institutions from across the United States, Mexico and Canada. Additionally, Nikon donated two high-end image analysis computers to the CIC to enhance our image analysis capability. The CIC and Nikon have been partnering on improving image analysis methods and imaging techniques such as Enhanced Resolution and SRRF.

The CIC added equipment and technical training in techniques to enhance users research. T93he 3022 Nikon A1R GaAsP system added luminescence imaging. This allows investigators to visualize luminescence at single-cell level. Also, the CIC began training users in new clearing techniques including Clarity, PACT, SeeDB, Cubic, and X-Clarity. Core personnel evaluated commercial clearing devices and added the Logos X-Clarity chamber to its shared equipment. The X-Clarity chamber is capable of clearing an adult mouse brain in as little as 3 hours. Finally, the CIC has implemented new techniques for super-resolution including Nikon's Enhanced Resolution (ER) and Super Resolution Radial Fluctuations (SRRF). ER provides lateral resolution to 140nm. SRRF provides localization based resolution to 50-100nm.

The CIC hosted [Dr. Scott Fraser, PhD](#), an internationally known researcher for a CCRF lecture in the Perinatal Seminar Series as well as a technical presentation as part of ORVCA Imaging and Cytometry Day.

The CIC director, [Dr. J. Matthew Kofron, PhD](#), gave the following presentations:

- 2015 ORVCA Imaging and Cytometry Day: Breakout session on single molecule FISH
- 2015 MCB seminar series
- 2015 DHC seminar series
- 2015 Nikon Pan-American meeting
- 2016 ORVCA Imaging and Cytometry Day: Breakout session on new super resolution techniques.
- 2016 Midwest ABRF meeting: Balancing budgets and institutional needs for technological advancement.
- The CIC provided 40 letters of support for investigator grant applications.

## Yutaka Yoshida Publication

The Yoshida lab published in Nature Neuroscience. This paper is a significant for finding a possible treatment for suppressed immunity from spine injuries. Infection, a consequence of immune suppression, is the leading cause of death for people with spinal cord injuries (SCIs). However, the underlying mechanisms are unknown. We show that profound plasticity develops within spinal autonomic circuitry below the injury, creating a sympathetic anti-inflammatory reflex. We further show that inhibition of neuronal activity involved this reflex circuitry blocks post-SCI immune suppression. These data provide new insights and potential therapeutic options for limiting the devastating consequences of post-traumatic autonomic hyperreflexia and post-injury immune suppression.

## Recruitment of Takanori Takebe

The Divisions of Developmental Biology, [Pulmonary Biology](#), and [Gastroenterology, Hepatology and Nutrition](#) have jointly recruited [Dr. Takanori Takebe, MD](#) (Taka). Taka is a world leader in developing liver and kidney organoids, and is particularly known for his dedication to reducing his technology to clinical practice. He won the "The 2016 NYSCF – Robertson Stem Cell Investigator Award", an R01 equivalent grant, for applying human iPSC-derived liver organoid towards the treatment of pediatric liver disease model. His work is highlighted as the best paper of 2015 in [Cell Stem Cell](#).

## Gene Expression Core

[The Gene Expression Core](#) works to stay at the forefront of small sample gene expression profiling. The Core purchased a Fluidigm C1 microfluidics machine three years ago for the RNA-Seq analysis of single cells. The Fluidigm C1 brought the capacity to carry out RNA-Seq analysis of single cells in a high throughput robotics driven manner. The machine places individual cells in discrete chambers and carries out a series of biochemical amplification reactions. The Fluidigm performs the amplifications in nanoliter volumes, which results in less nonspecific product and conserves reagents. It can optimally process about 96 cells per run. Because of the high use and limited availability of our Fluidigm C1 we purchased another machine in 2016.

In 2015, the McCarroll Lab described another technology for single cell RNA-Seq, called Drop-Seq. The Drop-Seq approach is quite remarkable in that it allows analyzation of many thousands of cells at a much reduced cost per cell. The concept is that a very simple and inexpensive microfluidics device creates nanodrops including a single bead and a single cell. Oligonucleotides coats the bead that carries a 12 base bead specific barcode. The RNA anneals to the polyT part of these oligos of a lysed cell. cDNA, made from the RNA,

incorporates the bead unique barcode, allowing the resulting RNA-Seq reads to be assigned to this specific cell. The net result is that the drops can be broken and the beads all combined into a single tube for subsequent reverse transcription and processing. Post RNA-Seq the reads can be deconvoluted to determine which reads came from which cell. The net result is that this technology allows RNA-Seq analysis of many thousands of cells, at a greatly reduced cost per cell compared to Fluidigm. During the past year the Gene Expression Core has set up Drop-Seq technology and carried out about 50 runs to optimize the procedure. For example, we have defined the single cell RNA-Seq profiles of several thousand mouse embryonic kidney cells. Another example is in the analysis of the developing mouse lung, as part of the LungMap consortium. Fig. 1 shows the results of a Drop-Seq analysis of about 12,000 P7 mouse lung cells, with the many cells divided into specific types using the Seurat program. Fig. 2 shows a heatmap of gene expression patterns of P3 mouse lung cells.

## Transgenic Animal and Genome Editing (TAGE) Core

The fiscal year 2016 (FY16) was a productive year for the Transgenic Animal and Genome Editing Core (TAGE). Its newly established CRISPR service remained in high demand in FY16. There were 48 requests for mutant mouse (or rat) production and 8 requests for cell editing-related services throughout the year. We also launched a new service for targeted transgenesis using the TARGATT system that allows the direct insertion of the transgene directly into the safe harbor locus in mice, instead of random integration. This service saw the completion of three projects. The conventional transgenic services also remained in high demand in FY16. We received 32 requests for the pronuclear injection, 92 for embryo transfer (re-derivation), 4 for blastocyst injection, 20 for in vitro fertilization, and 45 for sperm cryopreservation.

To deal with the high demand for services, the TAGE core had undergone a number of changes in personnel, facilities, and the experimental procedures in FY16. We recruited a research associate, Celvie Yuan, as a replacement for Huirong Xie who left for [Michigan State University](#), to perform CRISPR services, animal surgery, and in vitro fertilization service. We also hired a new tech, Evan Barr-Beare, to perform molecular biology experiments, animal surgery, and other mouse work. These two new additions greatly reduced the backlog of service requests and increased our revenue. The revenue they generated was able to cover and exceed the costs of their salary and benefits.

Because most of our services require the use of animals, the number of animals the animal room is able to hold became another limiting factor for our services. To address the issue, [Cincinnati Children's Hospital Research Foundation](#), and the Veterinary Services, provided the support and renovated the mouse room to increase the capacity from 420 to 598 mouse cages. The renovation also included two new animal hoods for changing cages and a brand new surgical hood to replace the old one that was partially functional. These new hoods allow for simultaneous performance of a variety of tasks. For instance, we can perform surgery and mouse biopsy at the same time when the Veterinary Services tech is changing the cages. The animal room renovation has substantially improved the effectiveness, flexibility, and availability.

We understand that increasing the efficiency of our services can improve the service flow, reduce the failure rate, cut the costs, and bring in more business. While providing the services, we constantly optimized every step of the procedures and tested new methods and reagents to improve the efficiency. The TAGE core director and staff also attended international conferences and workshops to gain new skills and knowledge. We also hosted cross-division journal club to ensure that our techniques are up-to-date. As a consequence, we had a low failure rate and a high efficiency in CRISPR services and other services, including in vitro fertilization, blastocyst injection, and sperm cryopreservation. Our results have impressed people around the world via presentations at conferences.

The TAGE director gave the following presentations:

- 2015 MCB seminar series
- 2015 Heart Institute seminar series
- 2015 Genome Engineering: CRISPR/Cas Revolution meeting, Cold Spring Harbor, NY
- 2016 Association for Research in Vision and Ophthalmology annual meeting, Seattle, WA
- 2016 Pulmonary Biology Division meeting 2016 ORVCA Imaging and Cytometry Day

- 2016 Midwest ABRF meeting

The TAGE has provided more than 40 letters of support for investigator grant applications in FY16.

## Pluripotent Stem Cell Facility

The mission of the [Pluripotent Stem Cell Facility](#) (PSCF) is to facilitate and support human pluripotent stem cell (hPSC) research at Cincinnati Children's Hospital Medical Center by providing centralized access to state-of-the-art human pluripotent stem cell technologies as well as reagents, expertise and training. Since the PSCF creation in 2008, we have provided services to >85 faculty members from Cincinnati Children's and numerous external institutions. Fiscal year 2016 saw an increase in demand for each of our major services. The generation of human induced pluripotent stem cell (iPSC) lines increased to 40 successfully completed projects in FY 2016 (compared to 18 in FY 2015 and 25 in FY 2014). These cells are now used in disease modeling applications at Cincinnati Children's and several external institutions. A key facet of our mission is dissemination of hPSC technologies to Cincinnati Children's investigators through training. In FY 2016, the total number of hands-on training courses delivered by the PSCF increased to 23 in FY 2016 (compared to 19 in FY 2015 and 20 in FY 2014).

The PSCF is responsible for the continued development/implementation of key hPSC technologies to ensure that Cincinnati Children's investigators have access to cutting-edge hPSC reagents and technologies. In FY 2016, the PSCF began implementing methods for the efficient genome editing of hPSCs using CRISPR/Cas9 technologies. These efforts are in collaboration with the Transgenic Animal and Genome Editing (TAGE) core (Dr. Yueh-Chiang Hu). All routine procedures including the transfection and cloning of hPSCs have been optimized and a basic hPSC genome editing service is now available to our clients (our first project has been successfully completed). We are continuing work to identify the most efficient methods to introduce and express CRISPR/Cas9 components to hPSCs in order to increase the robustness of these protocols. In the last year, we have also continued to optimize and improve methods for the generation of iPSCs. This includes the implementation of a new technique to generate iPSCs from blood samples, which has resulted in a ~10-fold increase in the efficiency of iPSC formation. We have also tested and begun to optimize methods for the generation of iPSCs from urine samples. Preliminary studies have been successful and we have generated iPSCs from urine-derived kidney epithelial cells using both integrating (lentivirus) and non-integrating (episomal plasmids) reprogramming methods.

Finally, in FY2016, in collaboration with [Dr. Ying Sun, PhD](#), in the [Division of Human Genetics](#), [Dr. Christopher Mayhew, PhD](#), received a pilot grant to study the therapeutic efficacy of iPSC-derived neural progenitors in a mouse model of neuronopathic Gaucher Disease (nGD). This grant involves the generation of human and mouse iPSCs harboring nGD mutations. Using CRISPR/Cas9 and iPSCs, corrected mutations are differentiated to neural progenitor cells (NPCs). Researchers administer a subset of these corrected NPCs to nGD mice by intravenous injection. Then they assess the ability of these cells to cross the blood-brain barrier, enter the CNS, and impact nGD phenotypes. In the first year of funding of this grant, we have optimized IV delivery (dose/schedule) and detected donor NPCs in the CNS of nGD mice. Furthermore, evidence of therapeutic benefit can be demonstrated by improved measures of key physiological consequences of neurodegeneration in nGD mice. These encouraging preliminary data have resulted in the awarding of a second year of funding for this grant. Larger foundation and [National Institutes of Health](#) grant applications are in progress.

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## Significant Publications

Chen S, Brunskill EW, Potter SS, Dexheimer PJ, Salomonis N, Aronow BJ, Hong CI, Zhang T, [Kopan R. Intrinsic Age-Dependent Changes and Cell-Cell Contacts Regulate Nephron Progenitor Lifespan](#). *Dev Cell*. 2015 Oct;1235(1):49-62.

Chen et al. explored the control of nephron progenitor lifespan which determines the number of nephrons an individual has by single-cell transcription profiling and heterochronic cell transplantation. They observed progressive age-dependent changes with increasing heterogeneity in older populations. Young cells can “rejuvenate” older progenitors, and age dependent changes alter the niche environment, affect inter-progenitor interactions, and contribute to the cessation of nephrogenesis.

Hass MR, Liow HH, Chen X, Sharma A, Inoue YU, Inoue T, Reeb A, Martens A, Fulbright M, Raju S, Stevens M, Boyle S, Park JS, Weirauch MT, Brent MR, [Kopan R. SpDamID: Marking DNA Bound by Protein Complexes Identifies Notch-Dimer Responsive Enhancers](#). *Mol Cell*. 2016 Oct 6:64(1):213.

Hass et al. developed SpDamID by splitting DAM into inactive halves. Proximity-enabled DAM reconstitution methylates adenine in GATC on genomic DNA bound in vivo by interacting or juxtapositioned transcription factors. SpDamID is a powerful tool that enables dynamic analysis of combinatorial protein interactions with DNA at a genome-wide level.

Imai F, Ladle DR, Leslie JR, Duan X, Rizvi TA, Ciraolo GM, Zheng Y, **Yoshida Y. Synapse Formation in Monosynaptic Sensory-Motor Connections Is Regulated by Presynaptic Rho GTPase Cdc42.** *J Neurosci.* 2016 May 25;36(21):5724-35.

This study shows that Cdc42 regulates synapse formation of monosynaptic sensory-motor circuits.

Rankin RA, Han L, McCracken KW, Kenny AP, Anglin CT, Grigg EA, Crawford CM, Wells JM, Shannon JM, **Zorn AM. A Retinoic Acid - Hedgehog Cascade Coordinates Mesoderm Inducing Signals and Endoderm Competence During Lung Specification.** *Cell Rep.* 2016 Jun 28;16(1):66-78.

The complex genetic networks controlling fetal lung development are poorly understood. Rankin and Han et al., show that an evolutionarily conserved cell signaling cascade coordinates tissue interactions that are essential for initial development respiratory system in frogs, mice and human stem cells. This work informs our understanding of congenital birth defects and our ability to make human lung tissue in a dish for regenerative medicine.

Ueno M, Ueno-Nakamura Y, Niehaus J, Popovich PG, **Yoshida Y. Silencing Spinal Interneurons Inhibits Immune Suppressive Autonomic Reflexes Caused by Spinal Cord Injury.** *Nat Neurosci.* 2016 Jun;19(6):784-7.

This study shows reorganization of spleen-spinal cord circuitry after spinal cord injury, and inhibition of excitatory interneurons inhibits immune suppression.

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## Division Publications

1. Agricola ZN, Jagpal AK, Allbee AW, Prewitt AR, Shifley ET, Rankin SA, Zorn AM, Kenny AP. **Identification of Genes Expressed in the Migrating Primitive Myeloid Lineage of *Xenopus Laevis*.** *Dev Dyn.* 2016; 245:47-55.
2. Alqadah A, Hsieh YW, Schumacher JA, Wang X, Merrill SA, Millington G, Bayne B, Jorgensen EM, Chuang CF. **Slo Bk Potassium Channels Couple Gap Junctions to Inhibition of Calcium Signaling in Olfactory Neuron Diversification.** *PLoS Genet.* 2016; 12:e1005654.
3. Bell A, Kofron M, Nistor V. **Multiphoton Crosslinking for Biocompatible 3d Printing of Type I Collagen.** *Biofabrication.* 2015; 7:035007.
4. Bhatt S, Connett J, Voelker H, Lindberg S, Westfall E, Wells J, Lazarus S, Criner G, Dransfield M. **Beta-Blockers for the Prevention of Acute Exacerbations of Chronic Obstructive Pulmonary Disease (?Lock Copd): A Randomised Controlled Study Protocol.** *BMJ Open.* 2016; 6:e012292.
5. Breidenbach AP, Aschbacher-Smith L, Lu Y, Dyment NA, Liu CF, Liu H, Wylie C, Rao M, Shearn JT, Rowe DW, Kadler KE, Jiang R, Butler DL. **Ablating Hedgehog Signaling in Tenocytes During Development Impairs Biomechanics and Matrix Organization of the Adult Murine Patellar Tendon Entesis.** *J Orthop Res.* 2015; 33:1142-51.
6. Broering TJ, Wang YL, Pandey RN, Hegde RS, Wang SC, Namekawa SH. **Baz1b Is Dispensable for H2ax Phosphorylation on Tyrosine 142 During Spermatogenesis.** *Biol Open.* 2015; 4:873-84.
7. Chen G, Wernig M, Berninger B, Nakafuku M, Parmar M, Zhang CL. **In Vivo Reprogramming for Brain and Spinal Cord Repair.** *eNeuro.* 2015; 2.
8. Chen S, Brunskill EW, Potter SS, Dexheimer PJ, Salomonis N, Aronow BJ, Hong CI, Zhang T, Kopan R. **Intrinsic Age-Dependent Changes and Cell-Cell Contacts Regulate Nephron Progenitor Lifespan.** *Dev Cell.* 2015; 35:49-62.

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13. Grant I, Balcha D, Hao T, Shen Y, Trivedi P, Patrushev I, Fortriede J, Karpinka J, Liu L, Zorn A. **The Xenopus Orfeome: A Resource That Enables Functional Genomics.** *Dev Biol.* 2015; 408:345-57.
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17. Hayashi Y, Nishimune H, Hozumi K, Saga Y, Harada A, Yuzaki M, Iwatsubo T, Kopan R, Tomita T. **A Novel Non-Canonical Notch Signaling Regulates Expression of Synaptic Vesicle Proteins in Excitatory Neurons.** *Sci Rep.* 2016; 6:23969.
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23. Kopan R. **The Unaimed Arrow Never Misses.** *Curr Top Dev Biol.* 2016; 116:547-50.
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26. LaBonne C, Zorn AM. **Modeling Human Development and Disease in Xenopus. Preface.** *Dev Biol.* 2015; 408:179.

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29. Liu Z, Brunskill E, Varnum-Finney B, Zhang C, Zhang A, Jay PY, Bernstein I, Morimoto M, Kopan R. **The Intracellular Domains of Notch1 and Notch2 Are Functionally Equivalent During Development and Carcinogenesis**. *Development*. 2015; 142:2452-63.
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35. Potter AS, Potter SS. **Molecular Anatomy of Palate Development**. *PLoS One*. 2015; 10:e0132662.
36. Raines AM, Magella B, Adam M, Potter SS. **Key Pathways Regulated by Hoxa9,10,11/Hoxd9,10,11 During Limb Development**. *BMC Dev Biol*. 2015; 15:28.
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54. Zhang Z, Rankin SA, Zorn AM. **Syndecan4 Coordinates Wnt/Jnk and Bmp Signaling to Regulate Foregut Progenitor Development.** *Dev Biol.* 2016; 416:187-99.

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## Grants, Contracts, and Industry Agreements

### Annual Grant Award Dollars

Investigator	Title	Sponsor	ID	Dates	Amount
Kenneth J Campbell, PHD Brian Gebelein, PHD	Roles of Gsx Factors in Telencephalic Neurogenesis	National Institutes of Health	R01 NS044080	3/15/2014 - 2/28/2019	\$547,413
Sang-wook Cha, PHD	Wnt/PCP Signaling in the Intestinal Epithelium	National Institutes of Health	K01 DK101618	4/15/2014 - 2/28/2019	\$128,976
Brian Gebelein, PHD	Hox Control of Cell-Specific EGF Signaling During Development	National Institutes of Health	R01 GM079428	8/9/2013 - 5/31/2017	\$290,700
Rashmi Hegde, PHD	Mechanism of Action of Retinal Determination Proteins	National Institutes of Health	R01 EY014648	4/1/2014 - 3/31/2018	\$351,000
Rashmi Hegde, PHD	EYA in Retinal Angiogenesis	National Institutes of Health	R01 EY022917	8/1/2013 - 7/31/2017	\$374,850
Rashmi Hegde, PHD	Eya Inhibitors in the Treatment of Peripheral Vascular Disease and	National Institutes of Health (The Cleveland Clinic Lerner Coll of Med)	U54 HL119810	3/1/2015 - 2/29/2016	\$78,000



	Pulmonary Arterial Hypertension				
Rulang Jiang, PHD	Molecular Patterning of Mammalian Dentition	National Institutes of Health	R01 DE018401	9/12/2013 - 6/30/2018	\$516,799
Raphael Kopan, PHD	Assessing the Therapeutic Window for Future Anti-Notch Dimerization Agents	National Institutes of Health	R01 CA163653	7/1/2013 - 4/30/2018	\$323,864
Raphael Kopan, PHD	The Mechanism Regulating Renal Progenitor Aging	National Institutes of Health	R01 DK106225	4/1/2016 - 1/31/2021	\$469,933
Xinhua Lin, PHD	Molecular Mechanisms Regulating Intestinal Stem Cell Activities and Homeostasis	National Institutes of Health	R01 GM115995	8/1/2015 - 4/30/2019	\$616,200
Jorge Munera, PHD	Human Intestinal Organoids as a Model of Ulcerative Colitis	Crohn's & Colitis Foundation of America	CCFA315366 - Munera,Jorge	7/1/2014 - 6/30/2017	\$58,250
Masato Nakafuku, MD-PHD Kenneth J Campbell, PHD	Molecular Control of Neurogenesis in the Adult Subventricular Zone	National Institutes of Health	R01 NS069893	4/1/2015 - 3/31/2020	\$482,627
S Steven Potter, PHD	Transcriptome Atlases of the Craniofacial Sutures	National Institutes of Health (Icahn School of Medicine at Mount Sinai)	0255-7191-4609 (U01 DE024448)	5/1/2014 - 4/30/2019	\$31,448
S Steven Potter, PHD James Wells, PHD	Single Cell/RNA-Seq Dissection of Human iPS Cell Development into Intestine	National Institutes of Health	R01 DK098350	9/20/2013 - 7/31/2017	\$332,775
S Steven Potter, PHD Jeffrey A Whitsett, MD	Lung MAP Atlas Research Center	National Institutes of Health	U01 HL122642	6/15/2014 - 4/30/2019	\$390,982
S Steven Potter, PHD	Recombineering Based Analysis of Hox Function in Kidney Development	National Institutes of Health	R01 DK099995	8/8/2014 - 4/30/2018	\$339,300
S Steven Potter, PHD	Generating Molecular Markers that Selectively Label Urothelial Sub-populations	National Institutes of Health (Columbia University Medical Center)	U01 DK094530	9/30/2011 - 8/31/2016	\$42,976
Stephen Riffle	Targeting Eyes Absent Proteins in the Treatment of Ewing Sarcoma	Cancer Free Kids	CFK_Riffle	7/7/2015 - 7/6/2016	\$35,000
James Wells, PHD Noah F Shroyer	Investigation of Regional Identity in Human Intestinal Stem Cells	National Institutes of Health	U01 DK103117	9/1/2014 - 8/31/2019	\$122,567

Jennifer A Schumacher, PHD	The Role of Fibronectin/Integrin and BMP Signaling in Endocardial Morphogenesis and Differentiation	American Heart Association	16SDG27330007	1/1/2016 - 12/31/2019	\$77,000
Saulius Sumanas, PHD	Role of Collagen XXII in Vascular Stability	Amer Heart Assoc - Ohio Affiliate, Inc	16GRNT27370004	1/1/2016 - 12/31/2017	\$77,000
Saulius Sumanas, PHD	Inhibition of ETS Transcription Factors as a Novel strategy for Blocking Tumor Angiogenesis	Cancer Free Kids	CFK_Sumanas	6/6/2016 - 6/5/2017	\$50,000
Quynh Van Ton, PHD	Validation of Aneurysm Associated Genes in a Zebrafish Model	National Institutes of Health	F32 HL124889	12/1/2014 - 11/30/2017	\$54,294
James Wells, PHD	Human Endocrine Cell Development	National Institutes of Health	R01 DK092456	4/7/2012 - 2/28/2017	\$455,040
James Wells, PHD Michael Anthony Helmrath, MD	Establishment of In Vitro and In Vivo Models of Human Gastrointestinal Organoids	National Institutes of Health	U18 EB021780	9/30/2015 - 7/31/2017	\$143,520
James Wells, PHD	Intestinal Organoids as a Model System for Studying Enteric Disease	National Institutes of Health (University of Cincinnati)	U19 AI116491	3/1/2015 - 2/29/2020	\$513,497
Yutaka Yoshida, PHD	Semaphorin Signaling and Regeneration of Corticospinal Circuitry	NJ Commission Spinal Cord Research (Rutgers School Biomedical & Health Scien)	CSCR14IRG001	6/15/2014 - 6/30/2017	\$98,000
Yutaka Yoshida, PHD	Axon Die-back and Regeneration	Craig Neilson Foundation	Neilsen Fndtn - Yosh	7/1/2014 - 3/31/2017	\$150,000
Yutaka Yoshida, PHD	Synapse Elimination in the Central Nervous System	National Institutes of Health	R01 NS093002	7/15/2015 - 6/30/2020	\$370,156
Aaron Zorn, PHD	Systematic Improvement of Xenopus Fene Annotations and Reference Genomes	National Institutes of Health (University of California-Berkeley)	00008617 (R01 HD0807	8/1/2014 - 4/30/2018	\$46,355
Aaron Zorn, PHD	Xenbase: The Xenopus Model Organism Database	National Institutes of Health	P41 HD064556	12/11/2015 - 11/30/2020	\$1,725,385
Aaron Zorn, PHD	Molecular Basis of Digestive System Development in Xenopus	National Institutes of Health	R01 DK070858	4/1/2014 - 3/31/2018	\$339,519
Aaron Zorn, PHD	Structure-Function Investigation of DAN-mediated BMP Antagonism	National Institutes of Health (University of Cincinnati)	R01 GM114640	4/1/2015 - 1/31/2019	\$44,529

Aaron Zorn, PHD	Production, Validation and Distribution of the Xenopus ORFeome	National Institutes of Health (University of Virginia)	R01 HD069352	8/1/2011 - 5/31/2016	\$88,482
Aaron Zorn, PHD	Deciphering the Gene Regulatory Network Controlling Vertebrate Endodermal Fates	National Institutes of Health (The Regents of the Univ of California)	R01 HD073179	7/5/2013 - 4/30/2018	\$121,742
Aaron Zorn, PHD	Osr Transcription Factors Regulate Embryonic Lung Development	National Institutes of Health	R01 HL114898	8/10/2012 - 6/30/2017	\$376,763

**Total Annual Grant Award Dollars**

**\$10,264,941**

### **Annual Industry Award Dollars**

<b>Investigator</b>	<b>Industry Sponsor</b>	<b>Amount</b>
Yutaka Yoshida, PHD	Japan Science and Technology Corporation	\$129,895
<b>Total Annual Industry Award Dollars</b>		<b>\$129,895</b>