

Developmental Biology

Division Details

RESEARCH AND TRAINING DETAILS

Faculty	19
Joint Appointment Faculty	27
Research Fellows and Post Docs	25
Research Graduate Students	61
Total Annual Grant Award Dollars	\$11,286,652
CLINICAL ACTIVITIES AND TRAINING	
Clinical Fellows	3



Row 1: J Park, J Waxman, K Campbell, F Hamada, Y Lan, R Kopan, S Brugmann, 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

☆ Visit Developmental Biology.

Division Highlights

Faculty Recruitment

This year was a highly successful year of faculty recruitment. We received over 180 applications, and invited over a dozen candidates to interview. We have recruited Dr. Ertugrul Ozbudak, PhD, from Albert Einstein College of Medicine; Dr. Makiko Iwafuchi-Doi from UPENN; and Dr. Amanda Zacharias, also from UPENN, as primary division faculty. We have also being instrumental in the recruitment of two joint appointment faculty into other divisions: Dr. William Zacharias from UPENN to the Division of Pulmonary Biology, and Dr. Juan Sanchez-Gurmaches, PhD, from UMASS to the Division of Endocrinology. The addition of these new faculty are a great asset to the Division of Developmental Biology.

Fundamental New Discoveries

Investigators in the division continue to make fundamental new discoveries ranging from: the mechanisms that maintain sensory-motor circuits in the nervous system (Ima, et al. *Cell Reports*. 2016); genetic programs controlling the earliest stages of lung development (Rankin, et al. *Cell Reports*. 2016); to the worlds first generation of human stomach organoids from pluripotent stem cells (McCraken, et al. *Nature*. 2017).

Division Publications

- 1. McCracken KW; Aihara E; Martin B; Rawford CMC; Broda T; Treguier J; Zhang X; Shannon JM; Montrose MH; Wells JM. **Wnt/beta-catenin promotes gastric fundus specification in mice and humans.** *Nature*. 2017; 541:182-187.
- 2. Session AM; Uno Y; Kwon T; Hapman JAC; Toyoda A; Takahashi S; Fukui A; Hikosaka A; Suzuki A; Kondo M. **Genome evolution in** the allotetraploid frog Xenopus laevis. *Nature*. 2016; 538:336-343.
- 3. Workman MJ; Mahe MM; Trisno S; Poling HM; Watson CL; Sundaram N; Chang CF; Schiesser J; Aubert P; Stanley EG. **Engineered human pluripotent-stem-cell-derived intestinal tissues with a functional enteric nervous system.** *Nature Medicine*. 2017; 23:49-59.
- 4. Gu Z; Serradj N; Ueno M; Liang M; Li J; Baccei ML; Martin JH; Yoshida Y. **Skilled Movements Require Non-apoptotic Bax/Bak Pathway-Mediated Corticospinal Circuit Reorganization.** *Neuron*. 2017; 94:626-641.e4.
- 5. He D; Wang J; Lu Y; Deng Y; Zhao C; Xu L; Chen Y; Hu YC; Zhou W; Lu QR. IncRNA Functional Networks in Oligodendrocytes Reveal Stage-Specific Myelination Control by an IncOL1/Suz12 Complex in the CNS. Neuron. 2017; 93:362-378.
- Cunningham TJ; Tabacchi M; Eliane JP; Tuchayi SM; Manivasagam S; Mirzaalian H; Turkoz A; Kopan R; Schaffer A; Saavedra AP.
 Randomized trial of calcipotriol combined with 5-fluorouracil for skin cancer precursor immunotherapy. Journal of Clinical Investigation. 2017; 127:106-116.
- 7. Lages CS; Simmons J; Maddox A; Jones K; Karns R; Sheridan R; Shanmukhappa SK; Mohanty S; Kofron M; Russo P. **The Dendritic**Cell-T Helper 17-Macrophage Axis Controls Cholangiocyte Injury and Disease Progression in Murine and Human Biliary

 Atresia. *Hepatology*. 2017; 65:174-188.
- 8. Burk K; Mire E; Bellon A; Hocine M; Guillot J; Moraes F; Yoshida Y; Simons M; Chauvet S; Mann F. **Post-endocytic sorting of Plexin-D1 controls signal transduction and development of axonal and vascular circuits.** *Nature Communications*. 2017; 8:14508-17.
- 9. Kovall RA; Gebelein B; Sprinzak D; Kopan R. The Canonical Notch Signaling Pathway: Structural and Biochemical Insights into Shape, Sugar, and Force. Developmental Cell. 2017; 41:228- 241.
- 10. Qi Y; Liu H; Lin X. sumoylation Stabilizes Smoothened to Promote Hedgehog Signaling. Developmental Cell. 2016; 39:385-387.
- 11. Nakafuku M; Gotz M; Petrik D. Neurogenesis in the Developing and Adult Brain-Similarities and Key Differences. *Cold Spring Harbor perspectives in biology*. 2016; 8:a018853.
- 12. Xu X; Abdalla T; Bratcher PE; Jackson PL; Sabbatini G; Wells JM; Lou XY; Quinn R; Blalock JE; Clancy JP. **Doxycycline improves** clinical outcomes during cystic fibrosis exacerbations. The European respiratory journal: official journal of the European Society for Clinical Respiratory Physiology. 2017; 49:1601102.
- 13. Carmell MA; Dokshin GA; Skaletsky H; Hu Y-C; van Wolfswinkel JC; Igarashi KJ; Bellott DW; Nefedov M; Reddien PW; Enders GC. A widely employed germ cell marker is an ancient disordered protein with reproductive functions in diverse eukaryotes. *eLife*. 2016; 5.
- 14. Du Y; Kitzmiller JA; Sridharan A; Perl AK; Bridges JP; Misra RS; Pryhuber GS; Mariani TJ; Bhattacharya S; Guo M. Lung Gene Expression Analysis (LGEA): an integrative web portal for comprehensive gene expression data analysis in lung development. Thorax. 2017; 72:481-484.
- 15. Imai F; Chen X; Weirauch MT; Yoshida Y. Requirement for Dicer in Maintenance of Monosynaptic Sensory-Motor Circuits in the Spinal Cord. *Cell Reports*. 2016; 17:2163-2172.

- 16. Liu X; Uemura A; Fukushima Y; Yoshida Y; Hirashima M. Semaphorin 3G Provides a Repulsive Guidance Cue to Lymphatic Endothelial Cells via Neuropilin-2/PlexinD1. Cell Reports. 2016; 17:2299-2311.
- 17. Nolan K; Kattamuri C; Rankin SA; Read RJ; Zorn AM; Thompson TB. **Structure of Gremlin-2 in Complex with GDF5 Gives Insight into DAN-Family-Mediated BMP Antagonism.** *Cell Reports.* 2016; 16:2077 -2086.
- 18. Salomonis N; Dexheimer PJ; Omberg L; Schroll R; Bush S; Huo J; Schriml L; Sui SH; Keddache M; Mayhew C. Integrated Genomic Analysis of Diverse Induced Pluripotent Stem Cells from the Progenitor Cell Biology Consortium. Stem Cell Reports. 2016; 7:110-125.
- 19. Honoré C; Rescan C; Hald J; McGrath PS; Petersen MBK; Hansson M; Klein T; Østergaard S; Wells JM; Madsen OD. Revisiting the immunocytochemical detection of Neurogenin 3 expression in mouse and man. Diabetes, Obesity and Metabolism: a journal of pharmacology and therapeutics. 2016; 18 Suppl 1:10-22.
- 20. Stevens ML; Chaturvedi P; Rankin SA; Macdonald M; Jagannathan S; Yukawa M; Barski A; Zorn AM. Genomic integration of Wnt/beta-catenin and BMP/Smad1 signaling coordinates foregut and hindgut transcriptional programs. Development (Cambridge). 2017; 144:1283-1295.
- 21. Arora N; Imran Alsous J; Guggenheim JW; Mak M; Munera J; Wells JM; Kamm RD; Asada HH; Shvartsman SY; Griffith LG. A process engineering approach to increase organoid yield. Development (Cambridge). 2017; 144:1128-1136.
- Asai A; Aihara E; Watson C; Mourya R; Mizuochi T; Shivakumar P; Phelan K; Mayhew C; Helmrath M; Takebe T. Paracrine signals
 regulate human liver organoid maturation from induced pluripotent stem cells. Development (Cambridge). 2017;
 144:dev.142794.
- 23. McCauley HA; Wells JM. Pluripotent stem cell-derived organoids: using principles of developmental biology to grow human tissues in a dish. Development (Cambridge). 2017; 144:958-962.
- 24. Brinkley JF; Fisher S; Harris MP; Holmes G; Hooper JE; Wang Jabs E; Jones KL; Kesselman C; Klein OD; Maas RL. **The FaceBase Consortium: a comprehensive resource for craniofacial researchers.** *Development (Cambridge)*. 2016; 143:2677-2688.
- 25. Lan Y; Zhang N; Liu H; Xu J; Jiang R. **Golgb1 regulates protein glycosylation and is crucial for mammalian palate development.** *Development (Cambridge)*. 2016; 143:2344-2355.

Grants, Contracts, and Industry Agreements

Annual Grant Award Dollars

Investigator	Title	Sponsor	ID	Dates	Amount
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	07/05/2013 - 04/30/2018	\$100,000
Rashmi Hegde, PhD	Mechanism of Action of Retinal Determination Proteins	National Institutes of Health	R01 EY014648	04/01/2014 - 03/31/2018	\$315,900
Sang-wook Cha, PhD	Wnt/PCP Signaling in the Intestinal Epithelium	National Institutes of Health	K01 DK101618	04/15/2014 - 02/28/2019	\$128,976
S Steven Potter, PhD	Recombineering Based Analysis of Hox Function in	National Institutes of Health	R01 DK099995	08/08/2014	\$339,300

	Kidney Development			04/30/2018	
Aaron Zorn, PhD	Molecular Basis of Digestive System Development in	National Institutes of Health	R01 DK070858	04/01/2014	\$339,525
	Xenopus			03/31/2018	
Kenneth J Campbell, PhD Brian Gebelein, PhD	Roles of Gsx factors in Telencephalic Neurogenesis	National Institutes of Health	R01 NS044080	03/15/2014	\$492,671
Brian Gebelein, Frib				02/28/2019	
Aaron Zorn, PhD	Systematic improvement of Xenopus Gene Annotations and Reference Genomes	National Institutes of Health (University of California-Berkeley)	R01 HD080708	08/01/2014	\$47,531
				04/30/2018	
Yutaka Yoshida, PhD	Semaphorin Signaling and Regeneration of Corticospinal Circuitry	NJ Commission Spinal Cord Research (Rutgers School Biomedical & Health Scien)	CSCR14IRG001	06/15/2014	\$98,000
				06/30/2017	
Quynh Van Ton, PhD	Validation of Aneurysm Associated Genes in a Zebrafish Model	National Institutes of	F32 HL124889	12/01/2014	\$57,066
		Health		11/30/2017	
Jorge Munera, PhD	Human Intestinal Organoids	Crohn's & Colitis	CCF -	07/01/2014	\$58,250
	as a Model of Ulcerative Colitis	Foundation of America	Munera,Jorge	- 06/30/2017	
Raphael Kopan, PhD	Imaging Notch Interactions with Members of Its Pathway	National Institutes of Health (Washington University)	P50 CA094056	01/01/2014	\$150,544
				- 12/31/2016	
James Wells, PhD	Intestinal Organoids as a	National Institutes of	U19 AI116491	03/01/2015	\$379,481
	Model System for Studying Enteric Disease	Health (University of Cincinnati)		- 02/29/2020	
Aaron Zorn, PhD	Structure-Function Investigation of DAN- mediated BMP Antagonism	National Institutes of Health (University of Cincinnati)	R01 GM114640	04/01/2015	\$20,678
				01/31/2019	
Masato Nakafuku, MD,	Molecular Control of	National Institutes of	R01 NS069893	04/01/2015	\$482,627
PhD Kenneth J Campbell, PhD	Neurogenesis in the Adult Subventricular Zone	Health		03/31/2020	
Yutaka Yoshida, PhD	Synapse Elimination in the Central Nervous System	National Institutes of Health	R01 NS093002	07/15/2015	\$345,382
				- 06/30/2020	
Xinhua Lin, PhD	Molecular Mechanisms Regulating Intestinal Stem Cell Activities and	National Institutes of Health	R01 GM115995	08/01/2015	\$277,290
				- 04/30/2019	
	Homeostasis			000,2010	
Aaron Zorn, PhD	Xenbase: The Xenopus Model		P41 HD064556	12/11/2015	\$1,733,118
	Organism Database	Health		- 11/30/2020	

James Wells, PhD Michael Anthony Helmrath, MD	Establishment of In Vitro and In Vivo Models of Human Gastrointestinal Organoids with a Functional ENS	National Institutes of Health	U18 EB021780	09/30/2015 - 07/31/2018	\$167,665
Raphael Kopan, PhD	The Mechanism Regulating Renal Progenitor Aging	National Institutes of Health	R01 DK106225	04/01/2016 - 01/31/2021	\$459,900
Saulius Sumanas, PhD	Role of Collagen XXII in Vascular Stability	Amer Heart Assoc - Ohio Affiliate, Inc	16GRNT27370004	01/01/2016 - 06/14/2017	\$77,000
S Steven Potter, PhD	Atlas of Autonomic and Neuromodulatory Lineages in the Developing Lower Urinary Tract	National Institutes of Health (Vanderbilt University Medical Center)	U01 DK110804	09/17/2016 - 05/31/2021	\$60,438
S Steven Potter, PhD	Exploratory Statistical Analysis of Differential Network Behaviors Based on Gene Expression Atlas of Palate Development	National Institutes of Health (University of Florida)	R03 DE025625	08/15/2016 - 07/31/2018	\$17,871
Jennifer A Schumacher, PhD	The Role of Fibronectin/Integrin and BMP Signaling in Endocardial Morphogenesis and Differentiation	American Heart Association - National	16SDG27330007	01/01/2016 - 12/31/2019	\$77,000
Saulius Sumanas, PhD	Characterization of a Novel Hematopoietic Site	National Institutes of Health	R21 Al128445	12/01/2016 - 11/30/2018	\$234,000
Raphael Kopan, PhD	Assessing the Therapeutic Window for Future Anti-Notch Dimerization Agents	National Institutes of Health	R01 CA163653	07/01/2013 - 04/30/2018	\$311,165
Heather A McCauley, PhD	Enteroendocrine Cells, Nutrition & Metabolic Disease	American Diabetes Association	1-17-PDF-102	01/01/2017 - 12/31/2019	\$53,680
Rulang Jiang, PhD	Molecular Patterning of Mammalian Dentition	National Institutes of Health	R01 DE018401	09/12/2013 - 06/30/2018	\$516,799
Rulang Jiang, PhD	Molecular Regulation of Palate Development	Shriners Hospitals for Children- (Shriners Hospital for Children)	85900	01/01/2017 - 12/31/2021	\$245,000
Aaron Zorn, PhD	Osr Transcription Factors Regulate Embryonic Lung Development	National Institutes of Health	R01 HL114898	08/10/2012 - 06/30/2018	\$382,500
James Wells, PhD	ASCENTAdvanced	California Institute	TRAN1-08471	07/01/2016	\$99,999

	Superdonor Cellular Enteric Neuropathy Therapy	Regenerative Med (Children's Hospital Los Angeles)		- 06/30/2017	
Yutaka Yoshida, PhD	A Novel Combinatorial Approach to Restore Motor Function after Spinal Cord Injury	National Institutes of Health	R01 NS100772	04/01/2017 - 03/31/2022	\$371,693
S Steven Potter, PhD	ENSMAP: Molecular and Functional Mapping of the Enteric Nervous System	National Institutes of Health (Vanderbilt University Medical Center)	OT2OD023850	09/27/2016 - 07/31/2018	\$284,570
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	09/20/2013 - 07/31/2018	\$332,775
Rashmi Hegde, PhD	EYA in Retinal Angiogenesis	National Institutes of Health	R01 EY022917	08/01/2013 - 07/31/2018	\$382,500
Rashmi Hegde, PhD	Linked Regulation of Tumor Angiogenesis and Chemo- resistance	National Institutes of Health	R01 CA207068	04/01/2017 - 03/31/2022	\$356,850
S Steven Potter, PhD	Using Cold Active Proteases for Single Cell Dissociation	National Institutes of Health (University of Southern California)	U01 DK107350	02/01/2017 - 01/31/2018	\$87,000
Rashmi Hegde, PhD	EYA in Ewing's Sarcoma	Andrew McDonough B+ Foundation	B+_Hegde	01/01/2017 - 12/31/2017	\$50,000
Saulius Sumanas, PhD	The Role of Collagen COL22A1 in Intracranial Aneurysms and Vascular Stability	National Institutes of Health	R01 HL134815	06/15/2017 - 04/30/2021	\$452,935
Rashmi Hegde, PhD	EYA Inhibitors in the Treatment of Peripheral Vascular Disease and Pulmonary Arterial Hypertension	National Institutes of Health (The Cleveland Clinic Lerner Coll of Med)	U54 HL119810	01/01/2017 - 07/31/2017	\$58,500
Michael Anthony Helmrath, MD James Wells, PhD	Investigation of Regional Identity in Human Intestinal Stem Cells	National Institutes of Health	U01 DK103117	09/01/2014 - 08/31/2019	\$210,130
Jeffrey A Whitsett, MD S Steven Potter, PhD	Lung MAP Atlas Research Center	National Institutes of Health	U01 HL122642	06/15/2014 - 04/30/2019	\$390,732.50
Jeffrey A Whitsett, MD Xinhua Lin, PhD	Role of EMC3/TMEM111 in Alveolar Epithelial Cell Function	National Institutes of Health	R01 HL136722		\$239,610.50