

Cell and Developmental Biology

Photo: Neurons (red)
differentiated from iPSC.

“Research demonstrating that stem cells can be derived from a small sample of skin about the size of a blueberry (1/4”) offers a novel approach to study how these conditions develop in a petri dish”

Stem Cells from Skin to Study Genetic Diseases

Many complex brain disorders appear to originate during prenatal development, but are not diagnosed until decades later. Because brain cells are not available for study and there are no good animal models of these degenerative and psychiatric disorders, little is known about how they form, the underlying causes, or disease progression. Now, research demonstrating that stem cells can be derived from a small sample of skin about the size of a blueberry (1/4”) offers a novel approach to study how these conditions develop in a petri dish.

Mature skin cells can be “reprogrammed” to stem cells that have the ability to form all of the types of cells in the human body, like embryonic stem cells. Stem cells derived from individuals diagnosed with a variety of conditions will allow CDB scientists to study the origin and progression of these diseases and to search for new treatments.

One such disease, which has puzzled scientists since the Age of Pericles in Classical Athens, is bipolar disorder. As its name suggests, individuals diagnosed with bipolar disorder cycle between periods of hyper-excitability and depression. Although the disorder affects over 6 million Americans, surprisingly little is known about how it develops, and there is a critical, unmet need for new therapies.

Scientists in Consortium for Stem Cell Therapies laboratory are developing stem cells from individuals who have been diagnosed with BP by Dr. Malcom McClinnis and his colleagues in the UM Depression Center. The value of this sample is that it is part of a long-term clinical study supported by the Prechter Fund, and there are many additional genetic, electrophysiological and family data available for comparison studies.

After receiving institutional clearance for the work, connective tissue cells (fibroblasts) from the skin of four individuals with BP and two control patients were expanded in tissue culture, then four genes were delivered to the cells to cause them to have stem cell characteristics. After careful studies were done to confirm that the induced stem cells no longer express skin genes, but now have genes present in embryonic stem cells, they are beginning the exciting phase of differentiating the new stem cells to neurons.

The ability to study how neurons from BP individuals are different from normal neurons will help scientists understand the progression of this devastating disorder, and develop more effective treatments to treat millions of patients who suffer from BP worldwide. This research also



Message From The Chair

“In 1978, approximately 1 in 3 submitted NIH grants was funded; now the number averages approximately 1 in 10.”

While this has been another banner year for the Department, it would be foolish to ignore the increasingly frequent challenges and hurdles that loom on the horizon nationally. CDB faculty and students have remained in the news locally, nationally and internationally for their many accomplishments in the laboratory. The Department’s research stature rose to its highest point in the last decade. Our national rankings reflect not only the outstanding scientific accomplishments and recognition of our faculty and students at every level as the Department matures, but also reflects our ability to support our research mission in an increasingly challenging federal funding environment.

“CDB has been both lucky and smart by hiring young faculty who can still effectively compete”

We all know the reasons for the current challenges to our research mission. The country is deeply in debt, and there are literally millions of people suffering unemployment; it seems, to some, difficult to explain to congress why we should continue to invest in basic research in the face of these individual tragedies. Against this backdrop, no one points out that the United States spends (per capita) less than any other developed nation on federally funded research. Another complication with federal research funding is that it is “discretionary”, and since we no longer have champions like John Porter, Lowell Weiker or Edward Kennedy to explain to their peers why research is important both economically as well as for our future health, our message is lost among the cacophony of competing (and simpler to understand) interests. We need to continue to educate our congressional representatives and their aides about the nature of how discoveries are made, and that it is not by riding an annual rollercoaster where the NIH (the National Institutes of Health) budget might vary by as much as 15% depending on the favorable or ill wind of politics.

Despite multiple challenges, the Cell and Developmental Biology Department has risen to a ranking of 16th in the nation over the last decade, meaning that we are continuing to compete effectively for the scarce research resources that are available. For those of you, like me, who remember the good old days, when I first entered the competition

for federal research dollars in 1978, approximately 1 in 3 submitted NIH grants was funded; now the number averages approximately 1 in 10. All of us who have served on scientific review panels know that probably 20 to 25% of all submitted research grant applications are highly meritorious and deserve to be funded, meaning that today, about half of the most promising research in the world,

offering many of tomorrow’s most important medical advances, goes unfunded. Clearly, it becomes more and more difficult for our outstanding young faculty to offer the highest quality of teaching, which we demand, while at the same time competing for increasingly scarce research resources, which we also demand. To date, CDB has been both lucky and smart by hiring young faculty who can still effectively compete for those diminishing resources, but that good fortune cannot last indefinitely. For those of you reading this annual update, please, whenever you have the opportunity, tell your congressional delegation how important NIH funding is to the financial and physical well being of the country: our work is more than “discretionary”, it is vital.

James Douglas Engel, Ph.D.
G. Carl Huber Professor and Chair



Faculty Recognized

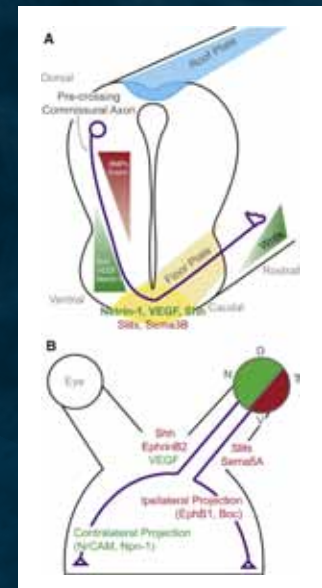
YUKIKO YAMASHITA MACARTHUR AWARD

Dr. Yamashita was one of 22 overall new MacArthur Fellows announced on Sept. 22 by the John D. and Catherine T. MacArthur Foundation. She will receive \$500,000 in “no strings attached” support over the next five years. Fellows are selected based on three criteria: exceptional creativity, promise for important future advances based on a track record of significant accomplishment, and potential for the fellowship to facilitate subsequent creative work. “Yukiko Yamashita continues the university’s national leadership in scientific research,” said President Mary Sue Coleman. “Her recognition by the MacArthur Foundation is powerful validation of the critical importance of exploring and understanding stem cells. It is a pleasure to congratulate her on receiving such a significant honor.” Yamashita’s lab investigates how adult stem cells decide upon their fate to maintain tissue stability. The lab also studies how stem cells orient their division plane in the context of the signaling microenvironment to divide asymmetrically, how this process is monitored, and how it changes during aging. “Dr. Yamashita’s work is of fundamental importance as we seek to deepen our understanding of stem cell division,” said Provost Phil Hanlon. “Her scholarly work exemplifies the excellence of our faculty.”

ROMAN GIGER DANA FOUNDATION AWARD

It has been known for a long time that the immune system can positively influence the regenerative capacity of injured central nervous system tissue. The molecular and cellular mechanisms by which specific aspects of the immune system promote regenerative growth hold great promise for therapeutic interventions following spinal cord injury, stroke or multiple sclerosis. In an ongoing collaboration with the laboratory of Benjamin Segal, we have uncovered a novel mechanism by which the immune system stimulates neuronal growth and regeneration. In adult mammals (including humans) injured axons in the optic nerve fail to undergo spontaneous regeneration, leading to permanent functional deficits. In mice subjected to retro-orbital optic nerve crush injury, activation of specific aspects of the innate immune system leads to very robust and long-distance axonal growth in vivo. Funds provided by the Dana Foundation will be used for an in-depth analysis of immune- and nervous system cross-talk to develop specific interventions that promote neurorepair.

Axon Guidance Mechanisms at the CNS Midline, Roman Giger



STEM CELLS FROM SKIN (CONTINUED FROM COVER)

sets the stage for similar studies of other disorders that lack cell or animal models.

Scientists agree that it is unlikely that these induced pluripotent stem cells will replace human embryonic stem cells, and that work on both types of cells, as well as with adult stem cells is required.

The stem cell core laboratory was established in the Department of Cell and Developmental Biology in 2004 with monies from the Medical School Endowment for the Basic Sciences, was supported as an Exploratory Center for Stem Cell Research by a grant from the NIH 2004-2009, and now is part of the A. Alfred Taubman Medical Research Institute and the University of Michigan. Dr. Sue O’Shea and Gary Smith are co-directors.

LAB MEMBERS



Nicholas Stefanski
Research Technician



Ajit Ramadugu
Undergraduate



Artun Kircali
Undergraduate



Kentaro Nabeshima

ASSISTANT PROFESSOR

B.S., Ph.D. Kyoto University
M.S. Shanghai Institute of Physiology

RESEARCH FOCUS

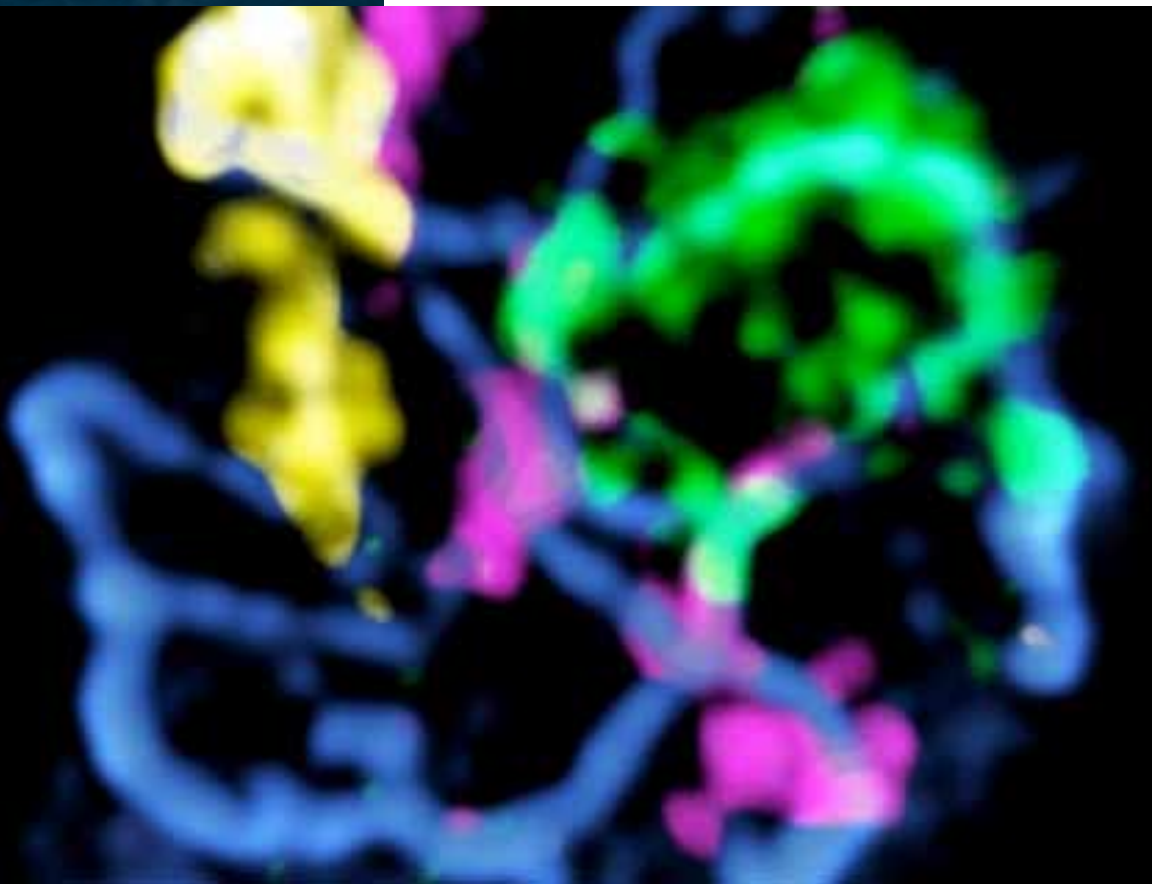
Meiotic failures cause reproductive problems in humans such as miscarriages, birth defects and mental retardations. In order to improve human reproductive health, it is critical to understand basic mechanisms for meiosis.

Pairing of homologous chromosomes is essential prerequisite for successful meiosis. We study the mechanism of this pairing process using the nematode, *C. elegans* as a model. This model organism provides a wealth of research tools such as classic genetics, cytology, biochemistry and modern functional genomics. In addition to these

tools, we have also developed novel methods such as chromosome paint to tackle a century-old problem: how do chromosomes establish homologous pairing?

In my laboratory, we have demonstrated that chromosomes reorganize their morphology as well as their spatial organization during homologous pairing process (Nabeshima et al., *PLoS Genetics*, 2011).

Recently, we have discovered a novel factor, MRG-1, that facilitates homologous pairing. Through the analysis of its function, we demonstrated the importance of pre-synaptic alignment in order to restrict assembly of the synaptonemal complex only between homologous chromosomes (Dombecki et al., *Developmental Cell*, in press).



This image shows a germ cell nucleus with chromosome paint and immunostaining of a component of the synaptonemal complex (SC) in *C. elegans* *mrg-1* mutant. In this squashed nucleus, subset of paint signals located at central part of the nucleus exhibit non-homologous synapsis: chromosome III and V (green and pink) are overlapped and associate along with the same SC stretch (light blue). This image is from Dombecki et al, *Developmental Cell*, in press.

Scott Barolo

ASSOCIATE PROFESSOR



Ph.D. University of California-San Diego
B.S. Pennsylvania State University

RESEARCH FOCUS

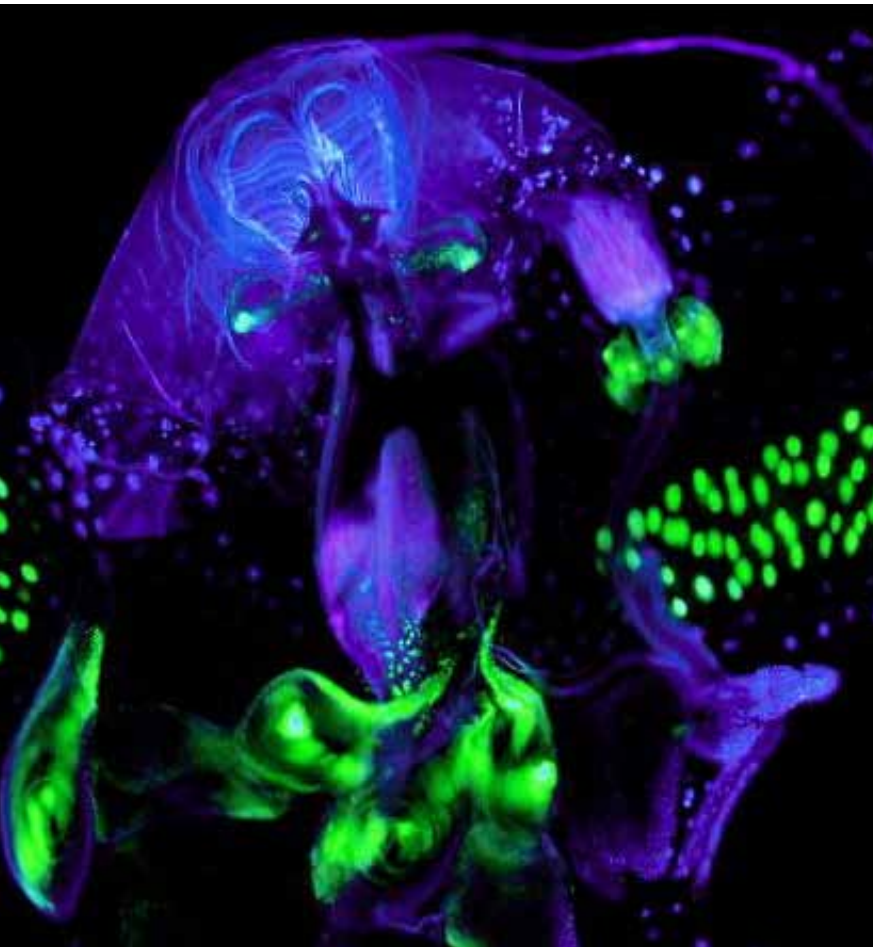
Gene regulation and signal transduction in development; Structure and function of transcriptional enhancers; Enhancer evolution.

Our lab studies enhancers, cis-regulatory DNA elements in the genome that control gene expression. Enhancers contain binding sites for transcription factors--proteins that bind DNA and turn genes on or off. A few highly conserved cell signaling pathways, including Hedgehog, Wnt, Notch, TGF-beta/BMP, and RTK/Ras/MAPK, control the development of most tissues and organs during animal development. The primary effects of cell signaling are

changes in gene expression, mediated by signal-regulated transcription factors. These factors bind to enhancers in target genes, turning them on or off in response to pathway signaling. Faulty signaling can result in diseases such as cancer, diabetes, autoimmune disorders, and neurodegenerative diseases, as well as developmental defects.

Signal-regulated enhancers have been intensively studied for years, but basic questions about these regulatory sequences remain unanswered. The gaps in our knowledge are best illustrated by the fact that "synthetic" versions of well-characterized enhancers (i.e., combinations of the known transcription factor binding sites) nearly always fail to drive gene expression in vivo. Therefore, it seems that we don't

yet know all of the component parts of the enhancer, or its basic structure. Using the *Drosophila* model system, we are employing genetic, biochemical, evolutionary, transgenic, and computational approaches to learn how enhancers control gene expression in developing tissues, and how these genomic elements evolve over time.



Shown here is part of a transgenic *Drosophila* larva in which cells that respond to the Hedgehog signaling pathway express GFP, a fluorescent protein cloned from a jellyfish, which causes those cells to glow green. Photo by Andrea Ramos (right).

LAB MEMBERS



Lisa Johnson
Research Lab Specialist



Nicole Evans
Graduate Student



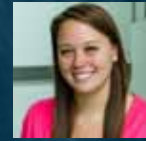
David Lorberbaum
Graduate Student



Andrea Ramos
Graduate Student



Amy Bennett
Undergraduate



Alex Chappell
Undergraduate



Jessica Frick
Undergraduate



Amy Strom
Undergraduate

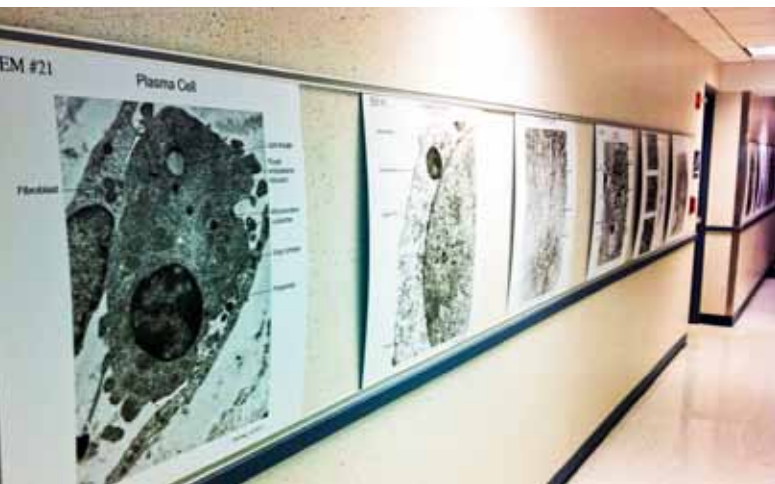


Diploma in Biochemistry, Free University Berlin
Ph.D. University of Heidelberg
Postdoctoral work at Stanford University and University of California at Berkeley

RESEARCH FOCUS

In 1991 I joined the department, at that time still called "Anatomy and Cell Biology", to establish my research laboratory. Using a *Drosophila* model system, my research was supported for the last 20 years by NIH, NSF and private foundations to investigate the role of the L1 family of neural cell adhesion molecules during nervous system development. When the opportunity recently availed itself to take over the directorship of the CDB histology courses, I decided to forego bench research and to concentrate on the educational mission of our department. This new direction not only includes running the three CDB histology courses, but also the opportunity to develop novel educational tools and to perform educational research.

During the 2006/07 academic year our department changed from the traditional format of teaching histology using real microscopes and glass slide sets to an online virtual microscopy set-up. All CDB-sponsored histology courses are now taught using a combination of regular lectures and laboratory sessions and modern electronic teaching tools, such as course websites providing links to the virtual slides and other digital resources. As the Michigan virtual slides are freely accessible worldwide, they are being used by a large number of non-Michigan students, who study histology at other universities. The University of Michigan Medical Histology websites receives about 16,000 hits per month, the majority from outside the State of Michigan. In the future, the Michigan slide collection



Michael Hortsch

ASSOCIATE PROFESSOR

will also be hosted as a special collection by the Cell Centered DataBase, which is housed in the National Center for Microscopy and Imaging Research (NCMIR) and is co-sponsored by the American Society for Cell Biology.

Currently, the CDB Department offers three histology courses, one each for medical and dental students and a third course for senior undergraduate and graduate students. One participating student wrote: "The course was the best I've taken in 4 years at Michigan".

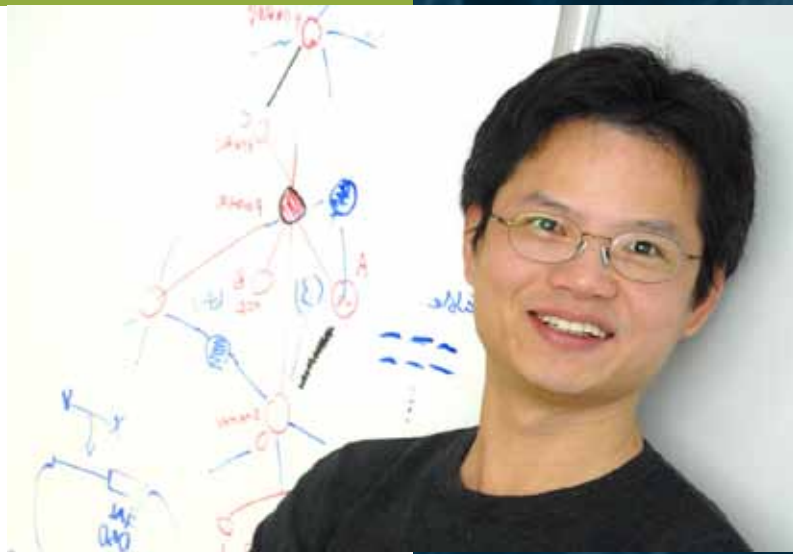
An important aspect of my current work is the development of novel educational tools that we will offer to Michigan students and to students at other institutions. I recently developed a series of PowerPoint files, which helps students studying histology to self-evaluate their knowledge before taking quizzes and exams. As this tool has proven to be extremely popular with students participating in CDB histology courses (95% of medical students named this "Second Look" series as one of the top three resources to learn histology), I am currently working with the support from the Medical School Dean's office to convert the original PowerPoint files into iPhone and Droid-based computer applications. In addition, I obtained grant support from the Center for Research on Learning and Teaching (CRLT) to study, how traditional and new electronic platforms, which are being used to teach histology at the University of Michigan, affect students' learning success.

Following the tradition and the high standard of numerous excellent teachers from our Department, among others, Drs. Matt Velkey and Sun-Kee Kim, I am excited to maintain the superb quality of CDB teaching and to develop innovative approaches for the courses offered under the CDB label. It is rewarding when our students recognize and appreciate these efforts. I am especially grateful to be recently voted by the medical students as one of the three most favorite M1 professors and together with my colleague Dr. Kim to be featured as a legendary professor in the 2011 edition of the student-edited "Code Blue – A Guide to the M1/M2 Years" book for new incoming medical students.

New electron microscope posters in the Furstenberg area. Now these images are also available on the CDB histology course websites, histology.med.umich.edu, in a digital format.

Jiandie Lin

ASSOCIATE PROFESSOR



B.S. Beijing University
Ph.D. Northwestern University
Fellow Harvard Medical School and Dana-Farber Cancer Institute

RESEARCH FOCUS

The laboratory research spans the fields of single molecule biophysics, protein biochemistry and cell biology and integrates a variety of experimental and computational approaches.

Metabolic syndrome has become a global epidemic that results in increased risk for type 2 diabetes, cardiovascular disease, and non-alcoholic fatty liver disease. Our lab is investigating the fundamental biology of metabolic control and homeostasis, and exploring their role in the pathogenesis of metabolic diseases. We focus our studies on dissecting the transcriptional networks that govern nutrient/energy metabolism and the mechanisms that integrate tissue metabolic activities with systemic physiological signals.

Transcriptional coactivators regulate chromatin states and are critical for the initiation and propagation of epigenetic signals. The PGC-1 family of coactivators (PGC-1 α and PGC-1 β) serves as "hubs" that integrate nutrient and hormonal signals and regulates mitochondrial biogenesis, glucose and lipid metabolism. To define the molecular components of this regulatory network,

we developed a genome-wide coactivation assay and interrogated over 1,700 human transcription factors and cofactors. These studies identified BAF60 family members as novel regulators of hepatic lipid metabolism and skeletal muscle fiber determination. Using proteomic tools, we investigated a hepatic PGC-1 β transcriptional complex that controls plasma lipid homeostasis and mediates the therapeutic action of a widely used lipid-lowering drug.

Organisms evolve diverse strategies to adapt their nutrient and energy metabolism to the light/dark cycles on the earth. How this temporal organization of metabolic functions is coordinated remains poorly understood. We previously identified PGC-1 α as a key factor that integrates the biological clock with energy metabolism. More recently, we discovered that autophagy, a process of controlled degradation of cytosolic materials, is highly rhythmic in vivo. Our current studies focus on understanding the mechanisms that mediate the crosstalk between the body clock and various metabolic processes. We are also interested in exploring how altered synchronization of metabolic rhythms leads to metabolic diseases.

LAB MEMBERS



Zhuoxian Meng
Research Fellow



Fang Fang
Research Fellow



Siming Li
Asst. Res. Scientist



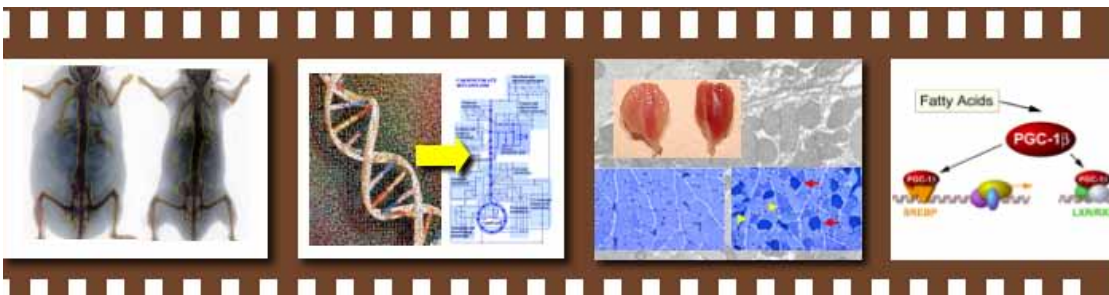
Di Ma
Research Fellow



Matthew Molusky
Graduate Student



Guoxiao Wang
Graduate Student



Cell and Developmental Biology Faculty



Ben Allen

Assistant Professor

The Allen Lab studies the mechanisms of growth factor and morphogen signaling during vertebrate embryogenesis using a wide range of approaches, including mouse developmental genetics, chick in ovo electroporation, biochemistry, and cell biology. The long-term goal of our research is to develop novel therapies for a broad spectrum of developmental diseases and childhood and adult cancers. We recently published back-to-back articles in *Developmental Cell* characterizing several essential co-receptors of the Hedgehog signaling pathway. We have received funding from The University of Michigan Comprehensive Cancer Center, Center for Organogenesis, and the American Heart Association to pursue this work.



Kate Barald

Professor

We discovered several years ago in studies, which the NSF labeled “transformative” (an accolade reserved for about 2% of all submissions) that the earliest neurotrophin in the vertebrate inner ear is an immune system inflammatory cytokine--macrophage migration inhibitory factor (MIF). This brings nervous system and immune system function even closer together--since they appear to share critical signalling molecules. Because neurons in the inner ear also carry receptors for MIF into adulthood, therapeutic approaches through very low concentrations of MIF (well below those that prompt an inflammatory response) might be able to prevent age-related deafness caused by nerve loss. MIF hydrogel coats could also be used to potentiate a cochlear implant, presently the only known “cure” for deafness.



Scott Barolo

Associate Professor

The Barolo lab studies the regulation of gene expression by genomic control sequences called enhancers. We are interested in how enhancers are structured, how they respond to extracellular signals, how they can act over great distances, and how their regulatory logic evolves over time. The summer of 2011 has been an important one for the lab: our work was featured on the covers of both *Science Signaling* (in June) and *Current Biology* (in July).



Maria Castro

Professor

Our laboratory explores the molecular and cellular interactions between cancer cells and hematopoietic stem cells, in particular we are interested in the development of the myeloid lineage. Work from our lab has uncovered that tumor secreted ligands can affect the development and maturation of antigen presenting cells, inhibiting anti-tumor immunity; resulting in tumor progression. Our work will uncover novel targets for the treatment of cancer; we have secured federally funded NIH RO1 grants to pursue this work.



Marina Di Magliano

Assistant Professor P: General Surgery

We study pancreatic cancer, one of the deadliest human malignancies. We seek to identify genes and activities the cancer needs for its maintenance, in order to identify potential therapeutic targets. Our research was initially funded by the Pancreatic Cancer Action Network, the American Association for Cancer Research, together with funding from the University of Michigan Biomedical Scholar Program and the University of Michigan Peptide Center. Thanks to that initial sponsorship, we were able to generate data that allowed us to be awarded an NIH/RO1 grant.



Andrzej Dlugosz

Professor P: Dermatology

We explore the pathogenesis of diseases that disrupt motor function, with a focus on Parkinson disease and dystonia. We have recently published work showing that Parkinson disease-causing mutations in the protein LRRK2 cause it to bind abnormally to microtubules, implicating the cytoskeleton in the step that cause Parkinson-related neurodegeneration. We also used a novel brain imaging technique (diffusion tensor imaging) to identify a neural pathway involved in the abnormal motor function in dystonia.



James Douglas Engel

Professor and Chair

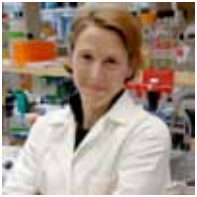
We recently discovered that a currently marketed antidepressant may be useful for treating sickle cell anemia. We also recently found that both transcription factors GATA2 and GATA3, originally discovered in the Engel laboratory, are each required for hematopoietic stem cell homeostasis.



Xing Fan

Assistant Professor P: Neurosurgery

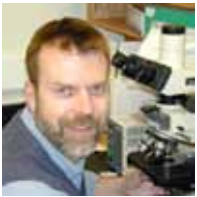
Our preliminary studies show that endothelial cells function as cancer stem cell niche to promote cancer stem cell self-renewal through Notch signaling in glioblastoma, the most common malignant brain tumor in human. Some of these data are published recently in the journal *Cancer Research*, 2011 Sep 6. [Epubahead of print] PubMed PMID: 21788346. The ongoing project (2011–2016) is supported by NIH R01 grant (R01CA148621). This study will help develop novel therapeutic strategies for this deadly disease.



Diane Fingar

Assistant Professor

Our goal is to elucidate the regulation and function of TOR (the target of rapamycin), an evolutionarily conserved protein kinase that coordinates a complex signal transduction network. Due to its control of fundamental cellular functions, mTOR dysregulation contributes to myriad disease states including diabetes, obesity, cancer, benign tumor syndromes, cardiovascular pathologies, and ageing. We recently published a paper in *Molecular and Cellular Biology (MCB)* that identified novel phosphorylation events on mTOR that promote cellular signaling, cell growth/size, and cell cycle progression.



Philip Gage

Associate Professor P: Ophthalmology & Visual Science

We use the mammalian eye to explore how cell signaling networks and transcriptional networks control development. We recently discovered evidence that the homeodomain transcription factor PITX2 controls successive steps in eye development through control of specific cell signaling pathways. We are continuing to pursue these interactions.



Roman Giger

Associate Professor

We are focusing on mechanisms that regulate: (i) developmental nervous system wiring, (ii) axonal regeneration following CNS injury, and (iii) CNS myelination in health and disease. We have demonstrated: (i) that select types of axon guidance molecules (Sema5A and Sema5B) are necessary for proper retinal stratification and visual information processing, (ii) members of the Nogo receptor family function as high-affinity receptors for inhibitory CSPGs that block axonal regeneration in the injured mouse optic nerve, and (iii) the lipid phosphatase Fig4/SAC3 is of critical importance for proper CNS myelination.



Jun-Lin Guan

Professor P: Molecular Medicine & Genetics

We study mechanisms of cell signaling in cancer and other diseases. Recent papers have reported the role of focal adhesion kinase and its associated signaling in breast cancer through regulation of mammary cancer stem cells as well as the function of a new autophagy gene in breast cancer, hematopoietic and neural stem cells and neurodegeneration



Deborah Gumucio

Professor

Ann Grosse's upcoming paper in *Development* will be featured in the ³In this Issue² column. This paper overturns several long-held ideas about intestinal remodeling during villus formation. The results have important implications for short bowel syndrome and bioengineering of intestinal villi. Ajay Prakash won an NIH F32 NRSA award for his studies on the role of Gata3 in pyloric patterning (with a perfect score!). Former student, Will Zacharias' paper on hedgehog control of intestinal smooth muscle (*Dev. Biol.* 355:152, 2011) was cited by Faculty of 1000.



Peter Hitchcock

Professor P: Ophthalmology & Visual Science

We investigate the molecular mechanisms that govern early retinal development and stem cell-based photoreceptor regeneration. This work utilizes zebrafish as a model and employs a variety of genetic and experimental approaches.



Michael Hortsch

Associate Professor

Director of histology courses, but also the opportunity to develop novel educational tools and to perform educational research. Research investigating the role of the L1 family of neural cell adhesion molecules during nervous system development.



Patrick Hu

Assistant Professor P: Internal Med Hematology/Oncology

We study the molecular basis of the control of development, metabolism, and longevity by insulin-like growth factor signaling in the nematode *Caenorhabditis elegans*. We have discovered a new conserved pathway that controls development and life span by regulating FoxO transcription factors. Our recent paper in *Cell Metabolism* on the novel conserved protein EAK-7 led to successful applications for grants from the American Cancer Society and the American Heart Association.



Ajit Joglekar

Assistant Professor

Our goal is to use “architecture-function” analysis to determine the emergent molecular mechanisms of kinetochore force generation and checkpoint signaling. As the first step in this process, we have established in vivo FRET and fluorescence polarization measurement assays in the lab to determine the nanoscale protein architecture of the kinetochore. Kaushik Gurunathan, a new post-doc in the lab, is now establishing spectroscopic methods to measure protein biochemistry in vivo and in vitro.



Cheng-Yu Lee

Assistant Professor P: Molecular Medicine & Genetics

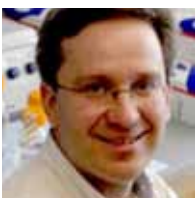
We study how stem cells and their progenitor cell progeny are functionally distinguished in the developing central nervous system. Failure to properly restrict the potential in progenitor cells perturbs development of the brain and leading to generation of tumor-initiating stem-like cells. We have identified several highly conserved tumor suppressor proteins that regulate the progenitor cell potential in the fly brain. Our study will likely provide novel insight into proper regulation of stem cells and progenitor cells in the context of normal development and suppression of tumor initiation.



Jiandie Lin

Associate Professor

We study the mechanisms that regulate nutrient and energy metabolism and explore their role in metabolic disease. We recently published a paper in the EMBO Journal describing how autophagy, a cellular process critical for homeostasis, is rhythmically activated and synchronized with the body clock.



Ivan Maillard

Assistant Professor P: Internal Med: Hematology/Oncology

We study the role of Notch signaling in the regulation of hematopoiesis and T cell immunity, as well as the epigenetic regulation of hematopoietic stem cells by Trithorax group genes. We recently published a paper in Blood describing a new essential role for Notch signaling in graft-versus-host disease.



Kentaro Nabeshima

Assistant Professor

We investigate the mechanisms for meiotic homologous chromosome pairing and synapsis. We recently published a paper in PLoS Genetics describing how chromosomes

are organized in the nucleus during this process. We also discovered a factor required for this process. A paper describing this work is under review of Developmental Cell.”



Sue O'Shea

Professor

Yao-Chang Tsan is examining the role of a novel microRNA in the lineage differentiation of neural stem cells to astrocytes and neurons. The microRNA is restricted in expression to the developing CNS, and when overexpressed, it inhibits neuronal differentiation by binding and inhibits expression of pan-neuronal genes including Elavl4. We are also collaborating with Dr. Melvin McInnis in the Department of Psychiatry to derive induced pluripotent stem cells (iPSC) from skin biopsies from patients diagnosed with Bipolar disorder. We have developed four iPSC lines from BP patients and two from control individuals, and are differentiating them into neurons, as a model to understand bipolar disease progression. The work is potentially important since there are no good susceptibility genes, no cell or animal models to study a disease that affects millions of Americans.



Sivaraj Sivaramakrishnan

Assistant Professor

We are interested in understanding the spatial and temporal dynamics of cell signaling in live cells. We have recently developed a biosensor to directly detect the coupling between a G protein coupled-receptor (GPCR) and G protein. We received the McKay award from the Cardiovascular center to apply these GPCR biosensors to understanding cell signaling in cardiac hypertrophy.



Billy Tsai

Associate Professor

We explore the molecular basis of viral and microbial pathogenesis. We recently published a paper in PLoS Pathogen describing how a large and intact virus (SV40) penetrates the endoplasmic reticulum membrane. Data from this paper helped to secure a federally funded NIH RO1 grant.



Kristen Verhey

Associate Professor

We study the microtubule cytoskeleton and associated motor proteins from the biophysical to the cell biological level. Our recent work has focused on primary cilia which are microtubule-based signaling “antennae” that protrude from the surface of nearly every cell in the body. We discovered that the import of motors and their cargoes into primary cilia utilizes molecules and

mechanisms similar to that of nuclear import (Nature Cell Biology 2010), indicating that there are structural, molecular and evolutionary parallels between cilia and nuclei.



Lois Weisman

Professor

We seek to understand how cellular events occur at the proper place and the correct time. One way that we address this question is through studies of myosin V, a molecular motor that moves many types of cargoes to different places at different times. We recently discovered that myosin V attaches to vesicles in a unique manner. Myosin V first attaches to the molecular machinery that forms the vesicles, and then recruits the molecular machinery that will ultimately be used to fuse the vesicles with the target membrane. Thus, the motor is attached throughout the life of the vesicle.



Deneen Wellik

Associate Professor P: Molecular Medicine & Genetics

We explore the function of Hox genes in developmental and regenerative processes. We have published papers this year on the role of Hox genes in limb development (Xu and Wellik, PNAS), kidney development (Yallowitz, et al., PLOS One), and prostate development (Xu, et al., Prostate). Additional ongoing projects are exploring roles for these genes in gut and pancreatic development and fracture healing processes.



Michael Welsh

Professor

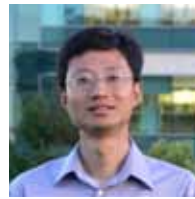
We collaborate with the lab of Mohammed Islam in the School of Engineering and with cardiovascular surgeons in the U of M Cardiovascular Center to develop medical applications for near and mid-infrared lasers. High blood pressure not adequately responsive to drug treatment affects 42 million Americans. Renal nerve block is a viable therapy for hypertension not responsive to drugs. Current research involves development of a minimally invasive, laser based approach to block renal nerves for long lasting treatment of high blood pressure. This collaboration is also investigating the use of infrared laser treatment as a therapy for atrial fibrillation, the most common form of heart arrhythmia. Other applications of the lasers could be in cardiovascular diagnostics or therapies in dermatology and ophthalmology



Yukiko Yamashita

Assistant Professor

The Yamashita laboratory investigates how stem cells contribute to the maintenance of tissues/organs during development, adult tissue homeostasis and aging. In particular, we are interested in how stem cells divide asymmetrically to produce a stem cell and a differentiating daughter, a fundamental process toward maintaining tissue homeostasis. We also initiated the very first study to understand how multiple stem cell populations coordinate their divisions to balance the cell numbers of distinct lineages.



Bing Ye

Assistant Professor

My laboratory investigates the mechanisms underlying the development and disorders of the nervous system. We focus on how neurons develop dendrites and axons and form specific connections with each other. We are particularly interested in human disease genes involved in these processes. We recently published a paper in the Journal of Neuroscience reporting that a novel gene, which separates dendrite and axon development, suppresses the expression of a gene mutated at high frequency in autosomal dominant hereditary spastic paraplegia. Our research is funded by NIH, Pew charitable trusts, and the Whitehall foundation.



Yuan Zhu

Associate Professor P: Molecular Medicine & Genetics

Our laboratory investigates cellular, genetic and molecular mechanisms underlying cancer development in the brain and peripheral nervous system. Our goal is to identify novel molecularly targeted therapies for these incurable human cancers as well as a neurological disease, neurofibromatosis type 1 (NF1).

Thesis Defenses



Jennifer Keller (Barald Lab): *Regulation and Function of the Mitotic Checkpoint Protein CHFR*

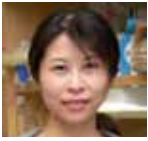


Mo Weng (Cheng-Yu Lee): *Keeping Neural Progenitors on a Short Leash: Distinguishing Progenitor Cells from Neural Stem Cells in Developing Drosophila Central Brain and Optic Lobe.*

Awards



Lihong Shi (Engel lab) received an American Heart Association postdoctoral fellowship.



Sakie Hosoya-Ohmura (Engel lab), research fellow, received a fellowship from the Cancer Research Institute.



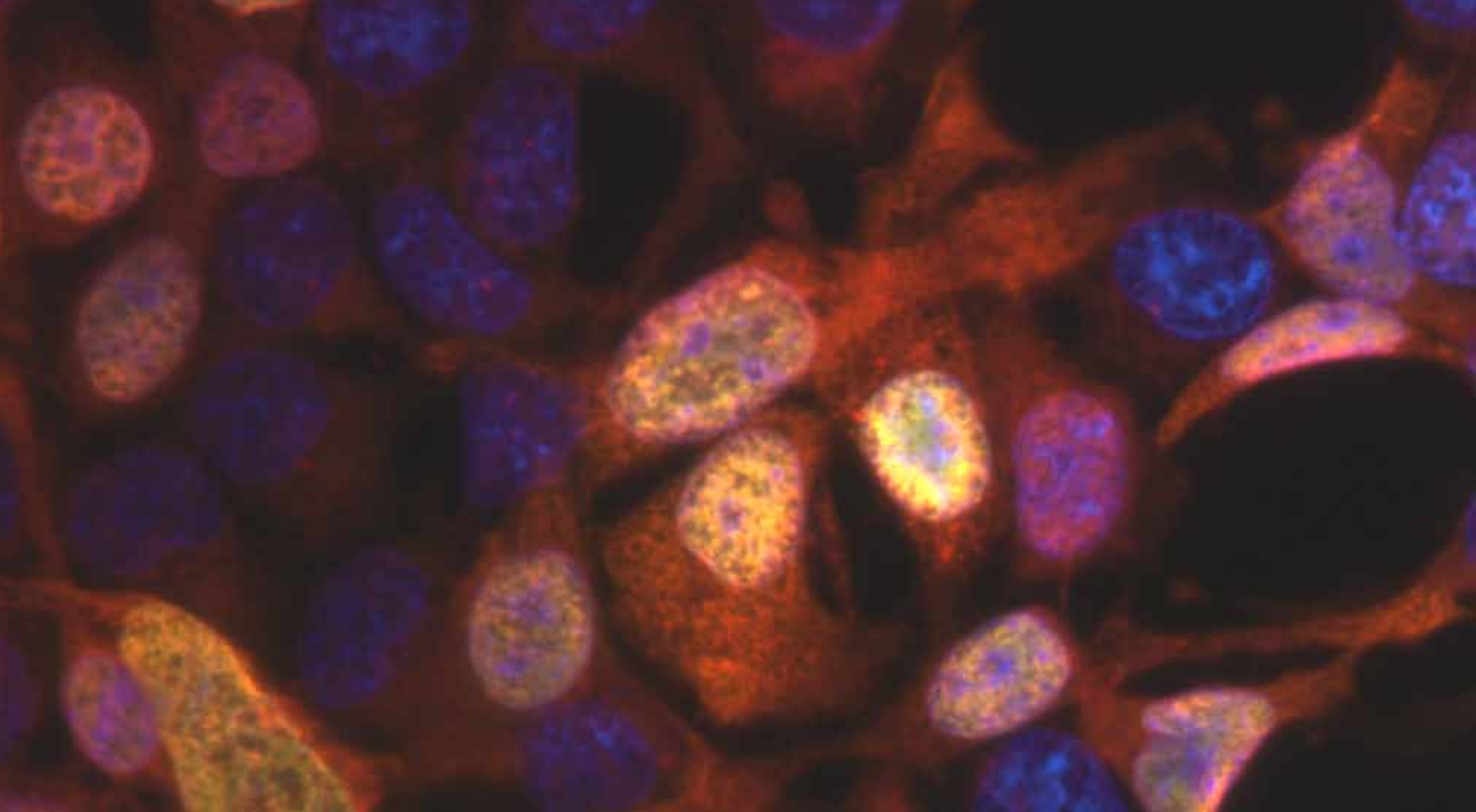
CDB WELCOMES NEW ADMINISTRATOR PAUL BRISTOL



Paul joins us from our sister Department of Chemistry in the College of Letters, Sciences and the Arts, where he was the Business and HR Manager. Previously he served in the LSA Deans' office.







Cultured cells transfected with a nuclear receptor, TR4 - Osamu Tanabe

“Due to the high quality of research performed by these individual investigators, they have added both strength and depth to the already cutting-edge research”

Research Professors and Investigators

Over the past several years, our department has seen an increase in the number of research professors and investigators (see list and a brief description of their research on the opposing page). As non-tenure track faculty, the main responsibility of this group of investigators is in performing research. Nonetheless, they are encouraged to be actively engaged in instructional activities when appropriate. In large part due to the high quality of research performed by these individual investigators, they have added both strength and depth to the already cutting-edge research conducted by tenured-track instructional faculty in the Cell and Developmental Biology department.

To qualify for these positions, the investigators typically have undergone rigorous training and demonstrated excellence during both their graduate and post-doctoral training. The measure for their excellence is generally assessed based on a combination of high-profile published papers and prestigious

fellowships. These positions are often used as a step immediately before entering a tenured-track faculty position.

As research investigators or professors, they enjoy many of the privileges of tenure-track faculty, including the opportunity to apply for independent locally and federally funded grants and a reasonable level of independent research direction. In addition, they enjoy more protected time to conduct experiments than tenure-track faculty due to the absence of any administrative duties. These attractive features, combined with the fact that tenure-track faculty positions are difficult to attain, have made these positions more popular in academic research.

Our department welcomes these colleagues, and is committed to ensure their successful professional development. They have already added a new sense of vitality and energy to the department. They have and will continue to contribute to the first-rate research expected of everyone in the department.

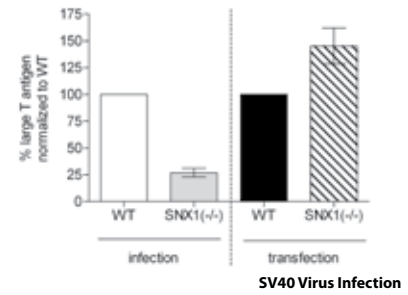
“research investigators or professors, enjoy many of the privileges as tenure-track faculty, including the opportunity to apply for independent locally and federally funded grants”



FAYE BRADBURY

*Research Investigator
Tsai Lab*

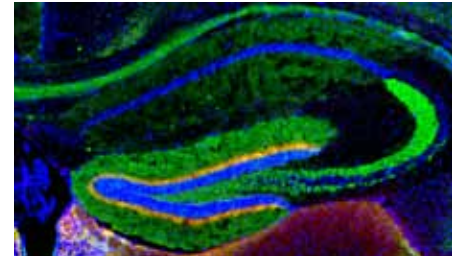
Early steps of SV40 viral infection. Identifying cellular proteins required for entry into the cell and transport through the endosomal system to the endoplasmic reticulum is the aim of my research.



YUNTAO DUAN

*Research Investigator
Giger Lab*

Functional characterization of the molecular and cellular mechanism of class 5 semaphorins in CNS development and in Autism Spectrum Disorders (ASD).



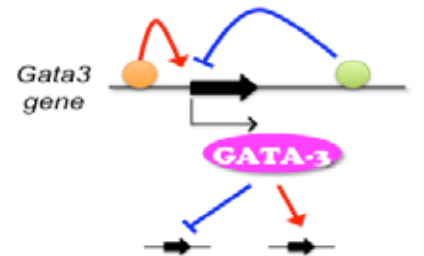
Hippocampus



TOMONORI HOSOYA

*Research Investigator
Engel Lab*

Transcriptional regulation during immature T lymphoid cells development; use molecular genetics to understand the mechanisms controlling early T-lymphopoiesis.



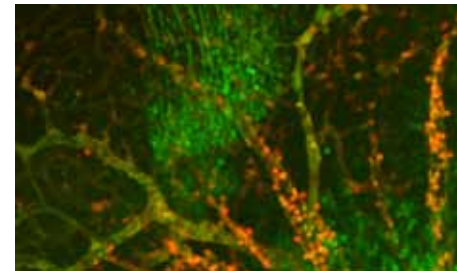
GATA-3 Transcriptional Networks



KIM-CHEW LIM

*Research Assistant Professor
Engel Lab*

Lineage decisions in vasculogenesis and hematopoiesis regulated by GATA transcription factors.



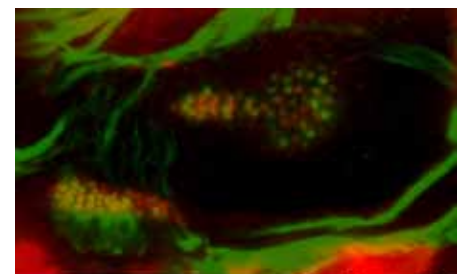
Blood vessels (orange) in brain (green)



YU-CHI SHEN

*Research Investigator
Barald Lab*

Cytokine macrophage migration inhibitory factor (MIF) signaling and inner ear development in zebrafish.



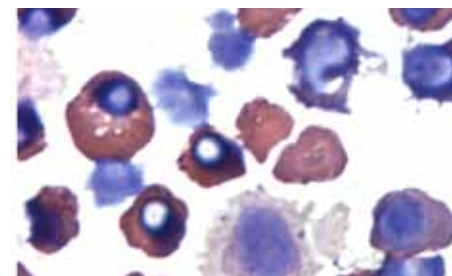
Zebrafish inner ear



OSAMU TANABE

*Research Assistant Professor
Engel Lab*

Understanding epigenetic mechanisms of lineage- and temporal-specific gene expression in development and cell differentiation.



Human blood cells differentiated *in vitro*

MAKE A DIFFERENCE

If you would like to support graduate education by making a gift to the Department of Cell and Developmental Biology visit

www.giving.umich.edu/give/med-cell

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