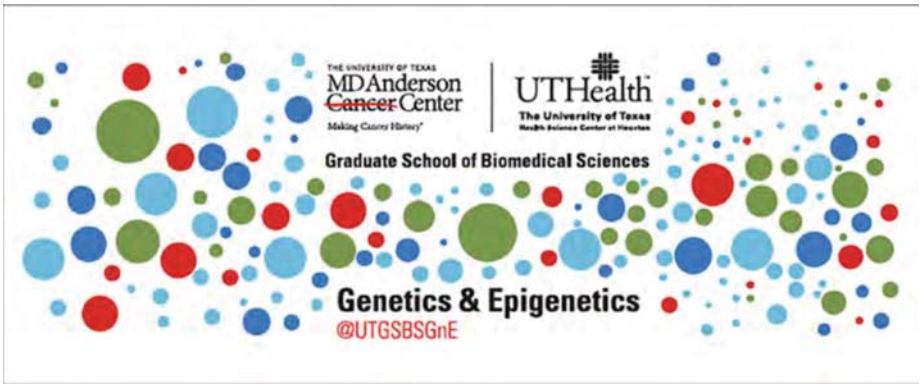



# Genetics and Epigenetics Program

# Research Summaries

# *of*

# Faculty Seeking Students

## Partial List 8/22/21

## See all faculty research profiles on GSBS website

## Genetics & Epigenetics Program

# G&E Faculty Seeking Students

**C. Marcelo Aldaz, PhD**
*Epigenetics & Mol. Carcinogenesis, MDA*

**Swathi Arur, PhD**
*Genetics, MDA*

**Blaine Bartholomew, PhD**
*Epigenetics & Mol. Carcinogenesis, MDA*

**Mark Bedford, PhD**
*Epigenetics & Mol. Carcinogenesis, MDA*

**Richard Behringer, PhD**
*Genetics, MDA*

**Krishna Bhat, PhD**
*Translational Molecular Pathology, MDA*

**Jichao Chen, PhD**
*Pulmonary Medicine – Research, MDA*

**Junjie Chen, PhD**
*Experimental Radiation Oncology, MDA*

**Xiaodong Cheng, PhD**
*Epigenetics & Mol. Carcinogenesis, MDA*

**Francesca Cole, PhD**
*Epigenetics & Mol. Carcinogenesis, MDA*

**Brian R. Davis, PhD**
*Institute Molecular Medicine (IMM), UTHealth*

**Giulio Draetta, MD, PhD**
*Genomic Medicine, MDA*

**George Eisenhoffer, PhD**
*Genetics, MDA*

**Walid Fakhouri, PhD**
*Diagnostic & Biomedical Science, UTHealth*

**Michael Galko, PhD**
*Genetics, MDA*

**Boyi Gan, PhD**
*Experimental Radiation Oncology, MDA*

**Yejing Ge, PhD**
*Cancer Biology, MDA*

**Yong-Jian Geng, MD, PhD**
*Internal Medicine-Cardiology, UTHealth*

**Giannicola Genovese, MD, PhD**
*Genitourinary Medical Oncology and Genomic Medicine*

**Vidya Gopalakrishnan, PhD**
*Pediatrics, MDA*

**Michael Green, PhD**
*Lymphoma-Myeloma, MDA*

**Michelle Hildebrandt, PhD**
*Lymphoma-Myeloma, MDA*

**Raghu Kalluri, MD, PhD**
*Cancer Biology, MDA*

**Ashish Kapoor, PhD**
*Institute Mol. Medicine (IMM), UTHealth*

**Georgios Karras, PhD**
*Genetics, MDA*

**Wenbo Li, PhD**
*Biochemistry & Molecular Biology, UTHealth*

**Wenliang Li, PhD**
*Institute Molecular Medicine (IMM), UTHealth*

**Han Liang, PhD**
*Bioinformatics & Computational Biology, MDA*

**Yonathan Lissanu Deribe, MD, PhD**
*Thoracic & Cardiovascular Surg – Research & Genomic Medicine, MDA*

**Guillermina Lozano, PhD**
*Genetics, MDA*

**Sadhan Majumder, PhD**
*Genetics, MDA*

**Sendurai Mani, PhD**
*Translational Molecular Pathology, MDA*

**Dianna Milewicz, MD, PhD**
*Internal Medicine – Molecular Genetics, UTHealth*

**Rachel Miller, PhD**
*Pediatrics – Research, UTHealth*

**Nicholas Navin, PhD**
*Genetics, MDA*

**Siddharth Prakash, MD, PhD**
*Internal Medicine, UTHealth*

**Kunal Rai, PhD**
*Genomic Medicine, MDA*

**Nidhi Sahni, PhD**
*Epigenetics & Mol. Carcinogenesis, MDA*

**Margarida Santos, PhD**
*Epigenetics & Mol. Carcinogenesis, MDA*

**Katharina Schlacher, PhD**
*Cancer Biology, MDA*

**Ambro van Hoof, PhD**
*Microbiology & Molecular Genetics, UTHealth*

**Consuelo Walss-Bass, PhD**
*Psychiatry & Behavioral Sciences, UTHealth*

**Bin Wang, PhD**
*Genetics, MDA*

**Hsi Ming (Sidney) Wang, PhD**
*Institute Molecular Medicine (IMM), UTHealth*

**Jun Wang, PhD**
*Pediatrics – Research, UTHealth*

**Han Xu, PhD**
*Epigenetics & Mol. Carcinogenesis, MDA*

**Xiangli Yang, PhD**
*Pediatrics – Research, UTHealth*

**Wantong Yao, PhD**
*Translational Molecular Pathology, MDA*

**Haoqiang Ying, PhD**
*Molecular & Cellular Oncology, MDA*

**Momoko Yoshimoto, MD, PhD**
*Institute Molecular Medicine (IMM), UTHealth*

**M. James You, MD, PhD**
*Hematopathology, MDA*

**Sheng Zhang, PhD**
*Institute Molecular Medicine (IMM), UTHealth*

**Zhongming Zhao, PhD**
*School Biomedical Informatics, UTHealth*

**Degui Zhi, PhD**
*School Biomedical Informatics, UTHealt*

*Rev 8/22/21*

# G&E Faculty Seeking Students

Faculty are listed in one or two categories

## Cancer Genetics

C. Marcelo Aldaz, PhD
Swathi Arur, PhD
Krishna Bhat, PhD
Junjie Chen, PhD
Giulio Draetta, MD, PhD
Boyi Gan PhD
Yejing Ge, PhD
Giannicola Genovese, MD, PhD
Vidya Gopalakrishnan, PhD
Michael Green, PhD
Raghu Kalluri, MD, PhD
Georgios Karras, PhD
Wenliang Li, PhD
Han Liang, PhD
Yonathan Lissanu Deribe, MD, PhD
Guillermina Lozano, PhD
Sadhan Majumder, PhD
Sendurai Mani, PhD
Kunal Rai, PhD
Nicholas Navin, PhD
Nidhi Sahni, PhD
Bin Wang, PhD
Haoqiang Ying, PhD
M. James You, MD, PhD
Zhongming Zhao, PhD

## Developmental Genetics

Swathi Arur, PhD
Richard Behringer, PhD
Jichao Chen, PhD
Francesca Cole, PhD
George Eisenhoffer, PhD
Walid Fakhouri, PhD
Michael Galko, PhD
Yejing Ge, PhD
Yong-Jian Geng, MD, PhD
Rachel Miller, PhD
Siddharth Prakash, MD, PhD
Ambro van Hoof, PhD
Jun Wang, PhD
Xiangli Yang, PhD
Momoko Yoshimoto, MD, PhD
Sheng Zhang, PhD

## Epigenetics

Blaine Bartholomew, PhD
Mark Bedford, PhD
Krishna Bhat, PhD
Jichao Chen, PhD
Xiaodong Cheng, PhD
Boyi Gan, PhD
Yejing Ge, PhD
Michael Green, PhD
Ashish Kapoor, PhD
Georgios Karras, PhD
Wenbo Li, PhD
Wenliang Li, PhD
Han Liang, PhD
Yonathan Lissanu Deribe, MD, PhD
Sadhan Majumder, PhD
Sendurai Mani, PhD
Kunal Rai, PhD
Nidhi Sahni, PhD
Margarida Santos, PhD
Consuelo Walss-Bass, PhD
Hsi Ming (Sidney) Wang, PhD
Han Xu, PhD

## Genome Maintenance & Repair

Blaine Bartholomew, PhD
Junjie Chen, PhD
Francesca Cole, PhD
Brian R. Davis, PhD
Georgios Karras, PhD
Kunal Rai, PhD
Nidhi Sahni, PhD
Katharina Schlacher, PhD
Bin Wang, PhD
Degui Zhi, PhD

## Human Genetics

C. Marcelo Aldaz, PhD
Han Chen, PhD
Brian R. Davis, PhD
Giulio Draetta, MD, PhD
Michelle Hildebrandt, PhD
Raghu Kalluri, MD, PhD
Ashish Kapoor, PhD
Georgios Karras, PhD
Wenbo Li, PhD
Dianna Milewicz, MD, PhD
Rachel Miller, PhD
Nicholas Navin, PhD
Siddharth Prakash, MD, PhD
Katharina Schlacher, PhD
Consuelo Walss-Bass, PhD
Hsi Ming (Sidney) Wang, PhD
Zhongming Zhao, PhD

*Rev 5/9/22*

# Swathi Arur, Ph.D.

Associate Professor, Department of Genetics, MD Anderson Cancer Center.

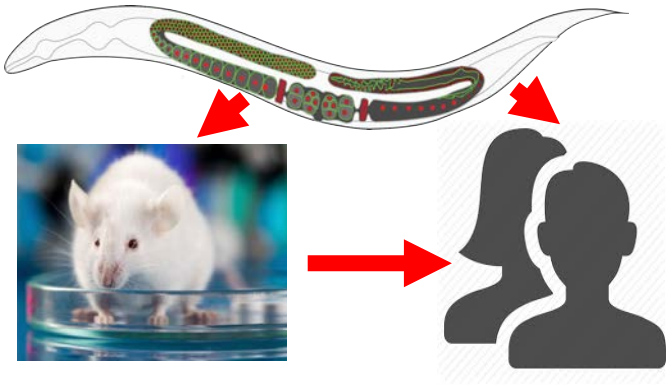
*The lab currently has four graduate students, please contact them for any questions about us!*

https://www.mdanderson.org/research/departments-labs-institutes/labs/arur-laboratory.html

**What do we do?:** Our research is focused on two major areas. (i) Female germ cell development and cellular reprogramming from an oocyte to a zygote: to identify principles that govern female fertility, and developmental birth defects independent of mechanisms that drive aneuploidy. (ii) Cancer Mechanisms and Therapeutics: To identify mechanisms that regulate tumor progression upon metabolic signaling rather than through an increase in mutational burden. Our research can be broadly divided into three categories, as below.

***Lab Team, 2019***. We have added a graduate student, Nick Newkirk, and a Research Assistant Sava Badimi since 2019. Updated lab picture to come!

**I. Discoveries from Fundamental Science: nutritional programs that govern female germ cell development.** Female meiosis I is completed *in utero* in vertebrates. Defects in meiosis I during female germ cell development manifest as sterility in later in her life, or as birth defects in her children. While we assume that maternal health and nutrition influences progeny health, we just never knew that maternal nutritional status regulates *female child's germ cell health* as well, until our lab discovered a direct link between maternal nutrition and regulation of female meiosis I and oocyte development. We discovered that the insulin signaling pathway in response to maternal nutrition status engages the RAS-ERK signaling pathway to directly regulate meiotic progression, and in collaboration with the Horvitz lab at MIT, we showed that maternal nutrition regulates transgenerational survival of the zygotes, and this is dependent on ERK signaling. The mechanisms, at the genetic and molecular level, that govern each of these events downstream to nutritional signaling, remain unresolved. Our goal is to determine the genetic, epigenetic, molecular and cell biological determinants that mediate the regulation of female meiotic 1 progression and progeny survival in response to nutritional availability and nutrient quality.



***Scientific philosophy of the lab.*** We study *C. elegans* germ cell morphogenesis to define underlying principles that link nutrition and environmental changes to gametes and progeny development. We use this data to apply to mammalian biology and better human health

**II. From Fundamental Discoveries to Cancer Science**: One of our goals is to advance knowledge gained from fundamental science discoveries to human health; we generate mouse models for this. We generated phosphorylated Dicer1 knock-in mouse model. We discovered that phosphorylated Dicer1 drives metabolism, aging and cancer metastasis. This is also the identification of the first metastatic driver that is regulated through phosphorylation. This is exciting because we could only have identified this molecule through our work in worms, multiple deep sequencing and now single cell sequencing efforts over the decade have failed to identify metastatic drivers of a KRas tumor. Second, because this is a phosphorylated epitope which drives tumors in mice, it also allows us to identify new small molecule inhibitors that can regress the course of cancer and halt it in its path.

**III. Translational Science: from discovery to patients:** We generated a monoclonal antibody to the phosphorylated Dicer1 epitope against the human protein, and screened endometroid endometrial cancers and non-small cell lung cancers. We find that Dicer1 phosphorylation significantly correlates with cancer invasion KRas mutant status and invasion in endometrial and non-small cell lung cancers. This antibody is currently being filed for US Patent and nationalized in US, Canada, Japan, China, UK and Europe for use as a diagnostic for early detection of metastatic cancers. In the future we hope to take these findings towards treatment.

**PI/Professor: Blaine Bartholomew PhD**
Dept Epigenetics and Molecular Carcinogenesis
UT MD Anderson Cancer Center, Science Park, Smithville, TX
Contact: bbartholomew@mdanderson.org

## Regulation of nuclear organization and chromatin dynamics by ATP-dependent chromatin remodelers

ATP-dependent chromatin remodelers are the gatekeepers of the cell and are crucial for maintaining cells in a pluripotent state as well as for switching to a differentiated state. Mutations of chromatin remodelers are therefore often drivers in oncogenesis and sought after frequently as therapeutic targets in cancer. A key class of these remodelers is the SWI/SNF or BAF family of complexes that regulate chromatin structure at promoters and enhancers and the long-range interactions that occur between them. Our current model is the activity most often affected in cancer when SWI/SNF is mutated is its role in establishing long-range interactions between enhancers and promoters that regulate gene expression. Our evidence suggests these mutations can promote de-differentiation by interfering with SWI/SNF's role in differentiation while not blocking SWI/SNF from promoting pluripotency. Like DNA translocations at the MLL locus or mutations of the MYC transcription factor, other well know drivers in cancer, mutations in SWI/SNF are tied to mis-regulation of RNA polymerase II pausing. My lab's objectives are to investigate and further validate/delineate these models using mouse embryonic stem cells and cutting-edge next generation sequencing (NGS) genomic methods.

Another family of chromatin remodelers called INO80 are also important in development and regulate chromatin composition by exchanging histone H2A variants. INO80 performs this function at only specific genomic locations and the molecular basis for this specificity is not known. We find an explanation for INO80's specificity is DNA sequence alone regulating the enzymatic activity of INO80. We have evidence for critical interactions of INO80 with nucleosomes varying in a DNA sequence specific manner that modulates INO80 activity, independent of INO80 recruitment. These studies involve diverse approaches including in vivo and reconstituted yeast genomic chromatin experiments along with chromatin biochemistry, cryo-electron microscopy, protein structure analysis using chemical crosslinking and mass spectrometry, and genomic NGS approaches. Our ongoing studies are to find in vitro and in vivo the DNA sequence requirements and corresponding changes in INO80's conformation.

**Environment**

Lab members receive a broad experience of chromatin biology combined with genomics so they can confidently address the involvement of epigenetics in cancer or other human diseases. While each member of the lab has their own distinct project, the work is highly collaborative and team based. Lab members often have additional networking and training opportunities in collaborations with other labs throughout the world. Previous lab members have gone on to tenure-track faculty positions at various universities, independent researchers at NIH and the USDA, and in the pharmaceutical and biotech industry.

*Seeking Graduate Student*

# PI/Professor: Mark Bedford PhD

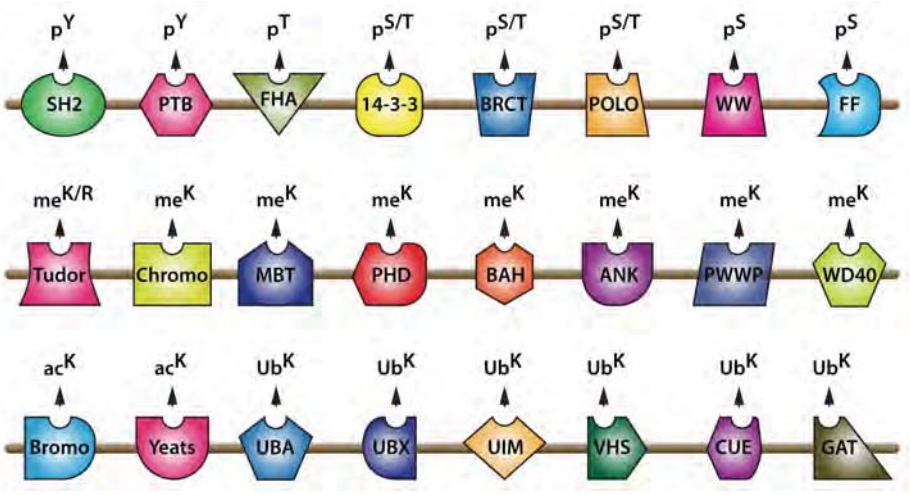
Dept Epigenetics & Molecular Carcinogenesis,
UT MD Anderson Cancer Center, Smithville TX
Contact: mtbedford@mdanderson.org (512 237 9539)

## Epigenetic Marks and Epigenetic Readers

***Interests***:
The Bedford laboratory focuses on two research topics: 1) we are elucidating the biological role of arginine methylation – an abundant modification that has been implicated in signal transduction and transcriptional control, and 2) we developed a protein domain microarray platform to interrogate the role of posttranslational modifications in driving protein-protein interactions in signal transduction. We have generated targeted disruptions and gain-of-function mouse models for these protein arginine methyltransferase enzymes (the PRMTs), with a primary focus on CARM1. Using our protein-domain microarray platform, we have identified and characterized novel protein interactions. In the past we have used these arrays to "read" the histone code. We have identified a number of novel proteins that interact with lysine and arginine methylated motifs, as well as with small molecules that can compete with these interactions.

***Appoaches***:

- Proteomic-based studies for PRMT substrate ID.
- Protein domain array studies for "read" ID.
- PRMT small molecule inhibitor studies.
- CRISPR-based screens for PRMTi vulnerabilities.
- Transgenic and knockout mouse models.




**Environment**. The PI places a high value on mentorship and has graduated seven PhD students. Currently, the lab is composed of two GSBS students and three postdoctoral fellows. Importantly, the PIs lab is located in Smithville, and not in Houston. The lab will be moving to Houston in 2021. Thus, a new student in this lab would have to start their research project in Smithville and then relocate to Houston.

**Positions available**. We have an NIH RO1 and CPRIT funding to support new graduate students.

# Jichao Chen's lab

**Research interest:** We have a cell-centric view of biology and are interested in three aspects of cells: (1) cell behavior, such as morphology and turnover; (2) cell lineage, such as differentiation and conversion; (3) cell signaling, such as paracrine and juxtacrine. We use the mouse lung as our model system and study how the lung is built during development and how it is repair upon injury. Our work is relevant to premature birth, infection, inflammation, and cancer.

**Projects:** One focus of the lab is on the lung epithelial progenitors and how they maintain the lung fate and orderly differentiate into airway and alveolar cells. We are dissecting the epigenetic mechanism and testing its relevance in regenerative medicine using lung cells derived from human embryonic stem cells.

A second focus of the lab is on the alveolar type 1 (AT1) cells, which are only 0.1 um in thickness but comprise nearly the entire gas exchange surface. We are unraveling the transcriptional control and cellular effectors of this highly specialized cell type. Furthermore, we have uncovered its unexpected signaling roles toward the nearby vasculature and fibroblasts. In particular, we have discovered a novel endothelial cell type in the lung that might be the tip cell equivalent in sprouting angiogenesis.

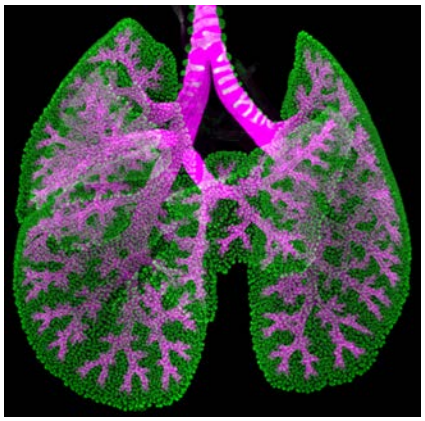
Recently, we have initiated several projects using single-cell RNA-seq and ATAC-seq to identify key intercellular interactions in multiple disease models, including a hyperoxia-induced model of lung immaturity and a virus model of lung injury-repair, as well as lung evolution.

**Techniques:** We employ what we consider to be the three pillars of modern biology: imaging, mouse genetics, and genomics. Specifically, we use 3D fluorescence imaging for fixed and live samples, CRISPR knock-in and conditional knock-out mouse models, and transcriptome and epigenome analysis including single-cell RNA-seq and ATAC-seq.

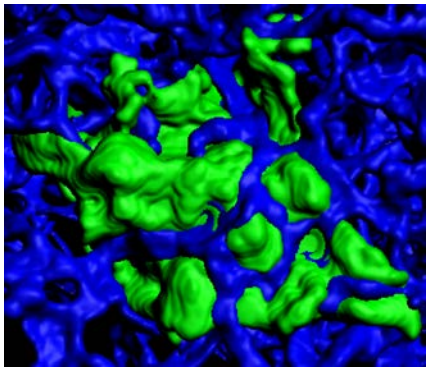
**People:** Lisandra (postdoc; K99 recipient), Vera (Baylor DB student), Annie (Baylor DB student), Celine (G&E student), Dalia (G&E student), Kamryn (Baylor DDMT student), Jonathan (research assistant), and Majo (G&E student).

**Contact:** Jichao Chen, Ph.D., M.H.S., Associate Professor, MD Anderson Cancer Center, jchen16@mdanderson.org

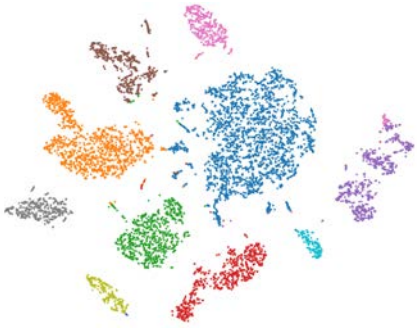
Scan the QR code for lab webpage.



Optical projection microscope image of an embryonic day 17 mouse lung, immunostained for progenitors (green) and airways (magenta).



Confocal image showing a single alveolar type 1 cell (green) intertwined with the vasculature (blue).



Single cell RNA-seq of >7,000 cells from an adult mouse lung, capturing >20 cell types of 4 cell lineages: epithelium, endothelium, mesenchyme, and immune.

*Seeking 1 or 2 Graduate Students*

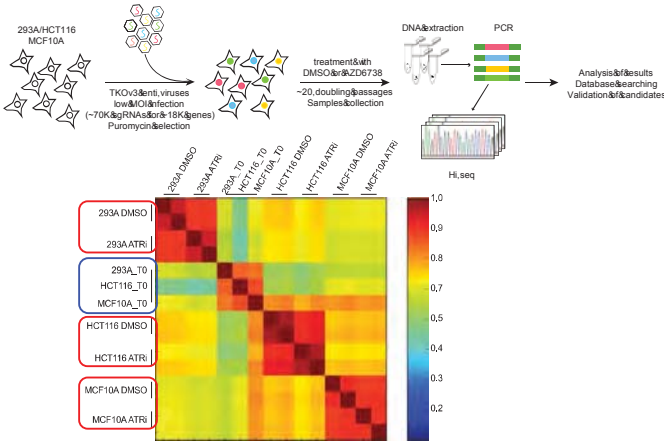

## PI/ Professor: Junjie Chen, PhD

Dept of Experimental Radiation Oncology, UT MD Anderson Cancer Center, Houston TX
Contact: jchen8@mdanderson.org


## "Proteomic, genetic, and functional investigation of DNA damage response and tumorigenesis"

The laboratory focuses on understanding molecular mechanisms underlying genomic instability and tumorigenesis. Maintenance of genome integrity following DNA damage requires the coordination of DNA repair with various cell-cycle checkpoints. The hope is that by understanding these DNA damage-responsive pathways, we will know how deregulation of them contributes to tumor initiation and/or progression and how to take advantage of this deregulation in cancer therapy. The laboratory has been studying DNA damage signaling and DNA repair pathways since 1999. We have identified and performed in-depth functional studies of many key cell-cycle checkpoint and DNA repair proteins in several DNA damage signaling and repair pathways.

With the increasing appreciation of intricacy of signaling pathways, it becomes evident that we need to go beyond our studies of individual proteins and pathways. We should achieve a comprehensive understanding of the network involved in DNA repair and determine how these proteins and pathways intersect, interact, communicate, coordinate, and collaborate for genome maintenance. Only by elucidating the complexity of DNA repair network will we be able to make meaningful and decisive contributions to cancer biology and treatment. With this in mind, we successfully carried out several genome-wide to medium- and small-scale network studies in various DNA repair and oncogenic signaling pathways. The goal is to combine our ability to conduct network analysis with our expertise in performing detailed mechanistic studies to establish physical and functional networks of DNA damage response, tumor suppressive and oncogenic pathways, which will facilitate the long-term goal of exploiting DNA repair and vulnerability in cancer to revolutionize treatment for cancer patients.




CRISPR/Cas9-based sgRNA screens with ATRi AZD6378 in multiple cell lines

**Environment**. Mentoring students and postdoctoral fellows and steering them toward cancer research has always been the most important goal of the laboratory. Over the past 20 years, I have trained more than 50 graduate students and postdoctoral fellows. 18 of my former trainees now have their own independent research groups. Therefore, I have ample experience to serve as a mentor and help their career development.

**Applying**. We seek students who are self-motivated and career-oriented to join an exciting and highly interactive research team. We allow students the freedom to pursue research of their interests. The lab is currently supported by several NIH R01s, a NIH P01, and two MIRA grants from CPRIT.

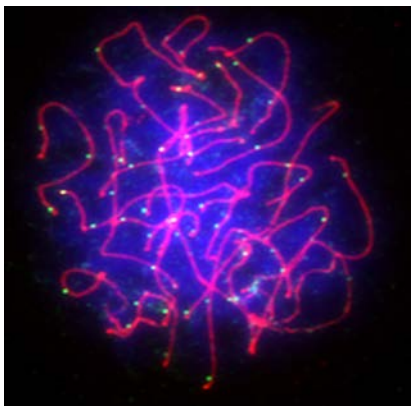
# PI: Francesca Cole, PhD

Associate Professor
Co-Director of the Genetics and Epigenetics Program
NIH Director's New Innovator and CPRIT Scholar
Epigenetics and Molecular Carcinogenesis,
UT MD Anderson Cancer Center, South Campus, SCRB4 4th floor Contact: fcole@mdanderson.org

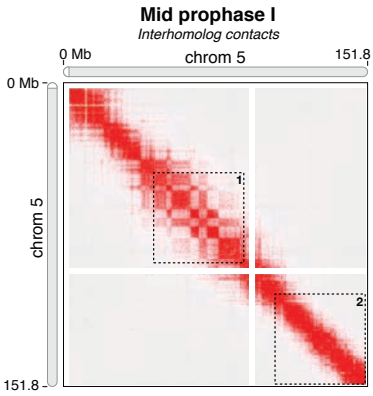
**"DNA repair and chromosome biology during meiosis"**

Compromised DNA repair is a common feature of cancers causing loss of genome integrity. Cancer cells frequently rely upon a single or few repair pathways to survive. This feature provides an approach to target tumor cells, leaving normal cells with a full complement of repair mechanisms unperturbed. Leveraging this approach requires a detailed mechanistic understanding of the interrelationships between DNA repair pathways in vivo. Our lab takes advantage of homologous recombination during meiosis, which is required to segregate chromosomes into sperm and eggs. Multiple pathways collaborate to repair programmed DNA breaks during meiotic prophase, and we investigate how they succeed or fail at this process primarily using mouse genetics.

We have developed assays to provide high-resolution mapping of recombination outcomes on all four chromatids (Cole F et al **Nature Genetics 2014** to determine the molecular nature of individual events and to biochemically and genetically delineate contributions from DNA repair pathways (Zelazowski M et al **Cell 2017**). We have recently developed methods to purify spermatocytes at specific stages to investigate the timing of recombination and chromosome organization during meiotic prophase (Patel L, Kang R co-first authors et al **Nature Structural and Molecular Biology, 2019**). We are currently developing whole genome single-cell sequencing to investigate recombination. Finally, the lab couples these molecular approaches with advanced microscopy (Cole F et al **Nature Cell Biology 2012**) to provide a holistic view of recombination during mouse and human meiosis.



Spermatocytes from young men have reduced recombination leading to high risk of fathering children with Down syndrome (Zelazowski et al Cell 2017)




The first whole genome mapping of interhomolog interactions during meiosis in any organism shown by HiC analysis of mouse spermatocytes (Patel, Kang et al NSMB 2019)

**Environment:** Our lab meetings, science journal club, and diversity and inclusion journal club alternate each week.

The lab currently has eight members: PI, two postdocs, two graduate students, two techs, and our lab manager. Our first student, Rhea Kang was awarded the Alfred G. Knudson, Jr., Outstanding Dissertation Award. All three of my students have received multiple awards for travel, scholarship, and service, as well as fellowships (CPRIT, Cockrell, and HEB).

All trainees attend a national or international meeting each year.

Our laboratory has funding and projects to support one to two new graduate students.

Ask our students and former members about the lab: Tolka Premkumar, Melissa Frasca, and your classmate, Ericka Humphrey!

# Brian R. Davis, Ph.D.


**Titles:** Professor and Director, Center for Stem Cell and Regenerative Medicine
**Endowed Chair** C. Harold and Lorine G. Wallace Distinguished University Chair Brown
**Title: Institution:** Foundation Institute of Molecular Medicine, UTHealth
**Contact:** brian.r.davis@uth.tmc.edu


**Title of Research program:** Genetic correction of stem cells for treatment of inherited lung and blood diseases

**Description of research program**

Dr. Davis's laboratory has as its primary objective the sequence-specific genetic correction of mutations in the chromosomal DNA of induced pluripotent stem (iPS) cells and/or tissue-specific stem cells derived from patients with inherited disorders affecting the lung or blood system. This is being pursued with the ultimate goal of developing stem cell-based therapeutic approaches. We have utilized DNA sequence-specific nuclease-mediated homology directed repair to correct the most common genetic mutations in iPS cell lines derived from patients with Cystic Fibrosis – and have demonstrated genetic and functional correction in lung epithelial cells derived from these corrected iPS cells. We have introduced lung-specific fluorescent reporters into iPS cells and utilized to specifically isolate early lung progenitors and then airway basal stem cells for purposes of molecular and functional characterization. One of our objectives is to employ CF patient-specific iPS cell-derived lung epithelium for testing sensitivity to specific CF drugs -- in order to facilitate a personalized therapeutic approach. We are also presently utilizing the fore-mentioned gene correction methodologies to correct the CF mutations in tissue-specific stem cells directly obtained from CF patients. The second major project in the laboratory focuses on the site-specific correction of gene mutations responsible for inherited blood disorders such as the Wiskott-Aldrich Syndrome (WAS), a primary immune deficiency. Again, we are seeking to correct the disease-causing mutations in patient-specific blood stem cells. In both the CF and WAS projects, the ultimate objective is the delivery back to patients of their own lung or blood stem cells, only differing from the original stem cells by the genetic correction of the relevant mutation.

**Research Projects (currently supported with funding from five grants)**

-Correction of airway basal stem cells and iPS cells from Cystic Fibrosis patients

- Derivation of airway basal stem cell from Cystic Fibrosis patient-specific iPS cells.

-Correction of blood stem cells from Wiskott-Aldrich Syndrome patients

**Key Recent Publications**


Suzuki S+, Crane AM+, Anirudhan V+, Barilla C, Matthias N, Randell SH, Rab A, Sorscher EJ, Kerschner JL, Yin S, Harris A, Mendel M, Kim K, Zhang L, Conway A*, **Davis BR***. Highly Efficient Editing of Cystic Fibrosis Patient-derived Airway Basal Cells Results in Functional CFTR correction. Mol. Ther. 2020 July 8; 28(7):1684-1695. PMID 32402246. +Co-first authors; *Corresponding authors.

King NE, Suzuki S, Barilla C, Hawkins FJ, Randell SH, Reynolds SD, Stripp BR, **Davis BR**. Correction of Airway Stem Cells: Genome Editing Approaches for the Treatment of Cystic Fibrosis. Hum. Gen. Ther. 2020, in press.

Laskowski TJ, Caeneghem YV, Pourebrahim R, Ma C, Ni Z, Garate Z, Crane AM, Li XS, Liao W, Gonzalez-Garay M, Segovia JC, Paschon DE, Rebar EJ, Holmes MC, Kaufman D, Vandekerckhove B, **Davis BR**. Genetic correction of iPSCs from a Wiskott-Aldrich Syndrome patient normalizes the lymphoid developmental and functional defects. Stem Cell Reports. 2016 Aug 9; 7(2):139-48. PMCID: PMC4982969


**Lab members**
Post Doctoral Fellows: Dr. John M. Avila, Dr. Cristina Barilla, Dr. Shingo Suzuki
Research Staff: Haipeng Xue

THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

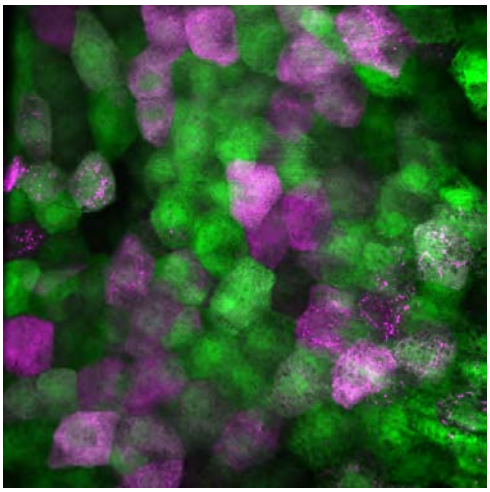

# George T. Eisenhoffer, PhD
Assistant Professor

CPRIT Scholar in Cancer Research
Department of Genetics

Office:
BSRB,, S11.8136c
gteisenhoffer@mdanderson.org
713-563-2754


## Research Interests

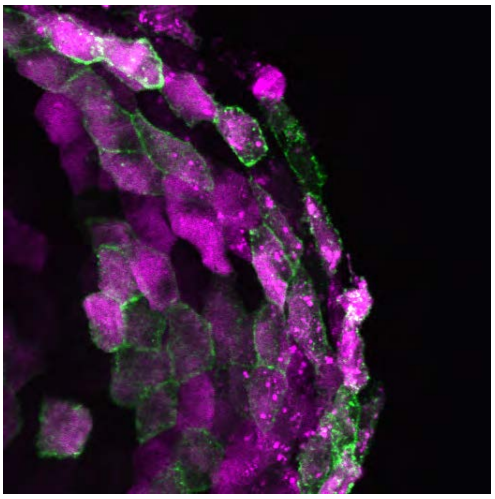
zebrafish development and genetics
epithelial tissue homeostasis
regeneration
stem cells
cell extrusion
metastasis



Our research focuses on understanding how cell division and death are coordinated to control overall cell numbers in epithelia.

**Goal:** To elucidate the mechanisms that regulate cell turnover while preserving barrier function in epithelia and identify specific alterations that go awry during pathogenesis.

**How we do it:** Use the powerful cellular and genetic tools available in the developing zebrafish to dissect cell turnover in a living epithelial tissue.



The Eisenhoffer lab utilizes a combinatorial approach that involves time lapse imaging and CRISPR/Cas9 genome editing techniques to characterize cell turnover under physiological conditions, after damage, and when extrusion is perturbed to gain a better understanding of how specific alterations may lead to epithelial pathologies and cancer.

# Michael J. Galko, Ph.D.

Professor, Department of Genetics
UT MD Anderson Cancer Center

Office: BSRB, S11.8116B
mjgalko@mdanderson.org
Tel: 713 792-9182

**Michael J. Galko**

## Research Interests:

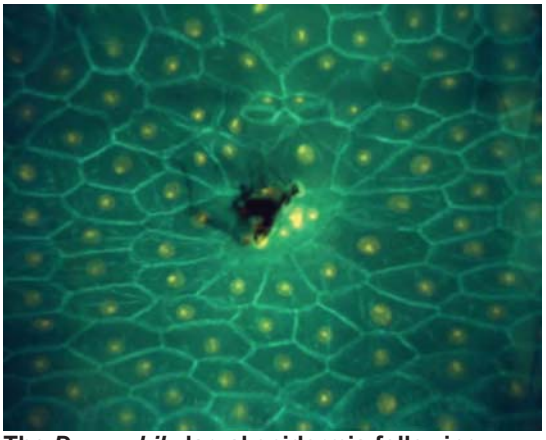
Tissue damage and tissue repair
Skin wound healing
Pain sensitization
*Drosophila* genetics

## Galko Laboratory

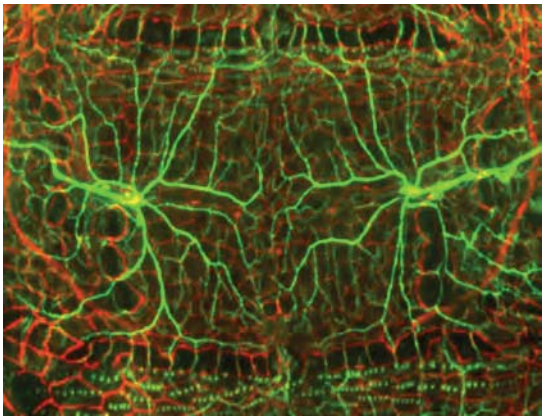
We seek to understand how organisms respond, at the cellular and behavioral levels, to tissue damage.

**Goal:** To discover and dissect the molecular/genetic mechanisms by which organisms sense and repair tissue damage, both in the normal animal and during disease or disease treatment.

**How we do it:** We combine tissue damage and behavioral assays developed in my laboratory with sophisticated *Drosophila* genetic analysis. Some of our projects involve cell biology and light microscopy while others are focused on neurobiology and behavioral analysis. All have the same goal- understanding how animals sense and respond to damage.



**The *Drosophila* larval epidermis following puncture wound (dark scab). Epidermal cells (green = membranes, yellow = nuclei) orient around the wound preparatory to healing.**



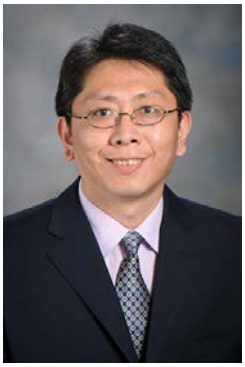
***Drosophila* larval epidermis (red) with underlying sensory eneurons (green). These cells sense and respond to tissue damage.**

**Student Awards:**
Total students graduated (6); AHA pre-doctoral fellowships (2); NIH F31 predoctoral fellowship (1); Larry Sandler Memorial Award for best doctoral thesis employing *Drosophila* (1; an international award sponsored by Genetics Society of America); GSBS fellowships (multiple); GSBS President's Research Award (1); Training grant appointments (every eligible trainee); Poster and speaking awards (multiple); Speaking invitations to national and international meetings (multiple).

**Student-driven publications:**

All students have graduated with first-author papers and student-driven publications have appeared in PNAS (2008), Current Biology (2009, 2009, 2011, 2016), Genetics (2010, Cover), J. Cell Science (2012), eLife (2015), Cell Death and Disease (2017), Developmental Biology (2017), and Development (2019).

# *Seeking Graduate Students*



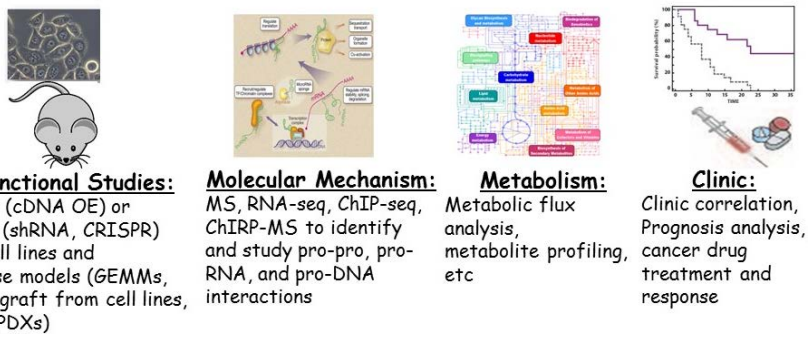

## PI/ Associate Professor: **Boyi Gan PhD**

ERO Dept., UT MD Anderson Cancer Center; Program of Genetics and Epigenetics, Program of Cancer Biology, GSBS. Contact: bgan@mdanderson.org; Lab webpage: https://www.mdanderson.org/research/departments-labs-institutes/labs/gan-laboratory.html


### "Targeting Ferroptosis and Metabolic Vulnerbility in Cancer"

My lab research is at the interface between cancer metabolism and cell survival/death. We are interested in the questions how cancer cell adapt to survive and grow under metabolic stress, and how to target metabolic vulnerabilities in cancer therapies. Our recent work has studied the regulatory mechanisms of ferroptosis, a form of cell death induced by lipid peroxidation, and its role in tumor suppression and cellular metabolism. Our recent study has also revealed an unexpected role of SLC7A11, the amino acid transporter that uptakes cystine and protects cells from ferroptosis, in promoting glucose dependency in cancer cells. Tumor cells with high expression of SLC7A11 are exquisitely sensitive to glucose starvation-induced cell death. Our study thus informs therapeutic strategies to target the metabolic vulnerability in tumors with high SLC7A11 expression. Currently we're employing multi-disciplinary approaches (see schematic on the right) to study these questions.

**Approach:**




**Training Environment**. My laboratory currently consists of ~10 trainees, including GSBS students, postdoc fellows, technicians, and research scientists. The lab environment allows extensive interactions between potential GSBS students and the PI as well as other trainees, but also encourages research independence development of potential students. Within this training environment, most trainees gain extensive training experience with high-profile publications (see representative publications below). GSBS students have played a major role in our research program. For example, Pranavi Koppula, a GSBS student made the discovery that SLC7A11 regulates glucose dependency in cancer cells, and has had multiple first-author publications and received several awards/fellowships, such as CPRIT Graduate Scholar Award and Dr. John J. Kopchick Research Award. The lab research is currently supported by three R01s and several foundation grants.

### Recent Representative Publications:

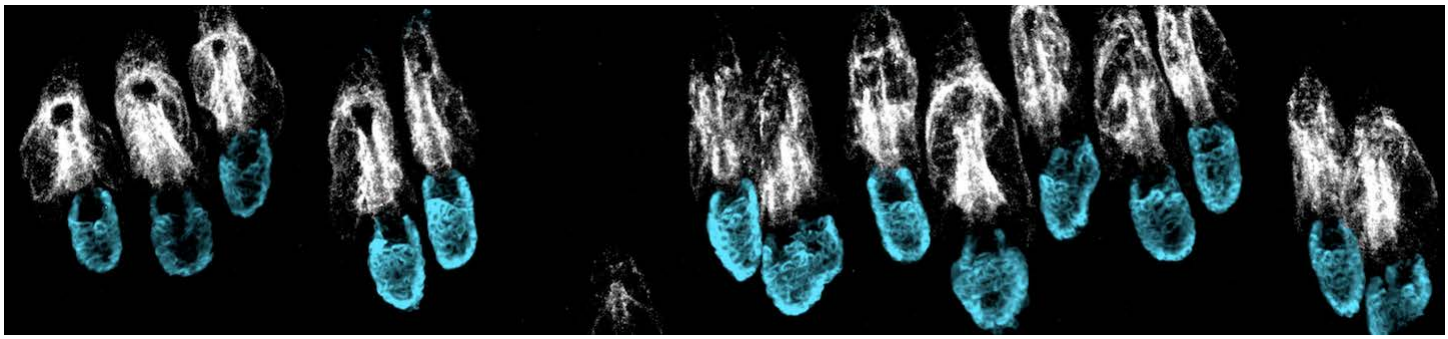

1. Zhang Y, et al., **Gan B**. BAP1 links metabolic regulation of ferroptosis to tumor suppression. **Nature Cell Biology**, 2018.
2. Lee H, et al., **Gan B**. Energy stress-mediated AMPK activation inhibits ferroptosis. **Nature Cell Biology**, 2020.
3. Liu X, et al., **Gan B**. Cystine transporter regulation of pentose phosphate pathway dependency and disulfide stress exposes a targetable metabolic vulnerability in cancer. **Nature Cell Biology**, 2020.
4. Koppula P, et al, **Gan B**. KEAP1 deficiency drives glucose dependency and sensitizes lung cancer cells and tumors to GLUT inhibition. **iScience**, 2021.
5. Zhang y, et al. **Gan B**. mTORC1 couples cyst(e)ine availability with GPX4 protein synthesis and ferroptosis regulation. **Nature Communications**, 2021.
6. Mao C, et al. **Gan B**. DHODH-mediated ferroptosis defence is a targetable vulnerability in cancer. **Nature**, 2021.

***Seeking PhD Student***

# PI: Yejing Ge, Ph.D.

Assistant Professor
Department of Cancer Biology
UT MD Anderson Cancer Center,
Houston TX
Contact: YGe1@mdanderson.org

Ge Lab
Skin Functional Genomics



Defined by golden standards of long-term self-renewal and multi-lineage differentiation, stem cells (SCs) come in different flavors. In mammals, adult SCs are essential units to orchestrate postnatal remodeling and repair damage. Upon stress, SCs often expand their fates and embark on behaviors distinct from their homeostatic patterns, known as plasticity. While plasticity is essential for organismal survival, its derailed regulation poses disease vulnerability to individuals, where SCs are subjected to functional exhaustion frequently observed in aging, or malignant transformation that occurs in cancer (Ge et al, **Nat Cell Biol**, 2016; Ge et al, **Cell**, 2017; Ge et al, **Nat Rev Genetics**, 2018; Ge et al, **PNAS**, 2020). Research in the Ge lab uses skin as our model system, and applies mouse genetics, functional genomics and development biology approaches to dissect molecular mechanisms underlying SC plasticity, and how its deregulation leads to human diseases, including wound repair, cancer, and aging. Come check us out at our website yejinggelab.com

We are excited to have talented and passionate individuals join our team!

## Our Core Values

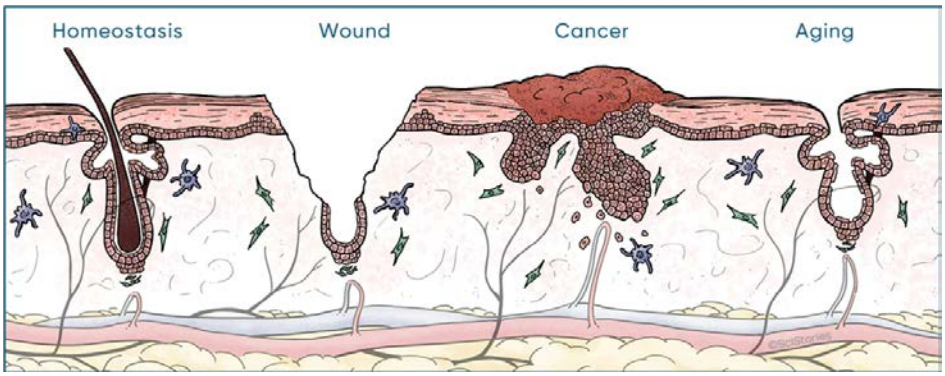
**Creativity**
Science is fun. Think outside the box.

**Rigor**
Never underestimate the importance of experimental rigor. It will take you far.

**Responsibility**
Be a good lab citizen. Do care.

**Perseverance**
Be faithful to your passion. Be tough.

**Freedom**
You are here only because you want to be.

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# PI: Dr. Michael Green, Ph.D.

Associate Professor, Director of Translational Research

Department of Lymphoma & Myeloma, and Department of Genomic Medicine

Email: mgreen5@mdanderson.org Twitter: @GreenLymphoLab

**Research Interest:** Our lab focuses on the epigenetic regulation of B-cell development, and how its dysregulation can lead to lymphoma. The process of B-cell development involves broad and dynamic changes in the epigenome and transcriptome that are coordinately regulated to allow for affinity maturation of immunoglobulins during the germinal center reaction. These normal processes often go awry as a result of genetic alterations and drive B-cell persistence and expansion that results in lymphoma. We are interested in understanding these processes and identifying synthetic dependencies associated with them that can be targeted by rational therapeutic strategies.

**Model Systems:** In addition to directly analyzing patient tumors, we have developed a variety of model systems for our research. This includes advanced CRISPR gene editing approaches in cell lines (Fig. 1), transgenic mouse models, and patient-derived xenograft (PDX) models. Students therefore have the opportunity to work with a mixture of *in vitro* and *in vivo* human and murine systems to explore the mechanistic consequences of genetic alterations and epigenetic programs.

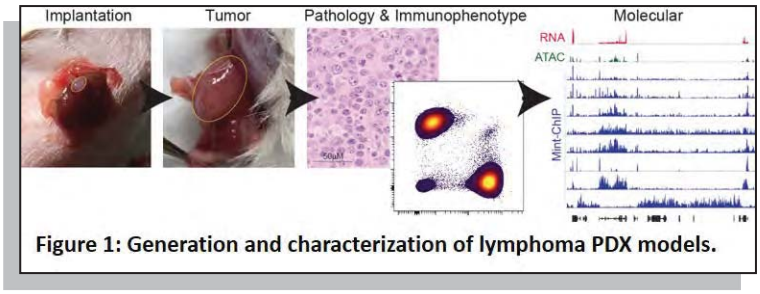



**Figure 1: Generation and characterization of lymphoma PDX models.**

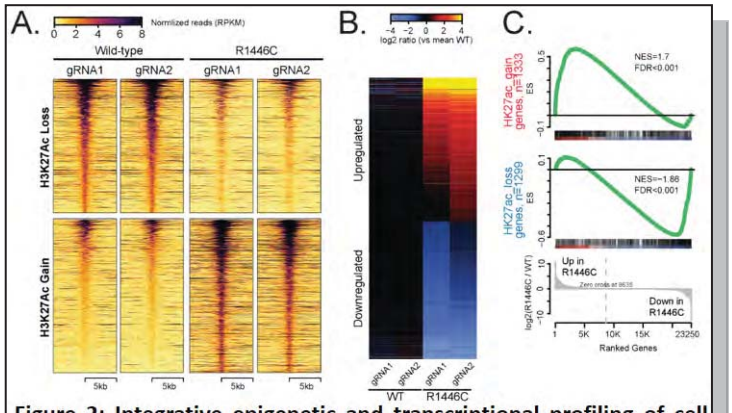



**Figure 2: Integrative epigenetic and transcriptional profiling of cell lines edited by CRISPR to incorporate R1446C mutations in the CREBBP histone acetyltransferase. A)** H3K27Ac ChIP-seq. **B)** RNA-seq. **C)** GSEA of transcriptional changes for genes with differential H3K27Ac. Recently published in Mondello et al., Cancer Discovery, 2020.

**Approaches:** We use a variety of standard genomic approaches such as whole-exome sequencing, RNA-sequencing, Omni-ATAC and ChIP-seq, in addition to other cutting edge genomic methodologies such as CUT&RUN, Mint-ChIP (Fig. 2), Hi-ChIP and single cell RNA-sequencing. In addition, we utilize spectral flow cytometry, biochemistry, molecular biology, CRISPR gene editing, and proteomic approaches to build a comprehensive understanding of how genetic alterations perturb the epigenetic regulation of important developmental processes. Students therefore learn and apply a wide variety of techniques.

Our lab currently includes an Instructor, 5 postdocs and two technicians. We have two R01s and additional philanthropic funding to support up to two graduate students.

**PI: Michelle Hildebrandt, PhD**
Associate Professor
Andrew Sabin Family Fellow
Department of Lymphoma/Myeloma
UT MD Anderson Cancer Center, Houston TX
Contact: mhildebr@mdanderson.org

**Research Interests:** Research interests in the lab are focused on two areas 1) genetic epidemiology of disparities in multiple myeloma and 2) survivorship and late-effect research in AYA and childhood cancer survivors.

**Disparities in Myeloma:** Multiple myeloma (MM) comprises approximately 13% of all hematologic cancers diagnosed. Racial differences in MM incidence and outcomes are well-described, particularly with regard to the 2- to 3-fold increase in incidence in individuals of African descent. However, there is little known regarding risk and clinical attributes of MM in the understudied Hispanic population. My research group is among the first to define the genetic, clinical, and prognostic features of MM in Hispanic patients. Our preliminary data suggests that Amerindian/Native American genetic ancestry may be protective for MM risk in the Hispanic population and that increased European genetic ancestry is associated with increased high-risk cytogenetic profiles in Hispanic MM patients. We are taking advantage of the diverse cancer patient population of MD Anderson and our collaborative sites to develop a Hispanic-focused MM cohort anchored by genome-wide genotyping, clinical, outcomes, and somatic expression profiling data. From this cohort, we will determine differences in patterns of MM clinical characteristics and outcomes by genetic ancestry and identify relationships between genetic ancestry and MM CD138+ expression profiles, as well as identifying race/ancestry-specific expression quantitative trait loci (eQTLs).

**Cardiotoxicity in AYA and Childhood Cancer Survivors:** Childhood and AYA (adolescent and young adult) cancer survivors are a unique population of cancer patients. The tremendous advances in treatment have dramatically increased the overall survival for these patients – however, this success has also resulted in a population of young adults with a wide-range of late-effects due to their previous cancer treatment as children. Cardiac dysfunction, often occurring years and decades following treatment, is a common late-effect and contributes to a high burden of excess mortality in these patients. My laboratory takes a bench-to-bedside approach to elucidate the mediators/mechanisms of cardiotoxicity and identify survivors at increased risk. My laboratory uses induced pluripotent stem cell (iPSC)-derived cardiomyocytes to model anthracycline response in the human target tissue using several "–omics" and phenotypic approaches – such as RNAseq, metabolomics, contractility, mitochondrial function. In parallel, I led two ongoing epidemiology studies of childhood and AYA survivors to collect detailed clinical, cardiac function, quality of life, and follow-up information from patients and bank blood biospecimens to identify biomarkers that predict risk of cardiotoxicity (and create a resource for other late-effects). The integrative analyses in the laboratory enable hypothesis-driven approaches that assesses the effect of genetic variation on cardiotoxicity risk in genes and networks implicated as anthracycline-responsive in the human cardiomyocyte. We are also able to link genetic associations with underlying biology using our cell line model system. We recently secured a protocol to generate patient-derived iPSC cell lines from our patient populations.

**Environment:** The PI's research team is small (compact and nimble!) and "all-hands on deck". My trainees learn all aspects of our research program from the clinic to the laboratory, providing wide-ranging experiences and broad skill sets. Our research efforts are enriched by close collaborations with faculty from MD Anderson, UTHealth School of Public Health, Texas Children's Hospital, and many outside institutions.

***Seeking Graduate Students***

# Dr. Raghu Kalluri, MD, PhD

Contact: rkalluri@mdanderson.org
Professor and Chair
Department of Cancer Biology
The University of Texas MD Anderson Cancer Center

My research focuses on investigating the mechanisms of cell-environment interactions essential for maintaining health, characterizing the disruption of these molecular communication networks in cancer and other diseases, and using these mechanisms to develop novel strategies for diagnosis and therapy of cancer and other diseases.

Current projects in the lab (below) encompass the full spectrum of medical research from patient to bench to bedside, and harness the unique basic science, translational science, clinical research and patient engagement available to cancer researchers and trainees at the Texas Medical Center.

- Tumor microenvironment and metastasis
- Cellular and tissue plasticity in cancer, tissue injury and organ regeneration
- The role of extracellular vesicles/exosomes in disease (cancer, vascular, cardiovascular and neurodegenerative diseases)
- Novel exosome-based therapeutics for cancer and other diseases (mechanism-based research, coupled to translation research and clinical trials)

A tutorial in my laboratory would provide an opportunity to participate in diverse projects that use a variety of molecular, cellular, functional and computational approaches to explore disease mechanisms. Animal models, cell culture models, immunological analysis, flow cytometry, genetic analysis, single cell sequencing/analysis, nanoimaging, machine learning, and other current and emerging technologies are used to address scientific questions.

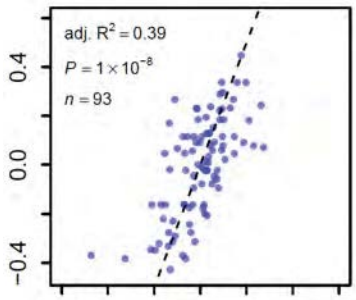
Students are encouraged to assess the research as well as the overall environment during their research rotation, and can reach out to any of the trainees or group members listed on our lab website. Graduate students are encouraged to develop independent projects while being fully supported and mentored by the PI as well as the senior members of the group. We strive to make teamwork and integrity central to our laboratory research culture.

# Ashish Kapoor, PhD

Assistant Professor, Center for Human Genetics
Institute of Molecular Medicine, McGovern Medical School, UTHealth
ashish.kapoor@uth.tmc.edu 713-500-2439

*Variable gene expression and disease risk or trait variation*

Human genetic mapping studies of common diseases and traits (largely genome-wide association studies) have indicated that variable gene expression likely plays a major role in disease susceptibility (such as diabetes) or trait variability (such as height). Variable gene expression has also been a key to development and evolution across species (such as humans vs. chimps). Although there are several biological processes that regulate gene expression, the major contribution is from the cis-regulatory elements (CREs) of gene expression, such as promoters, enhancers and insulators. However for most genes, as opposed to the coding regions, the CREs, which are largely non-coding, have not been identified, and the impact that extant sequence variation has on CRE function remains unknown. We seek to understand the specific molecular components and structure of this regulatory apparatus underlying gene expression variation (CRE and their variants, transcription factors, target gene) and the role it play in disease risk or trait variability. Specifically, we use electrocardiographic QT interval (time taken by heart muscles to repolarize in every heart beat), as a model trait to understand the molecular basis of QT interval variation across individuals. We utilize a wide variety of genetic, biochemical, cellular, functional genomic and computational approaches to identify CREs whose functions are altered by QT interval associated sequence variants, the transcription factors whose bindings are disrupted at the CREs due to causal variants, the target gene whose expression is modulated, and then link the perturbation of target gene expression to a QT interval relevant cellular or organismal phenotype.




Normalized observed *SCN5A* cardiac expression (Y-axis) in GTEx samples versus predicted expression (X-axis) based on a regression model using experimentally identified multiple causal CRE variants.

We encourage trainees interested in advancing their training and career goals, and at the same time contributing to the expanding field of variable gene expression and phenotypic variation, to contact and learn more about different existing projects in our research laboratory.

*Seeking 1-to-2 Graduate Students*


# PI/ Professor: Georgios Karras PhD

Dept Genetics, UT MD Anderson Cancer Center, Houston TX
Contact: gkarras@mdanderson.org


## "Protein Folding Chaperones Sculpting Evolution"

Proteins do most of the work in the cell, but they are not born ready for this. Proteins are synthesized as linear chains of amino acids that must fold into intricate 3D shapes to function. However, the crowdedness of intracellular milieu and the impetus of environmental change pose a serious challenge to protein folding. To resolve this issue, cells employ protein-folding chaperones, specialized proteins that help other polypeptides fold and function in the cell. In doing so, the abundant chaperone heat shock protein 90 (HSP90) provides a "protein-folding buffer" that allows the cell to tolerate genetic and environmental perturbations that are proteotoxic. We have demonstrated that the HSP90 buffer not only alters the biological effects of mutations in various model organisms, but also couples the biological manifestations of these mutations to changes in the environment of the cell. Investigating the mechanisms underlying HSP90-mediated gene-environment interactions revealed a role for this chaperone in beer evolution. We also identified a slew of seemingly benign environmental cues that influence HSP90's ability to buffer disease mutations in human cells. We are now investigating how HSP90 shapes the mutational landscape of tumors and how environmental cues shape this landscape and their impact on tumor evolution. Work in our lab employs multidisciplinary systems approaches, ranging from quantitative genetics to high-throughput biochemistry, in various model organisms, and aims to understand how HSP90 and the protein homeostasis network as a whole influence the penetrance/expressivity of human alleles associated with age-related diseases and aspires to explore new strategies to advance precision health.

**Lab Environment**. The PI places a high value on mentorship and trainee participation in setting research goals. Our group includes two post-docs and two research technicians. Incoming students will be immersed into a collegial and collaborative lab environment in which they will be able to develop research independence and leadership skills.

**Applying**. We are looking for highly motivated trainees who seek to advance their training in systems biology and quantitative genetics and wish to help us understand how protein-folding chaperones influence allele penetrance and expressivity. We have a CPRIT grant to support 1-to-2 new students.

# Wenbo Li Lab (enhancers, enhancer RNAs, epigenome, 4D Nucleome)

**Research Summary:** The Li lab focuses on RNA-mediated gene regulation and 3D chromatin organization. We aim to decipher the functions of noncoding DNA and RNA elements in the human genome in gene control and human diseases. We utilize biochemical and -omics approaches (e.g., ChIP-seq, Hi-C, PRO-seq, etc.), as well as (epi)genome editing tools and screening (CRISPR/Cas9/dCas9/Cas13). We have about 60-70% wet lab components, and 30-40% bioinformatic components. Students are encouraged to read the previous and recent publication of Dr. Li's lab (***Nature 2013***; ***Nature Rev. Genet***. 2016; ***Nature Communications***. 2019; **RNA Biology**. 2020). Full publication list can be found in NCBI MyBibliography: https://www.ncbi.nlm.nih.gov/myncbi/1Jip8J4DFUsQe/bibliography/public/.

*A recent lab picture taken in May 2021.*

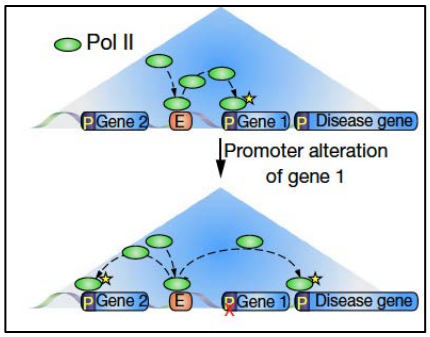



***Figure 1****. A diagram showing cancer mutations deregulate cancer genes via Enhancer release and retargeting (ERR).*

Recently, we found that cancer point mutations or common human genetic variants can rewire disease gene expression via a novel mechanism called Enhancer release and retargeting (Oh et al., 2021, ***Nature****, Figure 2*). Another set of studies from our lab found that RNA m6A methylation on retrotransposon RNAs can play important roles in deregulating disease-associated "long" genes (Xiong et al., 2021, ***Cell Research***), or that enhancer RNAs (eRNAs) may facilitate gene activation via promoting transcriptional condensates (Lee et al., 2021, ***Molecular Cell***, *Figure 3*). Very recently, we start to investigate how RNA virus such as SARS-CoV-2 impacts host chromatin architecture to cause COVID-19 (Wang et al., 2021, ***BioRxiv***).

**About the lab**: We currently have two postdocs, one Res Assistant and three GSBS students in the lab (by August 2021). Two of our students, Ruoyu Wang and Lana Al Hasani are actively involved in G&E activities; talk to them if you want to know more. We welcome students with an enthusiasm to uncover fundamental biology mechanisms of noncoding RNAs, epigenetics and 3D genome control. Both experimental and computational approaches are used. One main project is to study enhancer RNAs in human gene regulation and diseases such as cancer, and to explore novel RNA-targeting therapy of cancer. We study breast cancer mutations such as those of estrogen receptor (ERa) or FOXA1 in enhancer malfunction. Alternatively, students may be involved to investigate 3D genome deregulation in human neurodevelopment disorders, particularly the Down Syndrome. One unique opportunity in our lab is that we are the only team from Texas (and the entire southern US) that is a member of the NIH "4D nucleome consortium" (4DN) (https://commonfund.nih.gov/4dnucleome). Lab members have opportunities to attend 4DN consortium group meetings and will be exposed to world frontiers of 3D genome research.

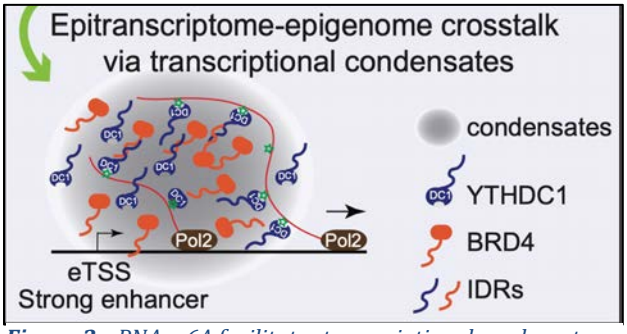



***Figure 2****. eRNA m6A facilitates transcriptional condensates.*

Our lab has funding to support two new graduate students for long term thesis projects. We already have some Master Students who have decided to join us this fall (so the numbers above are additional to these).

**Contact:** Wenbo Li, Assistant Professor, Biochemistry and Molecular Biology, UT McGovern Medical School. at Wenbo.li@uth.tmc.edu. You are welcome to inquire via email if you have questions or to arrange a meeting.

# Lissanu Lab

**Research Interests**: The Lissanu Lab is interested in identifying therapeutically amenable vulnerabilities of genetically defined subtypes of cancer. The long-term goal of the lab is to translate our basic cancer biology understanding to new cancer therapeutics. Specifically, we study lung cancers with mutations in epigenetic and chromatin regulators. Current efforts in the lab include elucidating the genetic vulnerabilities of cancers with mutations in the SWI/SNF chromatin remodeling complex using functional genomic approaches. We aim to leverage the insights from our basic studies to identify therapeutic targets and develop novel therapeutics. Further, we are actively pursuing targeted protein degradation by small molecule degraders as a new cancer therapeutic modality. In this respect, we design and synthesize novel small molecule protein degraders targeting critical epigenetic regulators.

## Projects

**Identification of synthetic lethal genetic interactions of SWI/SNF complex subunits**. Hypothesizing the existence of functional genomic interactions that affect cellular viability, we perform genome-wide CRISPR-Cas9 knockout screen on isogenic pairs of *SMARCA4* mutant and WT lung cancer cell lines (Fig. 1). The hits, putative synthetic lethal partners of *SMARCA4*, are validated by orthogonal approaches in vitro and in vivo. One such hit is SMARCA2, which we are actively investigating as cancer therapeutic target.

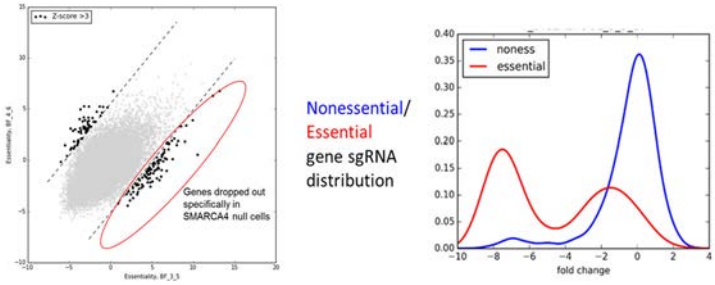



**Fig. 1 Genome-wide CRISPR knockout screen** is a powerful approach to discover synthetic lethal partners in isogenic pairs of cancer cell lines, *SMARCA4* mutant and *WT* cell lines (left panel). Right panel shows drop out of essential genes as positive controls.

**Discover and develop proteolysis targeting chimeras (PROTACs) as cancer therapeutics.** An important aspect of our research interest is the development of chemical probes to supplement genetic tools to understand chromatin biology in cancer. Proteolysis targeting chimeras (PROTACs) are exciting new molecular entities that have unique and potent pharmacologic properties. We have developed several PROTACs that induce selective degradation of target oncoproteins of interest including SMARCA2 as a therapeutic for SMARCA4 mutant lung cancer and glucocorticoid receptor (GR) as a combination therapy to circumvent resistance to chemotherapy in lung cancer (Fig. 2). These studies will provide first-in-class lung cancer therapeutics for clinical development.

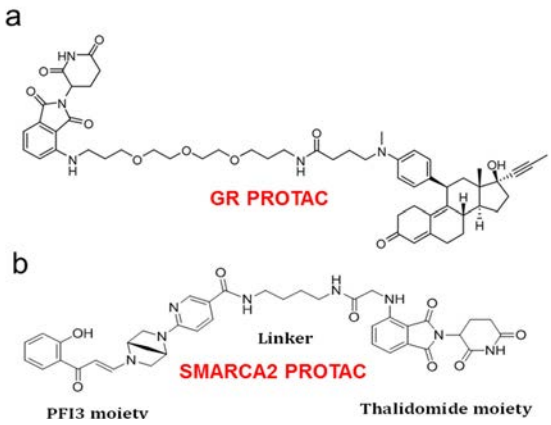



**Fig. 2 Chemical structures of degraders with potential as therapeutics**: typical GR and SMARCA2 PROTACs developed by the lab.

**Techniques:** CRISPR-Cas9 functional genomic screen, genetically engineered mouse (GEM) models, transcriptomic and epigenomic analysis (RNA-Seq, ATAC-Seq, ChIP-Seq),

Together with our collaborators and partners, **we offer unique opportunities to learn basic drug discovery and development processes** including target identification, PROTAC SAR, degradation assays, drug target engagement assays

**People**: Nicholas (Nick) Blazanin (postdoc), Sasi Kotagiri (postdoc), Poonam Pandey (postdoc), Yawen Wang (postdoc), Xiaobing Liang (senior research associate)

**Contact:** Yonathan Lissanu MD PhD, Assistant Professor, MD Anderson Cancer Center ylissanu@mdanderson.org

# *Seeking 1-to-2 Graduate Students*

PI/ Professor/Chair: **Guillermina Lozano PhD**
Dept Genetics, UT MD Anderson Cancer Center
Contact: gglozano@mdanderson.org

## The p53 tumor suppressor pathway

The p53 tumor suppressor is a DNA damage/stress response protein that functions as a transcription factor to regulate a large number of genes that prevent proliferation of damaged cells via initiation of cell cycle arrest and senescence, and via apoptosis and other mechanisms of cell death which are potent tumor suppressive mechanisms. Disruption of the pathway in tumors occurs most often through mutation or deletion of the *p53* gene itself, but elevated levels of two important p53 inhibitors, MDM2 and MDM4, also contribute to tumor development. We have developed *in vivo* mouse models that allow us to probe the specificity of the p53 response at the molecular and organismal levels. We plan to determine and functionally examine the p53 transcriptional program and the downstream pathways that are activated *in vivo* upon depletion of *Mdm2* in various tissues. In addition, high MDM2 levels as occur in some human cancers are not tolerated by normal cells. We have an ongoing CRISPR/Cas9 screen to identify factors that allow normal cells to survive despite elevated levels of MDM2 to identify and characterize synthetic lethal relationships with high MDM2 in tumors.

We have also created three novel conditional mutant p53 alleles in the mouse that are wild type to start with but recombine the *p53* locus in a Cre-dependent manner to create a few mutant cells in a sea of normal stroma and immune cells. Somatic p53 mutation in the breast epithelium produces breast carcinomas that metastasize to the lung and liver, common sites of human breast cancer metastasis. We are poised to decipher the changes that occur at each step of the metastatic process in this and other cancers by analyses of tumor evolution, circulating tumor cells, dormancy, and metastases.

**Environment** I have a large lab that consists of students, post docs, fellows and faculty. All work well together, and discuss and share their data.

**Applying** I would like to attract trainees who work independently with some direction. I have several NIH and CPRIT grants to support 1-2 new students. However, trainees are expected to apply for fellowships.

# Sadhan Majumder, PhD
**Professor, Department of Genetics**
**MD Anderson Cancer Center**
smajumder@mdanderson.org

## Lab Overview

The research in my laboratory is focused on (1) deciphering the mechanisms that control normal development and how aberrations of such mechanisms produce diseases, and (2) investigating how such knowledge can be translated into improved patient care. We begin by studying molecular mechanisms and then build on the lessons learned from those studies using a multi-disciplinary approach that encompasses genomics, bioinformatics, biochemistry, cell biology and mouse genetics. Our work involves close collaboration between basic scientists and clinicians. Our current work involves the roles of the transcriptional repressor REST in (i) brain tumors and in (ii) chronic pain.

Although REST regulates many genes, many of its biological functions still remain undiscovered. Overexpression (OE) of REST is found in many brain tumors, in ischemic insults, and in neurological diseases and behavioral disorders. However, progress in these areas has been hampered by the continuing absence of a conditional *Rest* OE mouse model. To solve this problem, we took up the challenge. Although it took us a while, we persevered and we have now created the first conditional REST OE knockin mouse line enabling study of the role of *Rest* OE in vivo. Our published results confirm that REST expression in these mice is physiologically relevant. Genome-wide analyses followed by biochemical and behavioral assays indicated that REST regulates spontaneous locomotion by repressing a new target, Dopamine Receptor 2. In a second line of work using these and *Rest* conditional knockout mice, we are studying the role of REST in cancer chemotherapy- and surgery-induced chronic pain and in subsequent opioid treatment. In that project, we proposed to study the central hypothesis that REST and G9a, a corepressor of REST, in specific neurons are involved in chronic pain caused by nerve injury and chemotherapy by regulating unique epigenomic and transcriptomic signatures (including mRNAs, miRs and lncRNAs).

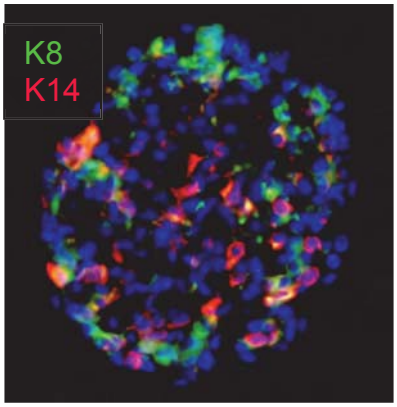
*Seeking Graduate Student*


## PI/ Professor: Sendurai A. Mani PhD

Dept: Translational Molecular Pathology
UT MD Anderson Cancer Center, Houston TX
Contact: smani@mdanderson.org
Website: www.mani.us


**"EMT and Cancer stem cells in treatment resistance, immunotherapy, and metastasis."**

Metastasis is the primary cause of cancer-related deaths but, surprisingly, one of the least understood processes in biology. Dr. Mani and his team demonstrated that the reactivation of the latent embryonic program known as the epithelial-mesenchymal transition (EMT) is necessary and sufficient for the development of metastasis (Yang and Mani et al., Cell 2004; Mani and Yang et al., PNAS 2007). Later, they found that the cancer cells not only acquire migratory and invasive properties through EMT but, also, stem-cell properties (Mani et al., Cell 2008).




A single breast epithelial stem cell developing into both luminal keratin K8 (green) and basal keratin K14 (red) positive epithelial cells in a sphere culture.

The EMT is a highly complex developmental program, reactivated in cancer cells. How the cancer cells initiate the EMT program, and what are the various growth factor and the associated signaling emanating from the tumor microenvironment regulate this process is unclear. Also, at the molecular level, how the EMT program induces stem cell properties to cancer cells is less understood. Mani's laboratory uses various experimental model systems, including cell lines, patient-derived tumor xenografts as well as mouse models to study the contribution of EMT and cancer stem cells (CSCs) to tumor progression, including their contribution to the development of resistance to chemo and immunotherapy.

**Environment**. Dr. Mani is passionate about teaching and mentoring graduate students and postdocs. He has recruited many talented postdoctoral fellows, graduate students, research assistants, and instructors to his laboratory. His fellows received fellowships from various funding agencies, including DOD, Susan G. Komen, Emil Aaltonen Foundation as well as T32. His trainees entered into academic as well as industrial career paths. One of his G&E graduate students started a highly prestigious and competitive cancer prevention fellow program at NCI. He is also a member of two T32 training grants, which will allow the students to compete for the T32 training fellowships. In summary, Dr. Mani's lab will provide an excellent environment and opportunities for incoming students to be successful.

**Applying**. The Mani lab is seeking for two trainees who are curious to understand how cancer develops to become resistant to chemo and immunotherapies. Trainees will have ample opportunities to advance their careers while enjoying their Ph.D. life. We have funding to support two new graduate students.

*Seeking Graduate Students*

# PI/ Professor: Dianna M. Milewicz, MD PhD

President George H.W. Bush Chair of Cardiovascular Medicine
Department of Internal Medicine, Division of Medical Genetics, UT McGovern Medical School, Houston TX
Contact: Dianna.M.Milewicz@uth.tmc.edu

**"Which Genes Trigger Vascular Diseases and Why?"**

Dr. Milewicz directs a translational research program to (1) identify the genetic causes of vascular diseases; (2) use model systems (mouseand induced pluripotent stem cells (iPSCs)) to understand the link between the mutant gene and the clinical disease; and (3) take the results of these studies back to the patients to improve clinical care and outcomes of their genetically triggered vascular diseases. The research program recruits patients with early onset or unusual vascular diseases, along with their family members, to identify genes for these conditions. Dr. Milewicz's research program has recruited over 20,000 individuals with vascular diseases worldwide. Her lab has identified many genes that predispose to thoracic aortic aneurysms, acute aortic dissections, early onset stroke, early onset coronary artery disease, and intracranial aneurysms. These results are translated into medical care through the inclusion of these genes on DNA genetic testing panels, which are used clinically to diagnosis individuals with vascular diseases.

As an example, Dr. Milewicz's research team identified a novel gene, *ACTA2*, for aortic dissections using a large family who requested to be part of her research. Through talking with and examining the family members who had survived an acute aortic dissection, Dr. Milewicz determined that mutations in *ACTA2* also cause early onset coronary artery disease and childhood onset strokes (see TEDx talk). These findings have altered the genetic basis of vascular diseases by demonstrating that alterations in one gene can lead to thoracic aortic aneurysms, early onset coronary artery disease and early onset strokes. Mouse models and iPSCs with *ACTA2* mutations are established to address how one gene triggers all these various vascular diseases.

**Environment**. The PI's research team includes graduate students, postdoctoral fellows, scientists, physicians, and genetic counselors. The weekly lab meetings and journal clubs provide an interactive educational environment. In addition, we collaborate with investigators within the Texas Medical Center, along with researchers and clinicians worldwide. It is a highly collaborative environment that focuses on understanding the molecular basis of vascular diseases to improve treatments and outcomes of these disease.

**Applying**. Interested students should contact Dr. Milewicz. Please feel free to contact the current graduate students in her laboratory:

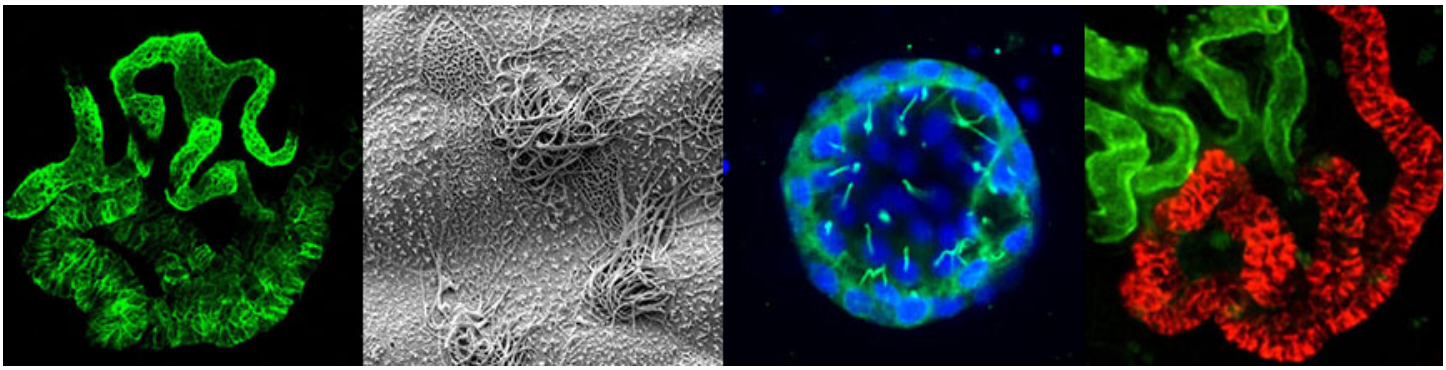
Kaveeta.Kaw@uth.tmc.edu

Jamie.M.Wright@uth.tmc.edu

Anita.Kaw@uth.tmc.edu

# PI: Rachel K. Miller, Ph.D.

Associate Professor
Pediatric Research Center
McGovern Medical School, MSE R413
Contact: Rachel.K.Miller@uth.tmc.edu
Webpage: https://med.uth.edu/pediatrics/miller-lab/

## "Modeling kidney development and disease in frog embryos"

The central goal of our research is to understand the processes that underlie the development of the kidney, and how disruption of these processes results in congenital anomalies of the kidney and urinary tract (CAKUT) that arise in human patients. Malformations of the kidney and urinary tract occur in almost 2% of the world population, representing nearly one-fourth of all birth defects. Because mutations in the genes causing these congenital abnormalities are only known in 14% of cases and often result in the need for kidney transplant, our goal is to understand how the mutated genes disrupt kidney development. We utilize the embryonic kidney of the frog (*Xenopus laevis*) as primary model of kidney development and to model human patient mutations within the kidney. We also utilize tissue culture of kidney cell lines to understand the cellular mechanisms driving nephron development. Our prior findings indicate that Wnt signaling pathway regulators play critical roles in kidney development and congenital disease. Therefore, we focus on understanding how these components regulate cellular processes that are important during kidney development.

**Environment**. We have a highly colloborative laboratory environment, and the contributions of our trainees have been integral to project successes. The valuable contributions of our laboratory's trainees have resulted in a steady record of publication. Collectively, trainees have been awarded the Gee Family Legacy Scholarship, the Gigli Family Endowed Scholarship, the Schissler fellowship and the Dean's Research Award. I look forward to advancing the scientific training of students in the future, as I feel it is one of the most rewarding parts of my job.

**Applying**. Please feel free to contact me if you are interested in rotating with our group. We would like to recruit one new graduate student.

*Seeking Graduate Student*

# PI/ Professor: Siddharth Prakash, MD,PhD

Dept of Internal Medicine, McGovern Medical School, UTHealth
Contact: Siddharth.K.Prakash@uth.tmc.edu

Siddharth Prakash earned a Bachelor of Science in Molecular Biophysics and Biochemistry from Yale University. He completed his M.D.-Ph.D. training with Dr. Huda Zoghbi in the Department of Molecular and Human Genetics and a fellowship in Cardiovascular Disease at Baylor College of Medicine. Since 2011, Dr. Prakash has worked in the John Ritter Research Program in Aortic and Vascular Diseases at McGovern Medical School, a part of the University of Texas Health Science Center at Houston (UTHealth), where he specializes in medical therapy, imaging and surveillance of patients with heritable aortic and vascular diseases. He is Associate Professor of Internal Medicine and is co-director of the Turner Syndrome Adult Comprehensive Care Center. Dr. Prakash's translational research laboratory focuses on the contribution of rare genomic copy number variants (CNVs) to bicuspid aortic valve (BAV), the most common adult congenital heart defect. Our lab uses an innovative strategy to identify new candidate genes for BAV, based in part on the hypothesis that reduced dosage of genes on the X chromosome is responsible for the increased prevalence of BAV in males and in women with Turner syndrome. We identified recurrent CNVs in diverse clinical cohorts with BAV and demonstrated that specific rare CNVs are an important contributing cause of thoracic aortic aneurysms. We were recently granted funding from the American Heart Association and an R01 from the National Institutes of Health to follow up on these observations in patients with early complications of bicuspid aortic valve disease.

**Active projects in the Prakash lab include**:

1. Characterization of induced pluripotent stem cells (iPSCs) from patients with Turner syndrome in a hydrogel model of embryonic aortic valve development.
2. Functional analysis of candidate genes for cardiovascular defects in iPSCs using CRISPR technology.
3. Functional analysis of candidate copy number variant loci implicated in left ventricular outflow tract development.
4. Exome sequencing of families with BAV and left-sided congenital heart defects. Findings are continuously fed back into aims 1-3.
5. Analysis of the role of tissue-specific mosaicism in Turner syndrome phenotypes using genomic copy number analysis, methylation profiling and RNA sequencing.

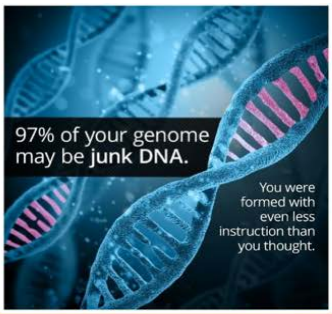
# KUNAL RAI's LAB

krai@mdanderson.org | Ph: 1-713-591-5303 | www.railab.org

**Research Interest**: Rai lab is focused on understanding how epigenetic processes contribute to human tumor biology and how we can exploit these aberrations to engineer novel therapeutic approaches. With the use of cutting-edge high throughput epigenomic methods, we have built chromatin maps from human tumor tissues and cancer cell lines with different genetic and clinical features. We are utilizing these datasets and cutting-edge computational methods to gain deeper understanding of underlying tumor biology as well as therapeutic approaches. Further, we are exploiting genome editing and high-throughput screening methods in cancer cell lines, animal models (mouse and zebrafish) to functionalize cancer epigenome and study epigenetic regulators of cancer progression with a focus on metastatic dissemination and resistance to immunotherapies.

**Projects:** Rai lab has a diverse array of activities which can be categorized under 6 different areas: 1) Chromatin structure and function in cancer; 2) Epigenome and personalized medicine; 3) Epigenetic drivers of metastasis; 4) Epigenetics of immunotherapy response; 5) Single cell epigenomics and 6) Machine learning in cancer epigenomics. Details of each of these areas can be found in our website (www.railab.org). Projects will be available in these areas as well as new areas, for example epigenome function during aging and obesity. We seek curious and motivated experimentalists and computational biologists. Lab provides great opportunity for learning computation analysis for experimentalists. Please contact Kunal to discuss potential projects and your interest.

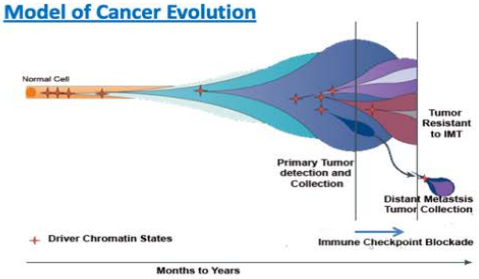
**People:** Rai lab is home to 7 PhD students (2 MD/PhD, 3 GSBS, 1 BCM, 1 SPH), 1 MS student, 6 post-doctoral fellows, 2 research scientists, an assistant professor, 2 research assistants and 3 UG students.



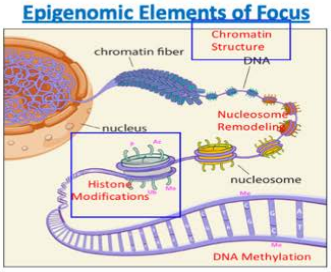

**Questions in Rai Lab**

1. **How is epigenomic landscape altered in cancer?**
2. **What is the impact of these alterations in cancer biology?**
3. **Can these alterations be used to identify novel biomarkers or guide therapeutic strategies?**

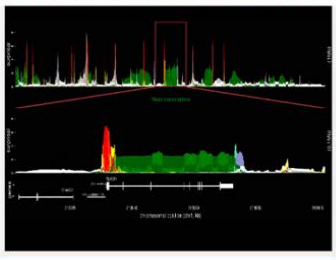
**Model of Cancer Evolution**



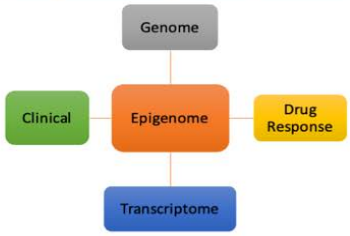

**Epigenomic Elements of Focus**



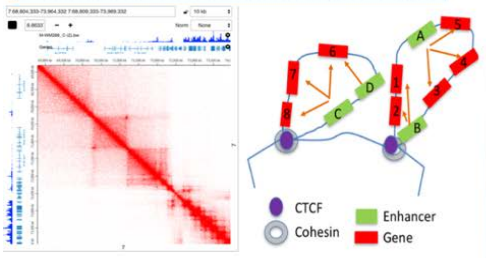

**Chromatin State in Cancer Evolution**



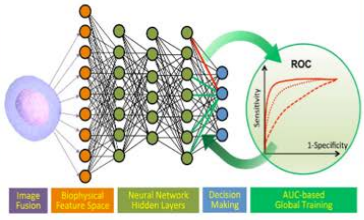
**Deep Integrative Analysis to Explore Biology**




**3D chromatin structure and Functionalization**




**Deep Learning in Cancer Epigenomics**




krai@mdanderson.org

*Seeking 1-2 PhD Students*


## PI/Assistant Professor: Nidhi Sahni, PhD

Epigenetics and Molecular Carcinogenesis, UT MD Anderson Cancer Center, **Science Park, Smithville** TX
Contact: nsahni@mdanderson.org


## "**Systems biology and precision medicine in human cancer**"

My laboratory is focused on systems biology of human cancer, integrating large-scale computational genomics and high-throughput experimental platforms to address fundamental problems in the modern era of personalized or precision medicine. The lab seeks a systems-level understanding of the underlying genetic and epigenetic aberrations in cancer heterogeneity and immunity. We aim to identify novel biomarkers and drug targets, and to have a major impact on cancer by translating into more effective prognosis and therapy for human cancer.

We use an advanced set of state-of-the-art technologies, including high-performance computing, signaling network analysis, Gateway technology, high-throughput screening, genome editing, proteomics and next-generation sequencing. To achieve systematic and significant insights in cancer progression, my lab focuses on the following areas:
(I). Systematic computational analysis of signaling networks in human cancer;
(II). Develop robust bioinformatics and computational algorithms to prioritize driver mutations from next-gen sequencing data;
(III). High-through CRISPR screens and proteomics to identify driver events contributing to tumorigenesis;
(IV). Functional characterization of genomic mutations in cancer cell models

Our lab is well-funded, supported by Sloan Research Foundation, Pinnacle Research Award, Rising STARs, CPRIT funds, among others. Recent representative publications include ***Cell*** (2015), 161: 647-60; ***Nature Rev Genet*** (2017), 18: 395-410; ***Cell*** (2015), 161: 661-73; ***Cell*** (2017), 168: 856-66; ***Cancer Cell*** (2018), 33: 450-462; ***Nature Commun.*** (2018), 9: 1317. For more information, please visit:
https://faculty.mdanderson.org/profiles/nidhi_sahni.html

**Environment:** Our laboratory values a friendly and interactive scientific environment. All graduate students and postdocs attend a national or international meeting each year. Tutorials in my laboratory can include a wide range of topics in systems biology, including computational analysis, statistics, bioinformatics, molecular biology, proteomics, and biochemistry. The integration of these technologies will provide valuable insights into genomic mutation-mediated signal transduction network alterations in cancer biology.

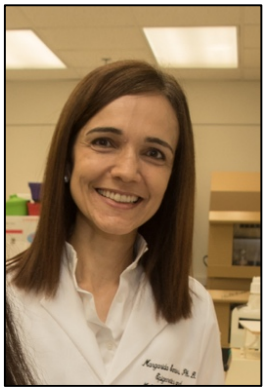
*Seeking PhD Students*

# PI: Margarida Almeida Santos, PhD

Assistant Professor
Dept. of Epigenetics & Molecular Carcinogenesis
MD Anderson

**Email:** MIAlmeidaSantos@mdanderson.org

**Lab Website:**
https://www.mdanderson.org/research/departments-labs-institutes/labs/santos-laboratory.html



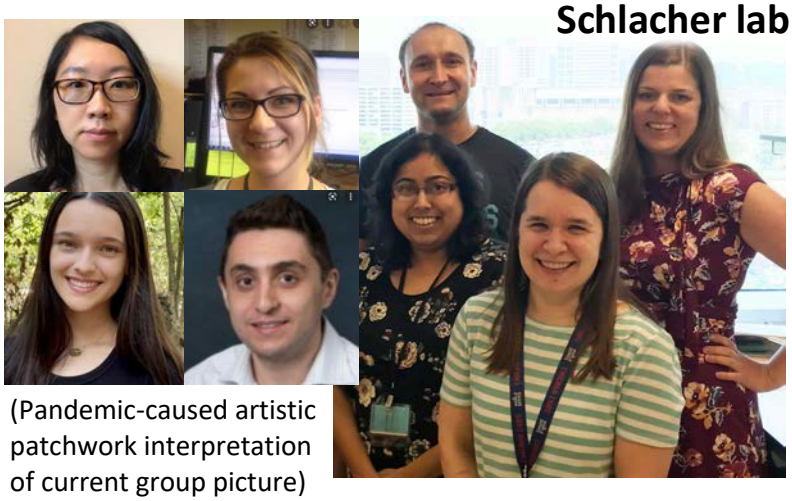
## Epigenetics and DNA Repair in Cancer Stem Cells

Our scientific interests are focused on replicative stress/DNA damage response and epigenetic regulators in cancer stem cells. Current studies in my laboratory focus on the hematopoietic system, since 1) it is a well-established system for adult stem cells studies and 2) the dynamic nature of the hematopoietic system places it in a vulnerable position with respect to genomic damage during DNA replication. Replicative stress can be defined as a slowing or stalling of replication fork progression and a source of spontaneous DNA lesions that drives genomic instability. “Oncogene-induced” replicative stress is a major driving force of hematological cancers. Aberrant oncogene expression induces precocious entry into S phase and perturbs replication fork progression, triggering the DNA damage response. The classical view of the DNA damage response (DDR) postulates that DDR is a crucial tumorigenesis barrier in early stages of cancer development, and a selective pressure that favors malignant clones with defects in DNA repair factors. My recent work showed that DNA damage induces the differentiation of leukemic stem-like cells in acute myeloid leukemia (AML) harboring the MLL-AF9 oncogene, thus uncovering an unexpected tumor-promoting role of genome guardians in enforcing the oncogene-induced differentiation blockade in AML (Santos et al., Nature 2014).

Current studies in my laboratory explore the concept of “DNA damage-induced differentiation of stem-like cancer cells” in AML and other aggressive hematological malignancies using mouse models, next generation sequencing and various DNA damage treatments and assays. Elucidating which DNA damage response proteins should be targeted in order to promote effective differentiation of leukemic stem cells is the next important step in designing new therapies against these cancers. We are also actively working on the epigenetic dys-regulation of leukemia stem cells, using our models of AML. We are particularly focused on methylation of lysine and arginine histone residues.

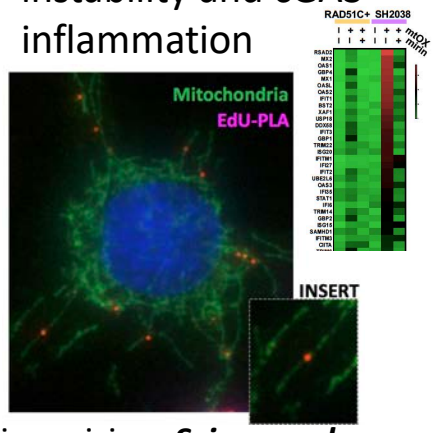
A tutorial with us provides experience in mouse work (in vivo leukemia studies), flow cytometry, next generation sequencing (ChIp-seq, RNA-seq and exome sequencing), immunofluorescence and cytology.

## Schlacher lab



(Pandemic-caused artistic patchwork interpretation of current group picture)

Mitochondria genome instability and cGAS inflammation

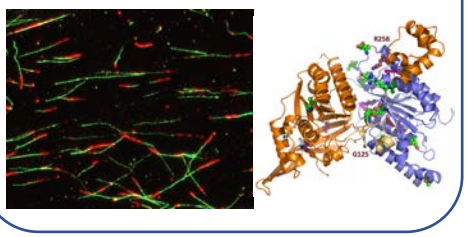



in revision, ***Science adv.***

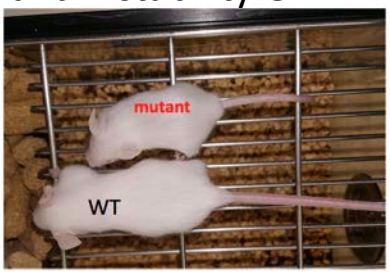
## DNA REPLICATION STABILITY FOR CANCER PREDICTION, TREAMTENT AND PREVENTION

Genome stability is a determining hallmark of development, fertility, neurodegeneration, cancer, chemo- and immunotherapy response. Our research focuses on DNA replication fork stability in the nucleus and in our most recent research expands to the mitochondrial genome. We are especially interested in the mechanistic and molecular foundational understanding to eventually inform clinical efforts for next-generation targeted therapy of the above phenotypes. Our research tools include newly developed single-molecule and single-cell microscopy in human cells and patient samples, as well as mouse models to unravel several exciting projects on DNA replication stability in the nucleus and mitochondria.

BRCA1/2/3, p53 + new in Breast, Ovarian & Heme Ca



Fanconi Anemia cancer and instability GEM




in revision, ***Nature comm.***

If you are **curious, motivated, have a strong desire to learn and innovate**, or want to simply find out more, just shoot an email our way to Katharina Schlacher, Associate Professor, Dep. of Cancer Biology, kschlacher@mdanderson.org


Roy et al, ***eLife***, 7. pii: e31723, **2018**
Schlacher, ***Nature***, 563(7732):478-480, **2018**
Roy et al, ***JCB***, 7. 217(4):1521-1536, **2018**
Schlacher, ***Cancer Cell***, 22(1):106-16, **2012**
Schlacher, ***Cell***, 145(4):529-42, **2011**



**Current Funding**
NIH (RO1)
CPRIT (RO1 equivalent)
CPRIT (PO1 equivalent)
Rita Allen Foundation (Scholar award)

# *Seeking 1 Graduate Student*

PI/ Professor: Ambro van Hoof PhD
Microbiology and Molecular Genetics, UTH Medical School
Contact: ambro.van.hoof@uth.tmc.edu

## “RNA processing and degradation in health and disease”

**Research** The generation of mature functional RNAs requires a wide variety of RNA processing steps that are each tightly regulated to control gene expression. Many of the RNA processing reactions require RNases. The same RNases also degrade RNAs when they become damaged, are misprocessed, or are no longer needed. Thus, during its life-time each RNA molecule is acted on by a number of different RNAses. The van Hoof lab studies how these RNases contribute to the gene expression program. Current reasearch in the van Hoof lab focuses on two RNases that are both multi-subunit protein complexes and mutated in pontocerebellar hypoplasia patients. Our research is supporterd by two NIH R01 grants (GM099790 through 2021 and GM13047 through 2022).

The RNA exosome acts on a wide variety of RNAs, yet is very specific for those RNAs. For example it degrades normal cellular mRNAs very slowly, but degrades aberrant mRNAs very rapidly. These aberrant mRNAs include mRNAs that have been cleaved by RNAi or any other RNase, mRNAs that lack a stop codon and viral mRNAs. We take advantage of the known structure of the RNA exosome and the power of yeast genetics to understand the mechanisms by which the RNA exosome acts specifically on its substrate RNAs.

One explanation for why tRNA splicing endonuclease (TSEN) and RNA exosome mutations both cause pontocerebellar hypoplasia is that they act in concert to degrade a specific RNA during neuronal development. It is therfore important to understand TSEN specificity. In contrast to the RNA exosome, the TSEN is only known to act on two RNAs. TSEN derives its name from its ability to cut introns out of tRNAs, but also cleaves one mRNA. Cleavage of this mRNA triggers further degradation by the RNA exosome. We have used yeast genetics combined with transcriptome sequencing to identify a small number of other mRNAs cleaved by TSEN, and map the cleavage sites.

**Training environment**. Students in the van Hoof lab work independently on their own project. This is reflected by all past students publishing papers with a limited number of co-authors in high profile journals suchs as PNAS, Molecular Cell, EMBO J. and Nature Structural and Mol. Biology and/or in leading society journals such as Genetics and RNA.

A project in the van Hoof lab exposes students to standard molecular biology techniques, forward and reverse genetic approaches to generate strains with mutations of interest, and RNA analysis by Northern blotting, qRTPCR, and transcriptome sequencing. The use of yeast means that an individual graduate student can be readily generate and test their own hypotheses. The genome of yeast is also small enough that we can easily identify mutations of interest. Because they diverged relatively recently, most of the genes and pathways implicated in human disease are conserved between yeast and human. Yeast research has a long track record of leading to fundamental understanding of molecular and cellular mechansims that are fundamental to all eukaryotes.

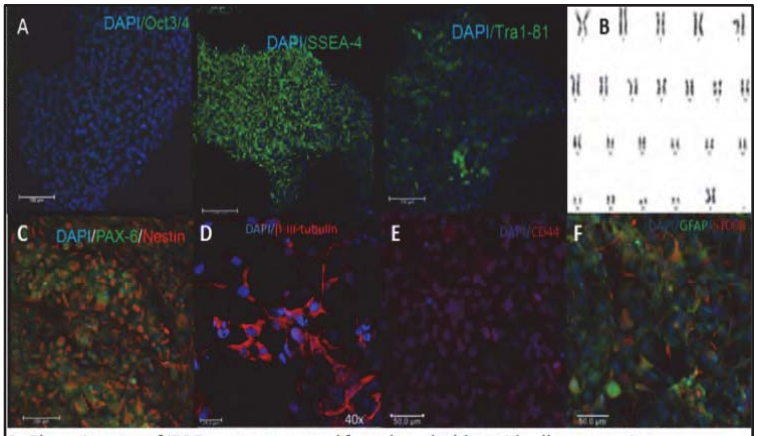
Ambro van Hoof is an experienced mentor who has trained 13 PhD students in three different programs. Most have subsequently obtained post-doctoral fellow positions at prestigious univeristies (Duke, UNC, UT Southwestern, BCM, UT MD Anderson) while others have directly moved into desired positions in biotech or health care industry (Regeneron, PPD, Houston Methodist). They all have used their yeast genetics training in other areas.

# Consuelo Walss-Bass, PhD

Associate Professor, Department of Psychiatry and Behavioral Sciences – UTHealth
**Contact**: Consuelo.WalssBass@uth.tmc.edu

The central focus of the Walss-Bass laboratory is to identify the genetic causes of severe psychiatric disorders such as schizophrenia, bipolar disorder and substance use disorders. Despite tremendous advances in genetics, molecular/cellular biology, and psychopharmacology, the fundamental biological nature of psychiatric disorders remains largely elusive. To address this problem, our laboratory utilizes a model of collaboration and dialogue between investigators working in the laboratory and investigators working directly with patients, to correlate behavioral outcomes with genetic underpinnings and biological mechanisms, in order to understand the biology behind psychiatric disorders.

The Walss-Bass lab utilizes genomic and proteomic techniques, in both humans and animal models, to investigate how changes in DNA sequence and epigenetic modifications cause changes in protein function, which in turn causes changes in brain function and behavior, and how this may lead to development of mental disorders. One key area of investigation focuses on understanding the role that the immune system plays in development of mental illnesses. We know that stress (either social stress or biological stress due to infections or illness) plays an important role in activating the immune system, and this in turn can have serious consequences in individuals who have a genetic predisposition to develop psychiatric disorders.




**A.** Phase images of iPSCs reprogrammed from lymphoblastoid cells, expressing pluripotent markers Oct4, SSEA4 and TRa1-81. **B.** The iPScs maintain a normal karyotype. **C.** NPCs are positive for PAX-6 and Nestin. **D.** Neuronal cells as positive for β-III-tubulin. **E.** LCL-derived astrocytes are positive for CD44. **F.** Astrocytes are positive for GFAP/S100B.

Dr. Walss-Bass established the UTHealth Brain Collection resource to help study brain disorders and create healthy changes for future generations. Brain tissue provides a crucial resource for understanding the biological causes of mental illness and other psychological challenges, such as substance abuse. In addition, Dr. Walss-Bass currently focuses on development of human induced-pluripotent stem cells and subsequent differentiation into neuronal cells and astrocytes to obtain virtual brain biopsies of individuals with psychiatric disorders.

Some questions we are trying to answer:

- What makes certain individuals vulnerable to developing different psychiatric disorders? How do changes in genetic/epigenetic architecture contribute to changes in biological functions that affect the outcome of mental illnesses?
- How can mental illness be treated if we know which genes are not working?
- Why do some mentally ill patients respond well to medications and others do not?

https://med.uth.edu/psychiatry/faculty/consuelo-walss-bass/

# PI: Bin Wang PhD

Associate Professor
Department of Genetics
UT MD Anderson Cancer Center, Houston TX
Email: bwang3@mdanderson.org

## Genome Maintenance/Tumor Suppression-
## *Cellular responses to DNA damage and replication stress*

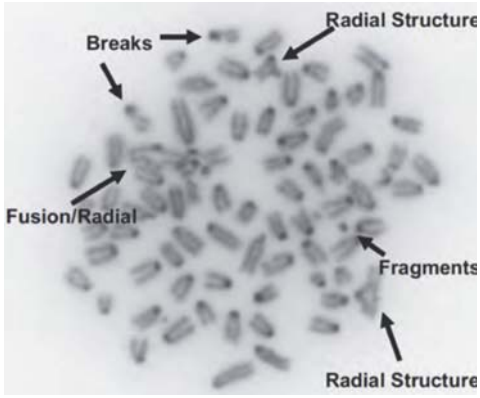
**Research Interests:** A hallmark of cancer is genomic instability. Our research is focused on understanding how cells respond to DNA damage, safeguard the integrity of the genome and prevent the development of cancer.

**Ongoing Projects:**

(1) how the hereditary breast tumor suppressor BRCA1 interaction network suppresses breast tumor development (*Castillo et al, Cell Rep 8, 807-817, 2014; Wu et al, Mol Cell 61, 434-448, 2016*);

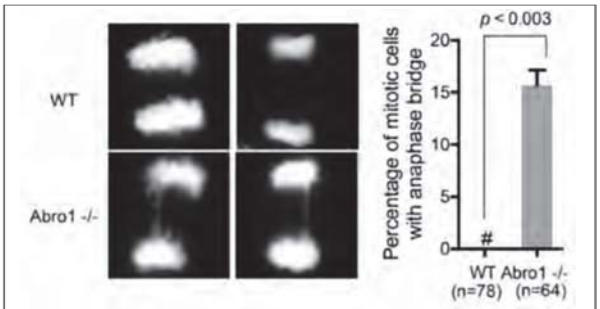
(2) how chromatin modification at sites of DNA damage regulates DNA repair and transcription (*Paul and Wang, Mol Cell 66, 458-472, 2017; Wu et al, Genes Dev 33, 1702-1717, 2019)*);

(3) how the cell protects genome stability in response to DNA replication stress (*Xu et al, Genes Dev 31, 1469-1482, 2017*).




Chromosome aberrations in a BRCA1-intearcting protein, Abraxas, -deficient cells.

**Approach:** We use a combinatory functional and molecular approach that involves imaging, CRISPR/Cas9 gene editing, genetics screens, high throughput sequencing, mass spectrometry, mouse model, etc.




Defect in DNA replication stress response leads to increased chromosome instability (increased anaphase bridge during mitosis) in Abro1-/- cells

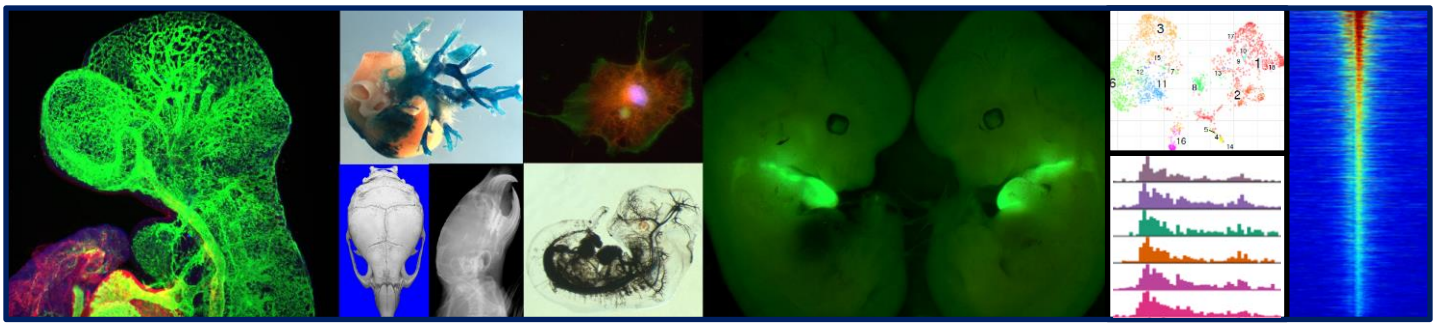
**Environment:** Our lab currently has six members including postdoctoral fellows and graduate students. Trainees in our lab have multiple opportunities to collaborate with and present their findings to the research community. We welcome motivated students who wish to advance their training and career goals by tackling some of the fundamental issues facing the understanding and treatment of cancer.

# PI: Jun Wang, PhD

Assistant Professor
Department of Pediatrics, McGovern Medical School
The University of Texas Health Science Center at Houston
Email: jun.wang@uth.tmc.edu
Website: https://med.uth.edu/pediatrics/faculty/jun-wang-ph-d/

## "Molecular regulation of heart and head development, diseases and regeneration"

Wang lab research is aimed at understanding signaling pathways such as Hippo, Wnt and Bmp pathways as well as non-coding RNAs in regulating craniofacial and cardiovascular development, diseases and regeneration, using approaches include a combination of genetic mouse models, molecular and biochemical techniques, imaging, cell culture and manipulation, genomics, proteomics, CRISPR-Cas9 genome editing and next generation sequencing techniques.



Research focus in the Wang lab: 1) the migrating multipotent cells named Neural Crest Cells (NCCs). NCCs make significant contribution to many different tissues and organs including the heart and head. 2) Cardiac Conduction System (CCS) homeostasis and regeneration. Dysfunction of CCS leads to cardiac arrhythmia, a major cause of death worldwide. 3) Congentital Heart Diseases (CHDs), the most common birth defects occur in everyone 1 out of 100 newborns.
For more information, please check our website: https://med.uth.edu/pediatrics/wang-lab/research/ .

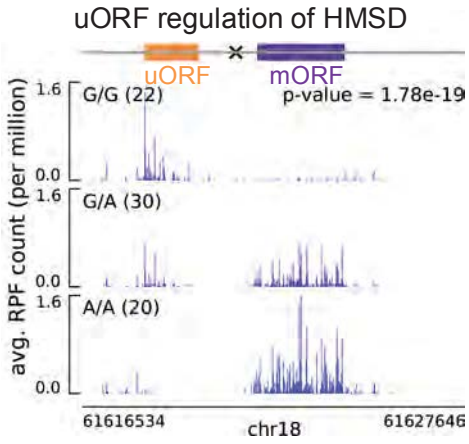
**Environment**. The PI has been devoted to on mentorship to advance students' training and reach their career goals. Wang lab, consist of postdoctoral fellows, graduate students, research associate and research assistant, is a highly collaborative team. Incoming students will take advantage of both in-lab collaborations and active collaborations with other labs including local collaborations at UT Health, MD Anderson Cancer Center, and Baylor College of Medicine, as well as national and international collaborations. We are currently well supported by funds from NIH, DOD and UT.

# Functional genomics laboratory recruiting students!

## PI: Sidney Wang PhD

Center for Human Genetics, Institute of Molecular Medicine, McGovern Medical School
**Contact**: hsi.ming.s.wang@uth.tmc.edu

Regulation of gene expression is fundamental to a wide range of biological processes. From cell fate determination during development to malignant transformation during tumorigenesis, precise control of gene expression forms the basis of these processes.
Our current understanding of gene regulation is, however, far from complete. Most published studies that profile gene expression are transcript-centric (i.e. they focus on measuring mRNA levels and levels of transcription factor binding). Our research program takes an integrative approach in order to better understand the principle of gene regulation and how it impacts critical biological processes. In particular, we focus on elucidating the impact and the principles of translational regulation of gene expression. Ongoing projects in the lab include: 1. Developing novel methods to systemically study RBP binding and its role in translational regulation. 2. Association mapping to identify genetic variants impacting translational regulation. 3. Functional validation of more than 7,000 novel coding regions we previously identified. 4. Developing tools for functional upstream Open Reading Frame (uORF) annotation and for investigating regulatory functions of uORFs. In addition, we are collaborating with other labs to investigate the role of translational regulation in muscle regeneration, cancer progression, and neuron differentiation.




*Using fine structures in ribo-seq data we have identified more than 7,000 novel coding regions in the human genome. These include regions in "non-coding" transcripts and additional translated ORFs in coding transcripts. A major effort of the group focus on functionally validating these regions, evaluating regulatory impact, and further developing tools to better study these and other novel genomic features. The diagram illustrates our previous results in identifying a novel translated region (uORF) at the HMSD locus. We found the uORF to negatively regulate translation of HMSD. We further identified a variant associated with the regulatory property of uORF.*

**Environment**

We are a small group of quantitative biologists interested in studying fundamental questions with new tools. Students in the laboratory have the opportunity to receive trainings in performing wet lab molecular biology experiments and dry lab statistical analyses of next generation sequencing data.

**Application**

Interested students are encouraged to directly contact Dr. Wang via email.

***Seeking One Graduate Student***


## PI/ Assistant Professor:  Han Xu, PhD

Epigenetics and Molecular Carcinogenesis, UT MD Anderson Cancer Center, Science Park, Smithville TX
Contact:  hxu4@mdanderson.org


## "CRISPR solutions for cancer drug target discovery"

In cancer drug target discovery, three questions are frequently asked: i) Which protein is the target for cancer treatment? ii) Which domain of the protein is the target for effective inhibition of the protein function? iii) Which biomarker(s) can be used for patient stratification? CRISPR-based functional screens have been proven to be powerful solutions to these questions. With large-scale pooled CRISPR screens, one can assess the functional importance of tens of thousands of proteins in a single experiment. With a CRISPR tiling-sgRNA screen, one can accurately identify the protein domains that are essential for tumor growth. Integration of CRISPR screens and genomic/transcriptomic data facilitates the search for reliable biomarkers, by which the right patient will be treated with the right drug.

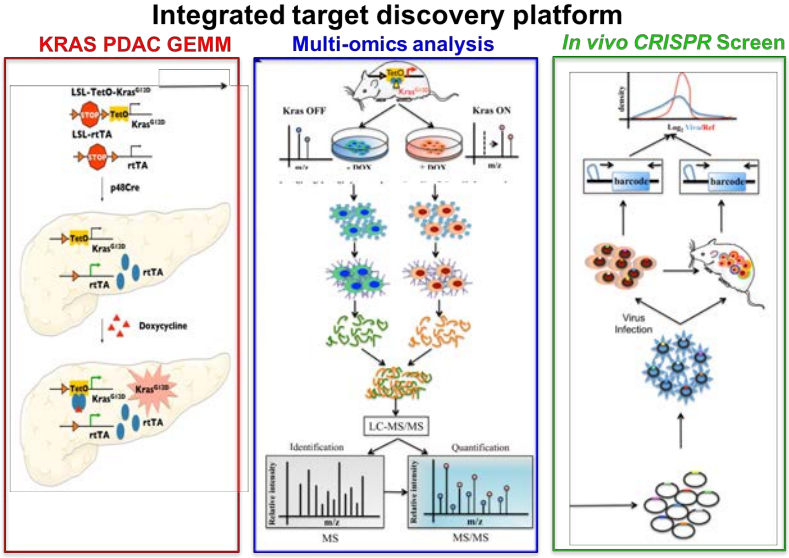
Our laboratory combines state-of-the-art biotechnologies and computational algorithms to develop optimized CRISPR solutions for cancer drug target discovery. Experimentally, our biologists are developing new vector systems and protocols to boost the performance of CRISPR screens, and are applying these systems for various biological studies through collaboration projects. Computationally, we have developed MaGeCK (Model-based Analysis of Genome-wide CRISPR/Cas9 Knockout), a widely-recognized tool for the analysis of CRISPR screens. We have also used machine-learning algorithms to predict effective sgRNAs for rational design of CRISPR libraries. Currently our computational scientists are working on the next-generation of software tools that implement novel library design rules and analysis pipelines. Through the integration of biotechnological improvement and advanced computational algorithms, we aim to establish powerful CRISPR platforms to accelerate the pace of cancer drug development.

**Environment**.  Our laboratory highly values interdisciplinary discussion and knowledge expansion through internal meeting, journal club, training and collaborations. Graduate students will be trained in both biochemistry and bioinformatics. The lab currently has two experimental postdocs, three computational postdocs, and a lab manager. The lab members are from various disciplines, including biochemistry, computer science, physics, and mathematics. We encourage graduate students and postdocs to present their work in national or international meetings each year. The lab is well-funded for the next three years.

# Wantong Yao Laboratory-Pancreatic Cancer Research

Contact: Wantong Yao, M.D., Ph.D.
UT MD Anderson Cancer Center
Contact: wyao2@mdanderson.org
Lab webpage: https://www.mdanderson.org/research/departments-labs-institutes/labs/yao-laboratory.html

**Research Summary** Pancreatic cancer is recognized as "King" cancer, with the worst prognosis and lowest survival of all major human cancers. Pancreatic cancer is a leading cause of cancer death largely due to the lack of early diagnostic markers and effective therapies in clinic. Thus, there is an urgent need to explore the basic and translational problems of this cancer type, with a long-term goal to improve pancreatic cancer prevention, diagnosis and treatment intervention for our patients. My laboratory is geared towards identifying accessible therapeutic targets for oncogenic signaling and function in pancreatic cancer, and further deeply understanding the molecular insights into the complicated array of oncogene driven tumorigenic events, in order to discover novel therapeutic approaches that targets mechanism essential for pancreatic cancer cell survival. The PI, Dr. Yao has been focusing on pancreatic cancer translational research for more than 15 years and is grantee of Pancreatic Cancer Action Network and Hirshberg Foundation for Pancreatic Cancer Research in US. *Dr. Yao would like to inspire, mentor and work with the next generation of scientists to study this lethal cancer type, desiring to cure it*.




Pancreatic cancer is unique among human cancers because its genetic landscape is dominated by a single oncogene, active mutant Kras, which occurs in > 90% of all pancreatic cancer cases and has been widely investigated as a potential marker and therapeutic target for pancreatic cancer. We have been focusing on gaining deep molecular insights into the oncogenic Kras -dependent and –independent events driving pancreatic cancer progression and maintenance. We have identified a key function of Hippo/YAP pathway in the bypass of KRAS-dependency in pancreatic cancer (***Cell, 2014***). More recently, our work on KRAS-driven surfaceome analysis leads to the identification of Syndecan1 and its vesicle trafficking pathway as critical players for therapeutic target development (***Nature, 2019***). We believe that our research background and current research programs match the interest of students in G&E program. *Please feel free to contact us if you would like to learn in details about our research programs.*

**Environment** We have lab meeting and journal club alternate every week. All trainees have opportunity to attend a national or international meeting each year. The lab currently has eight members: PI, one senior scientist, three postdocs, two graduate students, one lab tech, and our lab manager. Through diverse academic activities and social gatherings, we create a cohesive and flexible environment to foster ideation and collaboration with the strongest and most well-rounded pancreatic cancer researchers and clinicians across institution. *Our laboratory has funding and projects to support two new graduate students*.

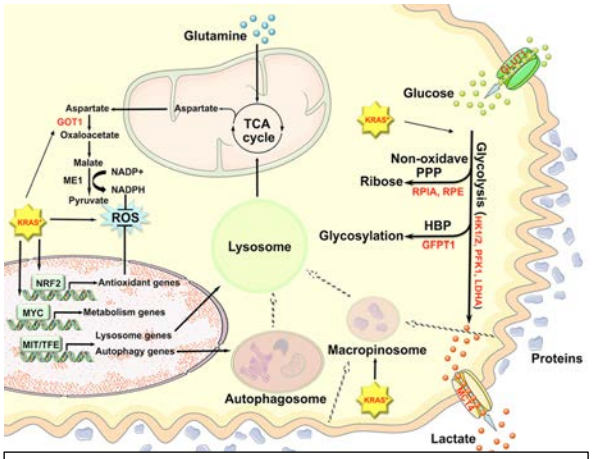
## *Seeking Graduate Student*


## PI: Haoqiang Ying, MD, PhD

Associate Professor, Molecular and Cellular Oncology, MD Anderson Cancer Center
Contact: hying@mdanderson.org


### Research Summary

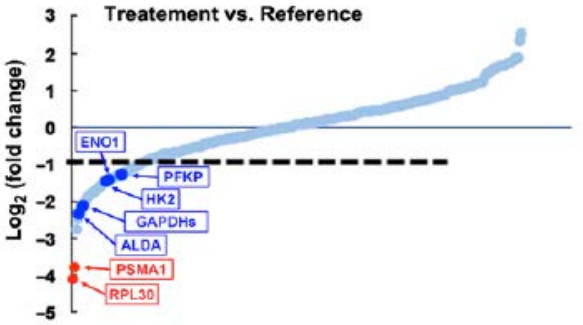
The Ying lab focuses on defining the pathways driving the pathogenesis of solid tumors, including pancreatic cancer and soft tissue sarcoma. We are using both genetic and biochemical approaches to characterized the roles of key cancer genes in metabolism reprogramming, tumor microenvironment and cellular lineage specification.




**Metabolism reprogramming of pancreatic cancer**

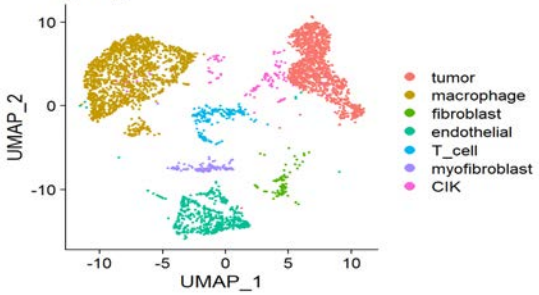
### Research Projects

*Targeting YAP1 oncogene in pancreatic cancer.* At the transcriptome level, pancreatic cancer is classified into several major clinically relevant subtypes, among which the squamous subtype exhibits the worst prognosis. Our recent work has identified YAP1 oncogene as a major driver for the squamous subtype tumors. We are several novel **genetically engineered mouse models** and **single cell technologies** to study 1) the role of YAP1 pathway during tumor maintenance; 2) the function of YAP1 in tumor microenvironment; and 3) modeling the therapeutic response of systematic YAP1 inhibition.




**In vivo loss-of-function screen to identify metabolism targets that sensitize pancreatic tumors to targeted therapy.**

*Metabolism reprogramming of pancreatic cancer.* Pancreatic cancer is characterized by an extensive fibrotic microenvironment, with a lack of effective blood supply that results in oxygen and nutrient deprivation. Tumors address these challenges through rewiring of metabolism programs to sustain nutrient supply and maintain redox homeostasis. We have made extensive contributions to the field of pancreatic cancer metabolism. We are employing **CRSPR-based genetic screens** in combination with **organelle metabolomics** and **isotype-labeled tracings** to characterize tumor-specific metabolism dependencies and develop novel therapeutic strategies. Ongoing projects include 1) unraveling the role of mannose metabolism on the nutrient salvage of pancreatic cancer; and 2) targeting novel lipid synthesis pathways to disrupt redox balance of pancreatic cancer.




**Single cell RNAseq of human undifferentiated pleomorphic sarcoma**

*Genetics and biology of soft tissue sarcoma.* Soft tissue sarcomas (STSs) are a collection of rare tumor types originated from the mesenchymal tissues. Recent large scale genomic studies, such as the TCGA project, have identified a collection of potential cancer drivers that are frequently mutated in STS. However, the function of these gene mutations remains poorly understood, largely due to lack of relevant preclinical models that faithfully recapitulate the genetics and biology of STS. To address this, we have successfully established novel genetically engineered mouse models and **patient-derived models** of STS to decipher the role of key cancer drivers in the regulation of lineage commitment and intra-tumoral heterogeneity using single cell technologies.

# PI: Momoko Yoshimoto MD, PhD

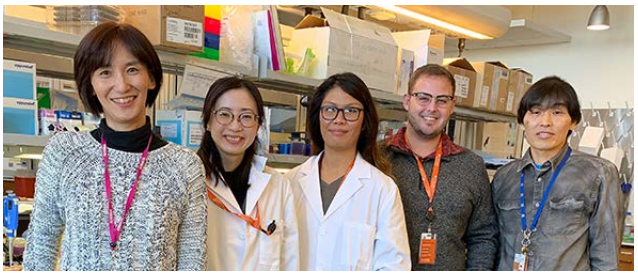
## Associate Professor

Center for Stem Cell Regenerative Medicine,
Institute for Molecular Medicine,
University of Texas Health Science Center at Houston
Momoko.Yoshimoto@uth.tmc.edu
**Lab website**: https://momokomykobay.wixsite.com/yoshimotolabwebsite

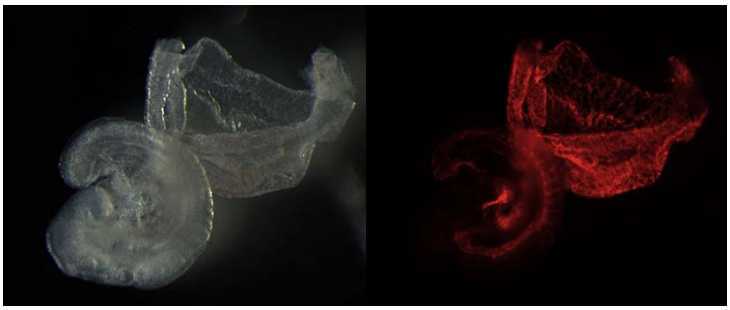

## *HSC and Immune Cell Development in the Mouse Embryo: Where do they come from and what are their contributions in the postnatal immune system?*

Hematopoietic stem cells (HSCs) reside in the bone marrow and produce all types of blood and immune cells throughout life. HSCs are first detectable in the mid-gestation of the mouse embryo; however, various blood cells, including innate lymphoid precursors already exist before the appearance of HSCs. We aim to understand molecularly how the first HSCs and immune cells are produced in the mouse embryo in the first place and how they contribute to postnatal immune system.

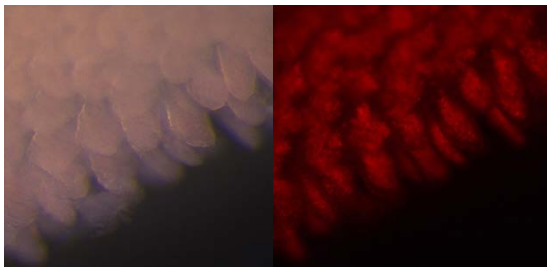
You can learn various transgenic/knock-out mouse models, lineage tracing mouse models, multi-color flow cytometry analysis/sorting, cell culture, human and mouse PSC culture, transplantation, immunhisto staining, qPCR, RNA-, and ATAC-sequencing, etc.



***We are dedicated to answer unsolved scientific questions in the field of developmental hematology-Immunology.***

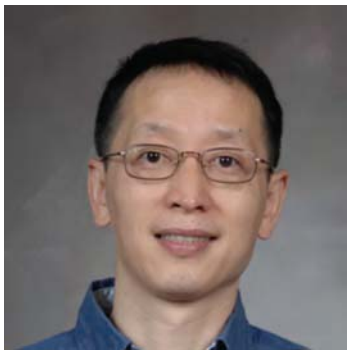


Endothelial-lineage tracing embryo. Endothelial cells were labeled at E8.5 and observed at E9.5



Adult mouse intestine. Lymphocytes are labeled Tomato+ in the villi.

## Seeking 1 Graduate Student



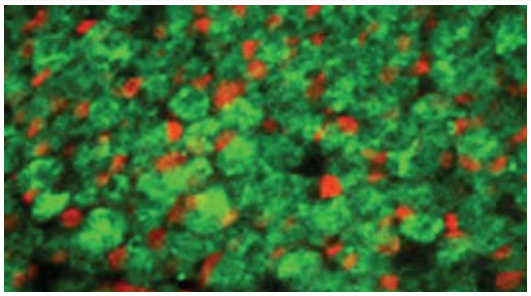
# PI/ Associate Professor: Sheng Zhang PhD

Brown Foundation Institute of Molecular Medicine
Department of Neurobiology and Anatomy
GSBS and McGovern Medical School at UTHealth
Contact: Sheng.Zhang@uth.tmc.edu

### "Confronting Neurodegenerative Diseases: A New Frontier"

Neurodegenerative disorders such as Alzheimer's disease (AD), Parkinson's disease (PD) and Huntington's disease (HD) are inflicting unbearably high emotional and financial toll to patients and their families, and together poses a pressing threat to the wellbeing of our society. However, currently there is no effective cure or preventions against any of these debilitating maladies.

One common pathological hallmark of almost all the neurodegenerative diseases is the presence of abnormal protein deposits, often known as tangles and plaques, in the affected brains. Cells normally operate several robust self-maintenance machineries, including *chaperones* that facilitate proteins to stay in shape, and *autophagy* (meaning "self-eating" in Greek) that cleans up and recycles worn-out or toxic cellular materials. These self-protective mechanisms often become inefficient or nonfunctional in aging neurons, causing and/or contributing to the brain diseases.



Abnormal protein deposits (red dots) in neurons (green) defective for autophagy

Using model organism *Drosophila* and mammalian systems, we study how disease genes, such as Huntingtin in HD and Parkin in PD, normally function in cells, and how *chaperones* and *autophagy* operate to recognize and efficiently clear mutated proteins and toxic agents, while spare and protect normal cellular constituents. Our goal is to harness these innate self-protective machineries to fight against ageing-related brain diseases.

**Research Projects**

- Mechanisms of protein folding and clearance pathways in brain degenerative disorders
- Functions of Huntingtin in autophagy and its perturbation in Huntington's disease
- Subcellular handling of neurotransmitter dopamine and Parkinson's disease
- Biogenesis of subcellular organelles (e.g., lysosome-related organelles) and human diseases

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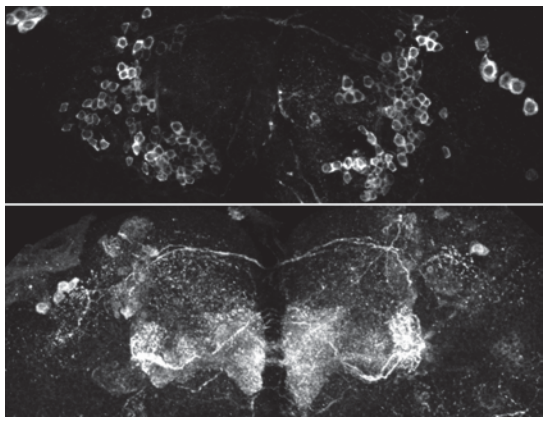


Dopamine neurons (top) and neurotransmitter dopamine (bottom) in *Drosophila* brains.

**Applying**. We look forward to motivated students to explore this new and important frontier, helping us to understand and fight these still un-curable brain diseases. We have NIH R01 grants to support new students.

***Seeking 2 Graduate Students***

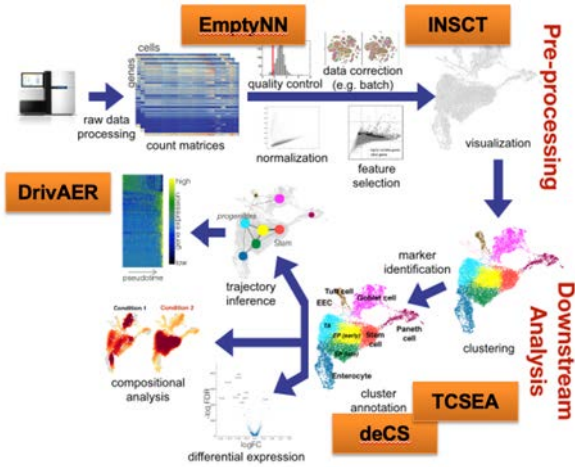
# PI/ Professor: Zhongming Zhao PhD

Center for Precision Health, School of Biomedical Informatics, UTHealth
Contact: zhongming.zhao@uth.tmc.edu

## "Deep learning for decoding genetic regulation and cellular maps in complex disease"

Dr. Zhao has broad interests in the areas of bioinformatics, machine learning, precision medicine, and data science. Representative projects are below. The students may work with Dr. Zhao to identify a long-term project for thesis.

**Predicting Phenotype by Deep Learning Heterogeneous Multi-Omics Data.** In this NIH renewal R01 project, we will develop a deep learning method for variant impact predictor, DeepVIP, single cell dense module search of GWAS signals (scGWAS) and a graphical neural network approach (GNN-scTP) to power the feature analysis from heterogeneous multi-omics data. These methods will be applied to 16 neurodevelopmental and neurodegenerative disorders and broad phenotypes using Vanderbilt Biobank (BioVU) and UK Biobank data.




Single cell omics methods and tools developed in BSML lab.

**Single cell sequencing approaches for studying early development and complex disease** (supported by a new R01 grant)

**Exploring big biomedical data for drug repositioning.**

**Environment**. The Bioinformatics and Systems Medicine Laboratory (BSML, web: uth.edu/bioinfo), directed by Dr. Zhao, has been very productive since it was originally founded in Vanderbilt University Medical Center in 2009 and later moved to UTHealth in 2016. The lab is in an interdisciplinary research environment, currently with 13 members in total (facultyx5, students x4, postdocs x1, research scientists x2, research coordinator x1). The lab has developed many NGS analysis pipelines, statistical methods, computational tools, biomedical databases, as well as conducted many discovery works in genomics, single cell omics, machine learning, and precision medicine areas. Dr. Zhao has trained over 70 students and postdocs (24 have become faculty, two CPRIT scholars).

**Applying**. We encourage those students who are interested in genomic medicine and translational bioinformatics to apply. We have several NIH/CPRIT grants as well as Dr. Zhao's startup and chair professorship fund. In addition, there is a recent CPRIT training grant titled "Biomedical Informatics, Genomics and Translational Cancer Research Training Program (BIG-TCR)".

*Seeking Graduate Student*

# PI/ Associate Professor: Degui Zhi PhD

School of Biomedical Informatics UTHealth, Center for Precision Health, Houston TX
Contact: Degui.Zhi@uth.tmc.edu

Our group is interested in using big data to advance precision medicine and health. We develop new algorithms and models for the big genetic and phenotypic data collected from biobanks and eletronic health records, and making new insights that are not possible with smaller scale data.

**Population genetics informatics**

Modern biobanks include genotypes up to 0.1%-1% of an entire large population. At this scale, genetic relatedness among samples is unavoidably ubiquitous. However, current methods are not efficient for uncovering genetic relatedness at such a scale. We developed ultra-efficient methods [https://github.com/ZhiGroup/RaPID] for detecting Identical-by-Descent (IBD) segments, a primary embodiment of genetic relatedness. Our RaPID method detected all IBD segments over a certain length orders of magnitude faster than existing methods, while offering higher power, accuracy, and sharper IBD segment boundaries.

We believe identifying IBD segments in population scale cohorts are the first step towards construction population scale genealogy which will be a fundamental infrastructure for future human society. We are enthusiastically working on improvement of the RaPID methods, and extending population genetics and statistical genetic approaches that leverage the information revealed by RaPID.

**Phenotyping of electronic health record (EHR) and imaging data using deep learning**

Large databases containing Patients' EHR data and imaging data are becoming available. This allows developing representation models that describe the inherent health status and treatment history of a patient. With access to multiple EHR databases with over 50 Million patients and biobank imaging data, we develop deep-learning-based phenotyping methods for uncovering the logic of medical practice and for multi-Omics integrative modeling.

**Environment.** We are a vibrant lab composed of around 3-6 graduate students and postdocs. The PI is devoted to mentoringship and the scientific and career growth of trainees. We have weekly group meetings, project team meetings, as well as one-on-one meetings with the PI. Our lab has extensive collaboration with other labs in school of biomedical informatics, school of public health, and other labs at the medical center and beyond. Students are expected to lead an individual project while at the same time collaborating in a team environment.

**Applying.** We encourage interest from ambitious trainees who are comfortable with working with biomedical big data and wish to pursue a career of informatics-driven discovery.