Genetics and Epigenetics Program

Research Summaries of Faculty Seeking Students

Partial List 8/22/22

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

Richard Behringer, PhD
Genetics, MDA

Jichao Chen, PhD
Pulmonary Medicine – Research, MDA

Jinjie Chen, PhD
Experimental Radiation Oncology, MDA

Xiaodong Cheng, PhD
Epigenetics & Mol. Carcinogenesis, MDA

Francesca Cole, PhD
Epigenetics & Mol. Carcinogenesis, MDA

Giulio Draetta, MD, PhD
Genomic Medicine, MDA

George Eisenhoffer, PhD
Genetics, MDA

Michael Galko, PhD
Genetics, MDA

Boyi Gan, PhD
Experimental Radiation Oncology, MDA

Yeijing Ge, PhD
Cancer Biology, MDA

Vidya Gopalakrishnan, PhD
Pediatrics, MDA

Michael Green, PhD
Lymphoma-Myeloma, & Genomic Medicine, MDA

Michelle Hildebrandt, PhD
Epidemiology, MDA

Raghu Kalluri, MD, PhD
Cancer Biology, MDA

Georgios Karras, PhD
Genetics, MDA

Wenbo Li, PhD
Biochemistry & Molecular Biology, UTHealth Houston

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

Han Liang, PhD
Bioinformatics & Computational Biology, MDA

Yonathan Lissau, MD, PhD
Thoracic & Cardiovascular Surg – Research & Genomic Medicine, MDA

Guillermina Lozano, PhD
Genetics, MDA

Kevin McBride, PhD
Epigenetics & Mol Carcinogenesis, MDA

Joseph McCarty, PhD
Neurosurgery, MDA

Dianna Milewicz, MD, PhD
Internal Medicine – Medical Genetics, UTHealth Houston

Rachel Miller, PhD
Pediatrics, UTHealth Houston

Margarida Santos, PhD
Epigenetics & Mol. Carcinogenesis, MDA

Katharina Schlacher, PhD
Cancer Biology, MDA

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

Peter Van Loo, PhD
Genetics, MDA

Bin Wang, PhD
Genetics, MDA

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

Jun Wang, PhD
Pediatrics – Research, UTHealth Houston

Han Xu, PhD
Epigenetics & Mol. Carcinogenesis, MDA

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

Zhongming Zhao, PhD
School Biomedical Informatics, UTHealth Houston
# G&E Faculty Seeking Students

Faculty are listed in one or two categories

## Cancer Genetics
- C. Marcelo Aldaz, PhD
- Swathi Arur, PhD
- Junjie Chen, PhD
- Giulio Draetta, MD, PhD
- George Eisenhoffer, PhD
- Boyi Gan, PhD
- Yejing Ge, PhD
- Vidya Gopalakrishnan, PhD
- Michael Green, PhD
- Raghu Kalluri, MD, PhD
- Wenliang Li, PhD
- Han Liang, PhD
- Yonathan Lissanu, MD, PhD
- Guillermima Lozano, PhD
- Joseph McCarty, PhD
- Katharina Schlacher, PhD
- Peter Van Loo, PhD
- Bin Wang, PhD
- Han, Xu, PhD

## Developmental Genetics
- Swathi Arur, PhD
- Richard Behringer, PhD
- Jichao Chen, PhD
- Francesca Cole, PhD
- George Eisenhoffer, PhD
- Michael Galko, PhD
- Joseph McCarty, PhD
- Dianna Milewicz, MD, PhD
- Rachel Miller, PhD
- Jun Wang, PhD
- Momoko Yoshimoto, MD, PhD
- Sheng Zhang, PhD

## Epigenetics
- Blaine Bartholomew, PhD
- Jichao Chen, PhD
- Xiaodong Cheng, PhD
- Boyi Gan, PhD
- Yejing Ge, PhD
- Vidya Gopalakrishnan, PhD
- Michael Green, PhD
- Raghu Kalluri, MD, PhD
- Georgios Karras, PhD
- Wenbo Li, PhD
- Wenliang Li, PhD
- Han Liang, PhD
- Yonathan Lissanu, MD, PhD
- Margarida Santos, PhD
- Ambro van Hoof, PhD
- Peter Van Loo, PhD
- Jun Wang, PhD
- Han Xu, PhD
- Zhongming Zhao, PhD

## Genome Maintenance & Repair
- Blaine Bartholomew, PhD
- Junjie Chen, PhD
- Xiaodong Cheng, PhD
- Francesca Cole, PhD
- Kevin McBride, PhD
- Margarida Santos, PhD
- Katharina Schlacher, PhD
- Bin Wang, PhD

## Human Genetics
- C. Marcelo Aldaz, PhD
- Michelle Hildebrandt, PhD
- Georgios Karras, PhD
- Wenbo Li, PhD
- Dianna Milewicz, MD, PhD
- Hsi Ming (Sidney) Wang, PhD
- Zhongming Zhao, PhD
My laboratory was the first to discover and clone WWOX (WW domain containing oxidoreductase) the target gene of chromosomal fragile site FRA16D, the 2nd most common site for spontaneous chromosomal breakage, deletion, and rearrangement in the human genome. Germline and somatic mutations affecting WWOX are common and intimately linked to an array of diverse human pathologies. In cancer WWOX behaves as a tumor suppressor. Deletions affecting WWOX and loss of expression are frequent in multiple cancers and indicative of poor prognosis. WWOX translocations and deletions are common in multiple myeloma a malignancy of plasma cells (differentiated B cells). Understanding the role of WWOX in multiple myeloma is a topic of interest in our lab.

Recent landmark studies by our lab and others have identified WWOX loss-of-function germline (i.e. familial) mutations as the culprit for neurodevelopmental, epileptic, and ataxic phenotypes of varying severity based on the level of WWOX dysfunction. Importantly, recent large-scale genome-wide association metanalyses and biomarker studies have also identified WWOX as a risk gene for common neurodegenerative conditions such as Alzheimer’s disease, Parkinson’s disease, and multiple sclerosis. Thus, the spectrum of complex brain disorders associated with WWOX is broad and heterogeneous, and there is little understanding of potential mechanisms at play. Studies to understand the role of WWOX in central nervous system development and pathology are major goals in our lab.

Cancer genomics and cancer chemoprevention are other areas of much interest in the lab. Ongoing studies in the lab are related to the translation of novel therapeutic and preventive approaches for breast and lung cancer. For example, we are currently carrying preclinical studies on the ‘Repurposing of the Macrolide Antibiotic Clarithromycin for the Prevention of Lung Cancer’.

We are always interested in recruiting passionate students!
**Swathi Arur, Ph.D.** 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?:** We use multidisciplinary approaches and model systems with a goal to gain knowledge into three specific biological questions. We hope to understand the basis of (i) environmental signaling and its role in male and female fertility, (ii) signaling and control of birth defects, with a specific focus on the Ras pathway and (iii) signaling based control of post-transcriptional regulation on cancer metastasis.

Below, I provide highlights of some of our ongoing research.

**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.

**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.
The mammalian SWI/SNF complex, whose functional roles are just beginning to be deciphered, is a master regulator in development and when mutated is the driving cause for large numbers of human diseases including cancer. Although SWI/SNF is highly enriched at enhancers and its basic chromatin remodeling activities have been studied for over 30 years, there is little known about how it regulates enhancer activity and enhancer-promoter interactions. By targeting a DNA/RNA binding module called the AT-hook in the catalytic subunit of this megadalton size complex, we have uncovered a role for SWI/SNF in de novo enhancer activation and nuclear architecture. Our model system for this purpose is the transition from a naïve pluripotent state an early step toward cell lineage priming and cell fate determination. In this transition, there is significant restructuring of the nuclear architecture as well as transcriptional rewiring, including de novo enhancer activation, that makes this such an ideal system for this purpose.

The INO80 ATP-dependent chromatin remodeler operates at promoters, telomeres and centromeres; and is involved in transcription regulation, 3-D organization of the genome, replication, DNA repair, and heterochromatin/centromere formation. Several lines of evidence show that INO80 promotes nucleosome disassembly and exchange of H2A.Z-H2B dimers, but our biochemical data has not provided many clues as to how INO80 disrupts chromatin. We want to find how INO80 promotes loss of canonical H3 at centromeres, increases accessibility at enhancers in several cancers, and promotes the exchange of H2A.Z at DNA double stranded breaks, pericentric and other regions by more fully understanding the mechanism of INO80 remodeling. We also want to find how DNA sequence has such large effects on the efficiency and maybe even the ultimate outcome of INO80 remodeling.

Environment: Join the ranks of those who have gone on from our laboratory to be successful faculty members, principal investigators at NIH and leaders in the biotech and pharmaceutical industry.
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), Vanja (postdoc), Vera (Baylor DB student), Annie (Baylor DB student; F31 recipient), Celine (G&E student; Kopchick Fellow), Dalia (G&E student), Kamryn (Baylor DDMT student), Jonathan (research assistant), Majo (G&E student), and Richa (G&E student).

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

https://www.mdanderson.org/research/departments-labs-institutes/labs/jichao-chen-laboratory.html
The laboratory focuses on understanding molecular mechanisms underlying genomic instability, tumorigenesis, and cancer therapy. 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.

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.
Looking for MS and PhD candidate students to study endogenous mutational mechanisms related to DNA methylation in the genesis of genetic diseases and cancer.

**Research activities** focus on addressing the following questions:

1. Is there a code for recognition of the five forms of cytosine modification by transcription factors?
2. Is there a specific pathway for epigenome reprogramming?
3. How are the patterns of DNA modifications altered by changes in associated histone methylation?
4. How are the patterns of DNA methylation altered in the context of human diseases?

**Recent publications:**


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 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 use our genomic, molecular, and cytological approaches to investigate recombination pathways in vivo (Premkumar T, et al BioRxiv, 2022) 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.

**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, three graduate students, a tech, and lab manager. Our first student, Rhea Kang was awarded the Alfred G. Knudson, Jr., Outstanding Dissertation Award. All 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 new graduate student.

Ask our students and former members about the lab: Tolka Premkumar, Melissa Frasca, Emely Larios, and Ericka Humphrey!
PI: Giulio Draetta, MD, PhD

Professor, Department of Genomic Medicine
Sewell Family Distinguished University Chair
UT MD Anderson Cancer Center, South Campus, SCRB4 6th Floor
Contact: gdraetta@mdanderson.org

Functional genomics, onco-metabolism, and innate and adaptive drug resistance in cancer

My laboratory focuses on disease mechanisms in pancreatic cancer and glioblastoma. We use classical genetic and biochemical analyses with functional genomics and state-of-the-art technologies to identify novel tumor dependencies and evaluate their potential for therapeutic translation. Some of our group’s accomplishments include identifying a dependency on oxidative phosphorylation in acute myeloid leukemia (Molina et al. Nature Medicine 2018) and pancreatic cancer stem-like cells (Viale et al. Nature 2014) and describing Kras-induced localization of Syndecan-1 to the cell membrane as a driver of macropinocytosis in pancreatic cancer (Yao et al. Nature 2019). We also described a novel WDR5–Myc interaction that is required to protect pancreatic cancer cells from DNA damage (Carugo et al. Cell Reports 2016). Most recently, discovered that medium-chain acyl-CoA dehydrogenase (MCAD) is essential to prevent toxic levels of fatty acid accumulation and oxidative stress in glioblastoma (Puca et al. Cancer Discovery 2021).

Environment. Students and trainees are expected to assert their independence, seek innovation, and work collaboratively. Team science is highly valued, and training in this laboratory includes myriad opportunities to collaborate. We have departmental lab meetings and smaller project group meetings weekly. My former trainees have been successful in obtaining scholarship/fellowship funding, and graduates have secured positions as academic postdocs or independent faculty and staff scientists in BioPharma.

Applying. We are always looking for trainees who are passionate about our research. Please email me if you are interested in learning more about research training in our lab.

MCAD is required to clear toxic lipids from brain tumor cells. This discovery introduces a new therapeutic concept for cancer cell metabolism: exploiting fatty acid metabolism to poison—rather than starve—cancer cells. (Puca et al. Cancer Discovery 2021)
George T. Eisenhoffer, PhD  
Associate Professor  
Department of Genetics  
gteisenhoffer@mdanderson.org

Research Interests
zebrafish development and genetics  
epithelial tissue homeostasis  
stem cells and regeneration  
carcinogenesis and metastasis

Cancer development has long been linked to a mis-regulation of the body’s normal homeostatic processes and regenerative responses during wound healing after injury. My laboratory studies the cellular and molecular mechanisms linking the birth and death of cells in living epithelial tissues to better understand how specific genetic changes drive an increase in cell numbers and lead to carcinogenesis. To study cell turnover in a living epithelial tissue, we use the developing zebrafish to rapidly elucidate mechanisms that regulate epithelial cell function under physiological conditions, after tissue damage, and after genetic perturbation. We monitor population dynamics and individual cell behaviors under normal and experimental conditions using high-resolution time-lapse microscopy to gain a clearer picture of how epithelia maintain overall numbers while sustaining a functional barrier.

Our studies have provided mechanistic insight into how localized changes in physical forces are coordinated to remove defective cells from living epithelial tissues (Atieh et al., 2021 Current Biology, Franco et al., 2019 MBoC). We have also interrogated the cell loss-induced signaling events and cellular responses, including inflammatory cell recruitment and epidermal cell proliferation, that drive turnover (Brock et. al., 2019 Nat. Comm; Wurster et al., 2021 Cell Reports). Together, our studies provide an in vivo characterization of epithelial cell turnover and create a system to identify new mechanisms controlling tissue regeneration and the changes that lead to cancer formation and progression.
Michael J. Galko, Ph.D.

Professor, Department of Genetics
UT MD Anderson Cancer Center

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Tel: 713 792-9182

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.

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:
**Seeking Graduate Students**

**PI: Boyi Gan, PhD**
Professor & Director, Radiation and Cancer Metabolism Research Program
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 Vulnerability 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:**

- **Functional Studies:** GOF (cDNA OE) or LOF (shRNA, CRISPR) in cell lines and mouse models (6EMMs, xenograft from cell lines, and PDXe)
- **Molecular Mechanism:** MS, RNA-seq, ChIP-seq, ChIRP-MS to identify and study pro-pro, pro-RNA, and pro-DNA interactions
- **Metabolism:** Metabolic flux analysis, metabolite profiling, etc
- **Clinic:** Clinic correlation, Prognosis analysis, cancer drug treatment and response

**Training Environment.** My laboratory currently consists of ~10 trainees, including graduate 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 (Nature Communications, iScience, JBC etc) 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 multiple R01s and several foundation grants.

**Recent Representative Publications:**

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; Lyu et al, 2022 revision submitted). 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 yejinggaelab.com

We are excited to have talented and passionate individuals join our team!
The lab of Vidya Gopalakrishnan, PhD.

The overall goal of research in the Gopalakrishnan lab is to identify molecular drivers of pediatric brain tumors and perform functional studies using genetically engineered mice (GEM) and patient derived xenograft (PDX) models. This information is used to study the contribution of these molecules to tumor biology, as well as to identify novel therapeutic vulnerabilities. Our work is broadly divided into 3 areas: (A) Cancer epigenetics: with a major emphasis on the transcription factor REST, and its role in initiation and progression of pediatric brain cancers. REST is a canonical regulator of neurogenesis. Its expression/function is dysregulated in pediatric brain cancers such as medulloblastoma, diffuse intrinsic pontine glioma and atypical teratoid rhabdoid tumors. Our multi-omics data from GEM and PDX models, and functional studies has revealed novel tumor cell-intrinsic and -extrinsic functions for REST, including cell proliferation, survival, migration, and effects on the vascular and immune microenvironment. These features are usually perturbed in high grade neoplasms. For therapeutics development, we use integrated multi-omics data and chemical screens. This approach allows us to not only identify and test new drugs, but also repurpose existing therapeutics in context-specific pre-clinical studies. (B) Cancer proteomics: with a focus on a component of the proteasomal machinery called USP37. We are studying its contribution to normal brain development and to the pathogenesis of medulloblastoma. (C) Immunotherapy for pediatric brain cancers: which involves interactions with a multidisciplinary team of scientists and physicians at MD Anderson Cancer Center. Our bench findings have been transitioned to clinical space as exemplified by the completion of a recent Phase-I clinical trial to show safety of intracranially administered Natural Killer (NK) cells. These studies are closely aligned with our clinical neuro-oncology and neurosurgical practice. Our team is currently working to show feasibility of tracking infused NK cells in mice using MRI, PET and biological reporter systems. Finally, our group is heavily invested in the development of a bio-bank of longitudinally collected pediatric brain tumors and sarcomas. Samples are annotated with correlative molecular data (epigenetic and immune) as well as information on survival and therapy response.

Overview of Therapeutic Approaches for Pediatric Brain Tumors
**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.

**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 3 Instructors, 5 postdocs, 2 clinical fellows and 3 technicians. We have four R01s, two CPRIT grants and additional philanthropic funding to support up to two graduate students.
**Research Interests:** Research interests in the lab are focused on two areas:

1. **Disparities in Myeloma:** Racial differences in multiple myeloma (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). We have also begun to investigate Social Determinants of Health (SDOH) measures in our diverse cohort to better understand the impact of the patient’s local environment on outcomes.

2. **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. 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, SDOH, 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 are also generating patient-derived iPSC cell lines from our patient populations. In parallel with our focus on disparities in myeloma, we have recently received funding to focus on disparities in cardiovascular health among AYA cancer survivors.

**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 used in patient-centric research. Our research efforts are enriched by close collaborations with faculty from MD Anderson, UTHealth School of Public Health, and many outside institutions through our involvement in the InterLymph Consortium.
**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.
Seeking PhD students

PI: Georgios Karras, Ph.D.

Assistant Professor
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UT MD Anderson Cancer Center
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Protein homeostasis is fundamental to healthy aging. The molecular chaperone Hsp90 safeguards protein homeostasis by interacting with partially folded polypeptides within the cell. Research in the Karras laboratory revealed that Hsp90 can alter the course of disease and evolution by shaping the consequences of genetic variation (Karras *Cell* 2017; Patel *et al*., Gracia *et al*., Pham *et al*., Economou *et al.*, under revision). We utilize proteomics, metabolomics, single-cell sequencing, and single-molecule approaches and develop new assays to study the dynamics of Hsp90 complexes and the influence they exert on the cellular hallmarks of aging and cancer.

We are looking for motivated students to join our diverse team @ Karras lab
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% wet lab components, and ~40% bioinformatic components. Students are encouraged to read the previous and recent publication of Dr. Li’s lab (Nature 2013; Nature Rev. Genet. 2016; Nat. Commun. 2019; RNA Biology. 2020; Mol Cell 2021, Nature, 2021, Cell Research 2021). Full publication list can be found in NCBI MyBibliography: https://www.ncbi.nlm.nih.gov/myncbi/1Jip8J4DFUsQe/bibliography/public/.

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 1). 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 2). Very recently, we investigated how RNA virus such as SARS-CoV-2 impacts host chromatin architecture to deregulate gene expression and may underlie COVID-19 pathology (Wang et al., 2021, BioRxiv).

About the lab: We currently have a Res Scientist, an instructor, four postdocs and seven GSBS PhD/MS students in the lab (by July 2022). Several of our students, Ruoyu Wang, Lana Al Hasani, Lanxin Bei 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. Alternatively, students may be involved to investigate 3D genome deregulation in human neurodevelopment disorders or neurodegeneration, particularly the Down Syndrome and Alzheimer’s Disease. 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.

Our lab intends to take one or two new graduate students for long term thesis projects in 2022/2023.

Contact: Wenbo Li, Ph.D., 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.
Han Liang, PhD

The fundamental question driving our research paradigm is how to take full advantage of cancer genomic data to elucidate the molecular basis of human cancer and develop effective therapeutic strategies, thereby contributing to the true promise of personalized or precision cancer therapy. Combining both computational and experimental approaches, my group research focuses on the following areas.

- **AI-driven bioinformatic tool development**
  One key goal of our group is to allow a broad research community to easily generate testable hypotheses and obtain biological insights from high-throughput genomic data. Over the past several years, we have developed several popular bioinformatics tools, including: (i) TCPA: an integrative bioinformatic data portal for visualizing and analyzing cancer reverse-phase protein array-based functional proteomic data. (ii) TANRIC: an interactive open platform to explore the function of IncRNAs in cancer. (iii) DrBioRight: the first nature language-oriented, AI-driven analytics platform for omics data. These tools collectively have >110,000 users from >100 countries.

- **Comparative genomics analysis within and across cancer types**
  Our group is one major contributor to large cancer genomics projects such as TCGA and ICGC. We systematically assessed the prognostic and predictive utility of TCGA genomic and proteomic data (Yuan et al. Nat Biotechnol 2014). We performed the first global analysis of sex effects on the molecular profiles of cancer patients and identified two classes of sex-effect cancer types (Yuan et al. Cancer Cell 2016). We performed a systematic analysis of hypoxia-related molecular features and their clinical values in terms of selecting cancer therapies (Ye et al., Nat Metab 2019). Collaborating with an international team, using ICGC whole-genome sequencing data, we performed a comprehensive molecular characterization of mitochondrial genomes in human cancers (Yuan et al. Nat Genet 2020). We focus on single-cell sequencing data to elucidate the interactions between tumor cells and tumor microenvironment and their effects on treatment responses.

- **Function and clinical utility of enhancer RNAs in cancer**
  Enhancer RNAs are a key class of regulatory elements in humans. We performed the first pan-cancer analysis of expressed enhancer RNAs and elucidated the enhancer-mediated regulatory mechanism of PD-L1 (Chen et al. Cell 2018). We demonstrated that fast-evolving human-specific enhancers are associated with cancer genes due to antagonistic pleiotropy (Chen et al. Cell Syst 2018). We constructed a high-resolution map of human enhancer RNA loci, enabling the quantification of super-enhancer activities (Chen and Liang, Cancer Cell 2020). These results highlight regulatory RNAs expression analysis as a new paradigm for investigating cancer mechanisms and discovering prognostic biomarkers.

- **Function and clinical utility of RNA modifications in cancer**
  RNA editing is an important post-transcriptional mechanism that can cause “mutations” at the RNA level. We have systematically characterized the A-to-I RNA editing events and demonstrated their clinical relevance in human cancer (Han et al. Cancer Cell 2015) as well as RNA editing hotspots in miRNAs (Wang et al. Genome Res 2017). We demonstrated a significant contribution of RNA editing to proteomic diversity (Peng et al. Cancer Cell 2018). RNA editing also plays a crucial role in immune response and we are studying the effects of RNA editing on immunotherapy. In addition, we are working on the m6A modifications and explore their roles as biomarkers and therapeutic targets.

- **Functional genomics/proteomics approaches for precision cancer medicine**
  With our collaborators, we developed a systems-biology approach to identifying cancer driver mutations by combining exome sequencing, high-throughput cell viability assays, and high-throughput protein expression arrays, which addresses a long-standing challenge in the field of cancer genomics (Li et al. Cancer Cell 2017; Ng et al. Cancer Cell 2018). We assessed the performance of different computational algorithms in predicting cancer driver mutations (Chen et al. Genome Biol 2020). Based on perturbed functional proteomics data, We developed a systems-biology approach to identify combination therapies based on "adaptive responses" (Zhao et al. Cancer Cell 2020).
Targeted protein degradation as a novel cancer therapeutic modality

Despite encouraging recent advances, most patients with advanced solid tumors lack effective therapeutic options, underscoring the dire need for additional treatment approaches. Genomic studies have identified frequent mutations in subunits of the SWI/SNF chromatin remodeling complex including *SMARCA4* and *ARID1A* in 20% of all solid tumors, making it the most frequently mutated complex in cancer. Unfortunately, there are no therapeutics approved for treating patients with these mutations. Research in the lab focuses on two major themes: identification of novel synthetic lethal genetic interactions to the SWI/SNF complex and discovery of novel chemical probes to degrade identified cancer targets. To this end we perform CRISPR-Cas9 functional genomic screens, utilize genetically engineered mouse (GEM) model developed in the lab and various epigenomic analysis (RNA-Seq, ATAC-Seq and ChIP-Seq).

For our chemical probe discovery efforts, we focus on an exciting and highly promising approach to degrade target proteins of interest termed proteolysis targeting chimera (PROTAC) technology. This approach enables us to not simply inhibit but eliminate cancer therapeutic targets. So far, we have successfully designed, synthesized and characterized two series of compounds against the glucocorticoid receptor and SMARCA2, two highly validated targets. Patents covering these compounds have been filed and active research is ongoing to study these compounds in vivo. These studies have the potential to provide first-in-class cancer therapeutics for clinical development.

**Environment:** We have a highly collaborative laboratory environment. Together with our collaborators and partners, we offer unique opportunities to learn basic drug discovery and development processes against epigenetic and chromatin targets including target identification, PROTAC SAR, degradation and drug target engagement assays. We look forward to inviting and advancing the scientific training of students interested in the intersection of epigenetics, chemical biology and translational research.

**People:** Nicholas (Nick) Blazanin (postdoc), Sasi Kotagiri (postdoc), Mohamed Qudratullah (postdoc), Yanyan Han (postdoc), Yawen Wang (postdoc), Xiaobing Liang (senior research associate)
“Modeling kidney development and disease in frog embryos”

The overall 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) in 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 known in only 14% of cases and often result in the need for transplant, our goal is to understand how these 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 kidney cell culture 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 in kidney development.

Environment. We have a highly collaborative 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 a position on an NIH Medical Student training award, a CPRIT undergraduate training award, a Rice Emerging Scholars Howard Hughes award, the Gee Family Legacy Scholarship, the Gigli Family Endowed Scholarship, the Schissler fellowship, the Dean’s Research Award and the GSBS Presidents’ Scholarship. 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. Our lab is growing! Please feel free to contact me if you are interested in working with our group. We would like to recruit one new M.S. student and one new Ph.D. student.
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.
MITOCHONDRIAL AND NUCLEAR GENOME STABILITY FOR DISEASE PREDICTION, TREATMENT 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 the mitochondria, and how the two communicate with each other. 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. In particular, we are interested in Fanconi Anemia (FA), which is a terrible but fascinating and prototypic genetic cancer-predisposition disease. It is signified by heterogeneous phenotypes including bone marrow failure, short stature, congenital abnormalities, infertility, sub-mendelian birth rate, genome instability, high inflammation, susceptibility to cancer, diabetes and neuroinflammation, and high cellular sensitivity to cancer therapeutics. Our research tools include newly developed single-molecule and single-cell microscopy in human and mouse cells, as well as patient samples, and unique and exciting mouse models. Our mechanistic and molecular focus is guided by human disease as well as by anatomic crystal structure information. Together, the data reveals new FA protein functions in mitochondrial and nuclear communication, inflammation, hematopoietic stem cell stability, development and sex-specific disease phenotypes, which are the latest focus of our research.

**Selected publications:**
in revision at *Nature communications*
Roy et al *eLIFE* 7:e31723. 2018;
Schlacher *Nature* 563, 478-480, 2018
Schlacher et al *Cancer Cell* 22, 106-116, 2012;
Schlacher et al *Cell* 145, 529-542. 2011
**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. Currently the van Hoof lab studies seven different RNases and an RNA modifying enzyme. Many of these RNases are mutated in human disease, but we don’t understand what mRNA or ncRNA these RNases digest and whether they function in RNA maturation or degradation. For example, pontocerebellar hypoplasia is caused by single amino acid changes in either the RNA exosome or the tRNA Splicing EndoNuclease (TSEN). We do know some of the functions of these multisubunit enzymes, but not all of the functions. We don’t know what functions are relevant to the disease, or the mechanism by which single amino acid changes affect these functions.

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 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 therefore 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 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 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 mechanisms 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 universities (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.

**Opportunity.** Our research is fully funded by an NIH R35 grant. Two current student are graduating during the 2022/2023 academic year and we have funding and projects for new students. Please contact me or any current or past student if you would like to consider joining the van Hoof lab.
Cancer Genomics and Evolution Laboratory

Our research focuses on large-scale pan-cancer genomics to gain insight into the genes, mutational processes, and evolution of cancer. Our work is highly data-driven, with a focus on large-scale data analysis to gain broad biological insight, and on the development of computational methods to enable conceptually novel analyses. Our research group is mostly computational with a small wet-lab component.

The cancer genome contains an archeological record of its past. The Cancer Genomics and Evolution Laboratory has pioneered methods to reconstruct a cancer's life history from massively parallel sequencing data and uses these ‘molecular archeology of cancer’ approaches to obtain detailed timelines of tumor evolution across many cancer types.

Since its inception, members of the Cancer Genomics laboratory have co-authored 15 papers in Nature, Science or Cell. Recent successes include pan-cancer studies of the evolutionary history of cancer (Gerstung et al., Nature 2020), intra-tumor heterogeneity (Dentro et al., Cell 2021), the mutational landscape in non-unique regions of the human genome (Tarabichi et al., Nature Biotechnology 2021), and biallelic mutations (Demeulemeester et al., Nature Genetics 2022).

Environment

We are a bold, imaginative, open, dynamic and collegial team. Students are mentored to complete ground-breaking research projects and successfully complete their PhDs in 4-5 years.

Applying

Our lab is growing, funded by a $6 million CPRIT award. We would like to recruit up to three new Ph.D. students. Please contact me at pvanloo@mdanderson.org if you are interested in working with us!

More info

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


(2) how chromatin modifications at sites of DNA damage regulates DNA repair and transcription (Paul and Wang, Molecular Cell, 2017; Wu et al, Genes & Dev, 2019);

(3) how the cell protects genome stability in response to DNA replication stress (Xu et al, Genes & Dev, 2017).

(4) how the failure of protection of stalled replication fork triggers activation of innate immune response (Emam et al, Nature Cell Biology, 2022).

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.

Environment: Our lab has regular weekly lab meetings and journal clubs. Students in our lab have won multiple awards and scholarships, such as CPRIT scholarship, Schissler Foundation Fellowship for Translational Studies in Cancer Research, President’s Research Scholarship, American Legion Auxiliary Fellowship, etc. 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.
Wang lab studies 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/biochemical techniques, electrophysiology techniques, imaging, cell culture/manipulation, CRISPR-Cas9 genome editing, and cutting edge next generation sequencing techniques such as single cell multiomics (scRNA-seq and scATAC-seq) and Cut&Run/Cut&Tag seq.

Projects in Wang lab focus on: 1) **Neural Crest Cells (NCCs)**, multipotent stem cells make significant contributions to different tissues/organs including heart and head, and defects in NCCs give rise to many diseases. Projects study NCCs proliferation/migration/stemness/cell fate decisions and NCCs derived heart development and congenital heart diseases, as well as NCCs derived cranial skeleton formation, repair and regeneration. 2) **Cardiac Conduction System (CCS)**, the tissue network in heart initiates and maintains normal heart contractions. Projects study CCS development, homeostasis and regeneration, as well as CCS aging and diseases.

**Wang Lab Environment.** Wang lab is a highly collaborative team, consist of regular lab members including postdoctoral fellows, graduate students, research associate and research assistant. We also have undergraduate researchers mentored by regular lab members. Our group is growing and actively seeking MS and PhD students. The PI has been devoted to mentoring trainees and helping them to reach their career goals. Trainees actively attend national or international meetings, and have received multiple awards and fellowships. Students will also take advantage of both in-lab collaborations and active collaborations with other labs including local, national and international collaborations. Please feel free to ask our current students about the lab: Shannon Erharht and Shuangjie You.
HSC and Immune Cell Development in the Mouse Embryo:
Where do they come from and what are their roles 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, immunohistochemistry staining, qPCR, scRNA-seq, and ATAC-sequencing, etc.

We are dedicated to answer unsolved scientific questions in the field of developmental hematology-immunology.
Neurodegenerative diseases: a new frontier

PI/ Associate Professor: Sheng Zhang PhD
Brown Foundation Institute of Molecular Medicine
Department of Neurobiology and Anatomy
GSBS and McGovern Medical School at UTHealth
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Neurodegenerative disorders such as Alzheimer’s disease (AD) and Parkinson’s disease (PD) are inflicting unbearably high emotional and financial toll to patients and their families and pose 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 machines, 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.

Using abundant tools in both model organism Drosophila and mammalian systems, we study how chaperones, autophagy and autolysosomal pathways operate and coordinate to recognize and efficiently clear toxic materials, while spare and protect normal constituents. Our goal is to develop strategy to employ these internal protection machineries to fight against ageing-related diseases.

Research Projects

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

We foster a highly supportive, collaborative and stimulating lab environment to learn and explore.

Applying. We are seeking motivated students to explore this new and important frontier, to understand and fight these still un-curable brain diseases.