Genetics & Epigenetics Program

Research Summaries of Faculty Seeking Students
Partial List as of 8/13/24
See all faculty research profiles on the GSBS website

Genetics & Epigenetics Program Faculty Seeking Students

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

Richard Behringer, PhD, Genetics, MDA

George Eisenhoffer, PhD, Genetics, MDA

Myriam Fornage, PhD, Institute Molecular Medicine (IMM), Research Center for Human Genetics, UTHealth Houston

Boyi Gan, PhD, Experimental Radiation Oncology, MDA

Yejing Ge, PhD, Cancer Biology, MDA

Priyatanash Gurha, PhD, Institute of Molecular Medicine, Center for Cardiovascular Genetics, UTHealth Houston

Shih-Han (Peggy) Lee, PhD, Genetics, MDA

Ruoyan Li, PhD, Systems Biology, MDA

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

Genetics & Epigenetics Program Faculty Seeking Students

Yuan-Hung Lo, PhD, Molecular & Cellular Oncology, MDA

Guillermina Lozano, PhD, Genetics, MDA

Rachel Miller, PhD, Pediatrics, UTHealth Houston

Margarida Albuquerque Almeida Santos, PhD, Epigenetics & Molecular Carcinogenesis, MDA

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

Peter Van Loo, PhD, Genetics, MDA

Bin Wang, PhD, Genetics, MDA

Jun Wang, PhD, Pediatrics – Research, UTHealth Houston

Wenyi Wang, PhD, Bioinformatics & Computational Biology, MDA

Zhongming Zhao, PhD, School of Biomedical Informatics and SPH, UTHealth Houston

Genetics & Epigenetics Program Faculty Seeking Students

Faculty are listed in one or two categories

Cancer Genetics:

Swathi Arur, PhD
George Eisenhoffer, PhD
Boyi Gan, PhD
Yejing Ge, PhD
Shih-Han (Peggy) Lee, PhD
Yuan-Hung Lo, PhD
Ruoyan Li, PhD
Guillermina Lozano, PhD
Peter Van Loo, PhD
Bin Wang, PhD
Wenyi Wang, PhD

Epigenetics:

Richard Behringer, PhD
Yejing Ge, PhD
Priyatanash Gurha, PhD
Shih-Han (Peggy) Lee, PhD
Wenbo Li, PhD
Margarida Albuquerque Almeida Santos, PhD
Peter Van Loo, PhD
Jun Wang, PhD
Zhongming Zhao, PhD

Developmental Genetics:

Swathi Arur, PhD
Richard Behringer, PhD
George Eisenhoffer, PhD
Rachel Miller, PhD
Ambro van Hoof, PhD
Jun Wang, PhD

Genome Maintenance & Repair:

Bin Wang, PhD
Wenyi Wang, PhD

Human Genetics:

Myriam Fornage, PhD
Wenbo Li, PhD
Rachel Miller, PhD
Ambro van Hoof, PhD
Zhongming Zhao, PhD

Swathi Arur, Ph.D: Professor, Department of Genetics, MD Anderson Cancer Center.
Lab on BSRB 11th Floor.

The lab currently has three Ph.D and one Masters 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. Nutritional programs that govern female germ cell development and transition to embryo 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. Trainee publications: *Lopez and Chen et al., Developmental Cell, 2013; Suen et al., Nat Str Mol Biol, 2013; Mattingly et al., J Biophy, 2015; Das et al., Science Advances 2020; Das et al., PNAS, 2022; Trimmer et al., Cell Reports, 2023.*

Lab team, 2023-2024. L-R (front): Jacob Ortega, Nick Newkirk, Swathi Arur, Tokiko Furuta, Melany Puente, Amelia Li, Janet Cheng.

L-R (back): Shin-Yu Chen, Deba Das, Lisa Watson, Kennty Trimmer, Han Bit Baek

Talk to them to learn about the lab culture!

Current students working on this broad topic: Han Bit Baek & You?

II. Small RNA pathways that control development: We discovered a direct intersection between environmentally activated signaling pathways and production of small RNAs that controls oocyte development, and oocyte to embryo transition. The discoveries include understanding the role of Dicer and Drosha phosphorylation, small RNA production, and determining why subsets of populations of small RNAs are generated, and what this may mean. Trainee publications: *Drake et al., Developmental Cell, 2014; Minogue et al., Nat Comm, 2018; Minogue et al., Current Protocols, 2019; Aryal et al., 2018, PNAS.*

Current students working on this broad topic: Nick Newkirk, Jacob Ortega, & You?

III. Dicer phosphorylation and nuclear role in cancer development: We discovered that Dicer is phoshorylated and translocated to the nucleus in *C. elegans*. We then generated mouse models to determine its role in cancer development. Phosphorylated nuclear Dicer drives tumor spread in mouse models of oncogenic KRas and mutant p53. We then discovered in non-small cell lung cancers that phosphorylated nuclear Dicer does not regulate microRNAs, instead it forms a large chromatin complex in the nucleus which helps open chromatin and affect transcription of lineage defining genes resulting in lineage reprogramming of lung tumor cells to gastric lineage. Trainee publications: *Aryal et al., 2018, Cancer Res; Reyes et al., 2023, Science Advances.*

Current students working on this topic: You?

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Reproductive organ development and disease

The overall goal of our research is to understand the molecular, cell, and developmental processes that result in the formation of the reproductive organs, the gene regulatory networks that control the differentiation of the male and female phenotypes, and how mutations result in reproductive organ variants and Diffences in Sex Development. Alterations in reproductive organ formation are associated with infertility, high risk pregnancies, and miscarriage. Our primary model system is the mouse but we also have a colony of brown anole lizards to explore these processes in reptiles, using CRISPR gene editing. We use cutting-edge microscopy methods, including time-lapse imaging of cell and tissue behaviors and 3D imaging platforms such as microCT, coupled with genomic approaches, including spatial transcriptomics to understand mutant phenotypes. More recently, we are exploring using a normal aspect of male sex differentiation as a novel model of cancer metastasis.

Environment. We have a very welcoming and supportive laboratory culture, appreciating the contributions of each lab member to make innovative discoveries in biomedical research.

Apply. Please contact me if you are interested in training in our group. We would like to recruit one new graduate student.

THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

George T. Eisenhoffer, PhD

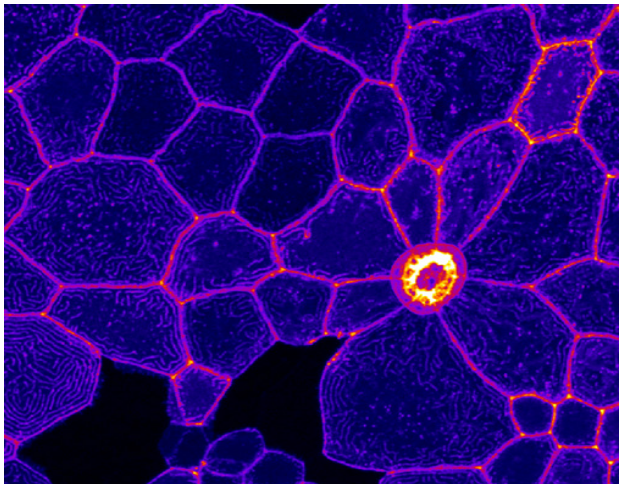
Associate Professor
Department of Genetics
gteisenhoffer@mdanderson.org

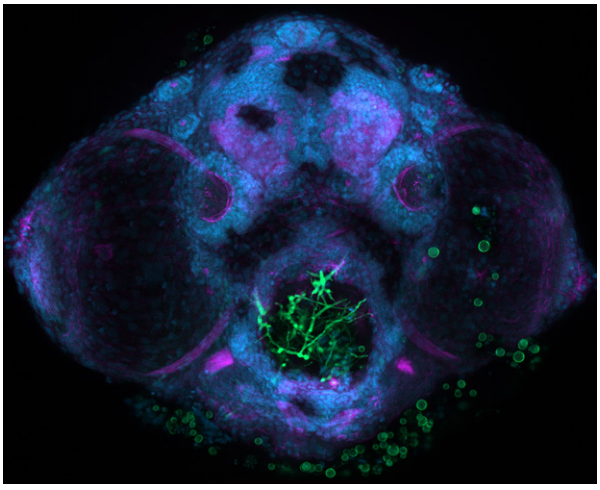
Research Interests

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.

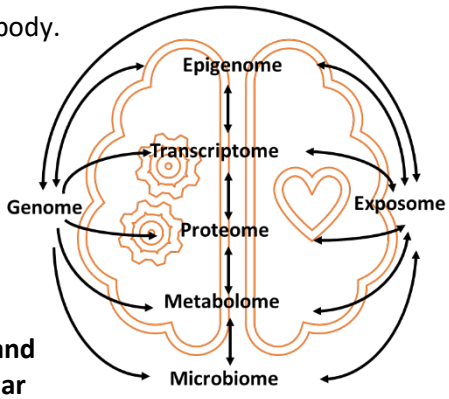
Our studies have provided mechanistic insight into how localized changes in physical forces are coordinated to remove defective cells from living epithelial tissues (Atieh et al., 2021 Current Biology, Franco et al., 2019 MBoC). We have also interrogated the cell loss-induced signaling events and cellular 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.





PI: Myriam Fornage, PhD
Professor of Molecular Medicine and Human Genetics
Laurence and Johanna Favrot Distinguished Professor
Brown Foundation Institute of Molecular Medicine
IMM Sarofim Research Building #530.F
Contact: myriam.fornage@uth.tmc.edu

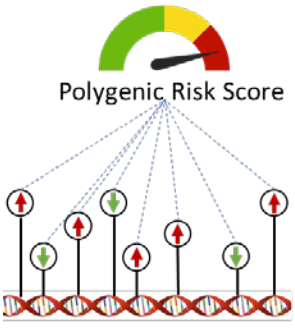
"Molecular Epidemiology of the Aging Brain in Diverse Populations and Across the Lifespan"

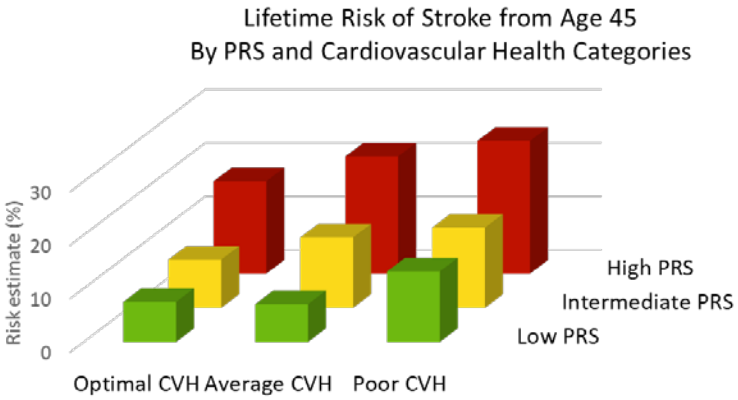


Throughout our lifetime our brain changes more than any other part of our body. Beginning in midlife, aging brings about subtle changes in brain structure, chemistry, and function. These changes are detectable by **neuroimaging techniques** and are associated with a greater risk of future stroke, cognitive and functional impairment, dementia, and death. Current "omics" technologies provide us with high-dimensional information about the sets of biological molecules that make up cells, tissues, and organisms on a population scale. **Our laboratory uses advanced computational techniques to make sense of multi-omic information with the goals to discover novel biomarkers for disease risk prediction and to enable informed preventive and therapeutic interventions that slow or reverse brain aging and brain vascular disease.**

With human genome sequence data, we seek to identify genes and gene variants that influence risk for stroke and Alzheimer's disease. These complex diseases are determined by DNA sequence variations occurring in many genes that have small effect sizes and act over long periods of time. With this genetic information, we can estimate a person's "polygenic risk score (PRS)" for a particular disease, which represents the total number of genetic variants influencing the disease that a person has inherited. A person's PRS provides a measure of disease risk due to their genes. Combining PRS with lifestyle and clinical risk factors can give a better idea of **how likely a person is to develop the disease during their lifetime** than considering either alone.

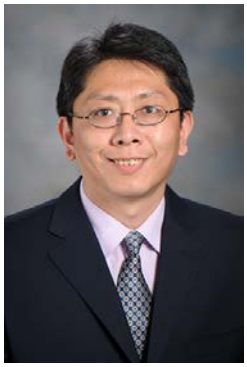
One of the most challenging aspects in the application of genetic information to precision medicine is ensuring that it is equally applicable to all so as to limit exacerbating health disparities. Our group is committed to working on diverse populations. Indeed, **we leverage diversity in population ancestry to map genes for brain health traits**, conducting population-specific GWAS accounting for global ancestry and admixture mapping.





Environment: Our laboratory is well funded through multiple NIH grants and has the necessary financial and networking resources to support the development of a graduate student. We meet weekly to discuss projects and all trainees attend at least one national meeting each year. Students are given the opportunity to participate in research consortium activities, including attending conference calls, presenting research, and attending in-person meetings. Please feel free to contact me or my current lab members if you are interested in working with us.

Seeking Graduate Students



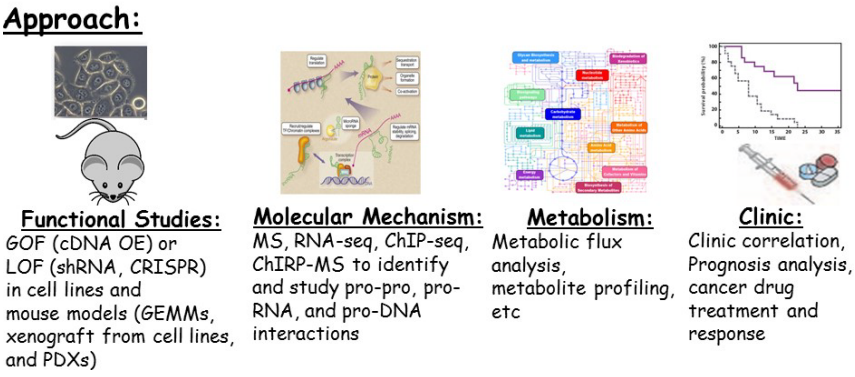
PI: Boyi Gan, PhD

N.G. and Hellen T. Hawkins Distinguished Professor for Cancer Research &
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 Disulfidptosis 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. We are studyiny ferroptosis and disulfidptosis, the forms of cell death induced by lipid peroxidation and disulfide stress, respectively, and and their roles in tumor suppression, cellular metabolism, and cancer therapy. Currently we're employing multi-disciplinary approaches (see schematic on the right) to study these questions.

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:

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. Mao C, et al. **Gan B**. DHODH-mediated ferroptosis defence is a targetable vulnerability in cancer. **Nature**, 2021.
5. Koppula P, et al, **Gan B**. A targetable CoQ-FSP1 axis drives ferroptosis- and radiation-resistance in KEAP1 inactive lung cancers. **Nature Communications**, 2022.
6. Liu X, et al, **Gan B**. Actin cytoskeleton vulnerability to disulfide stress mediates disulfidptosis. **Nature Cell Biology**. 2023 Mar;25(3):404-414. PMID: 36747082.

Seeking PhD Student

PI: Yejing Ge, Ph.D.

Assistant Professor
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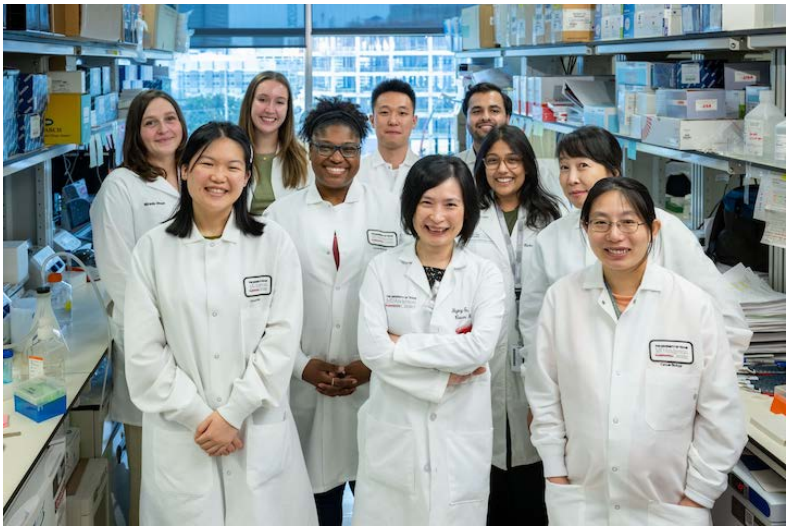
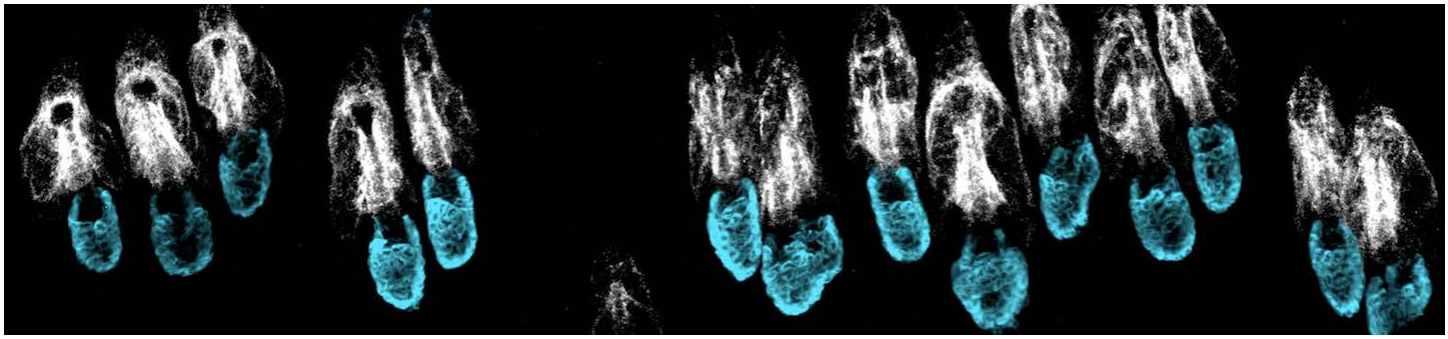
Ge Lab
Skin Functional Genomics





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; Lyu, Guan, Humphrey et al, 2022 **Genes & Dev**). Research in the Ge lab uses skin as a model, 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. We recently reported role of transposons in skin regeneration (Lyu, Kim, Humphrey, Nayak et al, **Cell**, revision submitted).

Come check us out at our website yejinggelab.com We are excited to have passionate individuals join our team!

Our Core Values

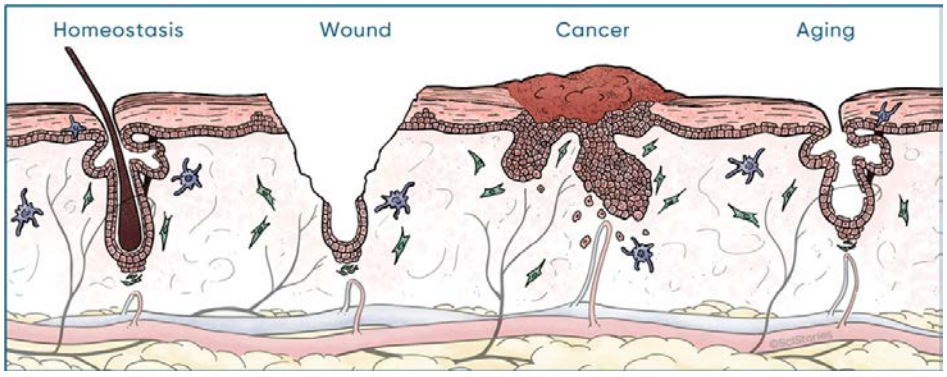
Creativity
Science is fun. Think outside the box.

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.



National Institutes of Health
The University of Texas MD Anderson Cancer Center
Making Cancer History
CPRIT
Department of Defense
afar
Women & Science
Robertson Foundation

Priyatanash Gurha, PhD
The University of Texas Health Science Center at Houston
Institute of Molecular Medicine
Center for Cardiovascular Genetics

Research program:

Molecular Mechanisms and Functions of Epigenetic Regulators and Non-coding RNAs in Heart Failure

1. Description of the research program

My primary research objective is to gain insight into the molecular mechanisms that regulate gene expression and contribute to the pathogenesis of heart failure. Within the context of this theme, we are investigating the role of epigenetics and non-coding RNAs in the proliferation, differentiation, and maturation of myocytes, as well as how perturbation of these interdependent processes ultimately results in cardiac dysfunction and failure. The epigenetic dysregulation of miR-184 and its role in the pathogenesis of ACM were identified in our previous research. In heart failure (HF), we are investigating how reprogramming of epigenetic code regulates gene transcription and the resulting cardiac phenotype. Recent research has revealed the significance of DNA methylation and Lamin Associated Domain in Human HF. These studies led to the identification of the KDM5 family of demethylases in the phenotype of HF. The function of KDM5 in the physiology and pathophysiology of the heart remains unknown.

We are investigating the cell-type-specific contribution of these regulators to cardiac physiology using induced pluripotent stem cells (iPSCs) and multiple mouse models. We discovered that KDM5 directly affects the maturation of iPSC-CMs. The reprogramming of iPSC-CM toward a maturation state is partially governed by KDM5 mediated epigenetic regulation of genes implicated in OXPHOS and sarcomere formation.

We recently implicate KDM5 as epigenetic regulators of dysregulated genes in HF caused by LMNA Loss of Function. The results suggest that KDM5A and KDM5B are involved in the pathogenesis of HF. Utilizing Gain of function and Loss of function approaches, the roles and underlying mechanisms governed by KDM5A and KDM5B in HF are been investigated. To address these problems, we take a multidisciplinary strategy that combines mouse genetics, biochemistry, and genomics.

2. Research Projects:

- Role of KDM5 family of Histone Demethylases in Heart
- Epigenetic regulatory mechanisms in Cardiomyopathies and heart failure
- Role of non-coding RNAs in Heart failure

Complete list of publication: https://www.ncbi.nlm.nih.gov/pubmed/?term=gurha+Priyatansh

PI: Shih-Han “Peggy” Lee, Ph.D.

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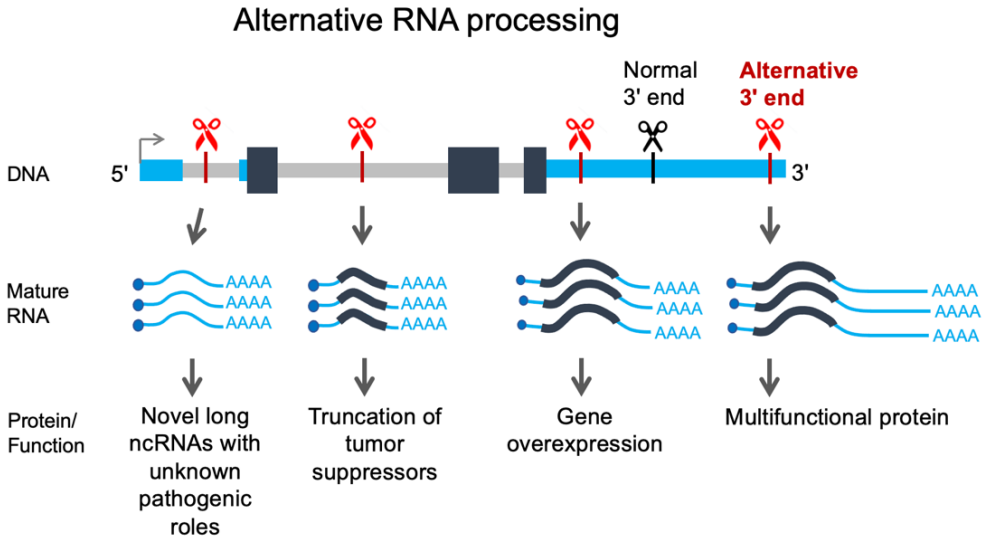
“The role of alternative RNAs in cancer”



Genetic alterations are known cancer drivers, but not all patients harbor sufficient driver mutations to elicit the onset and progression of the disease. There also exist cancers such as pediatric tumors and several liquid cancers that carry very few genetic alterations, highlighting a need for deeper understanding of non-genetic events that are equally potent to drive malignant transformation. Our lab investigates how aberrant RNA processing impacts tumor formation and progression. We have developed next-generation sequencing analyses to identify the expression of cancer-gained RNA isoforms in patient’s tumor cells (Lee & Singh, et al., Nature 2018; Singh, Lee, et al., Nature Communications, 2018). We integrate multidisciplinary approaches including molecular and cell biology, proteomics and advanced imaging to determine the pathogenic role of altered RNAs in tumor development (Lee and Mayr, Molecular Cell, 2019). Our studies reveal new cancer-implicated genes and pathways which have been overlooked by standard genetic profiling as their errors are hidden in RNA but not DNA. We hope to suggest innovative strategies to tackle cancer.

Environment:
People are the most important and valuable assets of our lab. We have a culture of collaboration and teamwork. The lab is currently supported by CPRIT and UT STARs awards. We are welcoming graduate students to join our team. It is our goal to nurture the next generation of scientists by building up necessary independence, scientific maturity, and out-of-the-box creativity.

Ruoyan Li, Ph.D.

Assistant Professor
Department of Systems Biology, MDA
Contact: rli11@mdanderson.org

Our lab is interested in understanding how cancer initiates from early normal cells and evolves into complex clonal architectures and multicellular ecosystems. We aim to understand this by leveraging and advancing cutting-edge genomics, single-cell multiomics, and spatial genomics technologies. Our overarching goal is to use the new knowledge from our research to facilitate the development of strategies for the prevention, detection and interception of cancer before it progresses to an intractable stage.

Cancer is a disease of the genome and an evolutionary process. We seek to understand the early steps of cancer initiation and evolution by focusing on somatic mutations and mutant clonal evolution in histologically normal human tissues. Recently, we have studied somatic evolution in normal human urothelium (Li et al. Science 2020) and compared somatic mutagenesis across multiple tissues from the same individuals (Li et al. Nature 2021).

Cancer is also a complex multicellular ecosystem where cancer cells interact with various cell types such as immune and stromal cells. By utilizing single-cell and spatial genomics, we aim to understand how cellular interactions within the ecosystem, along with oncogenic properties of cancer cells, influence cancer evolution and progression (Li et al. Cancer Cell 2022; Jin et al. Cell Research 2020).

Current research directions:

1. Studying somatic mutations in normal and premalignant tissues and their impact on cancer development.
2. Understanding premalignant progression and mutant clonal evolution.
3. Resolving the microenvironment of premalignancy and cancer in space and time.

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

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, Cut&Run, 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 ~30-40% bioinformatic components. Students are encouraged to read the previous and recent publication of Dr. Li's lab (**Nature Rev. Genet**. 2016; **Nat. Commun.** 2019; **RNA Biology**. 2020; **Mol Cell** 2021, **Nature**, 2021, **Cell Research** 2021; **Cell Reports**, 2022; **Nature Cell Biology**, 2022, **Nature Microbiology**, 2023; **eLife** 2024). Full publication list can be found in NCBI MyBibliography: https://www.ncbi.nlm.nih.gov/myncbi/1Jip8J4DFUsQe/bibliography/public/.

A lab picture taken in a recent annual lab BBQ party in Herman Park. Lab members and friends.

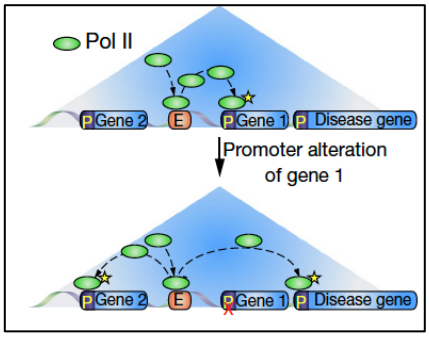


Figure 1*. A diagram showing cancer mutations deregulate cancer genes via Enhancer release and retargeting (ERR).*

Here are some examples of our recent findings. 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*). A 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, which may underlie COVID-19 pathology (Wang et al., 2023, **Nature Microbiology**).

About the lab: We currently have one senior lab Assistant Professor, eight postdocs, six GSBS PhD students and 2 lab assistants in the lab (by August 2023). We welcome students with an enthusiasm to uncover fundamental biology and mechanisms of noncoding RNAs, epigenetics and 3D genome, and to pioneer the frontier of cancer RNA medicine. 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. Another major disease/model we use are related to 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 exposure to frontiers of 3D genome research. Our lab intends to take one or two new graduate students for long term thesis projects in 2024/2025.

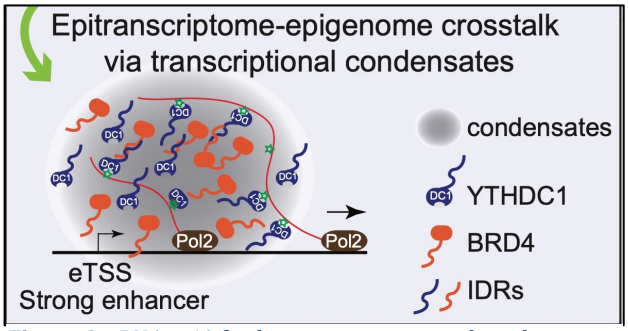
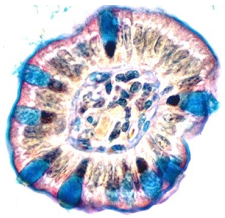


Figure 2*. eRNA m6A facilitates transcriptional condensates.*

Contact: Wenbo Li, Ph.D., Biochemistry and Molecular Biology, UTHealth McGovern Medical School; and TMC3 collaborative building at Helix Park. Email: Wenbo.li@uth.tmc.edu. You are welcome to inquire via email if you have questions or want to arrange a meeting.

PI: Yuan-Hung Lo, Ph.D.

Assistant Professor
University of Texas MD Anderson Cancer Center
Department of Molecular and Cellular Oncology
Office: Z11.5042, Zayed Building
Contact: YLo1@mdanderson.org



Who We Are?

We are a newly established laboratory comprising a dynamic team of passionate and creative researchers dedicated to advancing our understanding of gastrointestinal tract function and dysfunction. With **3D organoid models** and **cutting-edge genetic approaches**, we investigate fundamental and translational biology in pathogenesis. Our ultimate goal is to develop innovative therapies to improve patient outcomes and quality of life. Our lab is currently focused on three key areas:

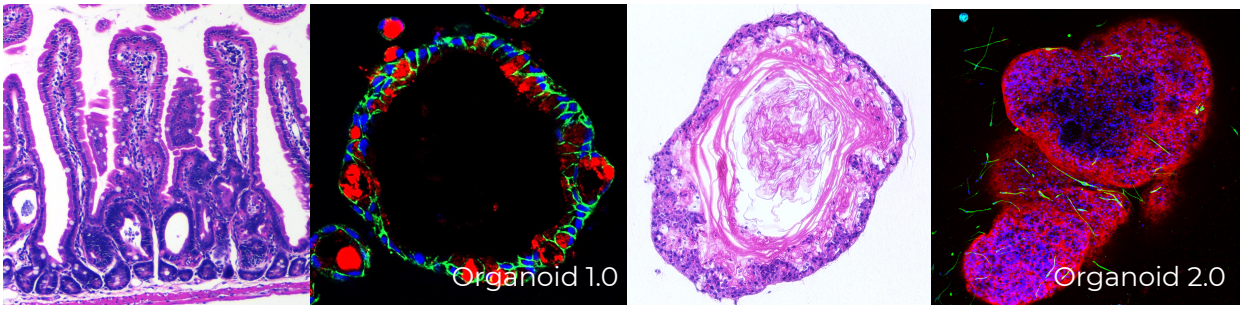
Modeling Gastric Cancer in Primary 3D Organoids. We are building innovative 3D tumor organoid models utilizing CRISPR/Cas9 genome-editing technologies. Our engineered tumor organoids faithfully mimic various stages of gastric cancer progression (**Organoid 1.0**). These models are valuable tools for investigating molecular mechanisms underlying tumor initiation, progression, and evolution.

Unveiling Gastrointestinal Stem Cell and Tumor Niche. We are pioneering sophisticated 3D culture systems (**Organoid 2.0**) to simulate stromal components of the tissue microenvironment. Using state-of-the-art imaging technologies, we aim to unravel the intricate interactions between normal and malignant epithelial cells and their surrounding microenvironment. We seek to understand the multifaceted processes underlying normal physiology and malignancies.

Elucidating Cell States Dynamics in Cancers. Gastric cancer development involves dynamic cell state changes and disruptions to signal pathways governing stem cell function and lineage differentiation. We are investigating tumor heterogeneity and therapeutic vulnerabilities of cancer cells using multi-omics single-cell technologies in our 3D organoid models. Our objective is to advance the understanding of cancer biology and develop new therapeutic strategies targeting cancer cell states.

Applying. Our team is dedicated to mentoring and supporting students. If you are passionate about gastrointestinal disease research and want to be part of a team impacting the field, we encourage you to apply!

References. (Lo et al., *Gastroenterology* 2017) (Lo et al., *Nature Cancer* 2020) (Lo et al., *Cancer Discovery* 2021) (Dao et al., *Trends Cancer* 2022) (Karlsson et al., *Nature* 2023)



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 *Mdm*2 in various tissues. In addition, high MDM2 levels as observed 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.

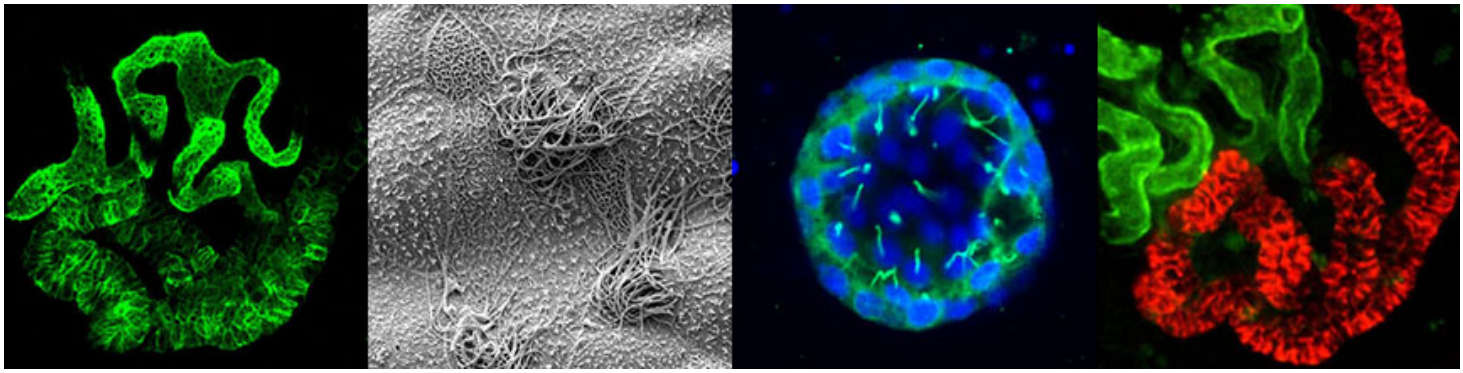
We have also created three novel conditional mutant p53 alleles in the mouse that are wild type to start with but recombine the *p53* locus in a Cre-dependent manner to create a few mutant cells in a sea of normal stroma and immune cells. Somatic p53 mutation in the breast epithelium produces breast 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 two NIH grants to support 1-2 new students. However, trainees are expected to apply for fellowships.

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”

Our overall research goal is to understand the processes that underlie kidney development and how their disruption results in congenital anomalies of the kidney and urinary tract (CAKUT). 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. Through our use of the frog (*Xenopus*) embryonic kidney, students in our group have made important discoveries related to kidney development (Krneta-Stankic et al. *Cell Rep* 2021) and congenital malformations (Blackburn et al. *Gen Med* 2019). Our trainees have also performed comparative kidney studies using single-cell transcriptomics (Corkins et al. *Kid Int* 2023) and made contributions enabling CRISPR/Cas9 genome editing in the kidney (DeLay et al. *Genetics* 2018). Building on these studies, we aim to understand the cellular processes that drive kidney development.

Environment. We have a highly collaborative laboratory culture, and the valuable contributions of our trainees have been integral to project successes, resulting 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, the GSBS Presidents’ Scholarship, an NIH R01 Supplement, and a Center for Clinical and Translational Sciences TL1 Fellowship. 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 get in touch with me if you are interested in working with our group. We wish to recruit one new graduate student.

Margarida Albuquerque Almeida Santos, PhD

The University of Texas MD Anderson Cancer Center
Department of Epigenetics and Molecular Carcinogenesis

Research in the Santos laboratory is focused on epigenetic regulation and transcription in normal and cancer cells, especially in Acute Myeloid Leukemia and B cell Lymphoma. Most recently the lab has been making novel discoveries uncovering the roles of both protein arginine methyltransferases and methyl-lysine readers on benign and malignant cell differentiation (Veazey et al., Leukemia, 2020; Van et al, JBC, 2022). The lab is also deeply invested in the understanding the function and regulation of the MLL3/4 complex in normal and malignant cells and is actively investigating the interplay of histone modifications and the DNA damage response. Ultimately the research in the Santos lab will define the mechanisms through which epigenetic regulation and transcription occur during normal differentiation and how these processes become disrupted in cancer, in order to develop specific and potent therapeutic strategies for treating cancer.

Other laboratory research interests include uncovering connections between replicative stress, epigenetic modifications, and DNA damage response and the epigenetic regulation of cancer stem cells. Replicative stress which can stem from the slowing or stalling of replication fork progression, is a source of spontaneous DNA damage 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 it is a crucial barrier to tumorigenesis during the early stages of cancer development, and that selective pressure favors malignant clones with defects in DNA repair factors, or genome guardians. Acute leukemias are typified by the accumulation of immature blood cells, or blasts, that are not fully differentiated. Dr. Santos showed that DNA damage induces the differentiation of leukemic stem-like cells in acute myeloid leukemia (AML) harboring the MLL-AF9 oncogene. This discovery uncovered an unexpected tumor-promoting role of the genome guardians in enforcing the oncogene-induced differentiation blockade in AML (Santos et al., Nature, 2014).

PI: Ambro van Hoof, PhD
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McGovern Medical School
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Twitter: @vanHooligans

“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. Currently the van Hoof lab studies seven different RNases and an RNA modifying enzyme. Many of these RNases are mutated in human disease, including cancers and human mendelian syndromes, 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 therfore important to understand TSEN specificity. In contrast to the RNA exosome, 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 as a graduate student, you can generate and test your own hypotheses. The genome of yeast is also small enough that we can easily identify mutations of interest. Because yeast and human diverged relatively recently, most of the genes and pathways implicated in human disease are conserved between them. Yeast research has a long track record of leading to pivotal 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 four 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 (Merck, 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. Several students will graduate in 2025 and we have projects for multiple new students. Please contact me or any current or past student if you would like to consider joining the van Hoof lab.

PI: Peter Van Loo, Ph.D.
Professor and CPRIT Scholar in Cancer Research
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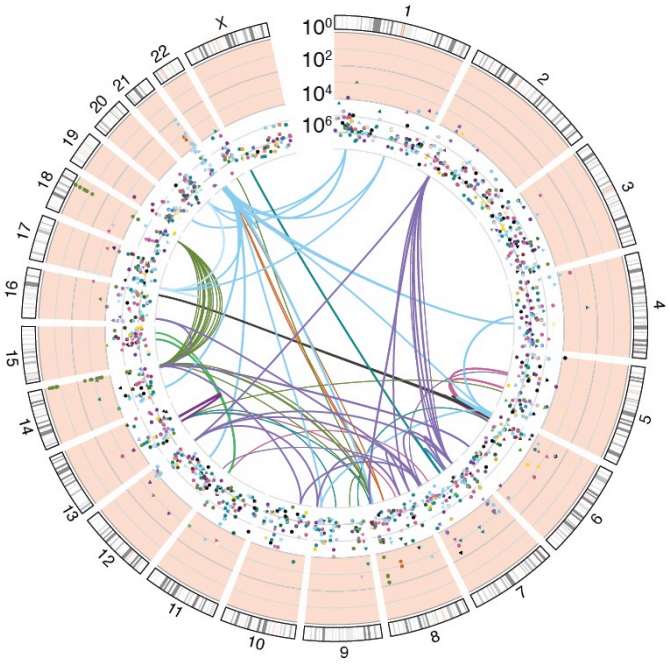
Cancer Genomics and Evolution Laboratory



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 18 papers in Nature, Science or Cell. Recent successes include pan-cancer studies of the evolutionary history of cancer (**Gerstung *et al.*, *Nature* 2020**, **Baker *et al.*, *Cancer Discovery* 2024**), 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 succesfully complete their PhDs in 4-5 years.

Applying

Our lab is growing, funded by a $6 million CPRIT award. 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

PI: Bin Wang, PhD

Professor
Department of Genetics
BSRB, S13.8116 a
UT MD Anderson Cancer Center, Houston TX
Email: bwang3@mdanderson.org

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

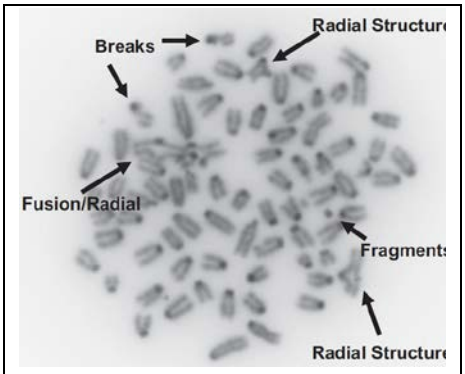
Research Interests: Our research is focused on understanding how cells respond to DNA damage and replication stress to safeguard the integrity of the genome, gaining insights into the development of cancer and the treatment of cancer.

Ongoing Projects:

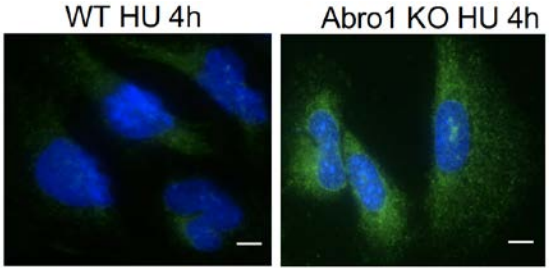
(1) how the hereditary breast tumor suppressor BRCA1 interaction network maintains genome stability and suppresses breast tumor development and metastases (Castillo et al, *Cell Report*, 2014; Wu et al, *Molecular Cell*, 2016; Wu and Wang, *Nature Communications*, 2021).

(2) how protein ubiquitin modification is involved in regulating DNA damage signaling and repair (Paul and Wang, *Molecular Cell*, 2017; Wu et al, *Genes & Dev*, 2019; Liu et al, *Nature Communications*, 2023).

(3) how the cell protects genome stability in response to DNA replication stress (Xu et al, *Genes & Dev*, 2017); and how the failure of protection of stalled replication fork triggers activation of innate immune response (Emam et al, *Nature Cell Biology*, 2022).



Chromosome aberrations in a BRCA1-intearcting protein, Abraxas, -deficient cells. (Castillo et al, **Cell Reports**, 2014).



Failure to protect stalled replication forks leads to single-stranded DNA (labeled in green) accumulation in the cytoplasm and triggers innate immune response (Emam et al, **Nature Cell Biology**, 2022).

Approach: We use combined functional and molecular approaches that involve imaging, CRISPR/Cas9 gene editing, genetic screens, high throughput sequencing, mass spectrometry, mouse model, etc.

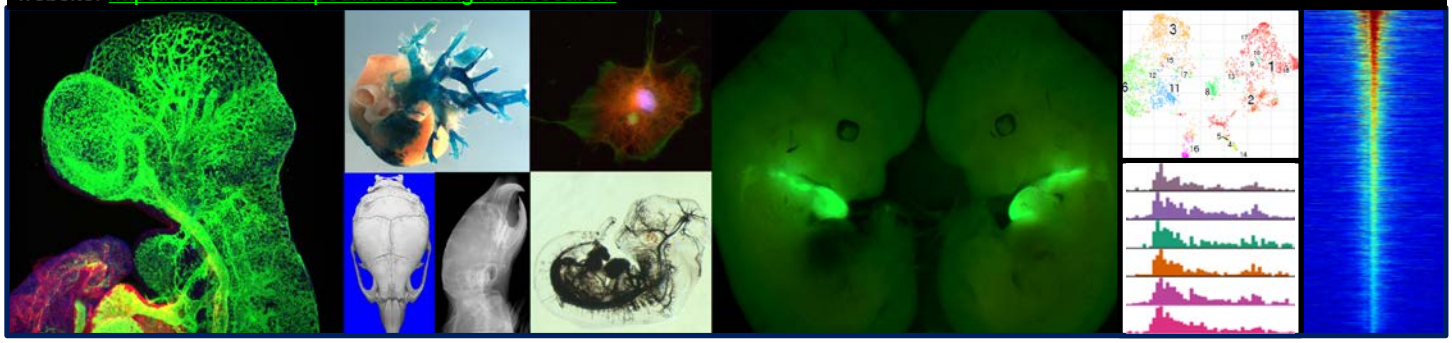
Environment: Our lab has regular weekly lab meetings and journal clubs. Students in our lab previously have won multiple awards and scholarships, such as CPRIT scholarship, Schissler Foundation Fellowship for Translational Studies in Cancer Research, President's Research Scholarship, American Legion 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.

PI: Jun Wang, PhD
Associate 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/

Wang Lab Research Interests:

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

website: https://med.uth.edu/pediatrics/wang-lab/research/



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, cell 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 Julianna Quinn.

PI: Wenyi Wang, Ph.D.
Professor
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Department of Biostatistics
The University of Texas MD Anderson Cancer Center
7007 Bertner Ave. Floor 12, 1MC12.2240
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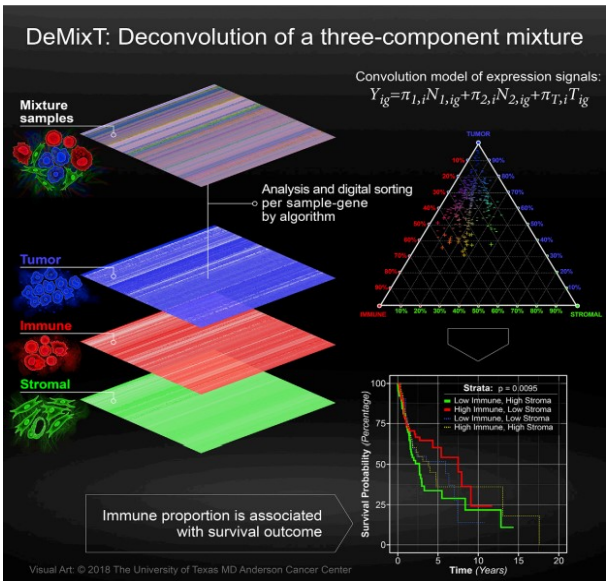
THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

Statistical Bioinformatics Lab

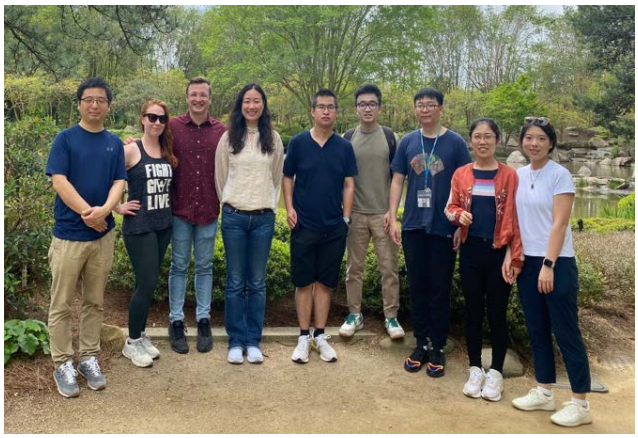


Our group passionately focuses on developing and applying computational methods to study the evolution of the human genome as well as the cancer genome, and to predict cancer risk to accelerate the translation of biological findings to clinical practice. The two main research programs in our laboratory are **1)** Deconvolution and single-cell modeling for intra- and inter- tumor heterogeneity and **2)** Semi-parametric survival modeling for cancer risk prediction.

We have been making pioneering contributions to developing methods and software tools for the studies of tumor heterogeneity and tumor evolution, such as MuSE for subclonal mutation calling (***Fan Y, et al., Genome Biol 2016***), with the recent MuSE 2.0 offering a 50-fold increase in speed (***Ji S, et al., Genome Res. 2024***), DeMixT for transcriptome deconvolution (***Wang Z, et al., iScience 2018***), and a pan-cancer characterization of genetic intra-tumor heterogeneity in subclonal selection (***Gerstung M, et al., Nature 2020***). More recently, our method to quantify tumor-specific total mRNA expression (*TmS*) from bulk sequencing data, considering tumor transcript proportion, was published in *Nature Biotechnology* (***Cao S, et al., Nat Biotechnol 2022***).

Our cancer risk prediction modeling has been focused on hereditary cancer syndromes associated with germline *TP53* mutations. Past trainees have developed modeling to predict the risk of de novo germline mutations and the risk of multiple unique primaries or cancer-specific risks in individual patients, as well as tools to be used by clinicians and genetic counselors to provide quantifiable cancer risks to patients (***Nguyen NH, et al., J Clin Oncol 2024, Nguyen NH, et al., JCO CCI 2024***). Current trainees are investigating the specific contributions of germline *TP53* point mutations on cancer development and how to stratify patients' risk based on germline mutations.

Our lab's original research on tumor heterogeneity and cancer risk prediction has also been published in other prestigious medical journals and top statistics journals such as *Cancer Research*, *JASA*, and *Cell.*



Environment

Our research group thrives in a highly collaborative environment, offering exceptional opportunities to partner with innovative cancer researchers and clinicians who specialize in clinical cancer genetics, breast, colorectal, and prostate cancer. Our collegial environment has encouraged many former trainees to continue collaborating with the lab once they enter academia or industry, creating a synergetic network.

Applying

We are recruiting similar-minded and enthusiastic PhD or master students who are interested in innovative analysis and interpretation of clinical data and/or multi-omic data using statistical methods, as well as therapeutic biomarkers and new treatment strategy development.

For more information on current projects in the lab please visit the lab website.

Seeking 2 Graduate Students

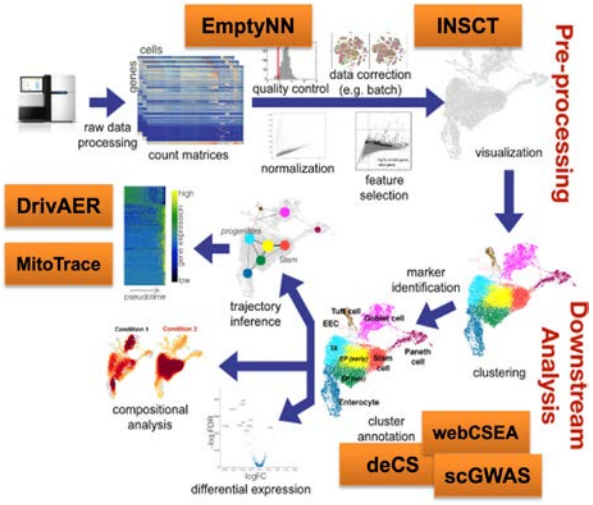
PI/ Professor: Zhongming Zhao, PhD

Vice President of Cancer Genomic Medicine, Chair Professor for Precision Health, McWilliams School of Biomedical Informatics, UTHealth
Contact: zhongming.zhao@uth.tmc.edu

"Multi-Scale, Integrated, and Contextualized (MUSIC) Approaches for Complex Disease Study"

The lab focuses on genomics, deep learning, precision medicine, translational science, and big data science. We develop novel computational approaches for deep understanding genetic variants and regulartory mechanisms in complex disease. Representative projects are below. The students may work with Dr. Zhao to identify a long-term project for thesis.

Multi-Scale, Integrated, and Contextualized Approaches for Complex Disease. In this NIH U01 project, we will develop and implement a robust AI framework, namely AIM-AI, for transforming the genetic catalog of Alzheimer's disease (AD) in a way that is Actionable, Integrated and Multiscale. We will engineer novel deep learning algorithms and GPT-based foundational models to build a powerful brain molecular chronological age predictor and further to dissect cell-type specific, genetic regulatory mechanisms in complex disease like AD.



Single-cell methods/tools developed in Zhao lab.

Predicting Phenotype by Deep Learning Heterogeneous Multi-Omics Data. In this NIH R01 project, we combine bioinformatics, statistical genetics, and phenotype and electronic medical record (EMR) data mining to develop novel analytical strategies that maximally leverage regulatory information from both genotype and expression (spatio-temporal and single cell levels).

Single-cell Sequencing Approaches for Neurodevelopmental Diseases and Cancer Immunotherapy.

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, with more than 400 publications in the past 14 years. The lab is in an interdisciplinary research environment, currently with 16 members in total (junior facultyx4, students x5, postdocs x4, research scientistx1, research coordinatorx1, program managerx1). The lab has developed many computational methods/tools and biomedical databases/resources. Sequencing facilities are in house. Dr. Zhao has trained more than 50 students and postdocs (24 have become faculty, including two CPRIT scholars).

Applying. We encourage those students who are interested in deep learning, genomic medicine and single-cell omics to apply. We have stable and abundant funding including several NIH/CPRIT grants as well as Dr. Zhao's startup and chair professorship fund.