THE UNIVERSITY OF TEXAS MD Anderson Cancer Center | UTHealth Houston
Graduate School of Biomedical Sciences

Genetics & Epigenetics Program

Research Summaries Of Faculty Seeking Students

Partial List as of 8/16/23

See all faculty research profiles
on the GSBS website

Genetics & Epigenetics Program
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

Francesca Cole, PhD
Epigenetics & Mol. Carcinogenesis, MDA

Giulio Draetta, MD, PhD
Genomic Medicine, MDA

George Eisenhoffer, PhD
Genetics, MDA

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

Michael Galko, PhD
Genetics, MDA

Boyi Gan, PhD
Experimental Radiation Oncology, MDA

Yejing Ge, PhD
Cancer Biology, MDA

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

Wenbo Li, PhD
Biochemistry & Molecular Biology, UTHealth Houston

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

Victor Lopez del Amo
Epidemiology, UTHealth Houston

Guillermina Lozano, PhD
Genetics, MDA

Kevin McBride, PhD
Epigenetics & Mol Carcinogenesis, MDA

Rachel Miller, PhD
Pediatrics, UTHealth Houston

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

Wantong Yao, PhD
Translational Molecular Pathology, MDA

Jihye Yun, PhD
Genetics, MDA

Jianjun Zhang PhD
Thoracic/Head & Neck Medical Oncology, and Genomic Medicine, MDA

Xiaotian Zhang, PhD
Biochemistry & Molecular Biology, UTHealth Houston

Genetics & Epigenetics Program
Faculty Seeking Students

Faculty are listed in one or two categories

Cancer Genetics

C. Marcelo Aldaz, PhD
Swathi Arur, PhD
Giulio Draetta, MD, PhD
George Eisenhoffer, PhD
Boyi Gan, PhD
Yejing Ge, PhD
Shih-Han (Peggy) Lee, PhD
Yuan-Hung Lo, PhD
Victor Lopez del Amo, PhD
Guillermina Lozano, PhD
Peter Van Loo, PhD
Bin Wang, PhD
Wenyi Wang, PhD
Wantong Yao, PhD
Jihye Yun, PhD
Jianjun Zhang, PhD
Xiaotian Zhang, PhD

Developmental Genetics

Swathi Arur, PhD
Blaine Bartholomew, PhD
Richard Behringer, PhD
Francesca Cole, PhD
George Eisenhoffer, PhD
Michael Galko, PhD
Rachel Miller, PhD
Ambro van Hoof, PhD
Jun Wang, PhD

Epigenetics

Blaine Bartholomew, PhD
Richard Behringer, PhD
Yejing Ge, PhD
Wenbo Li, PhD
Yuan-Hung Lo, PhD
Peter Van Loo, PhD
Jun Wang, PhD
Xiaotian Zhang, PhD

Genome Maintenance & Repair

Francesca Cole, PhD
Kevin McBride, PhD
Bin Wang, PhD

Human Genetics

C. Marcelo Aldaz, PhD
Myriam Fornage, PhD
Wenbo Li, PhD
Ambro van Hoof, PhD
Jianjun Zhang, PhD

PI: C. Marcelo Aldaz, MD, PhD

Professor
Epigenetics and Molecular Carcinogenesis,
UT MD Anderson Cancer Center, South Campus, SCRB4 4th floor
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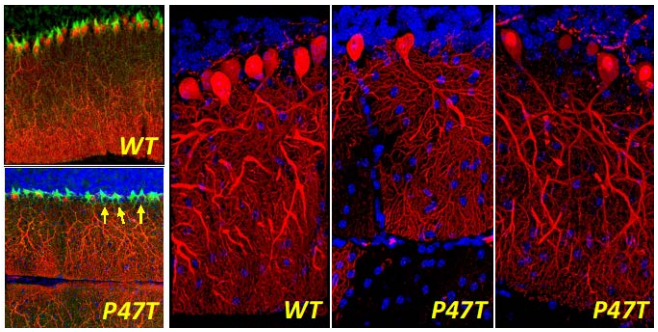
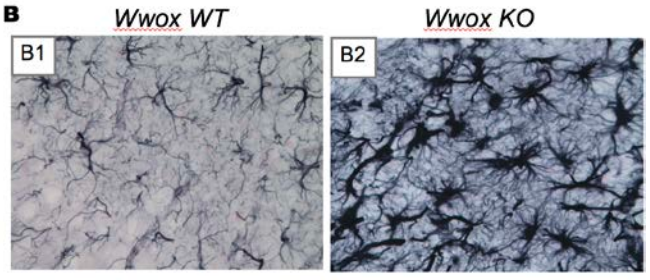
My laboratory was the first to discover and clone *WWOX* (WW domain containing oxidoreductase) the gene spanning chromosomal fragile site FRA16D, the 2nd most common site for spontaneous chromosomal breakage, deletion, and rearrangement in the human genome. Germline and somatic mutations affecting *WWOX* 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 analyses 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 the major objectives in our lab.



Purkinje cells degeneration in cerebellum of mice carrying a single amino acid loss-of-function knock-in mutation (P47T) in the WW domain of Wwox

We are always interested in recruiting passionate students !



Evidence of astrogliosis in brains of *Wwox KO* mice. (Hussain et al. Neurobiol. Dis. 2019 Jan;121:163-176)

Hussain T, et al**.** Wwox P47T loss-of-function mutation induces epilepsy, progressive neuroinflammation, and cerebellar degeneration in mice phenocopying human SCAR12. *Prog Neurobiol.* 2023 Apr;223:102425. PMID: 36828035. https://pubmed.ncbi.nlm.nih.gov/36828035/

Aldaz CM, Hussain T. WWOX Loss of Function in Neurodevelopmental and Neurodegenerative Disorders. *Int J Mol Sci.* 2020 Nov 24;21(23):8922. doi: 10.3390/ijms21238922. PMID: 33255508; PMCID: PMC7727818. https://pubmed.ncbi.nlm.nih.gov/33255508/

Hussain T, et al. (2019). Wwox deletion leads to reduced GABA-ergic inhibitory interneuron numbers and activation of microglia and astrocytes in mouse hippocampus. *Neurobiol Dis.* 121:163-76. PMCID: PMC7104842 https://www.ncbi.nlm.nih.gov/pubmed/30290271.

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.

Lab team, 2022-2023. Changes to this team: Raisa Reyes Castro graduated in 2023 May, Jake Seemann joined medical school in 2023 Summer.

Talk to them to learn about the lab culture!

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.*

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, Janet Cheng & 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?

Blaine Bartholomew, PhD
Professor
Epigenetics & Molecular Carcinogenesis
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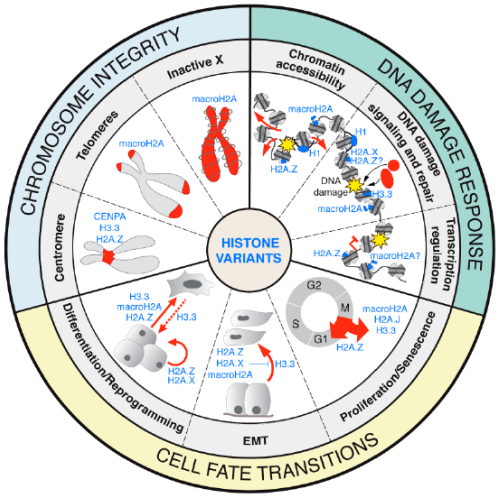
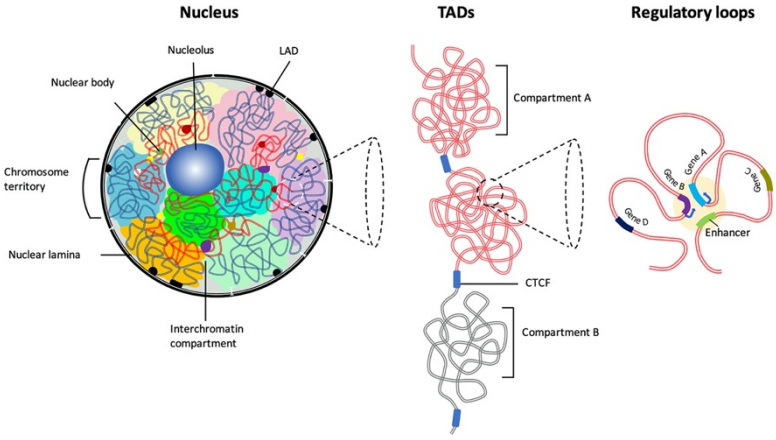
Nuclear Organization
Cell Differentiation &
Chromatin Remodeling

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.





Chromatin Dynamics
Transcription Regulation
DNA Replication & Repair

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

Behringer Lab

Our research focuses on the molecular and cellular mechanisms that lead to the formation of a mammalian embryo, the genesis of tissues and organs during development, and the pathological consequences of developmental defects. In addition, we study the genetic mechanisms that result in organ morphology and physiology differences that have evolved between species. We utilize genetic, embryological and comparative approaches.

The reproductive organs are essential for individuals to generate progeny and are a common source of disease. We are interested in defining the factors that cause the male and female phenotypes, including gonad and reproductive tract differentiation during embryogenesis and after birth. We are currently defining gene regulatory networks for reproductive organ development, using "-omics" profiling of developing reproductive organ tissues and generation of mutations in a variety of vertebrate species, including mammals, amphibians, reptiles, and birds.

PI: Francesca Cole, PhD

Associate Professor
Director of the Genetics and Epigenetics Program
NIH Director's New Innovator and CPRIT Scholar
Epigenetics and Molecular Carcinogenesis,
UT MD Anderson Cancer Center, South Campus, SCRB4 4th floor
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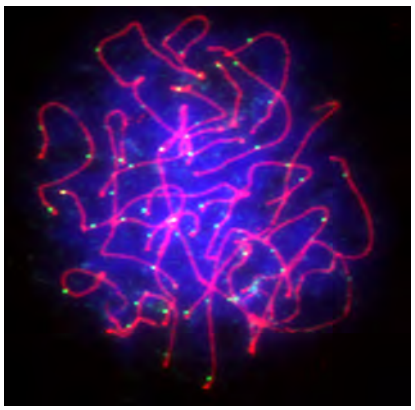
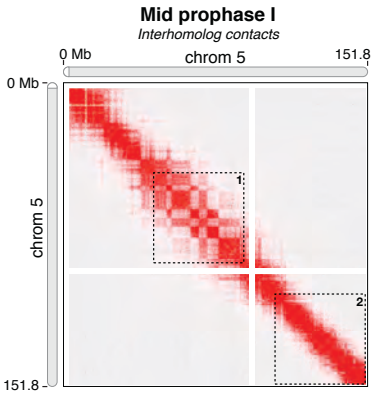
"DNA repair and chromosome biology during meiosis"

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

We have developed assays to provide high-resolution mapping of recombination outcomes on all four chromatids (Cole F et al **Nature Genetics 2014** to determine the molecular nature of individual events and to biochemically and genetically delineate contributions from DNA repair pathways (Zelazowski M et al **Cell 2017**). We have 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, **Molecular Cell, 2023**) We are currently developing whole genome single-cell sequencing to investigate recombination. Finally, the lab couples these molecular approaches with advanced microscopy (Cole F et al **Nature Cell Biology 2012**) to provide a holistic view of recombination during mouse and human meiosis.



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



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

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

The lab currently has eight members: PI, two postdocs, 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: Melissa Frasca, Emely Larios, and Ericka Humphrey!

Giulio Draetta, MD, PhD

I am a professor and Sewell Family Chair in the Department of Genomic Medicine, with a joint appointment in the department of Molecular and Cellular Oncology at The University of Texas MD Anderson Cancer Center. I also serve the institution as senior vice president and chief scientific officer. The research in 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. Focus areas include tumor heterogeneity, oncogenic reprograming of epigenetic and metabolic pathways, and mechanisms of disease adaptation and evolution. My research programs have initiated numerous drug discovery projects within MD Anderson's Therapeutics Discovery Division, including ongoing projects to identify drugs targeting the epigenetic and metabolism machineries.

I continue to train postdoctoral fellows and PhD students, and I am an active member of the Genetics and Epigenetics program faculty within the Graduate School for Biomedical Sciences. Since the 10 years that I have been here, twenty of my former MD Anderson trainees have moved on, six to academic tenure-track positions, six as research scientists in drug discovery environments, two in research administration, three to postdoctoral training, and three have returned to medicine. I am specifically focused on enticing our trainees to learn and apply genetics, biochemistry, and computational methods in pursuit of the identification of novel cancer mechanisms. I am insisting on avoiding the temptation to engage in poorly defined, observational translational/clinical science.

Ether phospholipids are required for mitochondrial reactive oxygen species homeostasis.
Chen Z, Ho IL, Soeung M, Yen EY, Liu J, Yan L, Rose JL, Srinivasan S, Jiang S, Edward Chang Q, Feng N, Gay JP, Wang Q, Wang J, Lorenzi PL, Veillon LJ, Wei B, Weinstein JN, Deem AK, Gao S, Genovese G, Viale A, Yao W, Lyssiotis CA, Marszalek JR, **Draetta GF**, Ying H. Nat Commun. 2023 Apr 17;14(1):2194. doi: 10.1038/s41467-023-37924-9.

Medium-Chain Acyl-CoA Dehydrogenase Protects Mitochondria from Lipid Peroxidation in Glioblastoma.
Puca F, Yu F, Bartolacci C, Pettazzoni P, Carugo A, Huang-Hobbs E, Liu J, Zanca C, Carbone F, Del Poggetto E, Gumin J, Dasgupta P, Seth S, Srinivasan S, Lang FF, Sulman EP, Lorenzi PL, Tan L, Shan M, Tolstyka ZP, Kachman M, Zhang L, Gao S, Deem AK, Genovese G, Scaglioni PP, Lyssiotis CA, Viale A, **Draetta GF.** Cancer Discov. 2021 Nov;11(11):2904-2923. doi: 10.1158/2159-8290.CD-20-1437. Epub 2021 May 26.

Syndecan 1 is a critical mediator of macropinocytosis in pancreatic cancer.
Yao W, Rose JL, Wang W, Seth S, Jiang H, Taguchi A, Liu J, Yan L, Kapoor A, Hou P, Chen Z, Wang Q, Nezi L, Xu Z, Yao J, Hu B, Pettazzoni PF, Ho IL, Feng N, Ramamoorthy V, Jiang S, Deng P, Ma GJ, Den P, Tan Z, Zhang SX, Wang H, Wang YA, Deem AK, Fleming JB, Carugo A, Heffernan TP, Maitra A, Viale A, Ying H, Hanash S, DePinho RA, **Draetta GF.** Nature. 2019 Apr;568(7752):410-414. doi: 10.1038/s41586-019-1062-1. Epub 2019 Mar 27.

Synthetic vulnerabilities of mesenchymal subpopulations in pancreatic cancer.
Genovese G, Carugo A, Tepper J, Robinson FS, Li L, Svelto M, Nezi L, Corti D, Minelli R, Pettazzoni P, Gutschner T, Wu CC, Seth S, Akdemir KC, Leo E, Amin S, Molin MD, Ying H, Kwong LN, Colla S, Takahashi K, Ghosh P, Giuliani V, Muller F, Dey P, Jiang S, Garvey J, Liu CG, Zhang J, Heffernan TP, Toniatti C, Fleming JB, Goggins MG, Wood LD, Sgambato A, Agaimy A, Maitra A, Roberts CW, Wang H, Viale A, DePinho RA, **Draetta GF**, Chin L. Nature. 2017 Feb 16;542(7641):362-366. doi: 10.1038/nature21064. Epub 2017 Feb 8.

Oncogene ablation-resistant pancreatic cancer cells depend on mitochondrial function.
Viale A, Pettazzoni P, Lyssiotis CA, Ying H, Sánchez N, Marchesini M, Carugo A, Green T, Seth S, Giuliani V, Kost-Alimova M, Muller F, Colla S, Nezi L, Genovese G, Deem AK, Kapoor A, Yao W, Brunetto E, Kang Y, Yuan M, Asara JM, Wang YA, Heffernan TP, Kimmelman AC, Wang H, Fleming JB, Cantley LC, DePinho RA, **Draetta GF.** Nature. 2014 Oct 30;514(7524):628-32. doi: 10.1038/nature13611. Epub 2014 Aug 10

THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

George T. Eisenhoffer, PhD

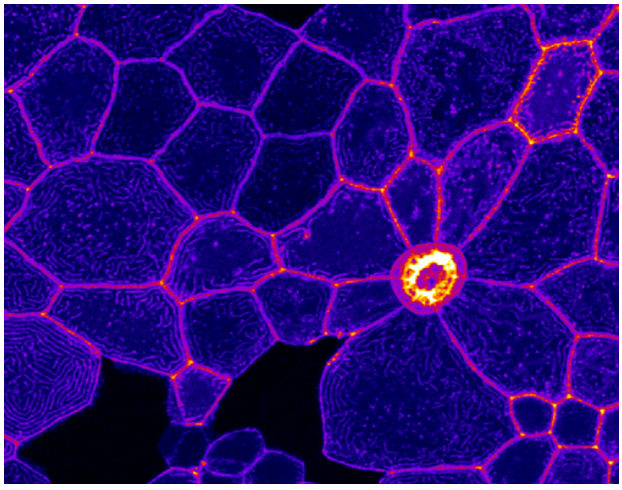
Associate Professor
Department of Genetics
gteisenhoffer@mdanderson.org

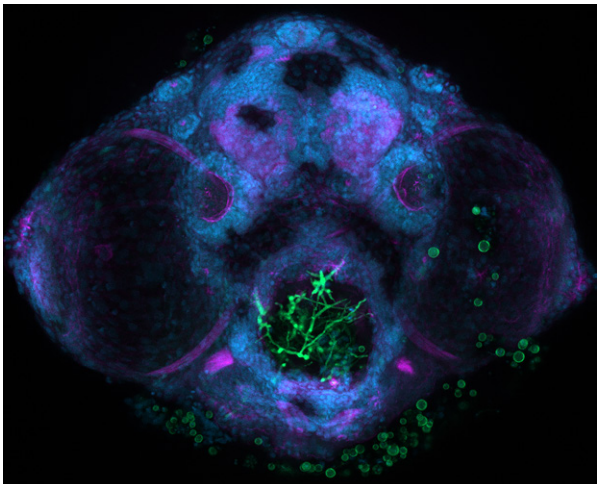
Research Interests

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.

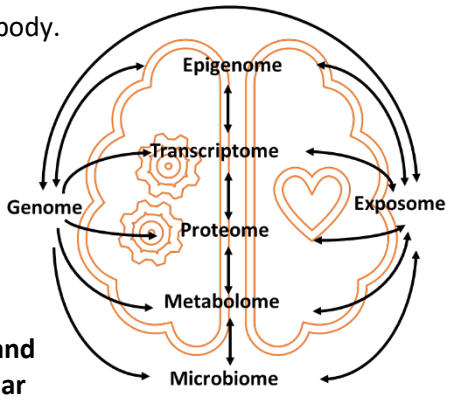
Our studies have provided mechanistic insight into how localized changes in physical forces are coordinated to remove defective cells from living epithelial tissues (Atieh et al., 2021 Current Biology, Franco et al., 2019 MBoC). We have also interrogated the cell loss-induced signaling events and cellular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

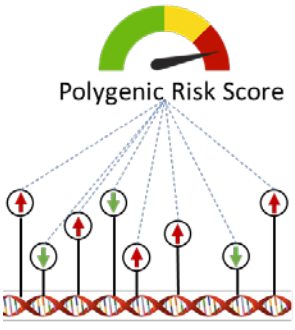
"Molecular Epidemiology of the Aging Brain in Diverse Populations and Across the Lifespan"

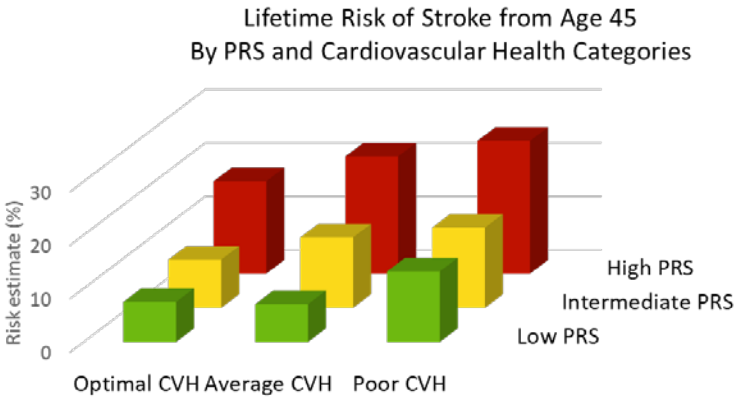


Throughout our lifetime our brain changes more than any other part of our body. Beginning in midlife, aging brings about subtle changes in brain structure, chemistry, and function. These changes are detectable by **neuroimaging techniques** and are associated with a greater risk of future stroke, cognitive 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.

Michael J. Galko, Ph.D.

Professor, Department of Genetics
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Michael J. Galko

Research Interests:

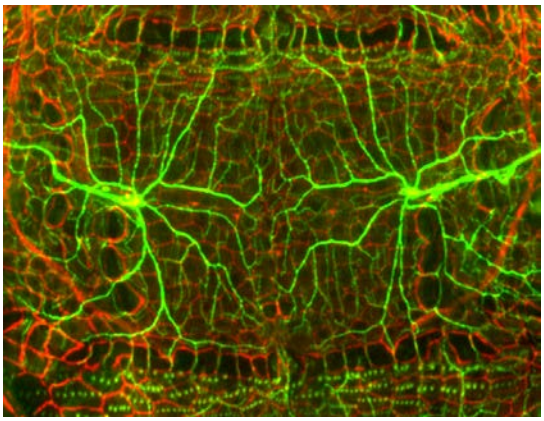
Pain sensitization
Analgesia
Skin wound healing
Drosophila genetics

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 damaging stimuli and repair tissue damage, both in the normal animal and during disease states or disease treatment (chemotherapy).

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.



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

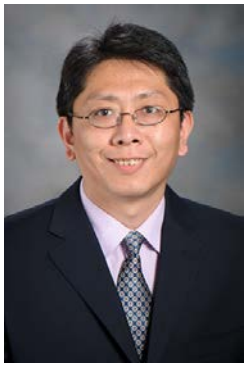
Student Awards: Total students graduated (6); AHA pre-doctoral fellowships (2); NIH F31 predoctoral fellowship (1); Larry Sandler Memorial Award for best doctoral thesis employing *Drosophila* (1; an international award sponsored by Genetics Society of America); GSBS fellowships (multiple); GSBS President's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

Student-driven publications: All past students graduated with first-author papers. Student-driven papers have appeared in PNAS (2008), Current Biology (2009, 2009, 2011, 2016), Genetics (2010, Cover), J. Cell Science (2012), eLife (2015), Cell Death and Disease (2017), Developmental Biology (2017), PLoS One (2018), Development (2019) and G3 (2022). Students are taught to write scientific papers.

Funding: My lab has two large active NIH grants that extend for the next 4-5 years. We seek to take two PhD-track graduate students in Summer 2024 to join two graduate students currently in the lab.

Lab environment: I run a smallish laboratory whose focus is graduate student training- in particular developing independent scientists working on creative projects. We have weekly group meetings/journal clubs that have a strong emphasis on data analysis, evaluation, and presentation. Students work on independent projects and meet in office bi-weekly (formally) to review data/progress and informally (in lab) more frequently. Students attend national meetings once per year. I am open to students interested in any future career path, though most former trainees have pursued postdoctoral research.

Seeking Graduate Students



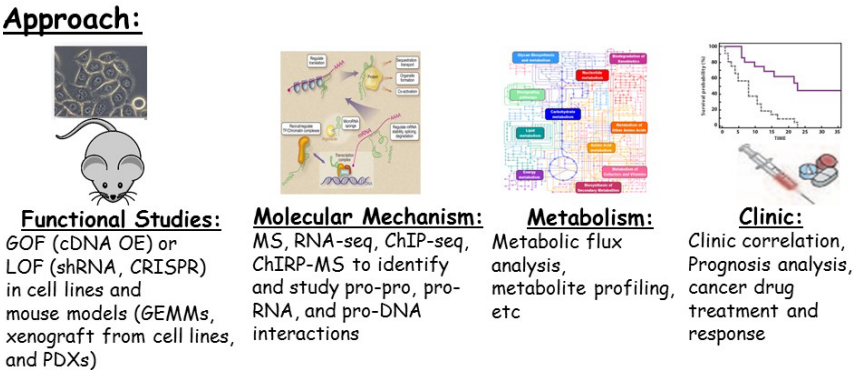
PI: Boyi Gan, PhD

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:

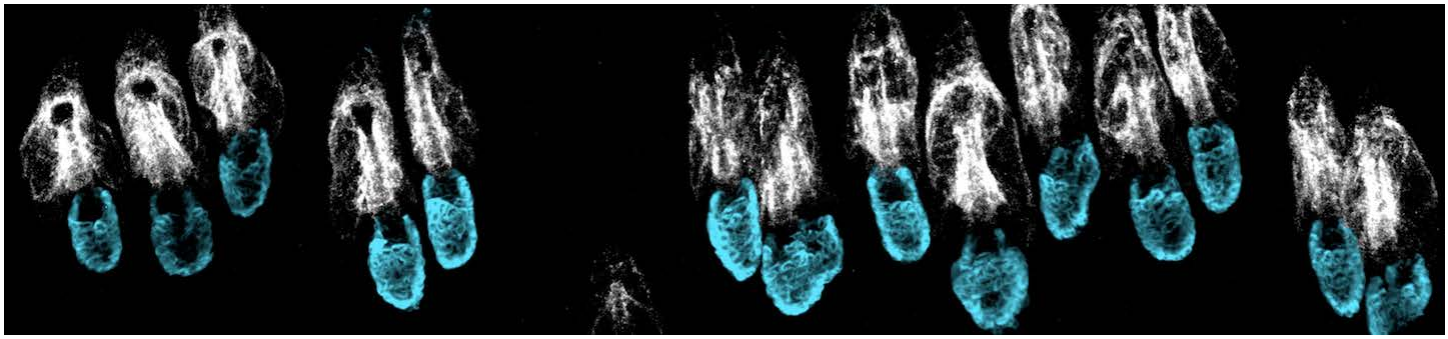
1. Zhang Y, et al., **Gan B**. BAP1 links metabolic regulation of ferroptosis to tumor suppression. **Nature Cell Biology**, 2018.
2. Lee H, et al., **Gan B**. Energy stress-mediated AMPK activation inhibits ferroptosis. **Nature Cell Biology**, 2020.
3. Liu X, et al., **Gan B**. Cystine transporter 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
Department of Cancer Biology
UT MD Anderson Cancer Center,
Houston TX
Contact: YGe1@mdanderson.org

Ge Lab
Skin Functional Genomics



Defined by golden standards of long-term self-renewal and multi-lineage differentiation, stem cells (SCs) come in different flavors. In mammals, adult SCs are essential units to orchestrate postnatal remodeling and repair damage. Upon stress, SCs often expand their fates and embark on behaviors distinct from their homeostatic patterns, known as plasticity. While plasticity is essential for organismal survival, its derailed regulation poses disease vulnerability to individuals, where SCs are subjected to functional exhaustion frequently observed in aging, or malignant transformation that occurs in cancer (Ge et al, **Nat Cell Biol**, 2016; Ge et al, **Cell**, 2017; Ge et al, **Nat Rev Genetics**, 2018; Ge et al, **PNAS**, 2020; Lyu, Guan et al, 2022 **Genes & Dev**). Research in the Ge lab uses skin as a model system, and applies mouse genetics, functional genomics and development biology approaches to dissect molecular mechanisms underlying SC plasticity, and how its deregulation leads to human diseases, including wound repair, cancer, and aging. Come check us out at our website yejinggelab.com

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

Our Core Values

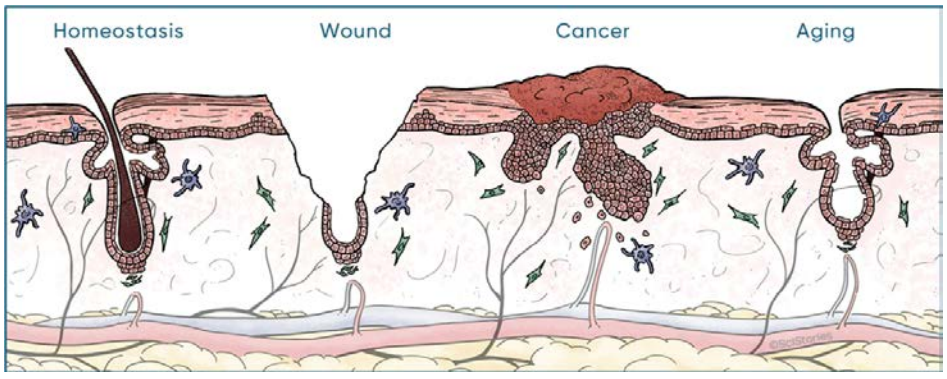
Creativity
Science is fun. Think outside the box.

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

Responsibility
Be a good lab citizen. Do care.

Perseverance
Be faithful to your passion. Be tough.

Freedom
You are here only because you want to be.



NATIONAL INSTITUTES OF HEALTH
THE UNIVERSITY OF TEXAS MD Anderson Cancer Center Making Cancer History
CPRIT
DEPARTMENT OF DEFENSE
afar
WOMEN & SCIENCE
ROBERTSON FOUNDATION

PI: Shih-Han “Peggy” Lee, Ph.D.

Assistant Professor, CPRIT Scholar
Department of Genetics,
UT MD Anderson Cancer Center, BSRB 11th floor
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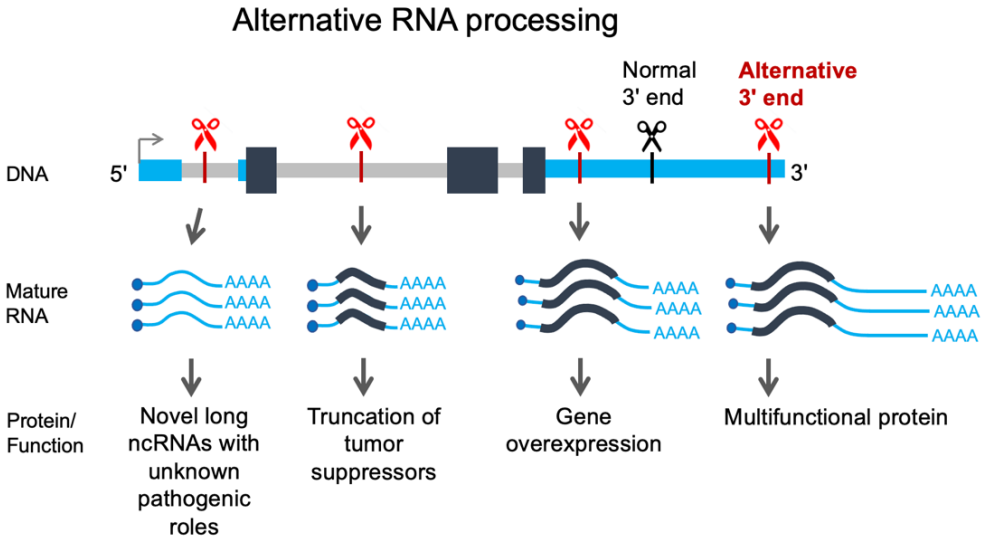
Webpage: https://www.mdanderson.org/research/departments-labs-institutes/labs/lee-laboratory.html

“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.

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

A recent lab picture taken in October 2022 (annual lab BBQ party in Herman Park). Lab members and friends.

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** 2013; **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). Full publication list can be found in NCBI MyBibliography: https://www.ncbi.nlm.nih.gov/myncbi/1Jip8J4DFUsQe/bibliography/public/.

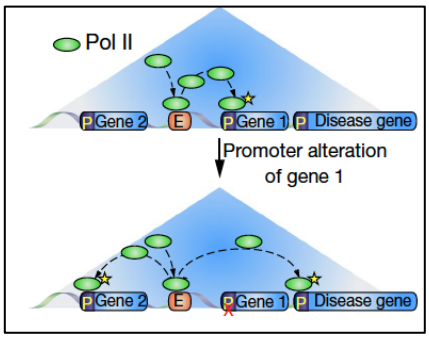


Figure 1*. A diagram showing cancer mutations deregulate cancer genes via Enhancer release and retargeting (ERR).*

Recently, we found that cancer point mutations or common human genetic variants can rewire disease gene expression via a novel mechanism called Enhancer release and retargeting (Oh et al., 2021, ***Nature***, *Figure 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, which may underlie COVID-19 pathology (Wang et al., 2023, **Nature Microbiology**).

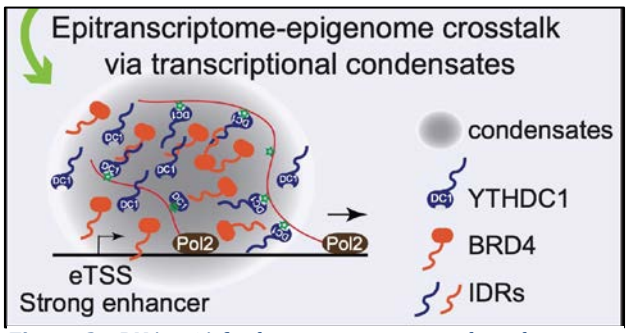


Figure 2*. eRNA m6A facilitates transcriptional condensates.*

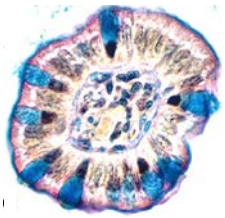
About the lab: We currently have two senior scientists/instructors, four postdocs, seven GSBS PhD/MS students and 3 lab assistants in the lab (by August 2023). We welcome students with an enthusiasm to uncover fundamental biology mechanisms of noncoding RNAs, epigenetics and 3D genome control, and in cancer therapy using RNA drugs. 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 exposure to frontiers of 3D genome research.

Our lab intends to take one or two new graduate students for long term thesis projects in 2023/2024.

Contact: Wenbo Li, Ph.D., Biochemistry and Molecular Biology, UTHealth 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.

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:

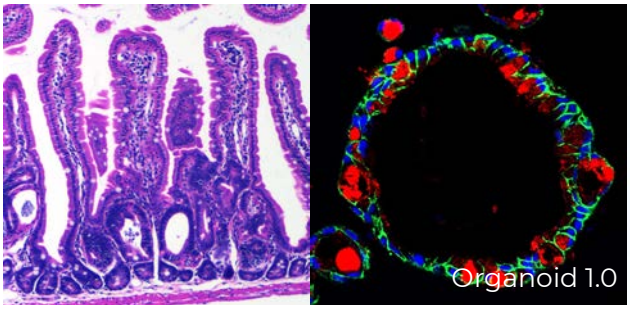
Modeling Gastric Cancer in Primary 3D Organoids. We are building innovative 3D tumor organoid models utilizing CRISPR/Cas9 genome-editing technologies. Our engineered tumor organoids faithfully mimic various stages of gastric cancer progression (**Organoid 1.0**). These models are valuable tools for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

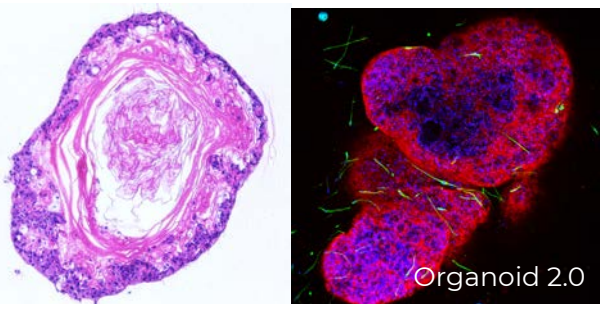
Unveiling Gastrointestinal Stem Cell and Tumor Niche. We are pioneering sophisticated 3D culture systems (**Organoid 2.0**) to simulate stromal components of the tissue microenvironment. Using state-of-the-art imaging technologies, we aim to unravel the intricate interactions between normal and malignant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





PI: Victor Lopez del Amo, Ph.D
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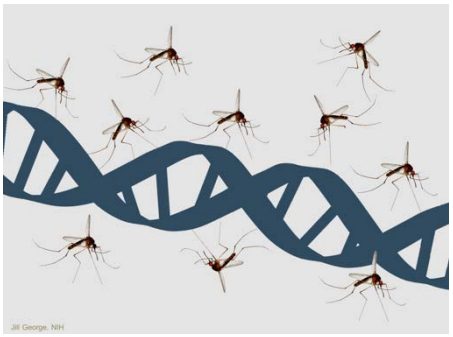
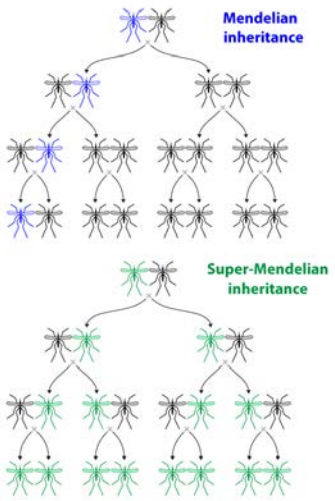
Website: www.lopezdelamolab.com



"***Using CRISPR-based genome editing approaches for reducing the impact of vector-borne diseases.***"

Background: Even with extensive work to curb its spread, mosquito-borne diseases such as malaria or dengue affect millions of people and causes over 800,000 deaths a year. Strategies for limiting the spread of these diseases mainly focus on curbing mosquito populations, with insecticides; yet, mosquitoes are evolving resistance to these chemicals, raising concerns about their long-term effectiveness. Vector control has also been explored through population suppression methods designed to crash a mosquito community by releasing sterile males that produce non-viable progeny; however, these strategies require complex continuous releases and large-scale mosquito rearing. Other strategies attempt to control susceptibility to the pathogens, such as vaccines to immunize the human population, though the most promising ones have only shown modest effects. Lastly, genetically engineering in effector genes to make mosquitoes resistant to the pathogen have been proposed as a tool for population modification, though the lack of a mechanism to spread these transgenes prevented their introgression into the target population.

CRISPR gene-drive technologies: The emergence of CRISPR-based technologies provides promising new tools for reducing the impact of vector-borne diseases. In particular, CRISPR gene-drive systems employ a Cas9 enzyme that acts like scissors to cut DNA at a specific location, and a guide RNA (gRNA) that directs the Cas9 where to cut. By surpassing the inheritance limit of 50% dictated by Mendel's law of gene segregation, these engineered cassettes allow for the introduction of a gene of interest that imparts new traits to modified animals. This offers tremendous potential for engineering wild populations due to their ability to self-propagate and spread quickly through a population via super-Mendelian inheritance rates (see **Image "spread of a gene drive"**).



Spread of a gene-drive element. The self-propagating gene drive promotes the spread of desired traits into a population by biasing Mendelian inheritance towards super-Mendelian.

Our main goal is to develop next-generation genome editing technologies toward controlling mosquito populations while reducing the burden of mosquito-borne diseases such as malaria. We have developed a split gene-drive system (Lopez del Amo, V., ***Nature Communications*** 2020), and a drug-inducible gene drive method (Lopez del Amo, V., ***Cell Reports*** 2020), which bring new opportunities for field implementation. Besides, I contributed to the generation of the first Cas9 line in *Culex quinquefasciatus* mosquitoes, the West Nile Vector, to facilitate the development of genome-editing methods for population engineering in these species (Xuechun Feng, ***Nature Communications*** 2021). Recently, we described and patented a new form of a gene drive that employs a nickase Cas9 to introduce paired single-strand breaks and promote efficient DNA homology directed-repair in the germline of a living organism (Lopez del Amo, V., ***Cell Reports*** 2022).

Environment: Our newly established lab is growing and seeking new students who are looking to grow both scientifically and personally in a peaceful and safe atmosphere. The PI is committed to the career development of all team members.

We use flies to optimize our CRISPR methods. Presence of the engineered DNA pieces are tracked with fluorescent markers.

(Left) Wildtype mosquito **(Right)** Transgenic mosquito expressing Cas9 marked with DsRed fluorescence (Feng, X., ***Nature Communications*** 2021)

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 occur in some human cancers are not tolerated by normal cells. We have an ongoing CRISPR/Cas9 screen to identify factors that allow normal cells to survive despite elevated levels of MDM2 to identify and characterize synthetic lethal relationships with high MDM2 in tumors.

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

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

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

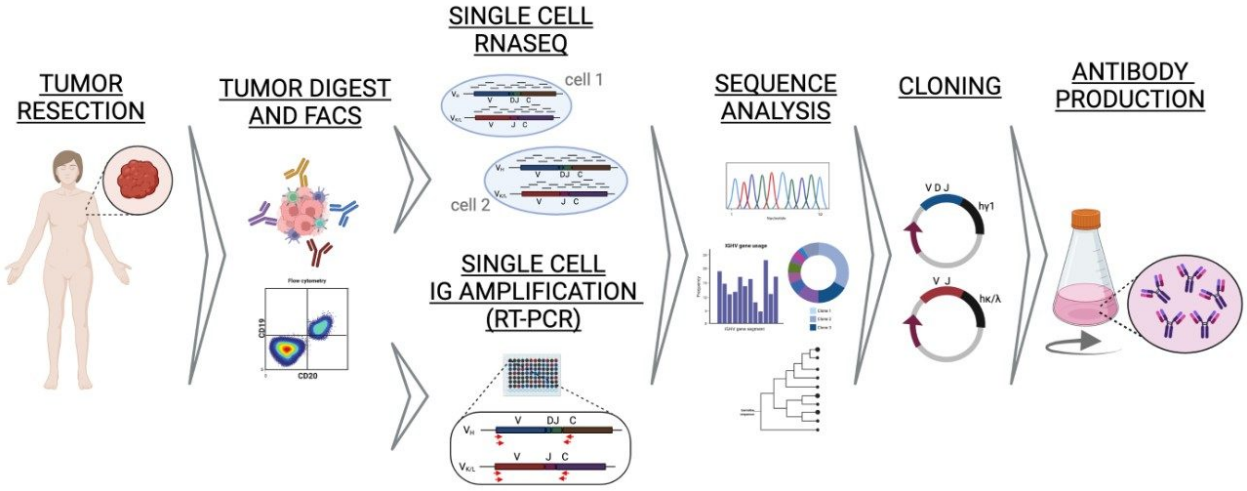
McBride Lab:

[B Cells in the Tumor Microenvironment and Patient Immunotherapy Response]

The McBride group is breaking new ground in understanding B cell responses in tumor immunology. They are highly focused on comparing the immunoglobulin repertoire from patients who do and do not respond to immune checkpoint blockade (ICB), but they also have many other collaborative projects based on defining the immunoglobulin repertoire in different disease states and experimental conditions.

Tertiary lymphoid structures (TLSs) are lymphoid organs that form in non-lymphoid tissues, often in response to chronic inflammation. In tumors, the presence of TLSs correlates with better overall patient survival and better patient response to immunotherapy. Preliminary evidence from the McBride lab indicates that *patients with a positive response to ICB may have B-cells that produce tumor-specific antibodies in the TLS*. However, it is unclear how TLSs interact with the tumor microenvironment or how a specific tumor microenvironment impacts B cell function in the TLS/tumor. To better understand these interactions, the McBride Lab is defining the immunoglobulin repertoire of tumor-infiltrating B cells in patients who do and do not respond to immunotherapy in melanoma, renal cell carcinoma, sarcoma, and non-small cell lung cancer.

The unique pipeline developed in the lab for recombinant antibody production has been adapted, as outlined below, for studying human patient samples. In this scheme, human tumor tissue samples are enzymatically digested to release single cells. The cells are sorted and analyzed to identify and isolate B cells recognizing a single antigen through a combination of fluorescence-activated cell sorting (FACS), single cell RNA-seq, and amplification of expressed immunoglobulin genes using RT-PCR. The amplified genes are sequenced and assessed for parameters including mutation profile. The genes are then cloned into expression vectors allowing for recombinant antibody production and testing for a number of applications including immunoblotting, immunohistochemistry and enzyme-linked immunosorbent assay (ELISA). Overall, this methodology can be used to identify antibodies that recognize tumors, the specific antigens the antibodies recognize, and characterize those antibodies that recognize tumor cell surface antigens. This opens the possibility of identifying and recombinantly producing antibodies with the potential to enhance ICB efficacy in patients who lack a robust response to conventional ICB therapy.



Projects within this research theme include:

• Defining the immunoglobulin repertoire of tumor-infiltrating B cells in patients undergoing ICB therapy
• Characterizing B cells and the immunoglobulin repertoire in melanoma, head and neck cancer, non-small lung cancer, sarcoma, and ovarian cancer
• Working with immunologists and other collaborators toward the goal of potentiating ICB therapy by evaluating the tumor-recognizing capacity and anti-tumor efficacy of the antibodies identified through the lab's pipeline

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

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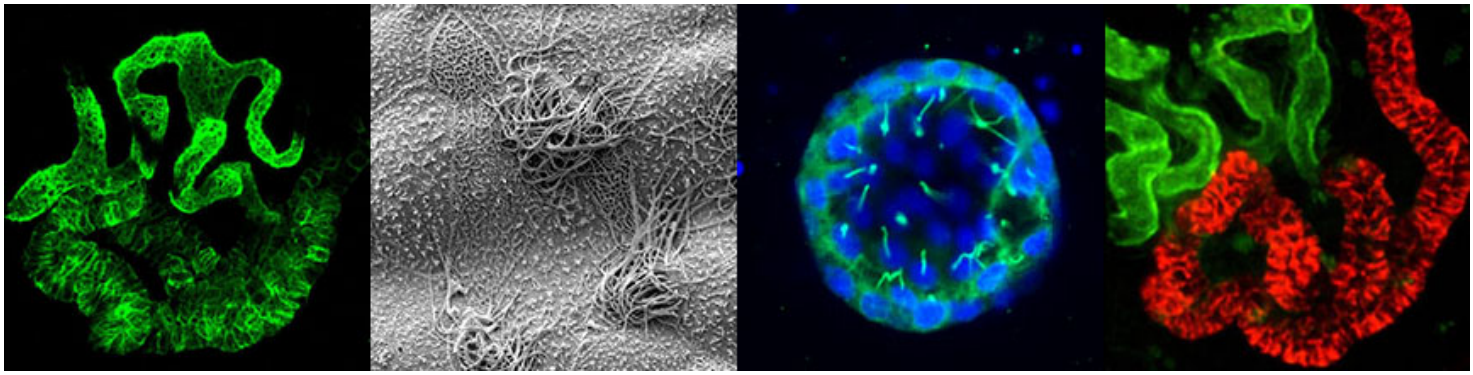

“Modeling kidney development and disease in frog embryos”

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 laevis*) 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 compartive 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, our goal is to underdand the cellular processes that drive kidney development.

Environment. We have a highly colloborative 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 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 graduate student.

PI: Ambro van Hoof, PhD
Professor
Microbiology and Molecular Genetics
McGovern Medical School
Contact: ambro.van.hoof@uth.tmc.edu or current students
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, 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 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 three different programs. Most have subsequently obtained post-doctoral fellow positions at prestigious univeristies (Duke, UNC, UT Southwestern, BCM, UT MD Anderson) while others have directly moved into desired positions in biotech or health care industry (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. Two students graduated during the 2022/2023 academic year and we have funding and 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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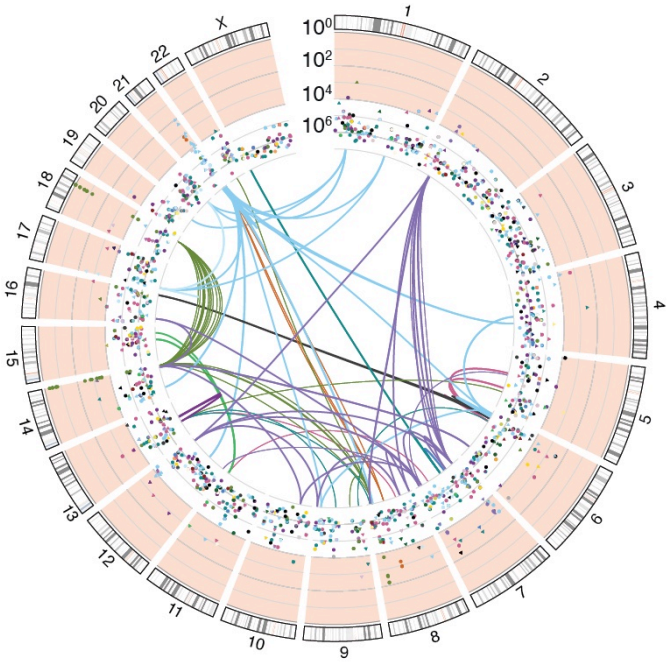
Cancer Genomics and Evolution Laboratory



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 s uccesses 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 succesfully 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

PI: Bin Wang PhD

Professor
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BSRB, S13.8116 a
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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.

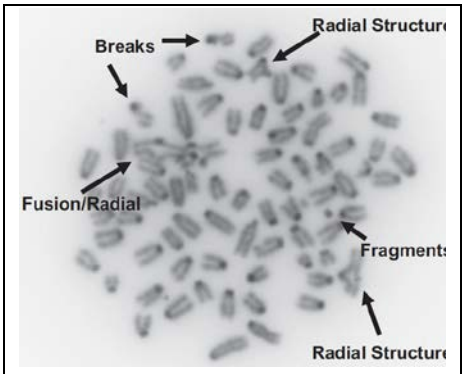
Ongoing Projects:

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

(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);

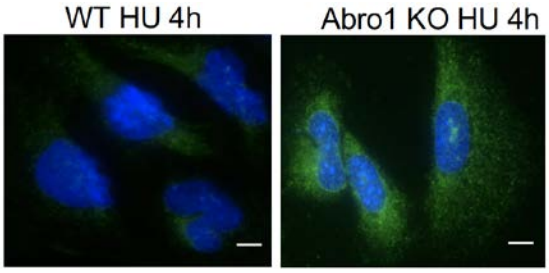
(3) how the cell protects genome stability in response to DNA replication stress (Xu et al, **Genes & Dev**, 2017).

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



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

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



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

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.

PI: Jun Wang, PhD
Associate Professor
Department of Pediatrics, McGovern Medical School
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Email: jun.wang@uth.tmc.edu
Website: https://med.uth.edu/pediatrics/faculty/jun-wang-ph-d/

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.

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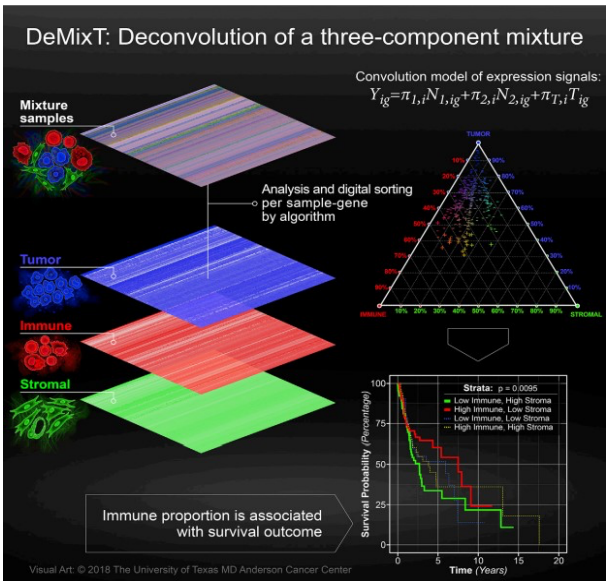
MD Anderson Cancer Center
Making Cancer History®

Statistical Bioinformatics Lab

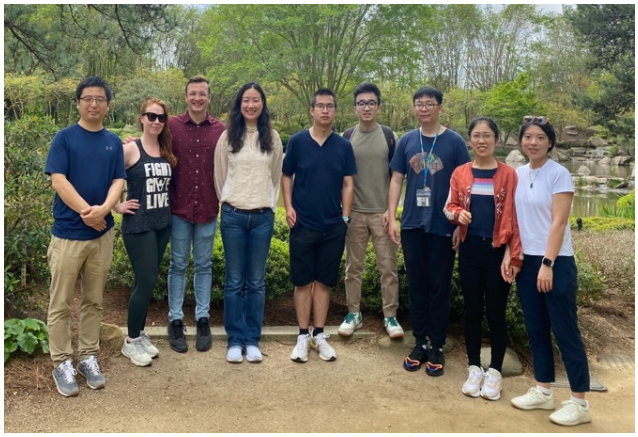


Our group passionately focuses on the development and application of computational methods to study the evolution of the human genome as well as the cancer genome, and predict cancer risk to accelerate the translation of biological findings to clinical practice. The two main research programs in our 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***), DeMixT for transcriptome deconvolution (***Wang Z, et al., iScience 2018***), and a pan-cancer characterization of genetic intra-tumor heterogeneity in subclonal selection (***Dentro et al., Cell 2021***). 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 predication modeling has been focused on hereditary cancer syndromes associated with germline *TP53* mutations. Past trainees have developed modeling to predict risk of *de novo* germline mutations (***Fan et al. Genome Research 2020***) and risk of multiple unique primaries or cancer-specific risk in individual patients. Current trainees are developing and testing tools to be used by clinicians and genetic counselors to provide quantifiable cancer risks to patients. Future research aims to investigate 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 have been published in prestigious medical journals and top statistics journals such as *Cancer Research*, *Genome Research*, *Genome Biology*, *JASA*, *Cell*, *Nature Biotechnology*, and *Nature*.



Environment

Our research group thrives in a highly collaborative environment, offering exceptional opportunities to partner with innovative cancer researchers and clinicians, specializing 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 making new discoveries in clinical data and/or multi-omic data using statistical methods, as well as developing therapeutic biomarker and new treatment strategy in cancer.

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

Wantong Yao Laboratory-Pancreatic Cancer Research

Contact: Wantong Yao, M.D., Ph.D.
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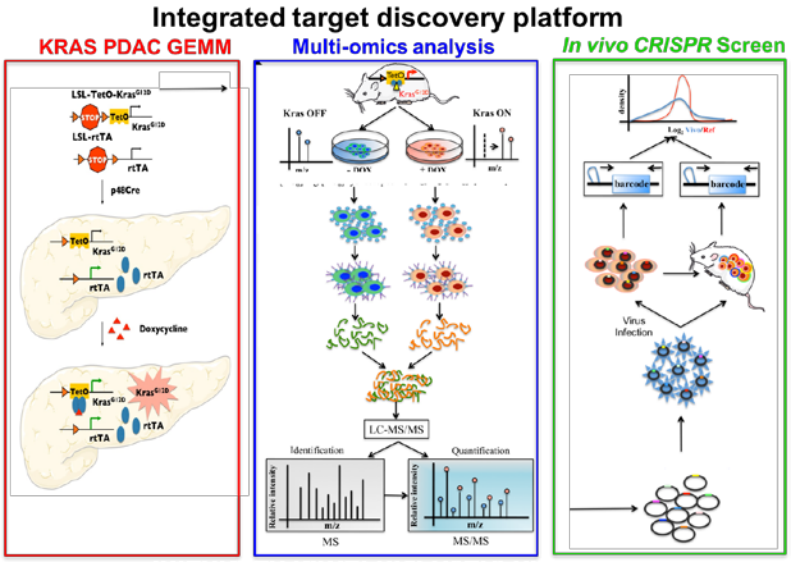
Lab webpage: https://www.mdanderson.org/research/departments-labs-institutes/labs/yao-laboratory.html

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



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

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

PI: Jihye Yun, Ph.D.

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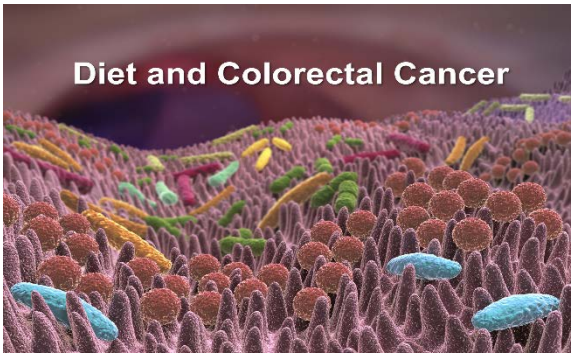
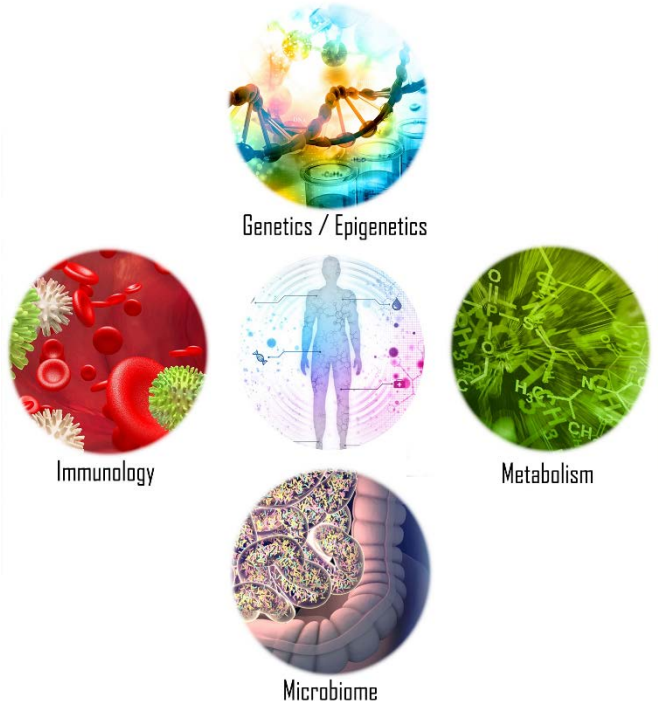


"The Role of Diet in Gut Microbiome and Colorectal Cancer: A Multi disciplinary Approach"



Our research goals are to understand the molecular mechanisms behind the interactions of diet and cells in the intestines. The intestine has many different types of cells including -but not limited to- intestinal stem cells, immune cells, microbiota, neural cells and cancer cells! The complex communications between diets and various cells in the intestines have profound effects on the development of chronic disease including colorectal cancer. Traditional monodisciplinary and reductionist approaches have limited potential for fulfilling our goals. **To overcome these limitations, we apply multidisciplinary and systems biology to unravel these complex and dynamic interrelationships using various mouse models, 3D organoids and state-of-the-art technologies.** We believe that discoveries from our research will have the direct and profound impact on our daily lives.

Environment: Our lab is a collaborative and supportive environment where students are encouraged to ask questions, take risks, and learn from each other. We work hard, but we also play hard. We believe that a healthy work-life balance is essential for productivity and creativity. We are looking for students who have a strong desire to learn and make a difference in the world. We value students who are passionate about their research, have a positive attitude, and are willing to work hard. If you are a motivated and passionate student who is looking for a challenging and rewarding PhD experience, then we encourage you to check our lab website and contact Jihye Yun to learn more about our lab.

Jianjun Jay Zhang Research Summary

I am an Associate Professor of Medical Oncology, a physician scientist dedicated to clinical and translational lung cancer research with specific training and expertise in lung cancer genomics and immunogenomics. My research has been focusing on elucidating the mechanisms and clinical implications of tumor heterogeneity; the impact of cancer molecular features on host anti-tumor immune surveillance during cancer evolution with or without therapy via integrative wet laboratory, bioinformatics and computational biology approaches. Our work mainly has focused on the following areas.

1. Discovered critical events in the initiation and progression of lung and oral precancers. (1) Revealed progressive genomic evolution at the single nucleotide level and demarcating evolution at the chromosomal level from lung precancer to invasive cancer; suggested neoplastic transformation of lung precancer is predominantly associated with a selective sweep of unfit subclones (*Hu, et al, Nat Commun, 2019*). (2) Demonstrated that hypermethylation is an early molecular event during initiation of precancer while hypomethylation takes place during the transition from precancer to preinvasive stages (*Hu, et al, Nat Commun, 2021*). (3) Demonstrated higher level of immunosuppression in invasive lung cancers compared to precancers and preinvasive cancers supporting immunotherapy for lung cancer prevention. (*Zhang et al, J Thorac Oncol, 2020; Dejima et al, Nat Commun, 2021*). These studies have led to the development of two unique lung cancer immunoprevention trials IMPRINT-lung (PI: Zhang), Can-Prevent-lung (PI: Zhang) and successfully secured grants including NIH R01, multi-institutional AACR Johnson & Johnson Innovative Cancer Research Grant, CPRIT IIRA etc. Moreover, these studies have also resulted in the filing of a patent for the immunoprevention of lung cancer.

2. Pioneered a series of studies on lung cancer heterogeneity. (1) Delineated intratumor heterogeneity (ITH) architecture of lung cancers in genomic (*Zhang et al, Science, 2014; Lee et al, Genome Biol. 2020; Chen et al, Nature Commun, 2021*), epigenetic (*Quek et al, Oncotarget, 2017; Hu, et al, Nat Commun, 2021*), transcriptomic landscape (*Lee et al, Mod Path, 2018; Lee et al, Genome Biol. 2020*) and in immune repertoire (*Reuben et al, Cancer Discov, 2017; Chen et al, Nature Commun, 2021; Dejima et al, Nat Commun, 2021; Francisco-Cruz et al, Mod, 2023*) and demonstrated that complex molecular ITH is associated with an immunosuppressive microenvironment and inferior survival. (2) Demonstrated genomic profiling may provide additional information to facilitate distinguishing potentially curable multicentric primary lung cancers from intrapulmonary metastasis (*Liu et al, Nat Commun, 2016; McLaughlin et al, J Thorac Dis, 2020*). (3) Explored the role of circulating cell-free DNA (cfDNA) analysis for investigating genomic ITH, prognostication, treatment decision making and disease monitoring (*Nong et al, Nat Commun, 2018; Lam et al, Clin Lung Cancer, 2018; Zhuo et al, Clin Cancer Res, 2020; Lam et al, J Thorac Oncol. 2020*). (4) Deciphered molecular and immune ITH evolution under treatment with chemotherapy, targeted therapy (*Jin et al, Oncogene, 2021*) or radiation (*Tang et al, Int J Radiat Oncol Biol Phys, 2020*) and discovered that induction of immunosuppression may be a common characteristic of cancer cells with metastatic plasticity (*Lee et al, Genome Biol., 2020*). These studies have merited grant support including ASCO Young Investigator Award, MD Anderson Physician Scientist Award and Lung Cancer Research Foundation, NIH U01 Award, CPRIT MIRA etc. Furthermore, these significant findings have offered invaluable insights that have directly influenced the development of our patent PRIORI-T: a method for the selection of tumor-reactive T cell receptors for adaptive cell therapy.

3. Elucidated the molecular mechanisms underlying immune evasion and identified novel biomarkers for immunotherapy. (1) Depicted the ITH architecture of T cell receptor (TCR) repertoire of lung cancers and discovered that heterogeneous TCR repertoire is associated with heterogeneous molecular landscape and inferior survival of lung cancer patients (*Reuben et al, Cancer Discov, 2017; Chen et al, Nature Commun, 2021*). (2) Discovered that a considerable proportion of the most active T cells in lung cancers were also prevalent in normal lung tissues, which appeared to be reactive to passenger mutations or viral infections. Therefore, a concise understanding of shared antigens and T cells between tumor and adjacent normal tissue is warranted to improve therapeutic efficacy and reduce the risk of toxicity in the context of immunotherapy (*Reuben et al, Nat Commun, 2020*). (3) Demonstrated that the impact of HLA diversity on clinical benefit from immunotherapy is disease-specific and it does not predict benefit from immunotherapy for lung cancer patients (*Negrao et al, J Thorac Oncol, 2019*). (4) Demonstrated substantial spatial and temporal heterogeneity in PD-L1 level across different anatomic sites and different time points during clinical course; and PD-L1 in lymph node specimens may not be a reliable predictor of benefit from immunotherapy in lung cancer patients (*Hong et al, J Thorac Oncol, 2020*). (5) Demonstrated that different oncodrivers are associated with distinct PD-L1 level and genomic features and patients with targetable mutations achieve inferior benefit from immunotherapy monotherapy in general with the exception of BRAF mutations (*Negrao et al, J Immunother Cancer*); (6) Pioneered using machine learning approach to investigate tumor biology and demonstrated that tumors of different genomic clusters are associated with unique immune features and response to immunotherapy, which provided a proof for principle that deep learning modeling may have the potential to discover cross-modality correlations of multifactorial input data to dissect the molecular mechanisms underlying resistance to immunotherapy (*Xie et al, Clin Cancer Res, 2020*). (7) Applied radiogenomics and pathomics analysis to study lung cancer biology and identified novel radiomics biomarkers that outperform benchmark biomarkers such as PD-L1 and tumor mutation burden for predicting benefit from immunotherapy in lung cancer patients (*Saad et al, Lancet Digit Health, 2023*).

Collaborative Research (leading to co-authored papers): We have provided support to numerous investigators, resulting in a series of high-impact publications in top-tier journals such as *Xiao et al, Proc Natl Acad Sci USA, 2023*; *Negrao et al, Cancer Disc, 2023; Cascone et al, Nat Med, 2023; Elamin et al, J Clin Onc, 2022; Gomez et al, Lancet Onc, 2016*. etc.

Publications: As of July 2023, I have had 198 papers (71 as a first/co-first/last/co-last author) published/accepted in peer-reviewed journals. I have authored 98 papers since September 2020, with 36 as a first/co-first or last/co-last author. Additionally, I have contributed over 200 meeting abstracts and proceedings. My scholarly impact is reflected in a Google Scholar H-index of 48 and an i10-index of 130, with over 12,000 citations to date.

Xiaotian Zhang, PhD

Spatial and temporal regulation of gene expression is a key to the organismal development. The dysregulation of such process could lead to the ectopic gene expression that initiate multiple diseases, particularly cancer. The Zhang lab focuses on the gene expression regulation in disease and development. We are interested in the gene expression regulation during the normal development process and more importantly, how these gene expression control programs are hijacked in diseases particularly cancer. Focusing on the normal and malignant hematopoiesis, the Zhang lab has pioneered in many fields of gene expression regulation including:

(1). The discovery of extreme long 3D genome interactions between Polycomb target loci in hematopoietic stem cells (Zhang et al, Molecular Cell 2020.).
(2) The discovery of the mutant NPM1 protein as a transcriptional amplifier on chromatin, which transformed the study of this common leukemic mutant protein in acute myeloid leukemia (Wang et al, Cancer Discovery, 2022).
(3). The discovery of novel non-coding genomic elements in globin switch regulation (Himadewi, et al, eLife, 2021).

We are currently working on the following research topics:
(1). The transcriptional hijacking mechanism by mutant NPM1 protein in acute myeloid leukemia (AML) through IDR and liquid-liquid phase separation.
(2). The regulation and therapeutic targeting of extreme long-range Polycomb loci interactions in acute myeloid leukemia stem cells.
(3). 3D genome organized by transcriptional factors in the hemoglobin switch and the novel gene therapy for hemoglobinopathies.

Zhang lab uses interdisciplinary approaches combining biochemistry and molecular biology, epigenomics, CRISPR/Cas9 genome editing, and bioinformatics. Zhang lab also extensively utilizes omics tools like ChIP-Seq, CUT&RUN, *in situ* Hi-C, and micro-C in leukemia cell line and mouse model. Interested students will learn to conduct one of these assays and perform bioinformatic analysis on omics data during her/his tutorial.

Pubmed list:
https://www.ncbi.nlm.nih.gov/myncbi/1jGTgZbxeDj5M/bibliography/public/
Google scholar:
https://scholar.google.com/citations?user=Bwbp6ssAAAAJ&hl=en