NEWS RELEASE 2021 NEW BMG FACULTY

In an effort to expand the breath, depth, and expertise in the Department of Biochemistry and Molecular Genetics and the Simpson Querrey Institute for Epigenetics at the Northwestern University Feinberg School of Medicine, we have been searching to identify exemplary candidates in the areas of relevant research for our department. We are delighted to report that our search for 2021 has been very successful and we have been able to bring on board four, superb scientists. We are delighted to introduce each individual recruit below:

EICHNER LABORATORY

DR. LILLIAN EICHNER

Exploring transcriptional deregulation in cancer has been the hallmark of Dr. Eichner's career. Dr. Eichner's postdoctoral work with Dr. Reuben Shaw at the Salk Institute for Biological Studies explored the mechanisms driving the tumor suppressor function of the serine/threonine kinase LKB1 in lung cancer. LKB1 is among the most frequently mutated genes in Non-Small Cell Lung Cancer (NSCLC), where it is inactivated in ~20% of cases. Clinically, LKB1 mutant tumors are resistant to the standard of care chemotherapy and immunotherapy, and targeted therapies are not available for this group of patients, necessitating a better understanding of this devastating disease. Leveraging immune-competent, genetically engineered mouse models to answer key questions in vivo, Dr. Eichner's work has proven that, contrary to expectation, AMPK does not mediate LKB1's tumor suppressor function in lung tumors (Eichner et al. *Cell Metab*, 2019). Instead, she found that LKB1 functions through the SIK kinases to impart tumor suppression (Hollstein, Eichner et al. *Cancer Discovery*, 2019). This mechanistic clarity spurred an exciting conceptual pivot in the understanding of molecular drivers of LKB1-mutant tumor biology. Downstream of LKB1, Dr. Eichner subsequently identified critical roles of the druggable epigenetic regulator Histone Deacetylase 3, HDAC3, in lung tumors (Eichner et al. *BioRxiv*, 2020). Dr. Eichner found that HDAC3 directly represses the SASP component of cellular senescence and cooperates with the lineage transcription factor NKX2-1 to mediate targeted therapy resistance. This led her to identify a novel therapeutic approach for recruiting T-cells into "immune cold" LKB1-mutant lung tumors in vivo. Throughout her postdoctoral work, Dr. Eichner has identified that transcription plays an important and previously under-appreciated role in mediating LKB1 function, which she has leveraged to reveal novel in vivo mechanisms and therapeutic liabilities that extend beyond LKB1 mutant tumors. Dr. Eichner's independent research will continue to investigate the interplay between HDAC3 and senescence, and transcriptional vulnerabilities unique to LKB1 mutant tumors. The overarching goal of her lab is to elucidate *in vivo* transcriptional dependencies at the intersection of epigenetics, signaling, and metabolism to reveal and harness therapeutically targetable transcriptional vulnerabilities in cancer.

GAO LABORATORY

DR. RULI GAO

In addition to her position as an Assistant Professor in the department, Dr. Gao is a member of the Center for Cancer Genomics in the Robert H. Lurie Comprehensive Cancer Center. Dr. Gao is joining us as she begins her first faculty position after completing her postdoctoral training at the MD Anderson Cancer Center with Dr. Nicholas Navin who developed the first single-cell DNA sequencing technology for human tumor cells, here is where she led the first large scale single-cell DNA sequencing project (N=1000 cells). Dr. Gao played key roles in the development of high throughput single-cell DNA sequencing (scDNA-seq) technologies and computational analysis of large-scale, single-cell genome and transcriptome sequencing data. She developed a paradigm shift punctuated copy number evolution model in solid tumors that challenges the Darwinian Gradualism (*Nature Genetics*, 2016; a bi-mode chemoresistance evolution model in triple-negative breast cancer that unified genotype and phenotype evolution into one model (*Cell*, 2018); and a high throughput nanogrid single nuclear RNA sequencing technology that opened the avenue of analyzing single-cell transcriptomes from archival frozen tissue samples (*Nature Communications*, 2017). Recently, Dr. Gao developed COPYKAT, a novel Bayesian approach to calculate genomic structures from single-cell RNA-seq data (*Nat Biotechnology*, Gao et al., 2021). Her current research is centered on the discovery and understanding of diverse genetic alterations and their functional outcomes in tumor evolution by developing and applying novel single-cell sequencing technologies and robust bioinformatic algorithms to patient-derived tumor and normal tissue samples. Dr. Gao's long-term goal is to translate her fundamental research findings into novel therapeutics to improve the quality of life of cancer patients and to extend their life span.

KELLEY LABORATORY

DR. SHANA KELLEY

Dr. Kelley who previously was a University Professor at the University of Toronto, is an internationally renowned researcher that has developed innovative and translational methods for tracking molecular and cellular analytes with unprecedented sensitivity. Her novel approaches integrate nanoscience, bioanalytical science, and engineering. She currently holds a professorship post in both the Chemistry Department and the Biochemistry and Molecular Genetics Department at Northwestern University. Work in Dr. Kelley's laboratory features a focus on high-throughput single-cell profiling and the application of new technology platforms of the characterization of pathways relevant to cancer progression and treatment. Recent efforts have focused on the development of *in vitro* and *in vivo* genome-wide screening approaches to identify factors that regulate the i) the expression of immune checkpoints; ii) aberrant signal transduction; and iii) tumor metastasis. These approaches are elucidating new disease biology as well as new therapeutic targets for cancer treatment.

LAUBERTH LABORATORY

DR. SHANNON LAUBERTH

Dr. Lauberth is joining us from the University of California San Diego where her primary research focused on making groundbreaking advances in basic and translational studies in the cancer epigenetic field. Her research program is centered on understanding: (i) enhancer elements that are key regulators of transcriptional circuits that ensure proper development and control numerous disease states. Her studies address a key gap in knowledge that relates to how enhancers are licensed for activation in cancer cells to regulate oncogenic gene expression programs and tumorigenic phenotypes; (ii) alterations in chromatin signatures and conformation that lead to enhancer reprogramming and aberrant gene regulation in cancer. Dr. Lauberth aims to identify alterations in the epigenetic states and chromatin structure in cancer genomes and *determine the functional consequences of these changes in the regulation of the tumor promoting gene expression programs; (iii) noncoding RNAs or the "dark matter" of the genome. Through novel sequencing technologies, Dr. Lauberth's lab identified classes of noncoding RNA molecules (ncRNAs) that are produced from enhancers (eRNAs) and downstream of genes (DOGs) in various human cancers. Her laboratory aims to unravel whether these abundant ncRNAs can serve as new molecular determinants of cancer initiation, risk, or susceptibility and to determine the mechanisms underlying their regulation and function in human cancers. These key goals build upon her laboratory's unique expertise in utilizing a combination of approaches that include cutting-edge high-throughput NGS technologies, state-of-the-art microscopy techniques, quantitative proteomics, biochemistry, and cell-based/genetic assays. Dr. Lauberth also employs powerful cell-free assays that fully reconstitute transcription on chromatin templates and are powerful in discerning direct (causal) effects of epigenetic and transcriptional regulatory mechanisms. Through her lab's comprehensive studies, she is well positioned to make significant strides in the identification of molecular markers that provide insight into the etiology and risk factors of human cancers and novel targets for therapies that will treat a broad range of human cancers.*

https://www.feinberg.northwestern.edu/sites/epigenetics/
https://www.feinberg.northwestern.edu/sites/biochem/