



Institute for
Diabetes,
Obesity, and
Metabolism

IDOM Laboratories
Seeking Graduate Students!



Arany Lab

Lab website: <https://www.med.upenn.edu/aranylab/>

Interests: The Arany lab focuses on cardiovascular metabolism. Such unfocused focus has led us to study a wide range of projects in the heart, liver, fat, etc, and has led us to use all techniques we can get our hands on, including human genetics, genetically engineered mouse models, cell culture, metabolomics, in vivo isotope metabolic tracing, and many more. In essence, the lab aims to ask fundamental questions within the (wide) space of cardiovascular metabolism and leverages all available state-of-the-art approaches to do so. Also, we have a great lab atmosphere, and a lot of fun!



Rotation Projects:

1. Delving into mechanisms underlying NAFLD, for which we have some impressive results in genetic mouse models.
2. Looking at molecular mechanisms that regulate branched chain amino acids, due to their strong association with insulin resistance.
3. Looking at the mechanisms of fatty acid transport by the vasculature.

Baur Lab

Lab Website: <https://www.med.upenn.edu/baurlab/>



Interests: Our research program is focused on understanding the molecular mechanisms that lead to aging, and how they can be influenced to promote health and longevity. Current projects in the lab are focused on elucidating how changes in nutrient intake, such as dietary restriction (DR), can exert beneficial effects on longevity and metabolism in mammals. A major area of interest is the role of changes in nicotinamide adenine dinucleotide (NAD)-metabolism in mediating consequences of aging and diseases. Our lab has characterized the physiological changes in mice that overexpress or lack the key NAD biosynthetic enzyme Nampt in a tissue-specific manner. The lab has also developed extensive methodology for measuring related metabolites, including via tracer studies to determine flux, and is currently working to understand the compartmentalization of NAD within mitochondria and other organelles. A second major focus is on understanding the mechanism of action for rapamycin, an inhibitor of the nutrient-sensing mTOR complexes. We have shown that rapamycin extends life at least in part via inhibition of mTORC1, but also causes detrimental side effects including hepatic insulin resistance via an off-target effect on mTORC2. Overall, the long-term goal of research in the Baur lab is to identify molecular mechanisms of DR that are amenable to nutritional or pharmacological manipulation and can be translated into therapies to prevent or treat age-related diseases in humans.

Rotation Projects:

1. Characterizing mouse models with altered NAD metabolism and/or mTOR signaling
2. Studying the influence of NAD metabolism and transport on mitochondrial function.

Jain Lab

Lab Website: <https://www.med.upenn.edu/jainlab/>



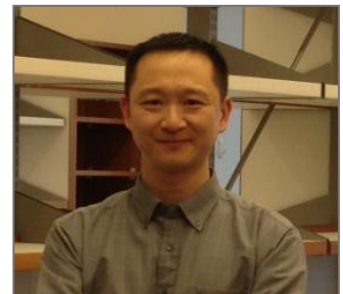
Interests: The Jain lab is interested in how nuclear architecture regulates cellular identity, lineage restriction and cell fate choices. We strive to understand the rules that govern genome organization and spatial positioning in the nucleus. We leverage classic models of stem cell biology and readily work across disciplines to dissect how genome organization shapes cellular identity and how this process goes awry in diseases such as cancer, diabetes and heart failure. Currently, we focus on two different areas of genome organization: 1. nuclear lamina-chromatin interactions, and 2. genome folding. We have multiple projects aimed at deciphering the molecular mechanisms which govern establishment and maintenance of spatial positioning and genome folding. We use a combination of techniques including ESC/iPSC differentiation strategies, mouse genetics, (epi-)genome engineering, genomics and imaging to tackle our hypotheses. The Jain lab is always looking for kind, creative and smart individuals to join the team.

Rotation Projects: Multiple rotation projects touching on various aspects of the aforementioned are available.

Pei Lab

Lab Website: <https://www.research.chop.edu/pei-laboratory/team> or <https://peilab.org>

Interests: His lab is mainly working on two areas of research: cardiac endocrinology, study of new heart-derived hormones in metabolism, physiology and disease; single-cell genomics analysis of organismal metabolism and disease, especially cardiac metabolism and disease. His lab is open to graduate students for rotation and thesis research. For more information and rotation, please visit the lab webpage and feel free to contact Dr. Pei: email: lpei@penncmedicine.upenn.edu



Rotation Projects:

1. Understand the basic biology of GDF15, a heart-derived hormone that impacts body growth.
2. Identify the liver GDF15 receptor and elucidate its signaling pathway in the liver.
3. Identification and functional study of novel heart-derived hormones.
4. Single cell genomics (snRNA-Seq, snATAC-Seq, etc.) study of heart biology and disease.
5. Understand cell type-specific regulatory mechanism of mitochondrial and metabolic functions.
6. Functional study of GWAS traits implicated in human metabolic diseases.

Lazar Lab

Lab Website: <https://www.med.upenn.edu/lazarlab/>



Interests: The Lazar laboratory studies the transcriptional and epigenomic regulation of metabolism. We are particularly focused on the interface between the environment and the genome in the development of diabetes, obesity, and metabolic diseases, using a combination of genomic, genetic, proteomic, bioinformatic, and metabolic phenotyping approaches. Special interest is placed on nuclear receptors (NRs), which are sequence-specific transcription factors that respond to hormones and metabolites. We are especially interested in circadian NRs called REV-ERBs, which are powerful repressors that function as key components of the circadian clock, linking metabolism to biological rhythms. REV-ERBs repress via NR corepressor complexes that contain the epigenomic modulator histone deacetylase 3 (HDAC3), and we learn a lot from comparing and contrasting the roles of these molecules in different tissues in response to environmental challenges including fattening diets and circadian disruption. We are also studying PPAR gamma, a NR that is the master regulator of adipocyte (fat cell) differentiation and function. Ligands for PPAR gamma have potent antidiabetic activity, and thus PPAR gamma represents a key transcriptional link between obesity and diabetes. The molecular, cellular, and integrative biology of these factors are being studied in mice and human systems.

Rotation Projects: Multiple rotation projects on any of our topics of interest are available.

Kaestner Lab

Lab Website: <https://www.med.upenn.edu/kaestnerlab/>

Interests: The Kaestner lab employs modern mouse genetic approaches, such as gene targeting, tissue-specific and inducible gene ablation, to understand the molecular mechanisms of organogenesis and physiology of the liver, pancreas and gastrointestinal tract. We also use next-generation sequencing to look at differences between the transcriptome and epigenome of normal vs diseased tissues. We derive sophisticated mouse genetic models, employ advanced epigenetic tools, and work on human islet specimens to determine mechanisms of blood glucose control and understand its failure in both type 1 and type 2 diabetes. Our group is a fun team made up of five graduate students, five postdocs and five staff members who like to help each and teach each other.



Rotation Projects: Multiple rotation projects available depending on the student's interest.

Merrick Lab

Lab website: <https://www.med.upenn.edu/apps/faculty/index.php/g275/p8653801>



Interests: The Merrick lab is dedicated to the discovery of cellular therapeutics for obesity. The metabolic consequences of obesity have been hypothesized to stem from a relative deficiency in new adipocyte formation from progenitor cells, leading to lipid spillover into liver and muscle and subsequent insulin resistance. We utilize cutting-edge technologies such as single-cell sequencing and the rapid generation of new transgenic mouse lines to identify and explore novel populations of mesenchymal progenitor cells in adipose tissue. Ultimately, our goal is to better understand these pathways in the context of metabolic disease in order to develop novel therapies for obesity and the metabolic syndrome.

Rotation Projects: Projects will focus on examining potential cell-cell interactions between these cell populations and macrophages within their connective tissue niche, the reticular interstitium, in adipose and other tissues.

Stoffers Lab

Lab Website: <https://www.med.upenn.edu/stofferslab/>



Interests: The Stoffers laboratory is a basic biomedical research group, encompassing clinical and basic postdoctoral fellows, MD, MD-PhD and PhD graduate students, and undergraduates, all striving to understand the development, maintenance and regeneration of pancreatic islet beta cells that produce the hormone insulin so critically required for normal glucose homeostasis. Our goal is to understand pancreatic islet biology in the context of health and disease. Our long-standing focus on the homeodomain transcription factor and human diabetes gene Pdx1 has positioned Pdx1 as a critical component of the transcriptional networks of endocrine progenitors and mature beta cells, resulting in fundamental observations of translational relevance to all forms of diabetes. We use genomic and proteomic approaches integrated with genetic mouse models and primary human islet investigations to define the partners of PDX1 and its downstream transcriptional targets. The exploration of PDX1 partners and targets takes us into new areas including mechanistic investigations of beta cell development, metabolism and postnatal beta cell survival.

Rotation Projects: Multiple rotation projects on any of our topics of interest are available. Current areas of focus in the lab include:

1. The Poly C Binding Protein (PCBP) RNA binding proteins in the beta cell
2. A stress inducible PDX1 transcriptional complex with ATF4 that governs postnatal beta cell survival
3. The role of OC1-PDX1 interaction in the development of the endocrine pancreas
4. The role of SPOP-PDX1 interactions in the developing and mature beta cell
5. Mechanisms of PDX1 mutations in the spectrum of human diabetes
6. Revelations from the Human Pancreas Analysis Program (HPAP) on the role of alpha cells in diabetes

Susztak Lab

Lab Website: <https://www.med.upenn.edu/susztaklab/>



Interests: Work in the Susztak laboratory is aimed towards the understanding of molecular pathways that govern chronic kidney disease development. Our work is mostly divided into two categories: hypothesis generating (high through-put, translational) and mechanistic studies. We hypothesize that integrative analysis of epigenetic and genetic settings in diseased cells can provide a rational basis for more accurately modeling the critical biological pathways involved in mediating the progressive phenotype in individual patients. We also predict that epigenomic integrative analysis can be used to determine the identity of chromatin and transcription factors that contribute mechanistically to aberrant transcriptional programming in chronic kidney disease, and that this information can be used for designing therapeutic strategies. We are specifically interested in defining cis-regulatory modules (promoters, enhancers and repressors) that govern the normal and altered epithelial phenotype in diseased kidneys. We use genetic approaches and mouse as a model organism to test the role of candidate signaling molecules and regulatory pathways directly in vivo.

Rotation projects:

1. Defining changes in gene expression and gene regulation in mouse and human kidney disease at a single cell level (scRNAseq and snATACSeq).
2. Understand how metabolic changes alter the epigenome and result in disease development. We know that substrates used to modify nucleic acids and chromatin are affected by nutrient availability and the activity of metabolic pathways. Thus, cellular metabolism constitutes a fundamental component of chromatin status and thereby of genome regulation.

Titchenell Lab

Lab Website: <https://www.med.upenn.edu/titchenelllab/>

Interests: Our lab investigates the molecular mechanisms of insulin action and insulin resistance to identify new therapeutic strategies for metabolic diseases such as diabetes, obesity and cancer. The Titchenell lab is focused on the regulation of metabolism by hormones and nutrients, with a particular emphasis on the anabolic hormone insulin. Alterations in insulin signaling and action underlie metabolic disease and lead to the development of deadly vascular and neuronal complications. Over the last several years, our main focus has been on understanding the signaling mechanisms by which insulin regulates systemic glucose and lipid metabolism. Through the use of various techniques encompassing molecular biology, biochemistry, metabolomics, transcriptional techniques and whole-animal physiology, we have unraveled several new molecular mechanisms that define how insulin controls liver, adipose, and skeletal muscle metabolism. Therefore, the long-term goals of our research program are to continue to explore and validate these pathways to define their contribution to organismal metabolism. Importantly, through the understanding of the basic mechanisms of hormone and nutrient signaling, we aim to identify the underlying mechanisms driving metabolic deregulation in disease with the goal of identifying new therapies to improve metabolic control.



Rotation Projects: Penn BGS students are welcome for rotations. Dr. Titchenell is a member of the Cell and Molecular Biology and Biochemistry and Molecular Biophysics graduate groups.