James S. McDonnell Department of Genetics

The Department of Genetics (http://genetics.wustl.edu) is at the forefront of the rapidly developing field known as genomic (or personalized) medicine, in which genetic and epigenetic analysis coupled with clinical information enables treatments to be tailored specifically to the individual patient. The rapid evolution of sequencing technologies, genome engineering, automated cellular imaging and mass spectrometry methods to rapidly perform proteomic and metabolomics studies, coupled with powerful computational tools, is revolutionizing the biological sciences. Investigators in the department are developing new methods of genomic analysis including technology and software, epigenomics and copy number variation as well as studies of disease pathways using model organisms, to identify and study genes responsible for human disease and treatment responses. The department supports a broad program of preclinical and graduate instruction in genetics, with research opportunities ranging from studies of transcriptional networks, population genetics, protein evolution, neurological disorders, developmental genetics, models of human disease, genome architecture, statistical genetics and computational biology, genome technologies and infertility.

A significant portion of the first-year course in basic medical sciences is devoted to human and clinical genetics, with emphasis on how genomic information will transform the practice of medicine. This includes specialized selective courses in addition to the core genetic curriculum. Advanced training in clinical genetics and in genetic research is available from the faculty in the Department of Genetics and from geneticists with principal appointments in many other departments within the School of Medicine (http://medicine.wustl.edu).

Advanced courses and seminars are offered that focus on the genetics of complex disease, gene expression, genome engineering, induced pluripotent stem cells, single cell genomics, molecular genetics, genetic epidemiology, computational biology, developmental genetics, microbial genetics, cancer genetics, and population and evolutionary genetics. Extraordinary opportunities for research training and experience are available in all of these areas and at all levels. The programs are tailored to meet the needs of medical students, graduate students, and both MD and PhD postdoctoral fellows pursuing advanced training in biomedical research.

Website: http://genetics.wustl.edu

Degrees & Requirements

While the Department of Genetics does not offer its own degree, some of the department's courses are open to students in the MD and MSTP (MD/PhD) programs. Further information about the MD and MSTP degrees can be found in the Degrees & Programs Offered (http://bulletin.wustl.edu/medicine/degrees) section of this Bulletin.

Research

M20 Genetics 900

Cross-listed with L41 Biol 590

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Our group has a long-standing interest in developing new methods for characterizing the origin and functional impact of human genetic variation. Recently completed projects have covered the following topics: mapping of copy number variants, measurement of sex-specific mutation rate and variation in mutation rate among decomposing the relative impact of different types of mutation (SNPs, indels, CNVs, etc.) on gene expression variation and disease susceptibility. Currently, we have a number of active projects that address fundamental unsolved problems related to human reproduction. First: We are trying to unravel the genetic basis for a common form of male infertility, non-obstructive azoospermia, using oligonucleotide arrays and exome sequencing. The short-term goal of this project is to define causal mutations in the >400 cases in which we have access. Our ultimate goal is to provide an unbiased view of the genetic architecture of the disease and establish a definitive reference panel of causal mutations that clinicians can use to facilitate diagnosis of spermatogenic failure. Second: We are using sperm DNA from a longitudinal cohort of semen donors to study the processes of mutation and selection within the population of germ cells of individuals. There are a number of other potential projects ranging from topics of medical relevance such as the biology of the placenta and maternal-fetal compatibility to more basic questions regarding genome biology and evolution. Training in this elective will be primarily computational, and can cover skills such as population genetic analysis, rare-variant association study methodology and other aspects of statistical genetics. However, parties interested in using other approaches to address the topics discussed here are welcome.
Our laboratory utilizes a variety of techniques spanning from human molecular genetics and informatics to mouse behavioral neuroscience and neuroanatomy. We develop and employ mouse models of psychiatric disorder, particularly those that mimic genetic variations we’ve identified from human patient populations, with the goal of trying to understand the cellular and molecular underpinnings of these disorders.

Studies on the role of centrioles and basal bodies in ciliary signaling, assembly, and motility using molecular genetics, computational, and biochemical approaches.

Growth control and morphogenesis in vertebrate development. Focus on genes and mechanisms affecting proportionate fin growth, fin regeneration and pigment stripe patterning in zebrafish.

Translating genetic and epigenetic molecular and analytical observations to physiological endpoints. We apply several complementary and integrated approaches including bench science, cultured cells, mouse phenotyping and husbandry, and computational and systems biology.

We are performing Cas9/CRISPR activation and repression screens in iPSC-derived neurons together with single-cell transcriptomics analysis to evaluate the causal effects of genetic variants associated with neuropsychiatric diseases. We are also studying how metabolism influences axonal/glial interactions important for proper nerve function. We use genetic and metabolomic analysis to identify molecular mechanisms of axonal degeneration, a self-destructive process that plays an important role in many neurodegenerative conditions.

Systems Biology, Gene Regulation, and Technology Development. Projects in the lab fall into three general categories: 1) Understanding the molecular logic of transcription factor cooperativity. 2) Mapping the gene regulatory networks that control developmental processes and using this knowledge to reprogram fibroblasts into useful cell types. 3) Developing novel technologies to more efficiently achieve the first two aims listed.

Engineering cell fate to generate clinically valuable cell populations: Stem Cell and Developmental Biology. Our research focuses on dissecting the gene regulatory networks that define cell identity, using the developing embryo and tissue regeneration as a guide to engineer fate in vitro. We apply insight from these analyses to generate clinically relevant populations by differentiating cells from a pluripotent state, or by directly converting cells between mature fates. We employ a combination of computational, single-cell transcriptomics, cell and developmental biology approaches.

Inter-individual variability in aging and lifespan. Developmental origins of longevity and adult health. Quantitative microscope and image analysis of C. elegans.

Development and evaluation of novel statistical genetics methodology, especially as applied to genomic identification and validation of variants for human complex quantitative traits, such as heart disease, cancer, pulmonary function, diabetes and human longevity.

Statistical genetics and psychiatric genetics. Development and application of analysis methods for studying the genetics of human disease and complex traits.

Inter-individual variability in aging and lifespan. Developmental origins of longevity and adult health. Quantitative microscope and image analysis of C. elegans.
Germ cell development in the model organism Caenorhabditis elegans. The major focuses are: control of the decision to proliferate or enter the meiotic pathway, control and coordination of meiotic prophase progression and gametogenesis, and control of meiotic maturation and ovulation.

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Identification of the genes and the elucidation of the molecular mechanisms that regulate the early events of Drosophila central neurogenesis; illumination of the mechanisms that form, pattern and specify the individual identities of the progenitor cells of the Drosophila embryonic CNS.

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We work in the general field of computational genomics and epigenomics. We study the evolution of human regulatory networks, with a focus on mobile elements (or transposable elements) and their impact on gene regulation, their genetic and epigenetic control, and their roles in human biology and diseases.

Faculty

Department Head
Jeffrey D. Milbrandt, MD, PhD

Director, McDonnell Genome Institute
Susan Dutcher, PhD (Interim)

Director, Division of Statistical Genomics
Michael Province, PhD

Director, Genome Technology Access Center
Rich Head, MS

Director, Genome Engineering and iPSC Center
Xiaoxia Cui, PhD

Visit our website for more information about our faculty (http://genetics.wustl.edu/faculty) and their appointments.

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Professor of Computer Science  
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BS California Institute Technolo 1972  
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W

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Y

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Instructor in Genetics (primary appointment)  
PHD Tongji University 1998  
BS Tongji University 1984  
MS Tongji University 1995  
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Courses


M20 Genetics 900 Research Elective - Genetics  
Research opportunities may be available. If interested, please contact the Department of Genetics.