Epigenomics Workshop

Friday, June 24, 2016

8:30 AM  Registration and Continental Breakfast

9:00 AM  Welcoming Remarks
Lawrence Silbart
Vice Provost for Strategic Initiatives
University of Connecticut

Charles Lee
Scientific Director and Professor
The Jackson Laboratory for Genomic Medicine

SCIENTIFIC PRESENTATIONS/Session One
Moderator/Justin Cotney

9:10 AM  X-chromosome Inactivation in Human: a Non-coding RNA tug-of-war?
Claire Rougeulle, Université of Paris

9:35 AM  Regulatory Riddles on & beyond the X chromosome
Stefan Pinter, University of Connecticut School of Medicine

9:53 AM  X Chromosome Imprinting and the Male Bias in Autism
Michael O’Neill, University of Connecticut

10:11 AM  (Epi)genomics of islet dysfunction and type 2 Diabetes
Michael Stitzel, The Jackson Laboratory for Genomic Medicine

10:30 AM  Break

SCIENTIFIC PRESENTATIONS/Session Two
Moderator/Stormy Chamberlain

10:50 AM  Prenatal stress and Epigenetic Regulations in the Developing Brain
Valérie Mezger, Université of Paris
11:15 AM  
*3D genome architecture and topological framework of transcription regulation*
Yijun Ruan, The Jackson Laboratory for Genomic Medicine

11:33 AM  
*Mapping cell-specific and disease associated regulatory elements with nascent RNA sequencing*
Leighton Core, University of Connecticut

11:51 AM  
*Comprehensive characterization of functional RNA elements encoded in the human genome*
Brenton Graveley, University of Connecticut School of Medicine

12:10 AM  
Lunch

1:15 PM  
*DNA methylation and disease: what have we learned from the ICF syndrome?*
Claire Francastel, Université of Paris

1:40 PM  
*Roadmap to identifying craniofacial enhanceropathies*
Justin Cotney, University of Connecticut School of Medicine

1:58 PM  
*The Epigenome and Chromatin Architectures of Pluripotent Cells*
Chia-Lin Wei, The Jackson Laboratory for Genomic Medicine

2:16 PM  
*A bipartite boundary element regulates tissue-specific imprinting of UBE3A*
Stormy Chamberlain, University of Connecticut School of Medicine

2:35 PM  
Break

2:50 PM  
*Epigenome maintenance in response to DNA damage*
Sophie Polo, Université of Paris

3:15 PM  
*The DNA damage response in human embryonic stem cell derived intestinal organoids*
Christopher Heinen, University of Connecticut School of Medicine
3:33 PM  Defining the epigenome of early colon neoplasia  
Daniel Rosenberg, University of Connecticut School of Medicine

3:51 PM  Knockout of the zinc finger protein ZNF274 in Prader-Willi syndrome-specific stem cells rescues the imprinted maternal 15q11-q13 transcripts  
Marc Lalande, University of Connecticut School of Medicine

4:15 PM  Closing Remarks  
Jeffrey Seemann  
Vice President for Research  
University of Connecticut

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**Biographies**

**Stormy J. Chamberlain, Ph.D.**
Stormy J. Chamberlain is the Raymond and Beverly Sackler Assistant Professor of Genetics and Genome Sciences at the University of Connecticut Health Center. Stormy obtained a B.A. degree in Molecular Biology from Princeton University and a Ph.D. in Genetics from the University of Florida. She performed post-doctoral research at the University of North Carolina-Chapel Hill and the University of Connecticut Health Center prior to joining the faculty at the University of Connecticut Health Center. Her lab uses induced pluripotent stem cell models of Angelman syndrome and 15q duplication syndrome to understand genetic and epigenetic regulation at the imprinted chromosome 15q11-q13 locus.

**Leighton Core, Ph.D.**
Leighton received a B.S. in Biology from Boston College in 1999. He worked as a technician in a microbiology lab at The Scripps Research Institute for three years. He did his doctoral and post-doctoral training in eukaryotic gene regulation with John Lis at Cornell University. Leighton joined the faculty of MCB at UConn, Storrs in 2014. His current research is focused on the genomics of gene regulation during development and disease.
Justin L. Cotney, Ph.D

Dr. Cotney received his undergraduate degree in Biology from Birmingham-Southern College in 2002. He then entered the Graduate Program in Genetics and Molecular Biology at Emory University. There he studied basic mechanisms of mitochondrial gene expression in the laboratory of Dr. Gerald Shadel. He uncovered novel activities of several key components of the human mitochondrial transcription machinery. He received his PhD for this work in 2008. He then joined the laboratory of Dr. James Noonan in the Department of Genetics at Yale University School of Medicine. There he was the recipient of a Rudolph Andersen fellowship that supported his work to develop functional genomics techniques to profile active chromatin signatures in small amounts of embryonic material. Using these techniques, he profiled promoter and enhancer activation states in early brain and limb development in human, rhesus, and mouse. During this postdoctoral work, Dr. Cotney was the recipient of a K99/R00 award from the National Institute of Dental and Craniofacial Research to apply functional genomics to early craniofacial development. Dr. Cotney joined the faculty of the Department of Genetics and Genome Sciences at UConn Health in May of 2015 and is actively recruiting graduate students and postdoctoral researchers interested in combining focused biological experiments with genome-wide sequencing techniques.

Claire Francastel, Ph.D.

Claire Francastel is the Research Director at INSERM (National Research Institute for Medical Research) and PI at the Epigenetics and Cell Fate, University Paris Diderot campus. Her work has been focused on the regulation of gene expression during normal and pathological cellular differentiation. She received her PhD in 1995 from the University Pierre et Marie Curie in Paris. She then turned to the emerging field of epigenetics and joined the Fred Hutchinson Cancer Research Center as a postdoctoral fellow (labs of David Martin and Mark Groudine) where she demonstrated a link between transcription factors occupancy at cis-acting elements and positioning of the linked genes within the nuclear space, with functional implication for its chromatin and expression status. She was recruited at INSERM in 2001 in the Hematology Department at the Cochin Institute in Paris were she started her own team and received an “Avenir” INSERM Junior Group Leader award in 2002. She then contributed to the creation of the Epigenetic and Cell Fate Unit in 2009. Her team is interested in non-coding transcriptional output of mammalian genomes, in normal and in disease situations, with special focus on transcripts arising from highly repeated sequences, which integrity relies on their methylated status, and the newly uncovered case of long or short regulatory ncRNAs originating from spliced introns.
Brenton Graveley, Ph.D.

Brenton Graveley is Associate Director of the University of Connecticut Institute for Systems Genomics and the John and Donna Krenicki Professor of Genomics and Personalized Healthcare in the Department of Genetics and Genome Sciences at UConn Health in Farmington, CT. Brent has studied RNA biology throughout his entire career. He performed his undergraduate studies at the University of Colorado, Boulder with David Prescott, his graduate studies at the University of Vermont with Greg Gilmartin, and his postdoctoral studies at Harvard University with Tom Maniatis. Brent is a lead investigator of the ENCODE and modENCODE projects, studies the mechanisms of alternative splicing using genomic, genetic, and biochemical approaches, and collaborates extensively to investigate various aspects of RNA biology. Brent was a member of the Board of Directors of the RNA Society, and currently serves as Editor of the journal RNA, as a member of the National Advisory Council for Human Genome Research, and was elected into the Connecticut Academy of Science and Engineering.

Christopher Heinen, Ph.D.

Chris Heinen is an Associate Professor of Medicine and an Investigator in the Center for Molecular Medicine. He is also an Investigator in the University of Connecticut Stem Cell Institute and the Institute for Systems Genomics. Dr. Heinen’s primary research interest is the hereditary cancer predisposition disease Lynch syndrome (LS). LS is caused by germline mutations in the genes of the DNA mismatch repair (MMR) pathway. His laboratory uses a variety of approaches to unravel the molecular mechanism of the MMR pathway and how defects in this pathway give rise to cancer. This work involves biochemical and biophysical approaches as well as utilizing cell culture models including human embryonic stem cells. In addition to studying the MMR pathway in stem cells, his lab differentiates these cells into human intestinal organoids to examine MMR function. The ultimate goal of the laboratory is to translate basic science findings into clinical applications that can help with the diagnosis, prevention and treatment of LS-associated cancers. Dr. Heinen obtained his undergraduate degree from Northwestern University and his PhD from the University of Cincinnati College of Medicine. He was a postdoctoral trainee at the Kimmel Cancer Center at Thomas Jefferson University. In addition to running his research lab, he is also the Director of Postdoctoral Affairs at UConn Health.
Marc Lalande, Ph.D.

Marc Lalande received a Ph.D. in Medical Biophysics from the University of Toronto in 1981. His postdoctoral training was with Dr. Samuel A. Latt in the Department of Pediatrics, Harvard Medical School and Children’s Hospital, Boston, MA. At Harvard Medical School, he was later an Associate Professor of Pediatrics and an Assistant Investigator of the Howard Hughes Medical Institute. In 1998, he moved to the UCONN School of Medicine. He is Director of the Stem Cell Institute and of the newly created Institute for Systems Genomics, a group with representation from 10 different UConn Schools and Colleges, the Jackson Laboratory and Connecticut Children’s. His research laboratory focuses on using induced pluripotent stem cell (iPSC) technology to study Prader-Willi syndrome, a chromosome 15q11-q13 imprinting disorder.

Valérie Mezger, Ph.D.

Valerie Mezger’s team (Interface between Development and Environment) has strong expertise in stress-responsive TFs (HSFs), and a leading position in the transcriptomic and epigenetic mechanisms underlying the stress response of the fetal brain (collab. P. Gressens; K. Hashimoto-Tori and P. Rakic, Yale, USA). Her team is one the founding groups of UMR7216, Epigenetics and Cell Fate (CNRS), created in January 2009 (Director J. Weitzman; Co-Director, V. Mezger) at the new campus (Paris-Rive Gauche) of Paris Diderot University. Dr. Mezger recently developed in her lab cutting-edge epigenomic techniques, ChIP-Seq, ATAC-Seq, DNA methylomic analysis par Capture Array, as well as pyrosequencing analysis of DNA methylation, in order to investigate the genome-wide modifications of the chromatin landscape induced by prenatal stress. The UMR is dedicated to the understanding of the role of epigenetic modifications in different cell differentiation systems, the maintenance of pluripotency and associated pathologies, and possesses all the expertise and technical facilities necessary to ensure the feasibility of the Team’s projects (Functional Epigenome Facility and L3 Lentivirus Facility). Dr. Mezger has also participated in the establishment of the LIA (International Associated Laboratory) EPIGENO STEM (Univ Connecticut) and the DHU PROTECT (P. Gressens) and is an active member of its Scientific Council.
Biographies

**Michael O'Neill, Ph.D.**

Michael O'Neill is Assistant Director of the Institute for Systems Genomics and Associate Professor in Genetics and Genome Sciences, Department of Molecular and Cell Biology at the University of Connecticut. He is also an investigator in the Connecticut Institute for the Brain and Cognitive Sciences. Dr. O'Neill obtained his BA and PhD from the University of Texas at Austin with Dorothea Bennett and Karen Artzt studying mouse t-haplotypes. He received post-doctoral training at the University of Melbourne with Dr. Andrew Sinclair studying the genetics of sex determination and at Princeton University with Dr. Shirley Tilghman studying genomic imprinting. Since starting his lab at UConn, Dr. O'Neill’s work has focused on the evolution of genomic imprinting in vertebrates and on the role of X-linked imprinted genes in reproductive- and neuro-development.

**Stefan Pinter, Ph.D.**

Dr. Stefan Pinter is an Assistant Professor in Genetics and Genome Sciences at UConn Health and member of the Institute for Systems Genomics at the University of Connecticut. His primary interest is to learn how chromosome folding, non-coding RNAs, and chromatin modifiers orchestrate gene expression, particularly in the context of allele-specific regulation. The vast majority of disease-associated variation does not change the content of genes but rather their dosage. Classic models of dosage compensation, such as X chromosome inactivation (XCI), provide a uniquely tractable perspective on these questions, because they use a variety of gene regulatory mechanisms. Building on his XCI, stem cell, and epigenomics work with GSA member Jeannie Lee at MGH/Harvard Medical School, the Pinter lab at UConn Health aims to develop scalable systems approaches to these questions, with a focus on genes that escape XCI and are implicated in Turner's syndrome (XO karyotype). Pinter's enduring interest in chromosome biology originated in his PhD training on DNA replication with Virginia Zakian at Princeton University, supported by a Komen Breast Cancer Research Foundation dissertation fellowship. His postdoctoral training was funded by the German Research Foundation and the Fund for Medical Discovery at MGH.
**Sophie Polo, Ph.D.**

Sophie Polo received her PhD in 2006 working with Geneviève Almouzni at the Institut Curie (Paris, France) on the role of chromatin assembly factors in cell proliferation and genome stability. She joined Steve Jackson’s laboratory at the Gurdon Institute in Cambridge UK for her postdoctoral studies on the function of chromatin remodelers in the response to DNA breaks. Since 2013, Sophie Polo has been leading the Epigenome Integrity group at the Epigenetics & Cell Fate Centre in Paris, France. Research in her group focuses on the chromatin dynamics in response to DNA damage in mammalian cells.

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**Daniel W. Rosenberg, Ph.D.**

Daniel W. Rosenberg has more than 30 years of experience in the field of cancer biology, using mouse models and human biospecimens. He is presently the Health Net, Inc. Chair in Cancer Biology and an Investigator in the Center for Molecular Medicine, directing an active research program that focuses on colorectal cancer etiology and development of novel chemoprevention strategies. He has established a translational research program in Cancer Prevention and serves as the Program Director. The research focus of the Program covers several areas of colon cancer biology, with translational applications in prevention and early detection, as well as therapeutic interventions. He has published several recent papers that identify early molecular signatures associated with neoplasia in laser-captured lesions obtained from colon biospecimens procured from screening colonoscopy subjects. He is studying the association of cigarette smoking, obesity, chronic inflammation and other risk factors with the early development of a subset of colorectal cancers that display a distinct spectrum of histological and molecular features. Importantly, these lesions occur primarily in the proximal region of the colon. An important feature of these lesions is a defect in the global epigenomic landscape, a process that his recent work has begun to unravel through global methylomic analyses.
Biographies

Claire Rougeulle, Ph.D.

Claire Rougeulle is a research director at the CNRS and a group leader at the Institute of Epigenetics and Cell Fate in Paris. Claire received her PhD in 1996 from University Pierre et Marie Curie in Paris. She was recruited to the CNRS in 1999 after her post-doctoral studies in Marc Lalande’s laboratory at the Harvard Medical School in Boston, where she studied the Angelman Syndrome and identified one of the first antisense transcript linked to an imprinted locus. She was awarded the Bronze Medal of the CNRS in 2007. Claire joined the Epigenetics and Cell Fate Institute in 2009, of which she is one of the founding members. Her group studies the function of long non-coding RNAs (lncRNAs) in controlling gene expression programs in stem cells, differentiation and development and their contribution to the plasticity of epigenetic regulation in evolution, using the X chromosome inactivation paradigm. Claire is also appointed as Adjunct Assistant Professor in the Department of Genetics and Genome Sciences, University of Connecticut School of Medicine.

Yijun Ruan, Ph.D.

Dr. Yijun Ruan is a genome biologist. He is currently Florine Roux Endowed Chair Professor in Genomics and Computational Biology and the Director of Genomic Sciences at The Jackson Laboratory for Genomic Medicine. Prior to joining the Jackson Laboratory, he was one of the founding members of the Genome Institute of Singapore, and served as a senior group leader and associate director for genome technology from 2002 to 2012. He played pivotal roles in establishing Singapore’s genomics capability and the award winning genomics programs. His current and primary research interest is to elucidate the 3D genome organization and the underlining regulatory functions in human and model organisms, with a focus to uncover the complex mechanisms of gene transcription regulation.
Michael Stitzel, Ph.D.

Type 2 diabetes is a disease of genes and environment. The Stitzel Laboratory studies the epigenome of human pancreatic islets and their developmental precursor cells. One aim is to use the epigenome as a read-out of effects of type 2 diabetes genetic variants on islet gene expression programs and function. Emerging evidence suggests that normal or disease-predisposing conditions can actually alter a cell's epigenome and lead to abnormal cellular functions. To this end, the Stitzel lab is investigating how the islet epigenome is altered under different stimulatory and stress conditions. Additionally, they are pursuing targeted modification of cells epigenomes to facilitate production of bona fide pancreatic islet cells from pluripotent stem cells or other terminally differentiated cells.

Chia-Lin Wei, Ph.D.

Dr. Wei joined the Jackson Laboratory in 2016 as the Director of Genomic Technologies, where she actively engages the development and application of innovative sequencing based genomic technologies to explore genome function and make genome-based medical discoveries for solutions in treating human disease. Dr. Wei got her Ph.D. (Microbiology) from the University of California at Davis. Prior to that she was at the Joint Genome Institute (JGI), joining in 2010. She was responsible for Department of Energy user facility genomic sequencing operation as well as sequencing related technology development effort within the Genomic Technology Department. Dr. Wei moved to JGI after an eight-year stint at Genome Institute of Singapore and was responsible for establishing a sequencing technology platform and genome biology program. She started her scientific career as a research scientist at Large Scale Biology Corporation where she built a research team specialized in cDNA-based analysis for gene discovery and as the key platform for the functional genomic program after a 3-year postdoctoral training at Massachusetts Institute of Technology focused on Drosophila development and apoptosis.

Dr. Wei group’s research activity involves the development of innovative sequencing-based genomic technologies to explore functional genomic elements for transcriptional and epigenetic regulation. She applies these approaches to interrogate genomic, characterize transcriptomes and chromatin structures pertinent to the pluripotency nature of stem cells, particularly uncovering the system biology networks in lineage specification and organism development and adaptation.