BIOGRAPHICAL SKETCH

NAME: Mason, Christopher Edward

eRA COMMONS USER NAME: CHMASON

POSITION TITLE: Associate Professor of Computational Genomics at Weill Cornell Medicine (WCM)

EDUCATION/TRAINING:

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Wisconsin-Madison	B.S.	05/01	Genetics
University of Wisconsin-Madison	B.S.	05/01	Biochemistry
Yale University	Ph.D.	09/06	Genome Evolution
Yale Law School	Fellowship	10/09	Biotechnology Intellectual Property
Yale Medical School	Postdoctoral	10/09	Neurogenetics and Clinical Genetics

A. Personal Statement

The Mason laboratory develops and deploys computational and experimental methodologies to identify the functional genetic elements of the human genome. To do this, we perform research in three principal areas: (1) molecular profiling in patients with extreme phenotypes, including brain malformations, aggressive cancers, and astronauts, (2) creating new biochemical techniques in DNA/RNA sequencing and DNA/RNA base modifications, and (3) the development of bioinformatics models for systems biology and metagenomics. We use high-throughput sequencing methods to generate single-cell, city-scale, and space-based multi-dimensional molecular maps of humans and their environments. We then develop algorithms to leverage these data for detecting, cataloging and functionally annotating interactions between these molecular changes and also connect them to larger datasets (ENCODE, TCGA, ICGC) for replication and contextualization. In the very long term, we hope these systems-based methods will enable an understanding of the functional elements of the human genome, such that we can begin to repair or re-engineer these genetic networks for ameliorating or attenuating disease and lay the foundation to enable long-term human space travel. These methods also being integrated for longitudinal multi-omic profiling of NASA astronauts and for improved methods for genetic and epigenetic diagnostics on the International Space Station (ISS).

B. Positions and Honors

Positions and Employment

1998-1999 *Network and Server Engineer*, Harley Davidson, Milwaukee, WI
1999 *Researcher*, Dept. of Genetics, University of Wisconsin-Madison, WI
2000-2001 *Researcher*, Depts. of Materials Science/Chemistry, University of Wisconsin-Madison, WI
2005-2009 *Visiting Fellow of Genomics, Ethics, and Law*, Yale Law School, New Haven, CT
2006-2009 *Post-doctoral Associate*, Program on Neurogenetics, Yale Univ., New Haven, CT
2007- *Scientific Advisor*, American Civil Liberties Union, New York, NY
2009- *Assistant Professor of Physiology and Biophysics,* Weill Cornell Medical College, New York, NY
2009- *Assistant Professor of Computational Genomics,* Weill Cornell Medical College, New York, NY
2011- *Member*, the Sandra and Edward Meyer Cancer Center, New York, NY
2013- *Visiting Scientist*, American Museum of Natural History, New York, NY
2014- *Assistant Professor of Neuroscience*, The Feil Family Brain and Mind Research Institute (BMRI), Weill Cornell Medical College, New York, NY
2015- *Associate Professor of Physiology and Biophysics,* Weill Cornell Medical College, New York, NY

Other Experience and Professional Memberships

2003-	Member, Genetics Society of America
2004-	Member, New York Academy of Sciences, NY
2009-	Member, Society for Genome Biology and Technology
2009-	Affiliate Fellow of Genomics, Ethics, and Law, Yale ISP, Yale Law School
2010-	Co-Director, New York City Synthetic Biology Association
2010-	Organizer for the International NGS Symposium of the Miptec Drug Conference
2010-	Board Member, GenSpace Community laboratory
2011-	Chair, HESI Genomics Working Group Committee
2013-	Member, ENCODE3 Analysis Working Group (RNA, Epigenetics)
2013	Organizer, Program in Quantitative Genomics - Harvard School of Public Health
2015	Editorial Board: Genome Biology, BMC Genomics
2015	Steering Committee, Genome in a Bottle (GIAB) Genome Standards Consortium at NIST

Honors

1994	Presidential Medal of Environmental Protection
1997	Ferdinand-Plaenert Scholarship
2001	UW-Madison CALS Leadership Award
2003	Graduate Research Fellowship, National Science Foundation (NSF)
2007	Science and Education Outreach Award, Racine, WI
2010-	Advisory Board Member for the Community Laboratory of "Genspace, NYC"
2011	Member, Scientific Advisory Board, PerkinElmer, Inc.
2011	Best Human Practices, Int'l Genetically Engineered Machines (iGEM) Competition
2011	2011 NIH Director's Transformative R01 Award
2012-	Scientific Review Panel, Shriner's Hospital
2013-2016	National Scientific Advisory Panel Member, Southwest National Primate Center
2013	Irma T. Hirschl/Monique Weill-Caulier Scholar Award
2013	CDC & ATSDR Honor Award for Standardization of Clinical Testing
2014	Bert L. and N. Kuggie Vallee Foundation Young Investigator Award
2014	"Brilliant 10" Scientist Award by Popular Science
2014	Selected as the First WorldQuant Foundation Scholar
2015	Selected as a TEDMED Speaker and Scholar
2016	The Pershing Square Sohn Prize for Young Investigators

C. Contributions to Science (selected from 126 total peer-reviewed publications)

1. Tumor Evolution and Cancer Epigenetics

We published the first demonstration that epialleles (phased epigenetic marks) show divergence and prognostic relevance during a tumor's evolution in AML. We have also published a suite of open-source bioinformatics tools (methylKit, eDMR, and methclone) with our novel biochemical methods (eRRBS, single-cell methylation, r-make) that enable integrative analysis for tumor profiling projects. We have used RNA-Seq, whole genome sequencing, and epigenetic analysis in cancer patients to find relapse-specific mutations that emerged after chemotherapy and found that these chemo-resistant variants can predict the aggressive type of the leukemia.

a. Akalin A, Garrett-Bakelman FE, Kormaksson M, Busuttil J, Zhang L, Khrebtukova I, Milne TA, Huang Y, Biswas D, Hess JL, Allis CD, Roeder RG, Valk PJ, Löwenberg B, Delwel R, Fernandez HF, Paietta E, Tallman MS, Schroth GP, Mason CE*, Melnick A*, Figueroa ME*. "Base-pair resolution DNA methylation sequencing reveals profoundly divergent epigenetic landscapes in Acute Myeloid Leukemia." *PLOS Genetics.* 2012 Jun;8(6):e1002781. PMC3380828.
b. Meyer JA, Wang J, Hogan LE, Dandekar S, Patel JA, Tang Z, Zumbo P, Li S, Zavadil J, Levine RL, Cardozo T, Hunger SP, Raetz EA, Morrison DJ, Mason CE, and Carroll WL. "Relapse Specific Mutations in Cytosolic 5'-Nucleotidase II in Childhood Acute Lymphoblastic Leukemia." *Nature Genetics*. 2013 Mar;45(3):290-4. PMC3681285.

c. Ricarte-Filho JC*, Li S*, Garcia-Rendueles ME , Montero-Conde C, Voza F, Knauf JA, Heguy A, Viale A, Bogdanova T, Thomas GA, Mason CE*, Fagin JA*. "Identification of kinase fusion oncogenes in post-Chernobyl radiation-induced thyroid cancers." *Journal of Clinical Investigation*. 2013. Oct 25. doi:pii: 69766. PMC380979.
d. Li S, Garrett-Bakelman F, Perl AE, Luger SM, Zhang C, To BL, Lewis ID, Brown AL, D'Andrea RJ, Ross ME, Levine R, Carroll M, Melnick A, Mason CE. "Dynamic evolution of clonal epialleles revealed by methclone." *Genome Biology*. 2014 Sep 27;15(9):472. PMC4242486.

2. Discovering Transcriptome and Epitranscriptome Function

Early publications leveraged high-throughput methods for functional genomics, leading to the first demonstration of widespread non-coding RNAs in an invertebrate system (*Drosophila melanogaster*) and demonstrated that the active areas of the genome are far more widespread than just the coding exons of genes. This work has led to additional characterization of human and cancer transcriptomes, and it has been validated by ongoing work with the ENCODE Consortium and our other collaborators. In 2012, we co-discovered and invented a method for characterizing a new kind of RNA modification (m^6A), called Methylated RNA ImmunoPrecipitation and sequencing (MeRIP-seq). We have since published and continue research on the roles for RNAs and RNA modifications, which includes RNA degradation rates, RNA editing, translation efficiency, miRNA interactions, and many RNA-binding roles for the epitranscriptome.

a. Stolc V*, Gauhar Z*, Mason C*, Halasz G, van Batenburg MF, Rifkin SA, Hua S, Herreman T, Tongprasit W, Barbano PE, Bussemaker HJ, White KP. A gene expression map for the euchromatic genome of Drosophila melanogaster. *Science*. Oct 22;306(5696):655-60. 2004
b. Meyer KD, Saletore Y, Zumbo P, Elemento O, Mason CE*, Jaffrey SJ*. "Comprehensive Analysis of mRNA Methylation Reveals Pervasive Adenosine Methylation in 3' UTRs." *Cell*. 2012. Jun 22;149(7):1635-46. PMC3383396.
c. Saletore Y, Meyer K, Korlach J, Vilfan I, Jaffrey S, Mason CE. "The Birth of the Epitranscriptome: Deciphering the Function of RNA Modifications." *Genome Biology*. 2012 Oct 31;13(10):175. PMC3491402.
d. Li S and Mason CE. The Pivotal Regulatory Landscape of RNA Modifications. *Annual Review of Genomics and Human Genetics (ARGHG)*. 2014;15:127-50. PMID: 24898039.

3. Next-Generation Sequencing (NGS) Methods and Standards Development.

We published the first cross-technology comparison of gene expression microarrays and RNA-sequencing, and we have since published methods for single-cell RNA-sequencing and a comprehensive comparison of all current RNA-sequencing methods and technologies. We have helped to establish the first principles and metrics for examining changes in RNA splicing and expression profiling, which have helped set standards at the FDA for clinical-grade RNA-sequencing. We now use these same principles to examine the best practices for genome sequencing as part of the Genome in a Bottle (GIAB) Consortium with the National Institute of Standards and Technology (NIST).

a. Marioni JC*, Mason CE*, Mane SM, Stephens M, Gilad Y. "RNA-seq: An assessment of technical reproducibility and comparison with gene expression arrays." *Genome Research.* 2008. Sep.; 18(9): 1509-17. PMC2527709.
b. Pan X, Durrett RE, Zhu H, Tanaka Y, Li Y, Zi X, Marjani SL, Euskirchen G, Ma C, LaMotte RH, Park I-H, Snyder M, Mason CE, Weissman SM. "Two methods for full-length RNA-seq for low quantities of cells and single cells." *Proceedings of the National Academy of Sciences*. 2013. Jan 8;110(2):594-9. PMC3545756.
c. The FDAs SEQC/MAQC-III Consortium, Mason CE*, Shi L*. "A comprehensive assessment of RNA-seq accuracy, reproducibility and information content by the Sequence Quality Control consortium." *Nature Biotechnology*. 2014 Sep;32(9):903-14. PMC4321899.
d. Li S, Tighe SW, Nicolet CM, Grove D, Levy S, Farmerie W, Viale A, Wright C, Schweitzer PA , Gao, Kim D, Boland J, Hicks B, Kim R, Chhangawala S, Jafari D, Raghavachari N, Gandara J, Garcia-Reyero N, Hendrickson C, Roberson D, Rosenfeld JA, Smith T, Underwood JG, Wang M, Zumbo P, Baldwin DA,

Grills GS, Mason CE. "Multi-Platform Assessment of Transcriptome Profiling Using RNA-Seq in the ABRF Next Generation Sequencing Study." *Nature Biotechnology*. 2014 Sep;32(9):915-25. PMC4167418.

4. Neurogenetics and Evolutionary Characterization of the Brain

Another long-standing interest of the laboratory is using genomics to understand human brain function, especially in the context of evolution. Using linkage analysis, GWAS studies, Mendelian genetics, and clinical applications of genomics technology, we have found novel risk loci for aneurysms, examined the complex transcriptome of the developing human brain, and established the first cross-primate comparison of region-specific gene expression profiles of the brain. These functional genomics map help us to prioritize genetic variants in both coding and noncoding regions of the human genome.

a. Bilguvar K, Yasuno K, Niemelä M, Ruigrok YM, Fraunberg M, Duijn CM, van den Berg LH, Mane SM, Mason CE *et al*. "Susceptibility loci for intracranial aneurysm in European and Japanese populations." *Nature Genetics*. 2008. Dec.; 40(12): 1472-7. PMC2682433.
b. Johnson MB, Kawasawa YI, Mason CE. Krsnik Z, Coppola G, *et al*. "Functional and evolutionary insights into human brain development through global transcriptome analysis." *Neuron*. 2009. May 28;62(4):494-509. PMC2739738.
c. Ercan-Sencicek AG, Stillman AA, Ghosh AK, Bilguvar K, O'Roak BJ, Mason CE, *et al.* "L-histidine decarboxylase and Tourette's syndrome." *New England Journal of Medicine.* 2010. May 20; 362(20):1901-8. PMC2894694.
d. Peng X, Thierry-Mieg J, Thierry-Mieg D, Nishida A, Pipes L, Bozinoski M, Thomas M, Kelly S, Weiss J, Raveendran M; Donna M; Gibbs R, Rogers J; Schroth G, Katze M, Mason CE. "Tissue-specific transcriptome sequencing analysis expands the non-human primate reference transcriptome resource (NHPRTR)." *Nucleic Acids Research.* 2015 Jan 28;43:D737-42. PMC3531109.

5. Large-scale Metagenomics and Longitudinal, Systems Biology

We have created new protocols and algorithms for clinical genomics, integrative, multi-omic analysis of biological data, and also pioneered new techniques for city-scale and space-based data collection. This includes our work in BioHDF for integrative genomics, the genetic map of DNA across the NYC subway system with our Pathomap/MetaSUB project, and the ongoing NASA Twins study of longitudinal profiling of two astronauts at the genetic, epigenetic, transcriptional, proteomic, metabolomic, microbiome, physiological, and cognitive levels during long-term space travel.

a. Mason CE, Zumbo P, Sanders S, Folk M, Robinson D, *et al*. "Standardizing the Next Generation of Bioinformatics Software Development With BioHDF (HDF5)." *Advances in Computational Biology.* Arabnia, Hamid (Ed.) 2010; 680:693-700. PMID: 20865556.
b. Mason CE, Porter S, and Smith T. "Characterizing Multi-omic data in Systems Biology." *Advances in Experimental Medicine and Biology*. 2014;799:15-38. PMID: 24292960.
c. Dubchak I, Balasubramanian S, Wang S, Meyden C, Sulakhe D, *et al*. "An integrative computational approach for prioritization of genomic variants." PLoS One. PMC4266634.
d. Afshinnekoo E, Meydan C, Chowdhury S, Jaroudi D, *et al*. Mason CE. "Geospatial Resolution of Human and Bacterial Diversity from City-scale Metagenomics." *Cell Systems*. 2015 Jul 29;1(1):72-87. PMC4651444.

Complete List of Work is Published and Linked at NCBI:
http://www.ncbi.nlm.nih.gov/sites/myncbi/christopher.mason.1/bibliography/41419218/public/

G. Research Support

ACTIVE

R01NS076465-03 (Mason, Ross) 09/01/11 – 05/31/16

Epigenome Interactions in Complex Neurogenetic Disorders

In this grant we will combine proof of principle studies in the mouse with investigations of human neural tube defect cohorts to examine the relationship between DNA/chromatin methylation and NTDs. Role: Co-PI

R01 ES 021006-04 (Finnell) 8/16/2012 – 6/30/2017

Study of Neural tube defects etiology: Genome and exposome

We aim to definine the relationships among maternal exposure, maternal nutrition, immune responses, maternal/embryonic genetics, and NTD risk. Moreover, the biological sample and data banks will allow us to continuously explore the genome and exposome of NTDs as our toolkit of investigation continues to mature. Role: Co-I

U10 CA180827-01 (Paietta) 4/14/14 – 2/28/19

ECOG-ACRIN Integrated Leukemia Translational Research Center

We will use genetic, epigenetic, and transcriptional profiles of leukemia samples during therapy to guide future therapy diretions and methods for patient stratification. Role: Co-I

NASA - NNX14AH50G (Mason) 04/01/14 – 03/31/17

The Landscape of DNA and RNA Methylation Before, During, and After Human Space Travel

We propose an integrated set of experiments on identical twins that will identify the genome-wide changes at the epigenetic (eRRBS), transcriptional (RNA-seq and miRNA-seq), and epitranscriptomic (MeRIP-seq) levels that occur before, during, and after space travel on the International Space Station (ISS). Role: PI

Hirschl/Monique Weill-Caulier Award (Mason) 07/01/14 – 06/30/19

The Dynamic Landscape of DNA and RNA Methylation Regulating Leukemia

We hypothesize that altered methylation of both DNA and RNA provide two routes for cancer cells to create and then maintain chemoresistant states, and we examine localization and genomic interplay in AML cancer cells. Role: PI

I7-A765, STARR Cancer Consortium (Mason) 01/01/2014-12/31/16

Single-Cell Resolution of Emergent Clones in the Myelodysplastic Syndromes (MDS) During Therapy and Disease Progression

We will examine divergent patient responses to chemotherapy, evaluate clonal selection and MDS stem cell transcriptional responses during disease progression as well as in response to MDS therapeutics. Role: PI

WorldQuant Foundation (Mason) 11/01/14 – 10/31/18

Integrated Systems Biology of Long-Term Human Space Travel

We developed computational approaches to genome interpretation and machine-learning tools for integrative data analysis from the NASA Twins Study. Role: PI

The Vallee Foundation Scholar Award (Mason) 9/1/2014 – 8/31/2019

Single-cell resolution of chemo-resistant clones in Acute Myeloid Leukemia

We propose to examine tumor evolution with our recently optimized single-cell RNA-sequencing (scRNA-seq) protocols and cell-purification techniques to investigate the genetic and functional heterogeneity of AML HSCs in a carefully selected group of AML patients. Role: PI

The Bill and Melinda Gates Foundation (and Sloan) G-2015-13964 (Mason) 4/1/2015 – 6/30/2017

MetaSUB: Metagenomics and Metadesign of the World's Subways

The metagenomic, geospatial distribution of taxa from highly trafficked surfaces at a city-wide scale has only recently been completed for one city (see below), and key questions remain about subway design, dynamics, and urban infrastructure. Role: PI

Pershing Square Sohn Prize (Mason) 7/1/2015 – 6/30/2019

Single-Cell Resolution of Leukemia's Epigenetic Evolution During Therapy

Goals: We aim to provide the first single-cell methylation profile of cancer during treatment, to determine the cell-to-cell epigenetic dynamics of leukemia.

PI has completed numerous federal and foundation grants.