Weill Cornell Medicine

Core Laboratories Center

Genomics and Epigenomics Core Facility

Epigenomics Services

ABSTRACT

The Genomics and Epigenomics Core Facility of the WCM Core Laboratories Center (CLC) provides state-of-the-art instruments and services, and expertise in their applications, to the Weill Cornell Medicine (WCM) community and to outside investigators. Resources and services include next generation sequencing, epigenomic assays, single cell genomics, nucleic acid mass spectrometry, and real-time PCR. The facility provides consultation on project design and data analysis, and offers seminars, educational workshops and training.

OVERVIEW

Background: Epigenomics is the study of the complete set of epigenetic modifications on the genetic material of a cell, known as the epigenome. Epigenetic modifications are reversible modifications on a cell's DNA or histones that affect gene expression without altering the DNA sequence. Similar to the genome, the epigenome can be inherited. Unlike the genetic code, the epigenetic code has plasticity and can be reprogrammed. Two of the most characterized epigenetic modifications are DNA methylation and histone modification. Epigenetic modifications play an important role in gene expression and regulation, and are involved in numerous cellular processes, including in differentiation, development and tumorigenesis.

History: The WCM CLC Genomics and Epigenomics Core Facility is the product of an ongoing process of integration of two previously separate core facilities, the Genomics Resources Core Facility (established in 2000) and the Epigenomics Core Facility (established in 2008).

Location: The core is located on the 1st and 4th floors of the "A" building and the 5th floor of the "C" building at 1300 York Avenue, New York, NY.

WCM Core Laboratories Center (CLC): The WCM CLC was established in 2015. In addition to genomics and epigenomics, the CLC includes core facilities that offer resources and services in proteomics and metabolomics, synthetic and analytical chemistry, NMR, flow cytometry, imaging (optical and electron microscopy, high content screening) CBIC (MRI, PET/CT, and ultrasound), biorepository, bioinformatics, and advanced technology assessment.

Next Generation Sequencing: The core facility has 5 Illumina instruments, including HiSeq 4000, 2 HiSeq 2500/1T, NextSeq 500, & MiSeq.

Genomics: Genomics applications include exome capture, whole genome and targeted region *de novo* sequencing and resequencing, targeted region and whole transcriptome profiling, small RNA analysis, and metagenomics.

Epigenomics: Epigenomics applications include (1) DNA methylation profiling, including whole genome bisulfite sequencing (WGBS), targeted methylome sequencing, enhanced reduced representation bisulfite sequencing (ERRBS), and 5-hydroxymethylcytosine (5hmC) profiling; (2) assessment of the functional state of chromatin by assaying for transposase activity (ATAC-seq); (3) genome wide protein-nucleic acid association mapping by chromatin immunoprecipitation sequencing (ChIP-seq); and (4) transcriptome profiling by RNA-seq.

Single Cell Genomics and Epigenomics: The core offers strong support for single cell genomics and epigenomics projects with a 10X Genomics Chromium system, a Drop-seq instrument, access to a Fluidigm C1 single-cell platform, and collaboration with the CLC Flow Cytometry Core Facility

Nucleic Acid Mass Spectrometry: The core offers the Agena Bioscience (Sequenom) Compact MassArray system, a platform that uses MALDI-TOF mass spectrometry to measure PCR-derived amplicons. Currently used for methylation analysis; other applications include genotyping and mutation detection, gene expression analysis, and pathogen detection.

Real-time PCR: An ABI 7900 HT Sequence Detection System provides real-time PCR for quantitative gene expression and SNP genotyping.

Sanger Sequencing & Fragment Analysis: The core offers a sample "drop and ship" location to facilitate WCM investigators' access to Sanger sequencing and fragment analysis services done on two ABI 3730xl DNA Analyzers in the BRC Genomics Facility on the Cornell University campus in Ithaca, NY.

Administration: The Genomics and Epigenomics Core Facility is part of the Weill Cornell Medicine (WCM) Core Laboratories Center (CLC).

Open to all: The resources and services of the core facility are open to all investigators at Weill Cornell Medicine, Cornell University and Cornell-affiliated institutions. The facility also provides services to external investigators at both academic institutions and commercial enterprises.

RESOURCES

Next Generation Sequencing: 5 Illumina NGS instruments, including HiSeq 4000, two HiSeq 2500/1T, HiSeq 2500, NextSeq 500, and MiSeq.

Single Cell Genomics and Epigenomics: 10X Genomics Chromium, custom built Drop-seq instrument, access to Fluidigm C1.

Nucleic Acid Mass Spectrometry: Agena Bioscience Compact MassArray.

Real-time PCR: ABI 7900 HT Sequence Detection System.

General: 2 Covaris S2, 2 Agilent 2100 Bioanalyzers, Agilent tape station, 2 Nanodrop1000 spectrophotometers, 2 Qubit fluorometers, Glomax plate reader, Gel Logic 200 Imaging System, 3 liquid handling robots (Eppendorf epMotion 5075m, Perkin Elmer Zephyr, Hamilton Starlet).

Epigenetic Profiling Services

Methylation profiling

- **Enhanced reduced representation bisulfite sequencing (ERRBS):** Methylation profiling of CpG enriched regions using MspI genomic digests.
- **Methylome capture:** Methylation profiling of CpG enriched regions using targeted probes.
- **Whole Genome Bisulfite Sequencing (WGBS):** Whole methylome profiling (5mC + 5hmC).
- **TrueMethyl-seq:** Methylome profiling of 5mC but not 5hmC modifications. NEW!
- **5hmC profiling:** Unique methylation calls for 5hmC modifications. NEW!
- **Nucleic acid mass spectrometry (MassArray):** Validation of methylation levels at specific genomic loci.

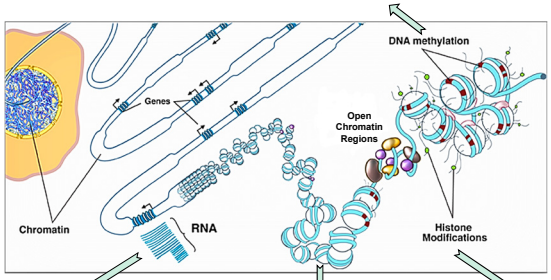


Figure from Roadmap Epigenomics Project www.roadmapepigenomics.org

Gene expression / transcriptome profiling (RNA-seq): Non-stranded or stranded RNA-seq with polyA selection; total stranded RNA-seq; ultra low input RNA-seq.

Assay for transposase-accessible chromatin (ATAC-seq): Identification of open chromatin regions NEW!

Chromatin immunoprecipitation sequencing (ChIP-Seq): Genome wide mapping of protein-nucleic acid associations.

Sample Management & Automation

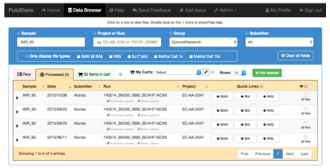
Laboratory Information Management System (LIMS)

We use custom built LIMS for process tracking, including service requests, sample submission, sample quality control, library preparation steps, sequencing parameters and provenance.

Robotics Automation

Library preparation protocols are standardized by use of high throughput equipment (such as pre-PCR and post-PCR liquid handling robots) to minimize variability and batch effects.

Bioinformatics Support



PubShare Portal and Data Storage

We provide distribution and long term storage of data generated by the core via our searchable portal (PubShare). This site provides options for easy downloads, sharing user defined lists of samples with external collaborators, and data access by one line commands or shell scripts for bulk downloading of data.

Analysis Pipelines

- Our in-house bisulphite sequencing analysis pipeline reports detailed methylation values for our methylation profiling assays.
- Automated genome alignment optimized for specific library types provided upon request for available genomes.

Custom Data Analysis

We provide customized data analysis services and consultation on a per project basis. These include but are not limited to:

- ERRBS differential methylation
- RNA-seq differential expression
- ChIP-seq peak calling / differential binding
- Functional annotation and analysis
- Custom alignments

New Technologies and Applications

Long Reads & Single Cell Genomics: 10X Genomics Chromium

- Deep profiling of complex cell populations with high-throughput digital gene expression on a cell-by-cell basis.
- Long-range information on a genome-wide scale, including variant calling, phasing and extensive characterization of genomic structure
- Long-range information for phasing, structural variant detection and copy number determination
- Sample-specific sequence and diploid genome structure.

Single Cell Reduced Representation Bisulfite Sequencing (scRRBS)

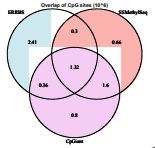
Single cell methylation using the Fluidigm C1 platform (variation of RRBS protocol using single cells). This is an ongoing methods development project being done by the core in collaboration with Dr. Chris Mason at WCM, NuGen and Fluidigm.

Low Throughput 5hmc Profiling

- Adaptation of MassArray Epityper to detect 5hmC.
- Adaptation of (E)RRBS towards genome wide detection of 5hmC using our new custom protocol in conjunction with NuGen and Cambridge Epigenetix (CEGX) reagents.

Comparison of Epigenetic Profiling Platforms

We evaluated three methylation profiling methodologies for differences in captured CpG sites and methylation levels, including enhanced reduced representation bisulfite sequencing (ERRBS), SureSelect methylation sequencing (ssMethyl-seq), and the Roche SeqCap Epi CpGiant enrichment method.



Consultation, Workshops and Training

Consultation on project design and data analysis available upon request. We also provide customized analysis and functional interpretation. In addition, the core provides support for grant applications (e.g., letters of support & experimental details).

Software analysis tools and training available through the CLC Genomics and Epigenomics Core Facility.

Educational workshops and hands-on training on data analysis available through the CLC Applied Bioinformatics Core (ABC).

Seminars on software tools organized by the CLC Applied Bioinformatics Core.

Seminars on emerging genomics technologies organized by the CLC Advanced Technology Assessment Facility.

Coordinated project design consultation and data analysis support available with the CLC proteomics and metabolomics, synthetic and analytical chemistry, NMR, flow cytometry, imaging (e.g., optical and multiphoton microscopy, high content screening, MRI, PET/CT, and high resolution ultrasound) biorepository, bioinformatics, and advanced technology assessment core facilities.

Contact Information

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For questions about the WCM Core Laboratories Center, please contact George Grills at gog2016@med.cornell.edu