

Albert Einstein College of Medicine

FACILITIES & RESOURCES

Overview

This document contains descriptions of core facility and other resources that can be used by Einstein investigators for inclusion in grant proposals. If you have any questions regarding a specific core facility or need a specific budget for your grant proposal, please reach out directly to the core director. Contact information for staff can be found on the Shared Facilities webpage. For general questions or to update this document with new information, please contact Brian Pelowski, Assistant Dean for Scientific Operations, at Brian.Pelowski@einsteinmed.org.

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NOTE: Individual word documents for each core can be downloaded on this webpage: http://einstein.yu.edu/research/shared-facilities/investigator-resources/

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Analytical Imaging Facility

Scientific Director: John Condeelis PhD

Administrative Director and Director of Electron Microscopy: Frank Macaluso MS

Co-Directors of Light Microscopy and Image Analysis: Vera DesMarais PhD and Peng Guo PhD

Introduction, Goals and Objectives

The Analytical Imaging Facility (AIF) is a comprehensive microscopy shared resource that offers imaging technologies ranging from macro-imaging with a stereoscope, classical microscopy including brightfield, darkfield, phase contrast, Nomarski differential interference contrast and wide-field epifluorescence and confocal microscopy for cell culture and tissues, to high speed spinning disk confocal microscopy for live cells, intravital multiphoton microscopy for live animals, and super-resolution (SIM and STORM) microscopy, through standard transmission and scanning electron microscopy, to cryoEM of macromolecules and whole mount cells. The wide range of imaging modalities is especially important for studying a diverse range of biological models to support the diverse biomedical research within the Einstein community. For instance, cells labeled with fluorescent reporter genes may be imaged at the whole animal or whole organ level down to single cells or cell compartments. Having the technology and staff in one location provides continuity and adds value to Einstein researchers who use microscopy. The goal of the AIF is to make routine and complex imaging technologies available to the entire Einstein community and provide needed image analysis training or assistance to its users. This is accomplished by supporting routine microscopy applications, training users in microscopy and image analysis software, hosting regular workshops to be an educator on microscopy and image processing and introducing innovative imaging technologies developed at this institution as they become available to meet the needs of Einstein investigators.

In addition to offering microscopy services, the facility also offers customized full service sample preparation for electron microscopy ranging from chemical fixation, embedding in resin and ultrathin sectioning, negative staining, immunogold labeling, critical point drying and metal shadowing. The facility also offers a full range of low temperature techniques for electron microscopy including quick freezing in the millisecond range by plunge, metal mirror or high pressure freezing. Subsequently frozen samples can be freeze-substituted and embedded at low temperatures, deep etched and rotary shadowed, freeze fractured, ultrathin cryosectioned or viewed directly in the cryoTEM.

The facility has traditionally emphasized teaching new users, on an individual basis, the imaging techniques they require for successful execution of their experiments. The AIF has further expanded its service to include more quantitative, rigorous and advanced image data analysis to the community with newly purchased commercial software as well as home written codes to support diverse research needs in the Einstein community. The AIF user group varies from the novice to experienced microscopist, encompassing graduate students, postdoctoral fellows, technicians, and principal investigators. Appropriate staff effort is expended to address the needs of these groups assisting them in experimental design, data collection, quantitative analysis and presentation. Novice users are trained in the specific imaging technology appropriate to address the specific research objective. Experienced users may customize any imaging station, utilizing the large inventory of optics and accessories that are available. Each imaging station is returned to a "standard configuration" at the end of a session. In this manner a large user group can be efficiently accommodated.

The science of Einstein faculty drives the technology offered in the AIF. State of the art technologies are regularly introduced by the AIF Directors to address these needs. Intravital Imaging was specifically developed within the AIF to support the Tumor Microenvironment and Metastasis Program. CryoEM development is continuing as the AIF supports structural biology research. The AIF staff is currently developing specimen prep protocols for correlative fluorescence and scanning electron microscopy. The need for high resolution SEM was addressed by a successful SIG to purchase a FESEM with cryotransfer stage for imaging samples sensitive to

dehydration artifacts, yeast capsule and bacterial biofilms for example, in a frozen hydrated state. This purchase included Atlas, for large area mapping, which will be used to reconstruct serial thin sections in 3D and Shuttle & Find for CLEM. Another successful SIG enabled the purchase of the 3D Histek P250 Panoramic Slide Scanner. This instrument will allow Einstein researchers to digitally scan and archive high quality images of large batches of slides in a very time efficient manner. Three most recent SIGs enabled the purchase of a Leica SP8 laser scanning confocal microscope for fixed and live cell imaging, a Nikon microscope equipped for Structural Illumination Microscopy (SIM) as well as localization based super-resolution (STORM/PALM) imaging and a JEOL 1400 Plus transmission electron microscope for ultrastructural studies in 2D and 3D.

Services and Technologies Provided

Light Microscopy - The light microscopy division of the AIF provides digital imaging from macro, on the order of cm, up to high resolution, on the order of $0.1~\mu m$, or even up to angstroms when including information from Forster Resonance Energy Transfer (FRET) technology. Einstein researchers may utilize the resource by having AIF staff perform work for a fee although most researchers are trained in use of instruments and thereby have unlimited 24 hour access. The facility offers assistance with experimental design, image acquisition and post-acquisition data analysis.

Light microscope imaging capabilities include epifluorescence, confocal and multi-photon imaging, as well as transmitted light options (brightfield, darkfield, phase contrast, Nomarski DIC). Available high quality optics represent current technologies of Olympus, Zeiss, Nikon, Leica, Perkin Elmer, and GE. Dynamic experiments with live material can be performed on three widefield epifluorescence microscopes, three confocal microscopes, one multi-photon microscope, and a STORM/SIM super-resolution microscope, all fitted with environmental chambers and able to capture time series and z-series in multiple fluorescent channels. Two Eppendorf microinjection systems are available for use on any of the inverted microscopes and can be used for cell manipulations such as microinjection and chemotaxis assays. An Eppendorf cell collector allows researchers to collect individual unattached cells for further analysis. In addition, the AIF offers support for advanced microscopy techniques such as Foster Resonance Energy Transfer (FRET), Fluorescence Recovery After Photobleaching (FRAP), photoactivation and photoconversion assays, as well as Fluorescent Lifetime Imaging Microscopy (FLIM). The multi-photon microscope is at the center of the Intravital Imaging Core of the Motility and Invasion Program Project Grant and the Tumor Microenvironment and Metastasis Program.

Widefield Epifluorescence Microscopes:

- **GE Delta Vision Core and Delta Vision Personal** stations are inverted microscopes using Olympus optics, with Applied Presicion programmable, high precision stages and environmental chambers. Objectives range from 4-150x and fluorescent channels range from DAPI to Cy5. Photometrics cool-snap cameras and an EMCCD camera are used for image acquisition. Due to the high precision stage, these instruments are ideally suited for acquisition of time-series and z-series in live samples. In addition, it is possible to mark coordinates, thus enabling point visiting and the acquisition of multiple time and z-series in each experiment. The software also allows for deconvolution of z-series post acquisition.
- **Digital Stations 1 and 2** are built around Olympus IX70 and IX81 inverted microscope stands and Cooke Sensicam CCD cameras operated with Scanalytics IP Lab software. Available objectives range from 4-60x. Each station can accommodate fluorescent probes ranging from DAPI to Cy5.
- Digital Station 5 is built around an IX70 inverted microscope and Cooke Sensicam CCD camera operated
 with Molecular Devices Metamorph software. It has a Sutter DG4 filter wheel for rapid switching of
 excitation wavelength and a Dual View for simultaneous image acquisition of two fluorescent channels.
 This station has an environmental chamber and is well suited for live cell experiments and for FRET.
- Digital Station 6 is built around a fully automated Olympus BX61 upright microscope stand with a Cooke Sensicam CCD camera operated with Scanalytics IP Lab software. Objectives range from 10-100x. It is equipped with filter cubes for 8 different fluorescent channels, ranging from DAPI to Cy7. It also has the Applied Spectral Imaging SKY SpectraCube and SKY camera for spectral karytyping of chromosomes. This station supports the microscopy requirements of the Molecular Cytogenetics Shared Resource.

- Zeiss AxioObserver with Shuttle & Find inverted microscope with objectives ranging from 5-100x. Brightfield imaging options include phase contrast and Nomarski/DIC. The microscope is equipped with two cameras, an Axiocam HRc for brightfield/histology color imaging and an Axiocam HRm for black and white fluorescence acquisition with Axiovision software and is equipped with a variety of fluorescent channels ranging from DAPI to Cy5. In addition, "shuttle & find" includes a Zeiss proprietary module in Axiovision to mark xy positions on samples in fluorescence and then find the same coordinates on the SEM microscope.
- **Zeiss Axioskop II upright microscope**. This microscope has objectives ranging from 1.25X through 100X. Imaging modes include brightfield, two types of darkfield, crossed polarization, and Nomarski DIC. Images are captured with a color Zeiss Axiocam using Axiovision software.
- **Zeiss Stemi 11 stereo microscope** with a Retiga Q-Image CCD Camera and a fluorescence module (DAPI, GFP and Rhodamine) for imaging entire yeast or bacterial plates and larger objects such as whole transgenic animals (for example C. elegans, zebrafish or mice).
- Olympus Stereo microscope. This microscope has a 1x lens with magnification boosters ranging from 0.7x to 11.5x. It is equipped with a cooled Olympus XM10 monochrome camera, four fluorescent filter cubes (CFP, GFP, RFP, CY5) and uses Cellsense Standard software.
- **3DHistech Pannoramic 250 digital slide scanner.** This instrument is a high capacity, high speed automated slide scanner. It can automatically scan up to 250 slides in one batch. It is equipped with a Lumencor LED light source, 20x and 40x air objectives and a scientific CMOS detector PCO edge 4.2. Imaging modes include brightfield as well as fluorescence (DAPI, FITC, TRITC and Cy5).

Laser Confocal Microscopes:

- Leica AOBS SP5 and SP8 confocal microscopes are point scanning confocal microscopes well suited for multichannel imaging of fixed samples. Objectives range from 10-63x. In addition, the SP5 has an environmental chamber and the SP8 has a stage top incubation system for live cell imaging. They are true spectral imaging systems due to their AOBS technology. The SP5 has seven laser lines for excitation, ranging from 405 to 633 nm, and four photomultiplier tubes allowing users to set up four separate fluorescent channels, plus one additional detector for simultaneous Nomarski DIC. The SP8 is a state of the art confocal microscopy platform. It is equipped with a pulsed White Light Laser covering the entire excitation range from 470-670nm in addition to a 405 nm laser and five detectors, including two highly sensitive HyD SMD detectors for super-sensitive imaging and fluorescence lifetime imaging, one HyD detector and two PMT detectors. In addition, the SP8 is equipped with PicoQuant hardware to conduct fluorescence lifetime imaging (FLIM) experiments. The AOTF allows for small regions of interest to be illuminated at high intensity for photoactivation, FRAP,acceptor-bleaching FRET, spectral scanning and unmixing for challenging samples. The SP8 is equipped with an 8K Hz resonant scanner for low phototoxicity live cell imaging.
- Zeiss LSM5 Live DuoScan confocal microscope is a dual laser confocal system that utilizes a point scanner
 for region of interest photobleaching or photactivation and a line scanner for very rapid (up to 60fps),
 simultaneous acquisition of intracellular dynamics, thus ideal for live cell confocal imaging. Objectives
 range from 10-100x. This instrument has an environmental chamber and is best suited for rapid acquisition
 of images of live samples, including FRET and FRAP.
- Perkin-Elmer UltraVIEW ERS spinning disc confocal microscope for live cell spinning disk (Yokogawa) confocal imaging. The system has laser lines at 488, 568 and 647 nm, a piezo for high-speed Z-axis control, an environmental chamber and Nikon optics, with objectives ranging from 10-100x. It utilizes Volocity acquisition software and a Hamamatsu 1394-ORCA-AG camera. Due to the nature of parallel excitation of spinning disk, this microscope is also faster than point scanning confocal, therefore ideal for fast confocal imaging on live specimen. A photokinesis module was added to perform FRAP experiments.
- Olympus Multiphoton PV1000-MPE utilizes a Spectra Physics Tsunami pulsed laser to excite fluorophores
 and enable second harmonics generation by femtosecond pulses of highly concentrated long wavelength
 light. Currently, three fluorescent channels can be detected (CFP, GFP, and mCherry). An additional
 channel is set up for second harmonic detection. This instrument is the centerpiece of the Intravital

Imaging Program and can accommodate a wide variety of samples ranging from anesthetized whole mice to whole organs, to sections of tissue. The deep penetration depth of multiphoton is ideal for intravital tissue imaging.

• **Nikon Super-resolution microscope** is a microscope with optical resolution beyond the traditional diffraction limit. It is equipped for TIRF imaging, Structural Illumination Microscopy (SIM) as well as localization based super-resolution (STORM/PALM) imaging. It has four laser lines at 405 nm, 488nm, 561 nm and 647 nm, a 100x (NA 1.49) oil objective, and an EMCCD (Andor iXon3) camera. It is fully motorized and equipped with environmental control in the form of a heated stage insert and objective heater.

Electron Microscopy - A wide range of sample preparation equipment and four electron microscopes permit AIF staff to offer full service sample preparation and imaging for standard and state of the art EM techniques. The AIF staff performs most of the specimen preparation protocols while some investigators with expertise in EM use the facility as an equipment resource. Investigators are trained as operators of the electron microscopes. The AIF offers all standard EM preparation protocols including embedding utilizing either epoxy or acrylic resins at ambient or low temperatures, thin sectioning, negative staining, immunogold labeling following pre or post embedding protocols. In addition, the AIF offers a full range of low temperature techniques for EM including cryofixation by plunge freezing, metal mirror freezing and high pressure freezing. Frozen samples can be further processed by freeze substitution and embedded at low temperatures. Specimens can be rotary shadowed for whole mount TEM, freeze fractured, and cryosectioned. Immunogold labeling can be performed using pre or post embedding protocols and by the Tokuyasu method for cryosections. Most traditionally prepared TEM samples are imaged with two JEOL TEMs (1400Plus and 1200EX) and recorded with Gatan digital cameras. Macromolecules and thin areas of whole mount cells frozen in vitreous ice can be imaged directly in the FEI Tecnai 20 cryo electron microscope under low dose conditions and recorded with a 4k x 4k TVIPS F415 CCD camera. 3D image analysis is performed with SPIDER or IMOD software. Surfaces of cells and tissues are imaged at high resolution at ambient or cryo temperature with a Zeiss Supra40 field emission scanning electron microscope (FESEM) with detectors for secondary backscatter and STEM signals.

Major equipment available for EM specimen preparation:

- Leica UC7 ultramicrotome with ATUM automatic serial section collection system.
- Leica UC6 ultramicrotome with FC6 cryo sectioning module.
- Leica UCT ultramicrotome with FC4 cryo sectioning module.
- Bal Tec HPM 010 High Pressure Freezer
- FEI Vitrobot
- Life Cell CF100 Slam Freezer
- Leica AFS2 and Bal Tec FSU-010 Freeze Substitution Units
- Cressington CFE-50 for freeze fracture and deep etch rotary shadowing.
- Tousimis Samdri 795 critical point dryer
- EMS 150T ES combination sputter coater, carbon coater and glow discharge turbopump unit
- Pelco 3450 Laboratory Microwave System
- Denton DV 502 vacuum evaporator.

Electron Microscopes:

- **JEOL 1200EX TEM**, accelerating voltage 20 KV to 120 KV, microprocessor control, equipped with side entry goniometer stage, side mounted Gatan 2k x 2k Orius CCD camera.
- **JEOL 1400Plus TEM** accelerating voltage 20 KV to 120 KV, LaB6 filament, bottom mount 11 megapixel Gatan Orius CCD Camera. SerialEM enables automated acquisition for electron tomography, serial sections and automated image montaging of large areas at high resolution.
- **FEI Tecnai 20 cryo TEM**, accelerating voltage from 60 KV to 200 KV, LaB6 filament, low dose software, Gatan cryo specimen holders, Gatan high tilt holder, Gatan dual axis cryo tomography holder, TVIPS

- TemCam-F415 CCD camera,. Electron cryomicroscopy of vitreous ice-embedded samples and electron tomography at ambient and cryo temperature have been developed utilizing this microscope.
- Zeiss Supra 40 FESEM with Gatan Alto 2500 cryotransfer stage, Oxford Inca EDS, Everhart—Thornley and inlens secondary, backscatter and STEM detectors, Atlas large area mapping and Shuttle & Find. The relative ease of high resolution surface imaging, detection of 10nm gold by backscatter imaging for localization of surface receptors, elemental identification and mapping, serial reconstruction in 3D of large areas, observation of biofilms and other dehydration sensitive materials at low temperature and correlative light and electron microscopy (CLEM) are all capabilities of this microscope.

Data Analysis - The AIF provides two high-end computer workstations and an arsenal of state of the art commercial software for quantitative image analysis in a user friendly environment. With various time and effort investment, the AIF also provides customized personal assistance on writing Matlab codes for image analysis on specific collaborations. The following commercial software is available:

- Volocity for Visualization, Restoration and Quantification is a high-performance 3D image analysis
 software for interactive, time-resolved volume visualization. It allows the user to identify, measure and
 track biological structures in 2D, 3D and 4D, and is able to deconvolve widefield fluorescence images to
 produce superior confocal quality images as well as quantify colocalization, ratio images, FRAP and FRET.
- GE Applied Precision SoftWorx for deconvolution and quantitative image analysis
- **Bitplane Imaris** is a powerful analysis software for data visualization, analysis, segmentation and interpretation of 3D and 4D microscopy datasets. It adds a set of high-performance tools to analyze multidimensional image data including interactive filtering, sorting, classifying, selecting and grouping objects based on statistical parameters. Its object tracking functionality is the best in the industry.
- 3DHistech QuantCenter for analysis of whole slides that were scanned on the 3DHistech P250 slide scanner. QuantCenter has many modules that quantify immunohistochemistry stains and immunofluorescence of the whole scanned tissue. These include pattern-based tissue segmentation, classification of nuclear stain, and measurements of immunostain intensity.
- Each confocal manufacturer provides its own software for data analysis including Zeiss and Leica.
- The AIF authors customized ImageJ macros and **Matlab** scripts for data analysis and presentation.
- **SPIDER** for 3D single particle analysis.
- **IMOD** for 3D electron tomography and 3D reconstruction of serial sections.
- Adobe Photoshop CS5 for publication-quality figure preparation.
- Ektron Content Management System 400 for web page presentation.

Animal Physiology Core

The Animal Physiology Core (APC) employs sophisticated research methodologies to assist Einstein investigators in the in vivo assessment of glucose and fatty acid metabolism, insulin sensitivity and energy homeostasis in mice and rats. The APC enables investigators to thoroughly characterize the effects of defined pharmacological, dietary, environmental and genetic alterations on glucose and lipid homeostasis, insulin action, and metabolism. The Core performs studies of adiposity distribution and facilitates NMR spectroscopy, fMRI and microPET analysis of experimental animal models of diabetes undergoing metabolic studies. The Core also provides specialized rodent surgeries for investigator laboratories and several cardiac functional assessments related to diabetic complications. To accomplish these goals, the Animal Physiology Core will: 1) advise investigators in the design of metabolic studies relevant to the control of glucose homeostasis and insulin action in rodents; 2) make available to investigators specialized measurements of whole body and tissue-specific glucose sensitivity and insulin action including, but not limited to insulin, pancreatic and hyperglycemic clamp studies; 3) provide specialized surgical models for the study of insulin sensitivity, energy balance, and glucose and fatty acid metabolism; 4) offer instruction to students, postdoctoral fellows, investigators and technical staff in performing surgical and physiological techniques necessary to evaluate the controls of glucose homeostasis and insulin action; 5) provide analysis of whole body carbohydrate/fatty acid oxidation, energy expenditure, feeding behavior, and locomotor activity using specialized metabolic (indirect calorimetry) and behavioral rodent cages; 6) provide assessment of the effects of spontaneous or scheduled exercise on glucose homeostasis and metabolism; 7) make available to investigators specialized measurements of rodent adipose tissue distribution using microCT and measurements of glycogen in liver and muscle, intrahepatic lipids and intramyocellular lipids using NMR; and 8) make available to investigators specialized measurements of brain energy and glucose utilization by functional MRI (fMRI) and microPET scanning. All these services are available to investigators new to diabetes research, as well as to investigators working on diabetes-related projects that can be enriched and extended by the use of the expertise and facilities of this Core.

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Biomarker Analytic Research Core

Biorepository

Biostatistics, Epidemiology & Research Design Core

Chemical Synthesis Core

The Chemical Synthesis Core is equipped with state-of-the-art instrumentations to perform demanding chemical reactions (Schlenk technique, low temperature, photochemical, chiral synthesis, organometallics, carbohydrates, peptides, pressure reactions, isotopic labeling, etc.). We offer services related to chemical synthesis and it is our goal to custom tailor solutions for each client. No matter if it is the simple synthesis of a reference compound or collaboration throughout an entire project – from the grant application to the published work – we will address your needs on an individual level. If there is a chemistry-related service that you do not find in our portfolio – please don't hesitate to give us a call. We are always curious about new ideas and directions.

- 1. Custom chemical synthesis
 - o Multi-step synthesis of single compounds
 - Library and analogue synthesis
 - Bioconjugation
 - o Scale-up and batch synthesis
- 2. Synthesis consulting & project planning
 - o Development of synthetic strategies in close collaboration with the client
 - Support in drafting chemistry sections for grant applications
- 3. Compound Purification
 - o LC (silica, alumina, reversed phase, ion exchange etc.)
 - HPLC (reversed phase, chiral columns etc.)
 - Vacuum distillation, recrystallization etc.
- 4. Analytical services
 - o NMR (1-D, 2-D; 1H, 13C, 19F etc.) (at the Structural NMR Resource Facility)
 - Infra-red spectroscopy
 - Mass spectrometry
 - o LC-MS
- 5. Data evaluation, editing and publishing support
 - Detailed evaluation of experimental and analytical data
 - o Preparation of synthetic sections and supporting material for publications
 - o Support on all chemistry related issues in the process of IP protection

Clinical Looking Glass

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Vice President Clinical IT Research and Development Montefiore Information Technology Professor of Clinical Epidemiology and Population Health and Medicine.

Montefiore Medical Center in the Bronx is composed of three adult hospital campuses Moses, Weiler, Wakefield, a stand-alone Emergency Department Westchester Square, and a Children's hospital. Data details for 2014 include: 1,491 beds, 92,117 discharges, 341,149 emergency department visits, 2,812,114 outpatient visits, and 2,455,353 outpatient prescriptions. The touched by Montefiore metric counts any individual seen in the inpatient, outpatient, or emergency department, or received a laboratory test, or a prescription. In 2014, 582,254 unique patients were touched by Montefiore in a borough of 1.4 million people.

An Electronic Medical Record Data Warehouse collects in real time clinical data from all these sites, obtains the social security death tapes from the social security administration, and vaccination information from the New York City Immunization Registry and provides access for IRB approved research, education, Quality improvement to researchers through Looking GlassTM Clinical Analytics (Streamline Health, Atlanta, Georgia).

Originally developed at Montefiore, and now a commercial Product, Clinical Looking Glass is a user-friendly interactive software application for the evaluation of health care quality, effectiveness, and efficiency. The system integrates clinical and administrative datasets allowing non-statisticians to produce epidemiologically cogent self-documenting reports globally assessing care quality while identifying the specific patients in need of clinical remediation.

Three core analytic patterns permit the user a near infinite capacity for creation of cohorts and query of cohort trajectory to outcome while protecting patient privacy. Montefiore IRB has ruled that use of CLG in its identity restricted mode is permitted under federal regulation as preparation for research permitting the research community to assess project feasibility in advance of obtaining IRB approval for a project ultimately requiring identifiers. As of June 2014, Montefiore CLG had 2,562,391 unique patients in its data repository which began on the inpatient in April 1997, captured laboratory data in both inpatient and outpatient facilities from 2002, and contains outpatient prescription information from 2005. Additional information can be obtained from http:\\exploreclg.montefiore.org.

A series of training videos for CLG use can be found on youtube: https://www.youtube.com/watch?v=wPmjQmLoKS0&list=PLf7raPnmlLOeAWU2cNf2jIMDRqQuUTCum&index=1

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A video demonstrating analyses expected of our students using Clinical Looking Glass in the recapitulation of research published by others in the New England Medical Journal can be seen: https://www.youtube.com/watch?v=2DiE3bc3dzg

Clinical Research Center

Community Engagement Consultation Core

Computational Genomics Core

The Computational Genomics Core (CGC) supports the Einstein community by providing essential informatics resources and infrastructure for the analysis and interpretation of large genomic and epigenomic datasets, providing for timely and standardized delivery of data to investigators, and to organize and present tutorials for data retrieval and analysis using the provided tools and methodologies. The CGC develop primary analysis pipelines, analysis and visualization tools for application-specific handling of data using open-source and commercial analysis tools. All tools are maintained and deployed in a manner that optimally supports the research activities of individual investigators. The CGC provides support pipelines for massively parallel sequencing based assays performed through the Epigenomics Shared Facility (ESF) and the Genomics core.

The facility directed by Dr. Fabien Delahaye consists of three full time bioinformaticians with expertise in the different levels of data analysis from primary stages when transforming raw sequence into biological information to more integrative analysis comparing different groups of assays and integrating with other sources of data.

The CGC pipeline catalogue includes quality control assessment and primary analysis for:

- Transcriptome Analysis (RNA-seq)
- Sequence Variant detection (Whole Genome Sequencing/Exome Sequencing)
- Chromatin Analysis (ATAC-seq/ChIP-seq)
- Methylome Analysis (Bisulfite Sequencing/HELP-Tagging/HELP-GT)
- Single cell Transcriptome Analysis (Chromium 10X)

Consultation on study design and customized analysis are also available and encouraged.

The delivery will vary depending on the analysis but always includes quality control report, raw and process data as well as code and settings used during the analysis to assure reproducibility of the findings.

The core is also involved in training by providing tutorials covering software and analysis methodologies.

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Epidemiology Informatics / Study Management Unit

The Epidemiology Informatics / Study Management Unit (EISMU) is based in the Department of Epidemiology and Population Health at the Albert Einstein College of Medicine. The EISMU provides informatics and database management expertise to investigators in all phases of their epidemiologic research, with a special focus on developing web-based 'Study Management Informatics Systems' (SMIS) designed to assist in implementing study protocols on an operational level for consortium and multi-centered epidemiological studies. These systems implement best practices and provide automated operational and quality assurance systems which ensure that the studies are conducted appropriately. The facility continually develops new informatics approaches based on emerging standards to enhance scientific research needs and initiates data mining, data sharing and research collaboration portals which maximize the potential for collaboration between investigators.

The EISMU facility focuses on building innovative systems that expand data collection and management abilities, ensure data integrity, improve laboratory process management and automate integration of data from various sources in order to provide for efficient research operations and improved data access. With each system design, the facility integrates previously designed informatics tools that have demonstrated success in the realm of the development of standards and best practices. System designs attempt to address broad needs across multiple projects. The EISMU provides user and technical documentation for systems and/or informatics tools developed to ensure long-term maintainability. The EISMU also collaborates with an honest broker at Montefiore Medical Center to provide linkage of clinical and research data across the institution.

IT Security

The EISMU has implemented a comprehensive Security Program that conforms to the National Institute of Standards and Technology (NIST) standards and the EISMU official Certification and Accreditation documentation has been accepted by the NIH. The EISMU provides secure data hosting, access and backup services and data security provisions are applied systematically at multiple levels to ensure safe and accountable data storage and access. Multiple factor authentication is required for access to critical systems which include login and password authentication, individual token verification and IP address restrictions. The system complies with HIPAA requirements and utilizes a Secure Socket Layer certificate to ensure data encryption during data transmission. Servers maintain audit logs of all connections and data modifications with access to users granted after certification criteria are met.

The EISMU offices are located in the Belfer building on the Einstein campus. Computer equipment currently resides in the same building in a secure and fully air-conditioned Network Operating Center which is accessible by electronic key card only. The EISMU systems and network environment provide reliable data availability and protection. A fully virtualized environment, built on Dell's hardware and VMware's enterprise level hypervisor, is utilized to provide high performing and highly available systems. Advanced backup and recovery systems are implemented to protect both complete server images and file level data. Redundancy is built into the infrastructure at various levels to minimize downtime in the event of an unexpected system failure including RAID disk arrays, bonded network interfaces, clustered VMware hosts, and file level replication. Cisco firewalls are used to protect all mission critical servers. Symantec Backup Exec and VMware Data Recovery are implemented as an enterprise backup/restore system. Critical database information is backed up at regular intervals to ensure minimal data loss in the event of a catastrophic disaster and to allow for both quick restoration of entire servers, as well as granular restoration of critical files. On site and off site backups include backups to disk (storage area network) and tape. A Virtual Private Network is available for remote access. The system employs a defense in depth model to safeguard data ensuring that only authorized users can access the network resources.

Services and Technologies Provided

- 1. Web based Communication\Collaborative Research Portals: An integral feature of each SMIS is the ability to provide a web-based secure and transparent communication and collaboration service utilizing customized Sharepoint sites which provide access to all study related components. The following components and services are made available and/or hosted via the collaborative portals: (1) protocol documentation and workflow processes for protocol implementation and tracking,(2) customized dashboards for coordinating sites and all subsites for multi-center studies, (3) electronic data capture, (4) project calendaring and shared document libraries with version control, (5) interactive QA reports and queries, (6) data extraction systems, (7) collaborative data analysis and study publication tracking system, (8) personnel electronic access management, (9) administrative functionality to monitor project plans and timelines, and (10) communication and training platforms. The system interoperates with email to distribute alerts and notifications, and audits all editing and updating of information on the site. In addition, the collaborative portals host and integrate with Citrix XenApp as an application delivery system which provides end-users with a fully encrypted session.
- **2.** Web-based Participant Registry and Research Recruitment System: This system generates a web site for each study, complete with a unique URL, consent form, questionnaires and clinical data forms. The system provides a user-friendly interface that allows study coordinators to design and administer an automated screening questionnaire which determines participant eligibility for the study based on pre-specified study criteria and presents eligible participants with an online consent form and printable postal indicia to submit a signed consent. Due to the potentially rich resource of access to a registry of potential participants, the system prompts users in order to obtain general consent for contact regarding other current or future studies from all participants deemed ineligible for any particular study.
- **3. Automated Instrument Design and Electronic Data Capture System:** This tool provides a user friendly interface for the creation of data collection instruments and assignment of each instrument to appropriate participation windows. The system automatically generates the database variables with all appropriate data validation rules, provides for controlled navigation during data entry to minimize human error and initiates data collection at appropriate intervals via preprogrammed customized reminder e-mails. The system is Section 508 compliant, tracks data collection activities at multiple sites, streamlines data management tasks, and provides a consistent framework to edit data. A user-friendly interface allows investigators in real time to access, query, and download collected data, generate monitoring and ad-hoc reports, and perform basic descriptive analysis online.
- **4. Database System Design and Implementation:** SQL Server serves as the core database for all EISMSR systems, with data transformation platforms in place to provide for the exchange of data from other database systems including Oracle MySQL etc. Common standards, form templates, database schemas and data definitions are utilized to maximize reusability of data and information sharing. Distinct databases are created for each study with unique access permissions assigned to study personnel. SQL Server Integration Services are utilized to consolidate data and automate all procedures. SQL Server Reporting Services are used to implement quality control and general data reporting systems. The SQL Server databases reside on firewall-protected virtual servers and strong encryption, authentication and authorization frameworks protect and secure data on the database level and during transmission.
- **5. Custom Programming and Data Analysis:** The EISMSR has extensive experience providing custom programming and web based applications for data presentation, integration, manipulation, management, and analysis. Mobile device enabled applications are developed and implemented in hospital settings for monitoring patient data providing physicians with the information necessary to administer research protocols Technological standards implemented integrate with commonly used platforms, and technologies implemented include .net technology, SSIS, SSRS, AJAX, XML and JQuery. Statistical packages such as SAS, STATA, SPSS and R are utilized for complex data and statistical analyses and complex data management.
- **6. Data Mining and Integration:** The data mining initiative strives to provide an enterprise approach for data acquisition and research information exchange by extracting and integrating data from disparate data sources

within the Montefiore electronic record and providing a presentation layer (see Reporting Services below) which can be accessed by multiple researchers. The EISMSR is developing automated procedures for data extraction utilizing Clinical Looking Glass, a cohort extraction tool from Montefiore EMR data data to identify various cancer cohorts (AIDS associated malignancies, ductal carcinoma in-situ, HPV etc.) and link with demographic, laboratory, medication clinic visit and pathological specimen storage data. Data transformation, harmonization and quality assurance are included in the workflow process to ensure that extracted clinical data meet the criteria of high quality research data and that data integrity is maintained across multiple data sources. Protocols for secure data transmittal and acquisition have been established, and identifiable data are encrypted and or de-identified before integration into the SMIS.

- **7. Study Documentation:** The EISMSR provides Operations Manuals and Data Dictionaries which detail all operational workflows, data management protocols, quality assurance systems, data tracking procedures and database design documentation. Database design and implementation are governed by the data dictionary that defines all data collection items, variable names, derived variables, and validation rules and outlines all decisions regarding data definitions and inclusion criteria for the master dataset that will be used for analysis. The Data Dictionary also serves to define rules for data integration from outside sources and sharing data for secondary reuse.
- **8. Quality Assurance and Audit Control Systems:** Best practices and standardized procedures are employed to design and implement quality assurance systems covering the various aspects of data collection, integration, verification, validation and monitoring, including adherence to protocols, audit and control and alerting for adverse reactions or data anomalies. The QA platform provides tools which monitor in real-time data collection and cleaning processes, flag data deviations from expected norms, track data mining activities and report summary statistics regarding the status of data curation across collaborative networks. QA results and appropriate suggested corrective actions are presented on each site's customized dashboard and the QA Officer investigates and oversees the resolution of all discrepancies reported by the system at the various sites.
- **9. Reporting Services:** The variety of robust and complex data sources mined and integrated for the investigators presents a challenge for information presentation, retrieval, data processing and analysis. Reporting Services are utilized to provide a sophisticated and user-friendly interface for the presentation of data in order to facilitate quick and easy access, querying, reporting, sharing, and processing of information for investigators. Summary data are presented by category (demographic, medication, medical history, laboratory results, cancer diagnoses etc.) as basic statistical summary data tables which allow investigators to drill down through categories of patient data to identify specific cohorts. The reporting feature is interactive and allows investigators to expand all statistical tables into new categories or collapse them in order to extract more specific information. In addition, an advanced level querying system allows for the selection of any variables and the implementation of automated simple descriptive statistics including means, frequencies and crosstabs etc. All identified cohorts and associated data can be exported to Excel or a variety of formats for import into a statistical package for analysis.
- **10. Web-based Image Annotation System:** The EISMSR has implemented across multiple institutions a web-based image annotation system which integrates various technologies to provide pathologists the ability to upload, annotate and score images from studies focusing on the tumor microenvironment of metastasis (TMEM). The system allows for tracking of inter-reliability and intra-reliability between and within pathologists, presents an interface to allow pathologists to collaborate via the web on designation of images and provides a collaborative teaching tool for TMEM scoring.
- 11. Integrated Clinical/Research Data Management Systems: An integrated data management system utilized by clinical personnel in various hospital departments was developed to collect and organize clinical information and facilitate the integration of research related data. A web-based clinical reporting feature allows physicians from multiple disciplines to probe and identify clinical trends. Components are continually being developed to incorporate new data sources (e.g. tissue microarray antibody staining, radiology/imaging, radiation toxicity, etc.) to allow for collaboration among researchers in a shared patient population.

- **12. Clinical Trial Management Systems:** For the New York Cancer Consortium, the facility has developed a Study Management Informatics System (SMIS) for management of multi-centered randomized clinical trials. This SMIS provides site-specific dashboards for document, scheduling and task management, an intuitive interface for screening and enrolling subjects based on pre-specified criteria, clinical data capture, protocol activity scheduling, automated email notifications, and query management. A quality assurance system has been integrated into this system and summary statistics on data curation and cleaning are generated and posted regularly. The EISMSR provides study management and monitoring, conducts regular trainings across all study sites, and has developed an automated electronic data submission process to CDUS.
- **13. Laboratory Operations Management Systems:** An extensive laboratory operations and management system has been developed which provides workflow processes, operational and processing guidance, quality assurance and specimen tracking for projects utilizing the Agilent Bio-analyzer and Illumina platforms.

Epigenomics Shared Facility

The Epigenomics Shared Facility (ESF) is a part of Einstein's Center for Epigenomics and now an Illumina CSPro (certified service provider) laboratory. The high-throughput molecular technological resources in the ESF include massively parallel sequencing (MPS) platforms Illumina HiSeq2500, Illumina MiSeq and Roche FLX; and TECAN freedom Evo® 200 Robotics. The core facility space is dedicated and customized, with MPS library preparation performed in a positive-pressure room isolated from the separate 'dirty' room in which tubes containing amplified libraries are opened within a fume hood. The MPS machines are connected by high-bandwidth networking to dedicated computing equipment located in a server room one floor below, thus keeping the computers separate from the molecular biology space.

The core facility is staffed by four dedicated full time personnel. The facility Director Dr. Shahina B. Maqbool has a Ph.D. and three of the full time technicians have Masters degrees and were hired to senior positions based on extensive experience. One full time staff member also has a Ph.D and was hired to develop and optimize automation of genomics and epigenomics assays.

Sample submission is coordinated through a laboratory information management system (LIMS) component of the WASP (an integrated LIMS and batch processing system: http://waspsystem.einstein.yu.edu/). This webbased system requires that the user enter data about the sample that will subsequently be used when uploading results to public data repositories. Facility users are provided with an account that allow electronic submission of libraries and real-time follow-up of the pipeline to which the samples are subjected. The facility has a turnaround of 2 to 3 weeks per library/job/project and once the sequencing data is available, users are sent an email directly on their account to alert them through WASP.

Quality control and assurance is a critical component of the functions of the Epigenomics Shared Facility. The MPS algorithms include error frequency testing as a function of read length and base composition. All primary data analyses are performed automatically on completion of data transfer from the Epigenomics Shared Facility, who assess data quality and release the results to the investigator by email. The data is backed-up and available for at least 6 months on the WASP server from the Albert Einstein College of Medicine.

ESF support diverse assays for MPS analysis:

- Epigenomic profiling of open chromatin (ATAC-SEQ)
- Chromatin immunoprecipitation assays
 - Massively-parallel sequencing-based (ChIP-Seq)
- Cytosine methylation assays
 - Massively-parallel sequencing-based HELP-Tagging
 - Whole genome Bisulphite sequencing (MethylC-Seq))
 - Epigenome-wide methylation analysis-SeqCap Epi (CpGiant/Choice)
- Directional RNA-Seq, miRNA-Seq
- Single Cell DNA/RNA-Seq (Single cell Genomics Core)
- Exome Capture Enrichment Sequencing (Human/Mouse) and Targeted Resequencing
- Whole-genome de novo or Resequencing and Amplicon-Resequencing

The services will include library preparation and sequencing plus primary data return, analysis and visualization through WASP (http://wasp.einstein.yu.edu). Secondary analysis is also provided on request through our Computational and Statistical Genomics/Epigenomics Groups

(http://wasp.einstein.yu.edu/index.php/AnalysisRequest). Pricing information is also available through WASP: http://waspsystem.einstein.yu.edu/ws/auth/sequencingPricing.do

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Flow Cytometry Core Facility

The Flow Cytometry Core Facility of Albert Einstein College of Medicine is a Cancer Center subsidized shared resource. Its function is to provide access to advanced flow cytometry and cell sorting instrumentation to all investigators at the college in a user-oriented environment and cost effective manner. The facility supports and maintains a wide array of equipment, and has a dedicated staff of four technical staff providing services and training. Analysis and sorting services and instrumentation are provided in facilities that allow management of potential biohazards, enabling sorting and analysis of many types of human and animal derived samples.

Services provided include:

- 1) Educational seminars on principles and applications of flow cytometry analysis and cell sorting
- 2) Hands-on training in use of all analytic flow cytometers and FACSAria cell sorters
- 3) Consultation on experimental design and data interpretation
- 4) Cell or subcellular particle high speed sorting based on fluorescence, size and granularity (Biosafety level up to BSL-2 with enhance aerosol containment)
- 5) Direct assistance with data acquisition and data analysis, including full service custom analyses performed by facility staff
- 6) Data storage and archiving
- 7) iLab online booking and billing system

Instrumentation:

- 1) Two Beckman Coulter MoFlo cell sorters (MoFlo XDP and MoFlo Legacy) providing up to 5 laser excitation and 15-color fluorescent detection. Includes 4-way sorting, plate sorting, aerosol containment, single cell cloning option and sample station/sort receptacle temperature control. (Operation by facility staff only).
- 2) Two Becton Dickinson FACSAria high-speed cell sorters providing up to 5 laser excitation and 14-color fluorescent detection. Includes optional 4-way sorting, index sorting, aerosol containment, cloning option and sample station/sort receptacle temperature control. They are available as a service operated by facility staff, or for self-operation by appropriately trained investigators.
- 3) Two Beckman Dickson LSRII Flow Cytometers. Each is configured with 5 lasers (355nm, 405 nm, 488 nm, 561 nm and 640 nm), and capable of analyzing up to 14-colors simultaneously. They are available for independent operation and assisted use.
- 4) Cytek upgraded DxP10 FACSCalibur Analyzer: This is a 4-laser, 10-color system, available for self operation and assisted analysis.
- 5) Becton Dickinson FACS Canto II analyzer: It is a 2-laser, 6-color system with multiple innovative features including a high throughput sampler (HTS) option that enables fully automated and rapid sample acquisition from 96- or 384-well microtiter plates. It is available for self operation and assisted analysis.
- 6) Thorlab iCys Laser Scanning Cytometer (LSC) (formerly Compucyte iCys LSC). This instrument combines the advantages of flow and image cytometry into a single system. It provides exceptionally flexibility and power for studies that combine cytometric data with cell imaging. It is equipped with three lasers (405 nm, 488 nm and 633 nm) and detects up to four simultaneous fluorescent parameters. It is available for self operation and assisted analysis.
- 7) Two fluorescent microscopes for standard image analysis.
- 8) Four computer workstations (three iMac and one PC) equipped data analysis software including FlowJo, Modfit and iCys programs.

Applications:

- High speed cell sorting, including single cell sorting for RNAseq
- Cell surface immunophenotyping

- Analysis of apoptosis and other cell death pathways
- Cell cycle analysis
- DNA damage and repair studies
- Fluorescent reporter and cellular translocation assays
- Calcium signaling analysis
- Single cell cytokine analysis

Cytokine measurement by cytometric bead array (CBA), including high throughput sampler

Gruss Magnetic Resonance Research Center

Please review the <u>information on this webpage</u> and contact Dr. Craig Branch at <u>craig.branch@einstein.yu.edu</u> to obtain a budget estimate for your project and language for your grant application.

Histology and Comparative Pathology Shared Resource

The Histology and Comparative Pathology Shared Resource of the Albert Einstein Cancer Center provides comprehensive, expert, and cost-effective pathology support to AECC investigators as well as to the Institute for Animal Studies Shared Facility. The facility routinely processes samples from animal models of cancer and disease, but also handles human tissue samples to promote excellence in translational research and provides the following services:

Comprehensive histology services – These services are provided by experienced histotechnicians and include tissue processing, embedding, and sectioning of paraffin and frozen samples. The facility offers routine hematoxylin and eosin staining, as well as an extensive inventory of special histochemical stains, enzyme histochemistry, and immunohistochemistry services. The facility offers numerous routine immunohistochemical stains such as those for cell proliferation and apoptosis, cell type including endothelial cells, and many other markers that are important in the study of cancer. In addition, the facility routinely optimizes antibodies for immunohistochemistry for investigators or makes available unusual histochemical or enzyme stains as requested; these projects involve extensive interaction with the researcher to define appropriate tissue collection methods, researcher expectations, and positive and negative tissue controls.

Pathology services – Both anatomic and histopathologic evaluation of animals and tissues are available to researchers and are performed by Dr. Amanda Beck, a board-certified veterinary pathologist and scientist with extensive rodent pathology experience and a scientific research background involving animal model of human disease. All such services culminate in a detailed report of findings, with or without gross photos or photomicrographs, and commentary on the significance of the findings and any recommendations for further studies. Dr. Beck's experience and knowledge promote valuable insight and close interactions with investigators regarding data interpretation and protocol development.

Clinical Pathology services – The facility is equipped with a desktop Oxford Scientific Hematology Analyzer with the OSI data management system for complete red and white blood cell parameters with differential white blood cell counts. Clinical chemistry analytic services are offered in collaboration with the Analytical Core Laboratory (Golding building GO2) affiliated with the Institute for Clinical and Translational Research at Einstein.

Study design, data interpretation, and documentation – The facility routinely interacts with investigators for consultation regarding study design (e.g. numbers of animals, ages, sex, strain), sample handling and submission, and histology protocols to best address the study objectives. Dr. Beck evaluates the samples submitted, interprets the data, and generates a report for the researcher.

Training - The facility provides training in animal necropsy, tissue fixation, tissue processing, tissue sectioning, and immunohistochemical techniques. Once trained, investigators can utilize the facility's rental microtomes and cryostats at a designated hourly rate.

Key Instruments:

- Custom built downdraft and backdraft table with 2 workstations
- 2 Tissue Processors (Sakura Tissue Tek VIP and Leica ASP300)
- 2 Embedding Centers (Sakura Tissue Tec TEC and Microm EC350)
- Automated H&E stainer with coverslipper (Leica Autostainer XL with Leica CV 5030)
- Automated immunostainer (Dako IHC Autostainer Plus)
- Cryostat (Leica CM 3050S)
- 3 Microtome Workstations (2 Leica RM2255 and 1 Microm HM335E)
- Microscopes
 - Pathologist microscope with digital imaging system (Zeiss Axio Imager.A2 with AxioCam and ZEN software)

- o Two-headed microscope for reviewing slides in tandem (Zeiss Axioskop 2)
- o 2 light microscopes (Olympus CH30 and Zeiss Primo Star)
- o 2 dissecting microscopes (Zeiss and Nikon)
- Oxford Science Forcyte Blood Analysis Unit
- Rental equipment
 - o 3 Microtome Workstations (Microm HM 325, Reichert-Jung 2030 and Shandon Finesse 325)
 - o 2 Cryostats (Leica CM1900 and Microm HM505 N)

Human Clinical Phenotyping Core

The Human Clinical Phenotyping Core (HCP) at the Albert Einstein College of Medicine serves to promote excellence in human phenotyping, and to provide outstanding training in clinical evaluation. HCP is a fully acting Core of the NIH funded IDDRC (1P30HD071593-01) whose mission is to advance diagnosis, prevention, and treatment of children and adults with developmental disabilities with a special focus on participants from minorities groups and women. Our multidisciplinary team includes expertise in a broad range of relevant areas including clinical assessment, psychometric evaluation, audiology, clinical trials studies, recruitment and community outreach, and database management. With a large research registry of deeply phenotyped children and adolescents with developmental disorders such as autism, RTT syndrome, ADHD, dyslexia, and rare disorders such as NPC Type 2, the Core provides Einstein investigators with a fully functioning operation for the recruitment and characterization of research participants for its studies. The broader goal of the HCP Core is to foster translational research by maintaining close links between the clinical and research communities at Einstein and by continuing to build the research registry. The HCP maintains a strong relationship with the local community and as of today its database include a pool of over 1700 research participants. The HCP Core maintains a centralized de-identified database of participants for access by Einstein investigators that includes information about data collection and provides continuity as they traverse different clinical projects.

The HCP Core will serve this project by providing well-characterized cohort of children and adults with XXX together with age and IQ matched typically developing control participants for enrollment in this research project. This objective will be achieved through comprehensive clinical evaluation using "gold standard" diagnostic, cognitive, and adaptive function evaluation. Our data base is managed by HCP staff under the direction of Dr. Molholm and includes extensive neuropsychological data, birth, medical and educational histories along with relevant socio-economic information. The HCP core will be responsible for participant recruitment and baseline evaluation to assess diagnostic eligibility and cognitive level. The HCP is equipped to perform clinical and cognitive assessment for children of all ages as well as adults, and for individuals of all functioning levels including those who are non-verbal.

HCP will advertise, recruit, diagnose and evaluate participants with XXX, as well as control participants (INDICATE TYPE OF CONTROL PARTICIPANT TO BE USED). The HCP Core will be responsible for the administration of the baseline phenotype assessments including medical examination, family medical history, cheeks swabs and blood draw. The core will also coordinate and assist in scheduling the visits for the project. HCP will work closely with PI and study coordinators to maintain computerized data files on all demographic, clinical, neuropsychological, biological and imaging information obtained on participants.

Recruitment and enrollment of participants, with an emphasis on diversity and minorities

The HCP recruits research participants through: 1) the existing database; 2) Einstein clinical services including CERC (Children Evaluation and Rehabilitation Center) and Montefiore children's hospital (Epilepsy Center, neurogenetic, Autism Center in Yonkers and the divisions of developmental pediatrics); 3) newspaper advertisements and 4) online list-serves, parent groups, local chapters of organizations (e.g., Autism Speaks), and special interest websites.

As part of the Albert Einstein Community, the clinical divisions of Einstein almost exclusively serve underprivileged minority populations of Latino, African, and Caribbean descent. Increasing their representation in research is a central mandate of the HCP. This is achieved through a number of specific recruitment efforts at selected clinical centers, advertisements, word of mouth, and our strong relationship with the community. HCP staff is trained to explain in appropriate details the goal of our research along with the enrollment and consent procedures. They are also trained to use screening instruments over the phone to optimize recruitment rate.

To provide targeted human phenotyping

HCP is equipped to provide overall phenotype (cognitive level, behavioral and developmental profiles) as well as more targeted clinical evaluation such as attention deficits, executive functions, learning disabilities, repetitive behaviors and social deficits. Each enrolled HCP participant will be evaluated by a highly qualified clinical psychologist with extensive experience in neurodevelopmental disorders. The evaluation encompasses a comprehensive battery of clinical diagnostic tests and tests of cognitive functions, language and adaptive functioning (see table xx). Dr. Bates is a licensed clinical neuropsychologist and supervises all evaluations and written reports sent to families after completion of the research protocol. The HCP team interfaces with project investigators to respond to their demand and assure optimal baseline evaluation. In addition, HCP works to develop novel metrics of phenotypes that are relevant to the specific research questions. The team and consulting panel of the HCP have expertise in a number of germane areas and are developing or have developed indices of the integrity of multisensory processing; tests to quantify executive functions, and automated recording measures of stereotyped movements.

To build an extensive database of enrolled children, young adults and families

The HCP maintains a state-of-the-art easily accessible and searchable database of de-identified potential research participants. A set of baseline phenotype measures is collected and applied across all participants with ASD to maintain a comprehensive database of information. Subsequently according to each project (e.g., age, IQ level, diagnosis) selected measures can be implemented (e.g., executive functions, attention, and language). In addition, HCP maintains a registry and database of typically developing (TD) children and adults. Maintenance of a central database ensures that the efforts that go into the recruitment and characterization of clinical and TD participants benefit both the individual investigator but also the broader Einstein research community.

STAFFING

Director: Dr. Sophie Molholm, Associate Professor of Pediatrics and Neuroscience, is responsible for overseeing all aspects of the HCP. She and the Senior Clinical Neuropsychologist, Dr. Juliana Bates, and Program Coordinator Margot Gardin, have weekly meetings to ensure that the Core is meeting the needs of its users, and that excellent patient management and relations are maintained. Dr. Molholm is a cognitive neuroscientist and has extensive experience in the management of large-scale research projects that include clinical populations. Over the past 6 years she has organized and overseen the clinical phenotyping of children on the autism spectrum and the characterization of their TD counterparts for her program of research on sensory processing and integration in autism (NIH, R01MH085322). She has expertise in the use of psychophysics, electrophysiology and neuroimaging to assay sensory processing and integration, mechanisms of selective attention, object processing and object recognition in adult and child populations, and in typical and atypical populations.

Clinical Psychologist: Dr. Juliana Bates is a licensed psychologist with over 15 years of experience in the diagnosis of neurodevelopmental disorders, and with particular expertise in autism. Her clinical expertise derives from working in a variety of environments including hospital, research, and private practice. At the HCP she supervises clinical postdoctoral fellows and and student trainees, and ensures reliability and consistency in administration of clinical evaluations across test administrators. She consults with investigators regarding appropriate evaluation instruments for their projects. Dr. Bates is highly skilled in working with more challenging participants.

Program Coordinator: Margot Gardin interfaces with the clinical staff at the various recruitment sites to ensure the smooth transfer of patient information into the HCP database. She is responsible for the daily updating of the database, assists investigators with database queries, and assists with scheduling of individuals in the research project as needed. She also provides the common thread for the family and participant as they interface with the HCP and the research personnel. Ms. Gardin will interface regularly with the PI and research personnel for whom she will provide biweekly recruitment and assessment progress reports.

Audiologist: HCP has access to audiometry through on-staff audiologist Janie Chobot-Rodd, M.A., CCC-A, who is the Co-Director of the Children's Hearing Research Program (CHRP) and Supervisor of Audiology at Montefiore/Einstein. She performs full audiological assessments as required by HCP protocols. She has extensive experience working with patients from all ages and cognitive functioning. Her testing and office space is being relocated from the Kennedy building (less than 100 meters away) to Van Etten, adjacent to the HCP.

Registered Nurse: Jill Kirschen is on staff to coordinate genetic testing and perform blood collection. She has over 10 years of experience working with children with developmental disabilities and is expert in drawing blood from children with developmental disorders.

Hybridoma Facility

The Hybridoma Facility produces monoclonal antibodies to antigens provided by investigators. For most investigators, the staff of the facility will carry out the whole process from immunization through the final cloning, freezing and production of mAb. In general, Dr. Scharff and Ms. Buhl will meet with the Principle Investigator, or his or her representative, to discuss the scientific problem and make decisions about how to immunize animals, to screen for positive hybridomas once a fusion is done and on the types of antibodies that are required. In cases where the screen for positive hybridomas requires special expertise, someone from the Pl's lab participates in the initial screening. Subsequent cloning and freezing is done by the staff of the facility and key clones are stored as a backup for investigators. In the course of making the hybridomas, students and fellows receive training on how to carry out the Hybridoma Technology. The facility can also provide approximately 100ml of highly concentrated monoclonals at around 1mg/ml in media. The facility also provides advice and assistance in characterizing monoclonal antibodies.

iLab Solutions Core Facility Management Software

The iLab Solutions Core Facility Management software (iLab) was made available to Albert Einstein College of Medicine cores and researchers in February 2015. iLab Solutions, now part of Agilent Technologies, is the leader in providing web-based management services to academic research institutions with customers that include leading NIH-funded universities, research hospitals, and independent institutes. iLab leverages a scientific advisory team comprised of active Pls with research backgrounds from Brigham & Women's Hospital, Dana-Farber Cancer Institute, EMBL, Harvard University, Huntsman Cancer Institute, Mt. Sinai School of Medicine, Stanford University, University of Melbourne, Vanderbilt University, and Yale University. The iLab leadership team includes executives with experience from Dana-Farber Cancer Institute, Deloitte, Facebook, Genentech, Intel, McKinsey, Microsoft, SAIC, and Vanderbilt University.

iLab offers a suite of web-based tools for academic research management. The functionality includes core facility service request management, enhanced sample management functionality, equipment reservation and usage tracking, billing and invoicing, reporting, and lab requisitioning and spend tracking tools. The system also allows each user a consolidated view of their recent activity in the system as well as the ability to search across all equipment, services and cores in the system. In order to ensure stability, security, scalability, and responsiveness, iLab conducts all software development, application maintenance, deployment, and user support internally. This internally-resourced approach results in a close relationship between iLab and our customers and ensures iLab can rapidly address customer needs.

Einstein has integrated iLab with the Banner financial system. Nightly feeds of sponsored and non-sponsored funds are fed into the system for use by researchers. Billing files are produced on a monthly basis and fed back into the financial system ensuring timely and accurate accounting for project costs. Single sign-on through integration with active directory allows any Einstein researcher easy access to a centralized marketplace for core services.

External users can register for an iLab account to access core services. After a project or service is completed, iLab generates and emails an invoice to the customer requesting payment. Data filters and an aging report allow cores to track the payment status of external projects.

Thirty core facilities at Einstein currently use iLab: Analytical Imaging Facility, Animal Behavioral Core, Animal Physiology Core, Biomarker Analytic Research Core, Biorepository Facility, Chemical Synthesis Core, Clinical Investigation Services Core, Computational Genomics, Epidemiology Study Management & Informatics, Epigenomics Shared Facility, Flow Cytometry Core Facility, Gene Targeting, Gene Modification, and Transgenic Mouse Facilities, Genetic Engineering and Gene Therapy Core, Genomics Core, Gruss Magnetic Resonance Research Center, High Performance Computing, Histology and Comparative Pathology Facility, In Vivo Imaging System Facility, Irradiator Facility, Macromolecular Therapeutics Development Facility, MicroPET Facility, Molecular Cytogenetic Core, Neural Cell Engineering and Imaging Core, Proteomics Core, Research Informatics Core, Stable Isotope and Metabolomics Core, Stem Cell Isolation and Xenotransplantation Core, the Structural NMR Resource, Tissue Engineering and Cellular Reprogramming Core and the Zebrafish Core.

In Vivo Imaging System (IVIS)

The IVIS facility provides access to the PerkinElmer IVIS Spectrum intravital imaging system that enables longitudinal three dimensional intravital imaging of animals or tissue expressing bioluminescent (e.g. Firefly luciferase) or far red fluorescent probes. The machine is equipped with a high sensitive CCD for imaging which is ideal for imaging single or multiple probes/reporters. Einstein investigators have used the system to follow tumor growth, tumor metastasis and progression of infectious diseases or the effects of drug treatments in infectious diseases. The facility is housed within BSL2 animal space for the convenience of animal works.

Services currently offered by the core:

- Intravital imaging of small animals
- Bioluminescence imaging (luciferase) of whole animals
- · Far red fluorescence imaging of whole animals

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Imaging and Cell Structure Core

The mission of the Imaging and Cell Structure Core (ICSC) of the Liver Research Center (LRC) is to provide Center Investigators with the reagents, equipment, analytic tools, and expertise to perform 'state of the art' microscopy techniques. The ICSC operates in conjunction with our Institutional Analytical Imaging Facility (AIF), which provides access to and training on expertly maintained top-of-the-line fluorescence and electron microscopes. Advanced analytical imaging techniques, available in the Core, are not readily available in individual laboratories. The Core facilitates use of imaging techniques in liver research by supporting and assisting with use of specialized instrumentation, including laser scanning confocal microscopy, deconvolution microscopy, multi-photon microscopy, and cryo-electron microscopy. In addition, the Core provides expertise in and assistance with specialized imaging techniques such as correlative microscopy, vesicle tracking, volumetric measurements, ultrastructural sample preparation, fluorescence recovery after photobleaching (FRAP), and fluorescence resonance energy transfer (FRET). We provide technical support for assisted or independent use of such instrumentation and Liver Center (LRC) Investigators receive priority and reduced rates (10% discount) for use of facility instrumentation and services. In addition, assistance is available for experimental design that utilizes imaging techniques, interpretation of light and electron microscopic data, design of fluorescent protein fusions, and selection of appropriate fluorescent dyes and proteins. The Core has an extensive catalog of fluorescent protein plasmids, dye-labeled antibodies, organelle markers, and other reagents available. In conjunction with the Gruss Lipper Biophotonics Center, the Core provides recommendations to update equipment, anticipate emerging imaging and cell structure methods, and to remain at the leading edge of imaging technology for LRC Investigators.

This Core builds on the expertise and success of Dr. Erik Lee Snapp, an Associate Professor in the Department of Anatomy and Structural Biology and an expert in advanced light microscopy techniques and fluorescent protein technology. Mr. Frank Macaluso provides considerable experience and expertise in electron microscopy sample preparation, image acquisition, and analysis. Funding for this Center Core will allow for services at a discounted 10% rate, support for the salaries of Dr. Snapp and Mr. Macaluso, and maintenance of a library of fluorescent protein plasmids, fluorescent antibodies, and cell dye reagents freely available to LRC Investigators. This Core offers services that are NOT part of the other Cores at Einstein such as 1) advice and reagents for fluorescent protein fusion design, 2) expertise and assistance with a range of fluorescence labeling technologies for cells and proteins, and 3) training in and/or performance of microscopy assays. *The ICSC provides leadership and personnel to perform or assist investigators in performing these* in vivo assessments using state of the art technologies at a discounted price. The services of this Core are available to LRC Investigators, members of the Einstein Community, and have been made available to other liver investigators both local and international and members of other Liver Research Centers to enrich and extend investigator studies.

The Goals of the Imaging and Cell Structure Core are to provide the following:

- 1. To advise investigators in the design of light and electron microscopy studies relevant to hepatocytes and liver tissue.
- 2. To provide specialized services in microscopy image analysis, training in light microscopy techniques, assistance with image acquisition, sample preparation, and experimental design.
- 3. To make available to investigators microscopes, software, training, and analysis for techniques ranging from standard fluorescence microscopy to advanced techniques including photomanipulation, FRET, cryo-EM, correlative microscopy, and coming soon superresolution SIM and STORM microscopy.
- 4. To make available to investigators access to and training in software for analysis of images.
- 5. To perform both quantitative and qualitative analyses of protein colocalization, mobility, and interactions in cells.

Key Instruments

- In addition to the full suite of microscopes available in the AIF, the Core Director has a Zeiss Axiovert 200 for imaging live and fixed fluorescent samples and a Zeiss Observer D1 equipped with a heated stage for multi-hour live cell imaging.
- The Director's lab has a Mac/PC image processing station loaded with Image Pro Plus.

Macromolecular Therapeutics Development Facility

The Macromolecular Therapeutics Development Facility provides expertise in protein purification production in prokaryotic and eukaryotic systems. A detailed description of our capabilities, suitable for grant applications, can be obtained by email from scott.garforth@einstein.yu.edu.

Molecular Cytogenetic Shared Facility

The Molecular Cytogenetic Core (MC) provides tools for the preparation of human and murine samples suitable for molecular genetic and cytogenetic analysis of the entire genome. These tools include the establishment of EBV transformed cell lines; enrichment of populations of cells from a variety of primary tissues (blood and other organs), isolation of DNA and mRNA from a variety of tissue culture samples as well as primary biopsies; preparation of metaphase chromosomes suitable for fluorescence in situ hybridization (FISH) and Spectral Karyotyping (SKY) or whole chromosome paints for human and mouse genome. The core personnel is trained to hybridize commercial probes and to designed locus specific probes for regions of interest to investigators. All the probes are custom designed and in house generated. The MC is located on the 4th floor of the Price Center Room 407 & 413A, the operations director is Dr. Jidong Shan and the scientific director is Dr. Cristina Montagna. Dr. Shan has been at Einstein over years and has extensive expertise in tissue culture and molecular biology techniques. She has long-standing expertise in the generation of EBV transformed cell lines and tissue culture. Under her supervision the average efficiency of EBV transformation is constantly above 90% while enrichment of cell population is above 95% depending on the cell type. Dr. Shan had been trained for the past year to master FISH techniques under the supervision of Dr. Montagna. The MC personnel include also Miss Debbie Lewis (level C technician) and Mrs. Yinghui Song (level C technician). The core's scientific supervisor (Dr. Montagna) has extensive and well-documented experience in the use of molecular cytogenetic tools. She trained initially with Prof. Renato Dulbecco and then with Dr. Thomas Ried, the founder of Spectral Karyotyping. Miss Lewis runs the daily experiments for the tissue culture part of this core wile Mrs. Song has been trained to carry on FISH and cytogenetic experiments.

Services: Probes labeling and hybridizations are carried out within the MC in the Department of Genetics at The Albert Einstein College of Medicine. The facility is located on the 4th floor of the Price Center for Genetic and Translational Medicine/ Block Research Pavilion. Presently, the core lab occupies 300 square feet. The facility is fully set up and has been operating for several years providing FISH services for locus specific probes, chromosome painting and SKY. SKY is a molecular cytogenetic technique that allows for differential visualization of all human or mouse chromosomes in distinct colors with a single hybridization and image exposure. SKY utilizes a combination of Fourier spectroscopy with epifluorescence microscopy and charge-coupled device (CCD)-imaging. Human and mouse single chromosome painting probes are generated from flow-sorted chromosomes and PCR-labeled through the incorporation of five spectrally distinct fluorochromes. Hybridized chromosomes can be visualized using an epifluorescence microscope. The MC core also provides customized services for the hybridization and analysis of tissue microarrays. The personnel has expertise in the establishment and maintenance of primary cell lines (EBV transformed); isolation of DNA and mRNA from a variety of sources (blood, scope, spit, hair and frozen buffy coat); PBMC isolation and cell population enrichment (eosinophils, B and T cells) and whole genome amplification.

Equipment: i) A microscope for SKY images acquisition is located in the AIF (Analytical Imaging Facility, a shared resource at AECOM located in the Price Center room 210). The system include an Olympus BX51 with automatic stage, 6 positions fluorescent turret with specific Chroma filter sets, DIC and equipped with a Sensicam CCD cooled camera. The microscope is connected to a SpectraCube (Applied Spectral Imaging), this technology is based on spectral imaging, which combines two existing technologies, CCD-imaging and spectrometry. CCD imaging produces a finely detailed monochrome image of an object. Spectrometry, on the other hand, measures the spectrum of selected areas on the object and then displays each spectrum as a separate graph. The SpectraCube system is made up of an interferometer, a CCD-camera, a computer, and spectral image analysis software available to all MC users. The SKY system is available to MC users upon reservation and its use is charged by the AIF at standard fee. This system is connected to a DELL computer running the full ASI acquisition and analysis package. This includes: FISH View for locus specific probes and chromosome painting analysis; BandView for standard cytogenetic karyotyping of inverted DAPI metaphases; SKY View for SKY analysis. ii) The Olympus BX51 besides being connected to the SpectraCube is also and equipped with a Cooke SensicamQE camera with IPLab for image acquisition. Custom made script for multifocal image acquisition for the fluorophores of interest have been generate and tested for this system;

thus for our purpose this function as a semi-automatic acquisition system. iii) The acquisition system has been recently fully upgraded with a SpotView C counting software for semi-automatic analysis of locus specific probes counting. iv) Metaphases for all experiments are prepared with the CDS-5 Cytogenetic Drying Chamber (Thermotron Industries). Locus Specific Probes are specifically labeled by nick translation with modified dNTPs. Chromosome painting probes are generated by (Degenerate Oligonucleotide Primer) DOP-PCR using an Eppendorf Mastercycler ep. v) Four laminar flow bio-safety cabinets, four tissue culture incubators and eight large liquid nitrogen storage units are available for tissue culture. vi) The Core is also equipped with three -80°C freezers and three refrigerators.

<u>Throughput and Capacity</u>: The MC core interacts with over 50 investigators at AECOM and provides FISH and cell culture services to investigators from other institutes. The facility has capacity to process over 1000 FISH samples/year. The personnel is also able to handle about 500 EBV transformations and up to 1,000 DNA or mRNA extractions /year.

Pluripotent Stem Cell Core Facility

Director: Eric Bouhassira

This facility occupies approximately 600 square-feet on the 9th floor of the Ullman Building and is equipped with 6 incubators, a BSL2 room for virus production and a semi-automated pluripotent stem cell culture system. There are two trained tissue culture technicians on staff that produce embryonic stem cells via manual passaging of both hES and iPS cells. The Core provides plates of hESCs or iPS cells on a fee for service basis. The facility has stocks of human H1 and H9 ES cell lines as well as a number of transgene-free control iPS cell lines. At no additional fee, the facility can initiate the production of embryoid bodies by seeding the undifferentiated cells in user specified differentiation medium.

The facility also produces transgene-free iPSCs using the Sendai virus method starting from peripheral blood cells or skin fibroblasts. Other donor cells can be used on demand. Once iPS cells are produced, they are analyzed by flow cytometry for expression of pluripotent stem cell antigens (e.g. SSEA-3, SSEA-4, TRA-1-60, Tra-1-80) and analyzed for EB and teratoma formation in collaboration with the human Stem Cell Isolation and Xenotransplantation Core. In addition, PCR is performed to ascertain that the Sendai virus genome is undetectable. Finally, karyotypes are performed to assess genome integrity. Three quality-controlled clones of iPS cells are provided to users.

The facility also provides consulting services for further characterization of the iPS cells by the genomics, epigenomics or proteomics facilities that are available at Einstein. The facility has been in operation for over 10 years and has served more than 30 users.

Project Acceleration Resource

Proteomics Shared Resource

The Proteomics Shared Resource (Laboratory for Macromolecular Analysis and Proteomics: LMAP) provides comprehensive mass spectrometry technologies for analysis of proteins, peptides, carbohydrates, lipids and unknowns that support the translational research mission and goals of the Albert Einstein College of Medicine. The laboratory interacts with scientists who routinely use mass spectrometry in their research programs, and helps those who wish to incorporate proteomics in their research but are unsure of how this can be done.

Comprehensive Mass Spectrometry Services -- The Proteomics Shared Resource provides Einstein researchers with comprehensive mass spectrometry (MS) technologies for analysis of proteins, peptides, carbohydrates, lipids and unknowns. Experienced staff scientists plan and execute MS-based assays, and carry out intensive data analysis. The core provides MALDI-TOF and ESI- mass spectrometry, experimental design services, methods development, bioinformatic analysis, and customized data analytical services. This includes:

- Identification of proteins from gel bands, immunoaffinity isolations, protein complexes or specialty preparations, homogenates, cell fractions or organelles
- Identification and localization of posttranslational modifications by bottom up approaches
- Top down analysis of small proteins or large fragments for localization of posttranslational modifications
- Confirmation of synthetic and recombinant molecules
- High-resolution analysis of metabolites, drugs, peptides and small molecules
- Quantitative analyses of metabolites, drugs, peptides and small molecules

Experimental Design, Sample Preparation, Training -- The Proteomics Shared Resource provides sample preparation and sample handling tips to avoid contamination and help ensure MS success, simplify workflows, and extend the dynamic range of analysis. Tested protocols and kits are available for fresh and frozen samples for cell fractionation, immunoaffinity purification, sample cleanup, ultrafiltration, serum depletion, and staining with MS compatible stains. The proteomics shared resource provides consultative help in the design of proteomics experiments and coordinates those experiments with analytical proteomic pathways available from our commercial partners.

- Consultation regarding experimental design
- Consultation regarding choice of global proteomics or selective proteomics strategies
- Advice or training in mass spectrometry-compatible sample preparation, resolving requirements that might differ between biological and analytical experimentation
- Review of published methods that can be optimized for a research project.
- Trypsin digestion, in gel or in solution, or other specialized enzymatic treatment or CNBr fragmentation
- Training for in-gel and solution enzymatic digestion
- Training in ZipTip or larger scale solid-phase extraction cleanup of samples
- Service or training in reproducible fractionation of fresh or frozen tissues or cultured cells to provide greater dynamic range of protein identification
- Service or training in isolation of phosphopeptides and glycopeptides
- Service or training in off-line FPLC, HPLC and UPLC for gel permeation, reversed phase, normal phase, and ion exchange chromatography

Data Analysis & Reports – MASCOT is used as a search algorithm, and databases are selected to suit each project. Custom databases can be generated. The Scaffold programs for data analysis are particularly useful in that a data reader is downloadable free online. Full unlimited versions of Scaffold and Scaffold PTM are maintained by the proteomics shared resource center. Workstations with MASCOT, Scaffold, and other analytical programs are available in the facility. This permits the end user to evaluate data in a variety of ways.

Staff scientists also train students and postdocs to analyze and mine their own data, as well as how to evaluate the quality of the data and what is meaningful.

Quantitative Proteomics and Mass Spectrometry – quantitative proteomics using SILAC, SILAM, ¹⁸O, iTRAQ and label-free methods are carried out in the Proteomics Shared Resource. Each has specific strengths and weaknesses for different types of experiments. These experiments are carried out using the ion trap or orbitrap mass spectrometers. Triple quadrupole mass spectrometry is now available to aid in quantitative analysis of drugs and their metabolites in biological fluids. Specific software applications are used for each method.

- Instruction and training in performance of quantitative proteomics experiments
- Instruction in preparation of stable isotope labeled cells in culture (SILAC)
- Stable isotope labeled mouse (SILAM) tissues from C57BI6 mice available for use
- Instruction in peptide labeling with iTRAQ reagents
- Multiple reaction monitoring assays and pharmacokinetics,
- Preparation of standard curves with and without biological fluid background

Structural Proteomics – Hydrogen/deuterium exchange-mass spectrometry studies can reveal details of protein dynamics and biomolecular interactions, using the orbitrap mass spectrometer.

Spatial Localization of Molecules -- Mass spectrometry imaging (MSISI) provides spatial localization of small proteins, small molecules, transmitters or metabolites in frozen tissue sections. The proteomics core coordinates preparation of samples for analysis with the Histology and Comparative Pathology Core. The Brucker imaging mass spectrometer system allows correlated analysis of mass spectrometry data and pathology over a wide range of m/z values. The proteomics core provides consultative help in the design of IMS experiments and discounted pilot studies for this technology.

- Preparation of tissue sections for imaging mass spectrometry of small molecules, drugs, metabolites, peptides, or proteins.
- Extraction and analysis of data obtained by MSI

Grant & Manuscript Support – The staff scientists of the proteomics core will provide consultative assistance to members of the Einstein community in the preparation of figures and tables to meet the highest standards required for publication of proteomics and mass spectrometry results. Assistance is also provided for analyzing MS results by pathway and gene ontology analysis, as well as statistical evaluation. Diagrams, writeups and sample data for manuscripts and grants are provided, as well as customized letters of support. Publications documenting successful implementation of novel methods by the Proteomics Core are also available. Staff scientists will also provide reviews of manuscripts and thesis chapters prior to submission.

Key Instruments:

- ThermoFinnigan LTQ Orbitrap Velos mass spectrometer with Waters NanoAcquity uplc
- Agilent 6490 triple quadrupole mass spectrometer (with nanospray)
- Bruker imaging mass spectrometer system
- Two ThermoFinnigan LTQ linear trap mass spectrometers
- Typhoon Imaging System
- Robotics for trypsin digestion of gel bands

Research Informatics Core

Rodent Behavioral Core

The Behavioral Core provides staff with over 15 years of experience in all aspects of laboratory animal behavior and maintains rigorous standards of reliability and quality control. We also have allocated space and testing equipment for a wide range of behavioral assays in mice and rats. These tests are broadly applicable to the study of heritable and developmental disorders, sensorimotor disorders, psychiatric, neurological and affective syndromes, neuropathological and infectious diseases, aging and reproductive function.

The Core aims to facilitate behavioral testing at every level. Some of our resources and services include:

- Dedicated space, software and apparatus
- Expertise in design, statistics, analysis and publication of behavioral studies
- Manuscript writing and dealing with reviews
- Maintain Core animal protocols and assist with user's animal protocols
- Training (staff, students and faculty)
- Assistance with grants
- Establish databases and baselines in commonly used strains
- Phenotype reference and information databases
- Model development
- Liaison with Animal Institute
- Other breeding, general animal health
- Support for statistics and graphing programs

Summary of Services

Cognitive Function

- Novel Object Recognition
- Object Placement VisuoSpatial Pattern recognition
- Social Discrimination Memory
- Spontaneous Alternation
- Spontaneous and Delayed alternation
- Morris Water Maze
- Sensorimotor gaiting (pre-pulse inhibition)
- Radial Arm Maze
- Conditioned Taste Aversion
- Conditioned Place Preference
- Labyrinth Maze
- Barnes Maze
- Set Shifting
- Fear Conditionint

Affective / Emotional Behaviors

- Social Interaction / Social Preference
- Social Transmission of Food Preferences
- Reproductive and mating behavior
- Open Field (exploratory behavior, risk)
- Marble Burying (neophobia, compulsions, anxiety)
- Elevated Plus Maze (anxiety)
- Light/Dark Box (anxiety)
- Acoustic Startle (anxiety and hearing)
- Porsolt (Forced Swim) Test (depression)

- Anhedonia (depression)
- Tail suspension test (depression)

Tests of Analgesia

- Von Frey (sensory, allodynia)
- Cold Tail Flick
- Hargreaves (thermal, pain)

Sensorimotor Function

- Open Field (activity, habituation, sensitization)
- Rotarod (motor coordination, motor learning)
- Grip Strength (sensorimotor function, muscle strength)
- Gait analysis and toe spread (motor coordination)
- Balance Beam (motor coordination)
- Visual Placing (visual acuity)
- Visual Cliff (visual acuity and depth perception)
- Pupil dilation
- Acoustic Startle and Prepulse Inhibition
- Gait analysis
- Tape removal test fine motor coordination
- Parallel Grid Floor test
- Negative Geotaxis and righting reflex

Other

- Functional Observation Battery (Primary Screen, Neurological Screen)
- Estrous Cycle Staging
- Behavioral Tracking software (Viewer, Biobserve)
- Grooming
- Stereotypies
- Developmental Milestones
- Homing behavior in pups
- Olfaction and olfactory discrimination
- Mating and breeding
- Behavioral Spectrometer
- Ultrasonic vocalizations

Stem Cell Isolation and Xenotransplantation Core

The Stem Cell Isolation and Xenotransplantation Core was initiated and built through NYSTEM funding, and currently provides services to about 25 laboratories at Einstein and elsewhere. The core provides the following resources:

Animal housing and irradiation

Animals are bred and provided by the facility to investigators and maintained under reverse isolation conditions in a barrier facility for protection from pathogens in a modern, AAALAC approved facility, supervised by three veterinarians. Pathogen-free use of a gamma irradiator (Cesium-137 gamma-ray irradiator (Mark I irradiator Model 68 with a 6,000-Ci source) is provided by the Core to irradiate mice as a conditioning process for stem cell xenografting. The Core also provides an ultra-sound instrument in a pathogen-free environment to monitor fetal development (for fetal liver stem cell transplantation), formation of solid tumors, as well as LSC-derived (liver stem cell-derived) formation of splenomegaly, hepatomegaly, etc.

Xenotransplantation procedure room

There is a dedicated 250 sq ft. procedure room, specifically built by the College tailored to the needs of the xenotransplantation facility. Four easily disinfectable injection stations and tables are available as well as anesthesia machines, animal restraint devices and injection equipment. The procedure room is part of the barrier facility so that mice do not have to be moved out of the facility for transplantation.

Stem cell isolation laboratory

Two cell sorters are available in the facility, and are located in dedicated, newly renovated space (350 sqft) provided by the Institution: (1) a 5-laser (including UV), 18 photomultiplier tube (PMT) Special Order BD FACS ARIA II integrated in a whole instrument biosafety cabinet (allowing for "biohazard sorting" of primary human stem cells from clinical specimens), and (2) a 3-laser, 14 PMT additional BD FACS ARIA IIu cell sorter.

Zebrafish Core Facility

The Zebrafish Core Facility at Einstein [http://www.einstein.yu.edu/research/shared-facilities/zebrafish/] is well equipped to maintain established transgenic and mutant zebrafish lines, provide 100's of embryos per week, and also able to rapidly produce new transgenic or mutant animal strains. The core facility has a dedicated technician who performs all the steps for production of new animal strains including microinjections, fluorescent screening, and animal maintenance. The Zebrafish Facility consists of ~450 square feet in Chanin 543C, an additional ~500 square feet on the 5th floor of the Ullman building and a small quarantine area of ~109 square feet in Chanin 521. The facility has dedicated space to hold approximately 2400 3L tanks. The Core Facility is allocated approximately 50% of the space.