

URSMD CORE FACILITIES AND SHARED RESOURCES SUMMARY

Overview and environment: The University of Rochester School of Medicine and Dentistry (URSMD) is highly committed to providing shared instrumentation and core facilities in support of basic, translational and clinical research across departments and centers. Indeed, core facilities and shared instrumentation play a central role in URM's 2007-2012 Strategic Plan. This is evidenced in part by the major increase in resources that URM has allocated for operational support (a 46% increase in core subsidies from FY 06 to FY 09, including a 15% increase from FY 08 to FY 09). It is also reflected by a major commitment to acquisition of new core instrumentation through NCRR/NIH supported Shared Instrumentation Grants and institutional investments.

New equipment and core enhancements: The University supported significant enhancement of multiple cores in the past 3 years with addition of state of the art instrumentation. A new Structural Biology and Biophysics Facility was added in 2010, with roughly \$1 million of newly acquired instrumentation. Equipment costing an additional ~\$1 million was also added to the Functional Genomics Core in 2009 and 2010, in the form of two high throughput DNA sequencing platforms (HTDS) – one being an ABI SOLiD4 HTDS and the second an Illumina GAIIX high throughput sequencer. An Olympus FV-1000 Confocal Microscope with SIM scanner capable of 2-laser synchronized scanning was added to the Confocal and Conventional Microscopy Core in mid-2008. A Fourier Transform Mass Spectrometer (FTMS) and a Triple Quad Mass Spectrometers capable of high sensitivity and resolution were purchased for the Proteomics Core in 2008. Three new cores were formed in the past three years including (1) the Multiphoton Imaging Core, which was established with the purchase of a multiphoton confocal microscope capable of live imaging, (2) the High Throughput Screening (HTS) core, which was established to permit the screening of libraries of small molecules, for desired biological activity, and (3) the Structural Biology and Biophysics facility (see above). A Gammacell 40 Exactor Low Dose-rate Research Irradiator was purchased and installed for animal work within the vivarium. In addition, the UR Clinical Translational Research Institute (CTSI) provided incremental support to multiple cores including an 18-color BD LSRII special order flow cytometer, an Amnis ImageStream GenX and additional equipment for the flow cytometry core.

Major core facilities: The UR Medical Center has a number of successful core research facilities that provide services to all researchers at the Medical Center. These facilities are listed below.

- **Biomolecular Interaction Laboratory.** The Biomolecular Interaction laboratory seeks to give access to custom affinity reagents to researchers in the University. We utilize phage display to generate recombinant antibodies to user provided target molecules and produce the single-chain Fv proteins for the user. We also can perform affinity measurements using surface plasmon resonance or provide access to trained users to this equipment. This facility is of special value to UR researchers with interests in immunology and/or flow cytometry. Specialized instrumentation includes a Reichert SR7000 Dual Channel surface plasmon resonance refractometer, Bio-Rad DuoFlow chromatography system, BioRobotics automated colony picker and PanVera fluorescence polarization spectrophotometer.
- **Biosafety Level 3 (BSL-3) Core.** The Biosafety level three facility (BSL-3) is available for the use of any researcher at the university whose work requires manipulation of biological agents which may cause serious or potentially lethal disease as a result of exposure by the inhalation route (such as TB). The BSL-3 Core laboratory is a fully self-contained facility and includes 4 biosafety cabinets, several incubators as well as -80 freezers and a liquid nitrogen storage tank. Additional equipment includes a tabletop centrifuge with high and low speed rotors, an inverted microscope (Olympus CK40), a sonifier, visible light spectrophotometer, electroporator, and cell lysis equipment.
- **Cold Storage Core (CSC).** The CSC provides a discrete area where investigators can keep freezers for long-term storage of research materials. The entire facility is alarmed and power protected.
- **Confocal and Conventional Microscopy Core Facility.** This core provides UR researchers the ability to obtain high quality imaging data using state-of-the-art microscopy instruments. It also serves as the information hub for UR resources centering around histological processing, imaging, and image processing and as a conduit for communication between imaging researchers on campus. Guidance for

quantitative assessment of image-based data is provided and core personnel are able to perform both the imaging and quantitation of data for investigators unfamiliar with microscopic research technology. Specialized instrumentation includes a newly (2008) acquired Olympus FV-1000 Confocal Microscope with SIM scanner capable of 2-laser synchronized scanning, an Olympus Vanox T Fluorescent Microscope (epifluorescence model), MicroBrightfield StereoInvestigator Software for image analysis, and a Pixcell II Arcturus Laser-Capture Microdissection instrument.

- **Electron Microscope Research Core.** The principal mission of the Electron Microscope Research Core (EM Core) is to provide University of Rochester researchers support in high magnification (1,000 to 600,000 range) image analysis of cells and tissue in the fields of Transmission Electron Microscopy (TEM), Scanning Electron Microscopy (SEM) and combined Scanning/Transmission EM (STEM). Specialized instrumentation includes a newly acquired (2007) Hitachi 7650 Analytical Transmission Electron Microscope with a sidemount Gatan 11 megapixel Digital Camera, an electron dispersive x-ray spectrometer (EDAX Instrument) for elemental analysis of nanoparticles, a Gatan Digiscan II undermount camera for STEM (scanning/transmission unit for darkfield EM and fine probe elemental analysis). Auxillary equipment includes a Reichert ultramicrotome, diamond knives, 2 Olympus light microscopes, a Bausch & Lomb dissecting microscope, centrifuges, a critical point dryer (for SEM specimens) and diamond knives.
- **Flow Cytometry and Immunologic Analysis Core.** The mission of URM C Flow Cytometry Core is to provide investigators with state-of-the-art instrumentation along with the expertise to push the limits of current technology to support cutting edge research. The core provides researchers with access to and training in the operation of flow instrumentation, as well as educational outreach to the research community. The Core currently has analytical, sorting and imaging flow cytometers including a FACSCanto II(8-colors) and 4 LSR-II's (a two 12-color and and two 18-color instruments) from BD Biosciences, BD 13-color FACS Aria and 18-color Aria-II cell sorters, two Amnis ImageStream Imaging Cytometers, including a state of the art Amnis ImageStream GenX, and an Accuri C6 cytometer. In close association with the Rochester Human Immunology Center, comprehensive training, consultation, method development and access to instrumentation is provided to investigators for maximizing quality, effectiveness and cost efficiency in flow research.
- **Functional Genomics Center.** The Functional Genomics Center (FGC) provides core laboratory services, technical advice, and assistance with experimental design and data analysis for various aspects of genomics research. The lab can extract DNA or RNA from cells, blood or tissues, and will check the quantity and quality of with a Nanodrop 1000 spectrophotometer and Agilent 2100 Bioanalyzer. Routine Sanger DNA sequencing and analysis of DNA fragments with fluorescent labels are done with a 48-capillary 3730 DNA Analyzer. Ultra-high-throughput sequencing (millions of short sequences done in parallel) is done with a SOLiD 3 Plus system. Real time PCR is done with a 7900HT thermal cycler, which also is available for a fee to investigators who set up their own 384-well PCR plates. Some genotyping projects can be done by the FGC, but it no longer accepts routine mouse genotyping projects. Microarray projects are done in conjunction with external labs to reduce costs and turnaround times and to offer more platforms (Affymetrix, Agilent, Illumina). The FGC staff analyzes microarray, real-time-PCR, and high-throughput sequencing data with no additional fee for projects using the lab services.. The following major equipment is located in the FGC: Applied Biosystems (ABI) SOLiD 4 high throughput sequencer, Illumina GAllx high throughput sequencer, Affymetrix GeneChip System (Hybridization Oven 640, Fluidics Station 450, Scanner 3000), Perkin Elmer ScanArray Microarray Scanner, ABI 7900HT real-time PCR instrument with autoloader and microfluidic card module, ABI 3730 Capillary Electrophoresis DNA sequencer, CAS 1200 liquid handling robot, 2 Agilent 2100 Bioanalyzers, BioRad gel documentation system, 3 NanoDrop ND-1000 spectrophotometers (two at FGC, one at medical center for public use), 25 Thermo Hybaid MBS PCR machines, 2 BioRad Dyad Disciple Thermal Cyclers, SciGene hybridization oven, Tecan HS4800 hybridization station.
- **Gene Targeting and Transgenic Core.** This core provides expertise and assistance in the production of transgenic mouse models by either DNA microinjection or gene targeting in embryonic stem (ES) cells. For gene targeting and transgenic projects, the Core assists in all phases of the project, including design and construction of gene targeting vectors, and microinjection of ES cells into mouse blastocysts in order to generate chimeric mice. Other services include mouse embryo and sperm cryopreservation, re-derivation of mice to obtain Specific Pathogen Free (SPF) status, generation of congenic mice (backcrossing). The Core consists of a barrier facility for procedures involving production

and maintenance of genetically modified mouse strains, a tissue culture facility for ES cells, and a molecular laboratory for generating gene targeting constructs and genotyping experiments.

- **High Throughput Screening (HTS) Core.** This core provides investigators with relatively cost effective access to screening chemical libraries for identification of novel molecules that can be used to perturb biological systems. It offers the capacity to develop assays for high throughput screening, the ability to screen relatively small libraries to obtain preliminary data for grant proposals, as well as to screen much larger libraries for identification of leads for therapeutics. The Core works closely with investigators to develop and initiate large or small scale screening campaigns and can direct investigators to resources for further lead development. Specialized instrumentation includes an Envision High Throughput Plate Reader, equipped with optics that allow for measurement of Fluorescence, Luminescence, Fluorescence Polarization (FP), Time Resolved Fluorescence (TRF), Absorbance, Alpha Screen, FRET and other assays in 96 or 384 well formats. The Core also has a Janus dual arm robotic liquid handling system, a Flexdrop plate filler, and a Biotek plate washer. This core was newly established in 2008.
- **Human Immunology Center Laboratory.** The Rochester Human Immunology Center (RHIC) and its core laboratory were established to acquire, refine and develop expertise in cutting-edge techniques and to support applications in Human Immunology research. The RHIC serves to enhance multi-disciplinary research initiatives catalyzing key clinical and basic immunology research in vaccines, HIV/AIDS, autoimmunity, allergy/asthma, transplantation as well as cancer immunology. The Center's core lab provides assistance and expertise in immunological method development, standardization and validation through individual and group training programs as well as collaborative projects. This core lab has served over 50 individual research projects over the past 6 years, resulting in >25 new grant awards; NIH funding of the HIC was renewed for another 5 years in 2009. The RHIC core lab works closely with the URSMD Flow Core facility to provide immunological and flow services.
- **Molecular Imaging Facility.** The Molecular Imaging Facility provides researchers at the UR with access to state of the art instruments capable of detecting and quantifying the levels and positions of radio- and fluorescently labeled molecules in a variety of formats including gels, blots and microtiter plates. Major instrumentation includes a Storm 820 Phosphorimager for phosphorimaging and a Typhoon 9410 (acquired in 2007). The Typhoon 9410 is housed within the Center for RNA Biology, and handles gel sandwiches, agarose and polyacrylamide gels, membranes, microplates, and microarrays, with the capacity for multiplexed detection of chemiluminescence, fluorescence and ionizing radiation.
- **Multiphoton Core Facility.** The Multiphoton Core Facility provides state-of-the-art multiphoton imaging capabilities to further biomedical and bio-optical research at the UR. Specialized instrumentation includes an Olympus Fluoview 1000 AOM-MPM imaging system and a Spectra-Physics MaiTai HP DeepSee Ti:Sa laser system with dispersion compensation. The multiphoton core is uniquely suited for intravital imaging and systems physiology in small animals, e.g., mice and rats. Small animal surgeries are routinely performed at two completely equipped surgical areas in direct proximity to the multiphoton microscope. Physiological measurements, such as arterial blood pressure, EKG, body-temperature, laser doppler, tissue oxygen, electrophysiology, pulse-oximetry, blood-gases, and blood-glucose. can be started during surgery and continued during the intravital imaging session. Further capabilities include engineering applications for opto-electronics and spectroscopy, and software development for quantitative image analysis, visualization and instrument control. This core was newly established in 2008.
- **Proteomics Center.** This core provides protein characterization support, predominantly in the form of proteomic technology. The analytical strengths of the core are mass spectrometry and separation sciences. In a classical proteomic application, a complex sample matrix, such as serum, is separated into individual protein fractions, the identities of which are then determined with mass spectrometry. The core processes a myriad of sample types, from complex clinical matrices to simple purified proteins, for identification of unknowns or verification of identity. Specialized instrumentation includes a Ciphergen PBS III (SELDI; Surface Enhanced MALDI), Thermo LCQ (Electrospray Spherical ion trap MS), Thermo LTQ (Electrospray linear ion trap MS), Autoflex III (MALDI TOF/TOF), ProteomeLab PF2D (Protein Fractionation system) as well as a Thermo Ultra (Triple quadrupole MS) (acquired in 2007) and a Bruker Apex Ultra 9.4T FT-ICRMS (Fourier transform MS) (acquired in 2008).

- **RCBI (Rochester Center for Brain Imaging).** The Rochester Center for Brain Imaging (RCBI) provides researchers at the UR, as well as neighboring institutions, with access to a state-of-the-art 3T magnet for research using magnetic resonance imaging (MRI). The Center is also able to provide structural images of any part of the human body, and spectroscopy of living tissues. The heart of the RCBI is a Siemens Trio 3T whole-body magnet, with maximum gradient amplitude of 40 mT/m and a slew rate 200T/m/s. A standard birdcage head coil as well as an 8 channel phased array head coil (capable of parallel imaging using SENSE/GRAPPA) are available for brain studies. Pulse sequences installed on the Trio system allow capability for many types of research applications, including functional MRI (EPI-BOLD), conventional structural MRI (including T1 and T2 weighted and perfusion imaging), diffusion-weighted scans including diffusion tensor imaging (DTI - for imaging white matter tracts in the brain), and single- and multi-voxel spectroscopy. Custom coils are available through the staff of the RCBI, permitting high resolution imaging of small animals. A \$750,000 upgrade to the Siemens Trio 3T is in progress (2009) and will upgrade the scanner to enable specialized coils to conduct whole-body imaging without repositioning the patient. The specific upgrade is a TIM (Total Imaging Matrix), consisting of hardware (RF coils and receivers, gradients, and new computers) and software (new pulse sequences and post-processing tools) that improve the speed of image acquisition, improve the spatial resolution of both structural and functional scans, add the capability of obtaining real-time fMRI, reduce susceptibility artifacts, and provide coils for whole-body scanning.
- **Vivarium.** The Vivarium is a centralized resource facility with staff and programs that support the research and educational uses of laboratory animals. These facilities are fully accredited by AAALAC and are in compliance with state law, federal statute and NIH policy. The Division of Laboratory Animal Medicine (DLAM) consists of one board certified laboratory animal veterinarian, two clinical laboratory animal veterinarians, a veterinary pathologist & a staff of trained and licensed technicians. Support is provided for research with all major animal species. Services provided by DLAM include colony health monitoring, quarantine services, animal acquisition from other research facilities, surgical support/anesthetic services, 24/7 on-call veterinary emergency services, clinical management of any cases of spontaneous or experimental disease, necropsy and histopathology services, training in specialized techniques (including inhalation anesthesia of rodents, blood collection, aseptic surgical technique) and rodent breeding colony management for PIs. Core services provided by the vivarium include daily husbandry practices, daily observations for health problems, special request services (special diets, water, fasting), provision of federally mandated enrichment to animals, and cage wash, autoclave and room sanitation services. Major equipment includes HEPA filtered ventilated cages & hoods for barrier maintenance of mice, inhalation anesthesia machines for rodents and large animals, diagnostic X-ray machine, autoclave for surgery packs, Intensive Care Unit, CO2 euthanasia stations and a new (2008) Gammacell 40 Exactor Low Dose-rate Research Irradiator for irradiation of small animals within the vivarium (used principally in support of bone marrow transfer studies in mice). The UR Medical Center has recently (2009) embarked on a major (20%) expansion of vivarium staff, aimed at better meeting needs of investigators using mice, that is being coupled with upgraded user training and a new "smart" card-swipe access on animal suites, intended to reduce potential for infection/contamination.
- **Xenogen IVIS *In Vivo* Imaging Core.** The mission of the *in vivo* bioluminescence imaging core is to allow the detection of bioluminescent tracer molecules in living small animals. Specialized instrumentation comprises a Xenogen IVIS Imager from Caliper Life Sciences, which is a first-generation instrument that documents bioluminescence across the visible spectrum.

Other Facilities

- **High performance computing (HPC):** The University of Rochester recognizes the key role of high-performance computing (HPC) in the advancement in research both within and across disciplines spanning all areas of academic scholarship. As a consequence, the University created the **Center for Computational Arts, Sciences, and Engineering (CASE)**. This University-funded center provides researchers across the university with the both the resources (i.e. CPU, storage, software tools, etc) and the assistance (training, operational support, software development support, etc) necessary to fully utilize high-performance computation in their research activities. CASE maintains two high-performance computing (HPC) clusters: the 7 teraflop BlueHive cluster, consisting of 84 compute nodes totaling 672

CPU cores, 672GB RAM, and 24 TB storage; and the Nova cluster, consisting of 144 CPU cores, 144GB RAM, 1.2 TB storage. CASE provides supporting software applications and tools, including Intel, GNU, and IBM compilers, parallel communications libraries, math libraries, and domain-specific applications, and cross-domain scientific applications including R and MATLAB. All of these resources are supported and maintained by a dedicated support team. In addition to computing resources and tools, CASE staff assists researchers to apply these tools to their own research by providing expertise and training, including: technical assistance applying computing to research; training in general HPC use, application use, and software development; and assistance in porting and tuning applications. The UR has further expanded its research facilities through a recent joint HPC research alliance with IBM. This activity provides researchers across the University with the resources and the assistance necessary to fully leverage high-performance computation in support of their research activities. The acquisition of a 13.9 teraflop BlueGene supercomputer, with 2048 processors, 2TB RAM, Storage Server with 90 TB storage, Front End Server, and 8 File Servers, complements the existing IBM Linux cluster in the CASE (see above). These high performance resources are professionally managed in the University's new state-of-the-art data center and offer researchers the power and the complete suite of software tools, including Intel optimizing compilers, Math and MPI libraries, IBM compilers, IMSL, ESSL, GPFS, the R statistical computing system, Matlab, Mathematica, System S, and SolidDB. In addition to this extensive computational research environment, University staff assists researchers to apply these tools to their own research by providing expertise and training, including: technical assistance applying computing to research; training in general HPC use, application use, and software development; and assistance in porting and tuning applications.