Center for Biomedical Shared Resources (CBSR) Overview

Owner: Doug Taatjes, Director CBSR, Amy Gilman, CBSR Administrative Assistant
Email: douglas.taatjes@med.uvm.edu, amy.gilman@med.uvm.edu
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Douglas J. Taatjes, Ph.D., Director, CBSR
Nicole DeLance, B.S., CBSR Budget Manager
Amy Gilman, CBSR Administrative Assistant

Core Directors
Roxana Del Rio Guerra, Ph.D.,SCYM, Flow Cytometry, RRID SCR_022147
Douglas Taatjes, Ph.D., Microscopy Imaging Center, RRID SCR_018821
Ying Wai Lam, Ph.D., Proteomics, RRID SCR_018667
Julie Dragon, Ph.D., Vermont Integrated Genomics Resource, RRID SCR_021775

Facilities and Other Resources
Resources of the CBSR include the Flow Cytometry and Cell Sorting Facility, Microscopy Imaging Center (MIC), Proteomics Core Facility, and Vermont Integrative Genomics Resource (VIGR).

Overview: The shared resources are founded on the principles of providing comprehensive services from experimental design, selection of appropriate technologies, services, data analysis, publication and grant support, training and education. The CBSR extends these capabilities enhancing new applications such as spatial transcriptomics and multiplex imaging. The success of the CBSR will be based upon the state-of-the-art capabilities, scientific expertise, and the outstanding reputation of VIGR, MIC, and Proteomics Facility. This comprehensive iterative approach is not available commercially.

CBSR occupies approximately 10,000 sq.ft on the main first floor level of the state-of-the-art and LEED certified Firestone Medical Research Building. CBSR opened its doors in January 2023 with all of the cores occupying the adjoined research space. Below we provide an overview of the foundational cores' capabilities, facilities, and equipment:

CBSR Microscopy Imaging Center (MIC)

Directory: Doug Taatjes
Core Marketplace Link (for Facility RRID, LIMS, equipment, and citations): RRID SCR_018821; https://coremarketplace.org/?FacilityID=22
Email: douglas.taatjes@med.uvm.edu
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Facilities and Other Resources
The Microscopy Imaging Center (MIC) is a Larner College of Medicine Core Facility designed as a multi-user resource for educating and assisting investigators in all aspects of sample preparation and collection and analysis of images for biological and materials applications. The MIC, established in 1994, has a long track record in supporting biomedical research both locally and regionally and serving the imaging needs of researchers regionally and nationally, including multiple corporate investigators. The MIC consists of multiple microscopy-based imaging systems, computers, and software for image analysis, providing state of the art, rigorous, quality assured, morphologically oriented services. It is operated on a fee for service basis and provides professional consultation and

assistance with experimental design, performing complex imaging-based experiments, training users in various immunohistochemical protocols and use of the complex imaging systems, equipment uses, and interpretation and analysis of results. MIC also provides full experimental imaging services, including testing of new antibodies and developing new experimental protocols and quantitative image analyses procedures. The MIC is staffed by multiple talented and experienced laboratory technologists and research professionals who can provide guidance with experimental design, sample preparation, tissue sectioning, high-resolution microscopy-based imaging, and data analysis and interpretation. The instruments provided in the MIC are state of the art tools that are used with the assistance and guidance from laboratory technologists for optimal results.

From a regional (and even national perspective), the MIC possesses some unique attributes. 1) Unlike many microscopy-based core cores which specialize in a specific area of microscopy, MIC incorporates in one location multiple types of high-resolution instrumentation including electron microscopes, confocal microscopes, super-resolution microscopy, laser microdissection, Nanostring GeoMX, Akoya Fusion-Phenocycler, atomic force microscopy, and whole slide imaging. (2) A major expansion of the imaging capabilities of the MIC has led to the creation of a large and unique imaging center through the recent NNE-CTR investments. (3) A full histology suite including paraffin microtomes, cryostats, Leica RM 2165 microtome for thick acrylic sections, ultramicrotomes, a Leica BOND RXm autostainer for immunohistochemistry, in situ hybridization, and RNAscope technologies, and a full special stains workstation with hood is located in MIC. (4) MIC staff not only train investigators in the use of the imaging and analysis equipment, they also perform experiments, develop new protocols and procedures, and analyze investigator images using a variety of analysis software packages (“All-Inclusive Services”).

The MIC houses 10 microscope/preparation rooms, rooms with computer workstations, printers, scanners, filing cabinets and desk space for personnel. Each microscope room is individually climate controlled and contains storage shelves and cabinets. Variable lighting controls are provided with overhead LED bulbs connected to a dimmer switch to provide complete darkness to full room luminance. Air tables for the light, confocal, and atomic force microscopes and accompanying air supply inlet line are conveniently located and can be rearranged, if necessary, as can countertops. Ample shelf space and file cabinets are installed for storage of manuals and accessories. The rooms maintain their own temperature thermostat control for adjustments within +/- 3.0^{o} F. The rooms are biohazard safety level II certified by the Department of Risk Management.

Personnel: Douglas J. Taatjes, Ph.D., Director: experienced in all forms of microscopy-based imaging and image analysis offered in the facility. Nicole Bouffard, B.S., Lab Manager: experienced in light microscopy, immunohistochemistry, confocal microscopy, super-resolution microscopy, atomic force microscopy, laser microdissection, scanning electromicroscopy, spatialomics, Leica BOND RXm autostainer, and image analysis. Brad Vietje, B.S.: experienced in light and electron microscopy, immunohistochemistry, confocal microscopy, and image analysis. Kyra Lee B.S., M.S.: experienced in confocal microscopy, multiplex immunofluorescence, Spatialomics, Leica BOND RXm autostainer, and image analysis.

Equipment
Major imaging systems and equipment include:
Electron Microscopy

- JEOL 1400 transmission electron microscope (TEM)
- JEOL 6060 scanning electron microscope (SEM) with attached Oxford INCA EDS system

Atomic Force Microscopy

- Asylum Instruments MFP-3D-BIO atomic force microscope
- Asylum Instruments Cypher ES atomic force microscope

Super-Resolution Microscopy

- Nikon N-STORM super-resolution microscopy system

Confocal Microscopy

- Nikon A1R HD confocal scanning laser microscope with spectral detector and high-throughput imaging upgrades

Light Microscopy

- Olympus BX50 Upright widefield fluorescence imaging system
- Olympus IX70 Inverted microscope
- Leica-Aperio VERSA-8 whole slide imager
- Applied BioPhysics ECIS

Other Imaging

- Nanostring GeoMX – Spatial omics
- Akoya Biosciences Fusion Phenocyler Multiplex Immunostaining System
- Arcturus XT-TI laser capture microdissector

Image Analysis

- Dell Optiplex 7040 workstation
- Z4 Advanced Imaging workstation
- Indica Labs HALO
- NIS Elements
- Improvision Volocity
- MBF Stereo Investigator
- Universal Imaging MetaMorph

Histology Core Lab

- Reichert Ultracut microtomes (ultramicrotomes)
- Reichert and Leica paraffin microtomes (paraffin microtimes)
- Cryostat Thermoshandon Cryotome E
- Reichert RM 2165 microtome for thick sections
- Leica BOND RXm autostainer
- RNAScope for automated in situ hybridization
- ACD RNAScope hybridization oven
- Bench-top histochemistry station

SOFTWARE:

- Multiple dedicated computer workstations for image analysis and processing, including the image analysis software packages:
    - NIS Elements
    - MetaMorph
    - Volocity
    - HALO
    - Stereo Investigator

CBSR Harry Hood Bassett Flow Cytometry and Small Particles Detection (FCSPD) Facility

Director: Roxana del Rio-Guerra, http://www.med.uvm.edu/flowcytometry/home
Core Marketplace Link (for Facility RRID, LIMS, equipment, and citations): RRID SCR_022147; https://coremarketplace.org/?FacilityID=16
Email: rdelrio@uvm.edu
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Facilities and Other Resources

The Harry Hood Bassett Flow Cytometry and Small Particles Detection (FCSPD) facility is a shared resource laboratory at the UVM-LCOM. We have more than 20 years of experience using flow cytometry technology for both basic and applied research as well as characterization and quantification of small particles (nm). The FCSPD facility consists of 4 flow cytometers (including a cell sorter) and a small particle detector analyzer. We provide strategic design, troubleshooting, validating, implementing, and analyzing multicolor flow cytometry experiments for a wide variety of applications, including water contamination, food science, animal science, materials, as well as preclinical and clinical research. Using our instruments, we can simultaneously measure 30-35 proteins, RNA and/or DNA per cell basis. Some of the applications are immune-phenotyping, cell cycle analysis, apoptosis, DNA content, stem cell analysis, cancer research, microbiology (bacteria, viruses, and other microorganisms in environmental samples, such as water and soil), drug discovery, and aquatic analysis, among others. We assist with manuscript and grant preparation, as well as provide training and educational services to the broad scientific community of Vermont. All our services aim to achieve a high standard of rigor enabling reproducible flow cytometry experiments. We have excellent social, cultural, and communications skills, along with a strong customer-oriented mindset to understand the flow cytometry needs of diverse investigators, and innovative approaches to foster collaborations to develop methods to address future needs of our users.

By providing cutting edge flow cytometry solutions, we are committed to doing second-to-one research at UVM-LCOM to innovate and accelerate discoveries that will improve the health of Vermonters and their environment. To achieve this, we work in partnership with UVM scientists and other clients. Their achievements are our achievements, we succeed together.

The core values that we live by each day:

We commit to do second to none research at UVM-LCOM
We innovate and challenge ourselves
We succeed together
We respect and care for each other

Vision

Our vision is to bring the most advanced and innovative high-parameter flow cytometry solutions to address unmet environmental and biological needs and accelerate discovery at the University of Vermont. We aim to advance medical knowledge through research for the benefit of our community and our environment.

Mission

Our mission is to provide our customers with state-of-the-art fluorescence-activated cell sorting (FACS) and high-parametric analytical flow cytometry services. We work in partnership with scientists to provide cutting edge flow cytometry solutions to address environmental, water, food, animal, materials, preclinical and clinical researcher needs.

We offer the most advanced of this technology to all UVM investigators, nearby colleges peers (including the Vermont IDeA/EPSCoR network), and biotech companies in the area.

Personnel: Roxana del Rio-Guerra, Ph.D.; SCYM (ASCP^{BOC}), Director.

Equipment:

- Beckman CytoFlex is a bench top flow cytometer equipped with 2 lasers: 488 nm (blue) and 638 nm (red) laser. This analyzer detects 6 parameters (4 fluorescence detectors plus forward and side scatter) at one time. Equipped with a 96-well plate reader.
- MACSQuant VYB analyzer is equipped with a 561 nm yellow laser plus a 405 nm and 488 nm lasers; it can detect 10 optical parameters.
- Cytek Aurora spectral flow cytometer equipped with four lasers: UV/355 nm, Violet/405 nm, Blue/488 nm, and Red/640 nm, and 54 fluorescence channels; forward scatter (FSC) off 488 nm and side scatter (SSC) off 405 and 488 nm laser; it has a multiplate reader.
- BD FASC Aria III is a bench top highspeed cell sorter equipped with four lasers: 405 nm, 488 nm, 561 nm, and 633 nm. This instrument provides 14 fluorescence detectors plus forward and side scatter and performs up to 4-way sorts at a flow rate of upwards of 20,000 cells/ second. The instrument can also sort directly into microtiter plates of varying sizes.
- Particle Metrix ZetaView Twin NTA. This is a nanoparticle tracking analyzer for the analysis of size, concentration, fluorescence, electrophoretic mobility and sub-populations of individual nanoparticles such as extracellular vesicles (EVs), exosomes, viruses, or virus-like particles. Equipped with 2 lasers: 405 nm and 488 nm, and 2 long pass emission filters.

CBSR Vermont Biomedical Research Network (VBRN) Proteomics Facility

Director: Dr. Ying Wai Lam;
Facility website: https://vbrn.org/proteomics/;
Summary of the facility's impact on the development of the network can be found at
https://vbrn.org/proteomics-impact/
https://vbrn.org/proteomics-publications/ (publications)
Core Marketplace Link (for Facility RRID, LIMS, equipment, and citations): RRID SCR_018667; https://coremarketplace.org/?FacilityID=44
Email: ying-wai.lam@uvm.edu
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Facilities and Other Resources

The VBRN Proteomics Facility (https://vbrn.org/proteomics/), supported by INBRE funding (P20GM103449), is located in the Firestone Medical Research Building 143. There are bench spaces for accommodating up to ten persons working simultaneously for sample preparation. The Proteomics Facility enables investigators to use an array of state-of-the-art mass spectrometry-based techniques for proteomics experiments, ranging from routine protein identification, post-translational modification characterization and finding protein interacting partners, to large-scale quantitative proteomics analyses using stable isotopes. Since its inception in 2006, the facility has analyzed over 20,000 samples and facilitated data acquisition to support over 200 publications (https://vbrn.org/proteomics-publications/) and 50+ grants. The facility has proven expertise in training investigators in experimental design and proteomics methods, while assisting with data interpretation, manuscript preparation, and grant submission. Working closely with the *VBRN's Data Science Core*, the Proteomics Facility staff provide "tailored" bioinformatics solutions to investigators. Our user base includes investigators from UVM and from institutions in 15 states.

Central to our mission is our ongoing practice of developing collaborations and methods to address future user needs (e.g., crosslinking mass spectrometry and deuterium exchange mass spectrometry). We have helped incorporate proteomics into undergraduate curricula at a number of Vermont Colleges over the years and have established a robust internship program to prepare undergraduates for STEM career.

A summary of the facility's impact on the development of the network can be found at https://vbrn.org/proteomics-impact/.

Personnel
Ying-Wai Lam, Ph.D., Director, Bin Deng, Ph.D. Manager, Sydney Cohn-Guthrie, B.S. technician are full- time staff with over three decades of combined proteomics experience.

Equipment
The Proteomics Facility is equipped with standard laboratory equipment (freezers, centrifuges, incubators, microscopes, and analytical balances, etc.), a Shimadzu analytical HPLC system with UV detection for offline high-pH reversed-phase fractionation, electrophoresis systems, a Sutter P-2000 laser puller, a Savant SpeedVac concentrator, a Labconco lyophilizer, five mass spectrometers from Thermo Fisher Scientific, as well as a hydrogen deuterium exchange (HDX) workflow station:

- Orbitrap Eclipse Tribrid mass spectrometer (MS) coupled to an EASY-nLC 1200 UPLC system
- Orbitrap Exploris 240 MS coupled to an EASY-nLC 1200 UPLC system
- LTQ Orbitrap Discovery MS coupled to a Surveyor HPLC system
- LTQ XL Linear Ion Trap MS equipped with electron transfer dissociation (ETD) coupled to a Surveyor HPLC system
- LTQ Linear Ion Trap MS coupled to a Prominence (Shimadzu) HPLC system
- HDX workflow station, HDx-3 PAL (Leap Technologies), which can be coupled to the LTQ or LTQ-Orbitrap Discovery MS with a Workplace Modular systems cart for conducting HDX MS experiments

The Data Processing unit maintains five computers (4 Dell Optiplex 7060 Workstations, i7 Processor, 32GB RAM, 2 displays for each, and 1 Dell Precision Tower 5810 with 1 display), and offers a suite of software including three copies of Proteome Discoverer 3.1 embedded with SEQUEST, MASCOT and Byonic, SCAFFOLD Q+S, SCAFFOLD DIA, PEAKS, Skyline, SimGlycan, and HD Examiner to evaluate the datasets generated from various types of proteomics experiments.

CBSR Vermont Integrative Genomics Resource (VIGR) Facility
Director: Julie Dragon
Core Marketplace Link (for Facility RRID, LIMS, equipment, and citations): RRID SCR_021775; https://coremarketplace.org/?FacilityID=245
Email: Julie.Dragon@uvm.edu
Date Last Updated: 1/10/25

Overview

The Vermont Integrative Genomics Resource is a multi-faceted facility that offers a full range of genomics and bioinformatics services. The facilities primary goals include consultation for

experimental design, data generation, troubleshooting assays, full service to bioinformatics analyses, and support for data management and publication. VIGR employs a director of technologies, and three laboratory technicians, and three bioinformatics that have over 30 years of combined experience in advanced genomics, molecular and microbiology, and bioinformatics analysis, with over 50 publications and numerous national and internationals presentations.

Personnel

	Julie A. Dragon, Ph.D., Director	
Vermont Integrative Genomics Resources		
Advanced Genome Technologies Core (AGTC)		**Bioinformatics Shared Resource (BSR)**
Scott Tighe, B.S. Director of Technologies		Princess Rodriguez, Ph.D.
Kirsten Tracy, Ph.D.		Ramiro Barrantes, Ph.D.
Stacia Richards, B.S.		Emily Guswa, Ph.D.*
		Heather Driscoll, M.S.*

**Affiliated through the Vermont Biomedical Research Network*

Facilities and equipment

The AGTC facility is located in the UVM College of Medicine complex in the new Firestone Building, and the BSR is located in the Given Courtyard 4th floor South.

Massively Parallel Sequencing (MPS): MPS includes single-cell genomic analysis, chromosome conformation capture techniques, RNA-Seq, Exome-Seq, ChIP-Seq, Methyl-Seq, whole genome sequencing, metagenomics and microbiome, and small RNA sequencing to name a few.
Major equipment includes:

- Singular G4 sequencer plus an Illumina MiSeq sequencer for short reads
- Multiple Oxford Nanopore systems, including MinION MK1B, a GridION X5 MK2 and two P2 Solo sequencers with appropriate compute support for adaptive sequencing (2 x Origin dual DDR5 5600MT/s 48GB 40-40-40-77 computers, for long read and whole amplicon sequencing
- 10x Single Cell Genomics System

General Genomic Services (GGS): GGS provides a vast array of analysis services including DNA/RNA extraction, PCR and PCR troubleshooting, primer design, Sanger sequencing, (SNP/MSI/AFLP), human cell line authentication, quantitative PCR, nucleic acid and protein quantification. Major equipment includes:

- ABI SeqStudio Genetic Analyzer (4 capillary)
- ABI Quant Studio 6 RTqPCR system and Prism 7500 Fast RTqPCR
- BioRad QX200 Digital Droplet qPCR
- BioRad QRS+ ChemiDoc imagers
- Agilent 2100 Bioanalyzer
- NanoDrop (ND-1000) Spectrophotometer
- Quantas Spectrofluorometers, and 3 Qubit spectrofluorometer

- Logo Quantum Microbial imager
- Zeiss digital AxioScope with DIC and full spectrum fluorescence
- Benchmark Beadbug6 Homogenizer
- 4 PCR-free Clean Air HEPA cabinets; 1 Biosafety II hood
- Savant SpeedVac
- 4 Biometra TAdvanced 60 Thermal Cyclers with Exchangeable Blocks
- 2 BioRad PTC200 Gradient Thermocyclers
- 1 Techne Gradient Prime thermocycler with 60 and 96 well blocks
- Omni International Homogenizer
- Isopure DNA Extraction robot
- InnovaPrep Concentrator
- Covaris Acostical hydroshear s220

Bioinformatics Shared Resource (BSR): The BSR provides cutting edge bioinformatics analysis that includes data processing, visualization, archival storage, and deposition in public repositories. Services also include data quality assessment, calculation of probe set statistics, sequence reads, alignment to a reference genome, variant calls, linear modeling, and multivariate analysis. Resource staff run nextflow-core standardized, containerized pipelines as well as custom pipelines. They provide custom reports, text describing methodology, figures for manuscripts, and assist in the deposition of data into public databases. In addition to providing established resources, staff assist in implementing new bioinformatics tools to provide innovative solutions for bioinformatics challenges, for instance spatial omics and multi omics. Resource personnel also support use of tools associated with the Vermont Advanced Computing Cluster (VACC), a multi-core cluster that will run computationally intensive applications.

The BSR has infrastructure to support analyses of multiple and integrated data types and leverages the VACC for high performance computing and data storage, which are continuously updated. Major equipment includes:

- **>10 dedicated multi-core processing nodes** (2-20-core (256 GB RAM) and 8-12-core (32GB RAM), and **30 TB storage** in the Vermont Advanced Computing Core cluster (VACC).
- An **independent VIGR queue** on the high-performance compute cluster so our jobs start immediately and are not interrupted by smaller, lower memory requiring jobs.
- **50 TB of secure long-term archival storage** provided by ETS. The entire 50 TB is backed up on a three-month rotating schedule to provide archival backup capability.
- **20 TB local external storage**, configured as a RAID array providing 3.25TB mirrored working space for project files, and a 1.5 TB hourly desktop backup.

The VACC provides access to three HPCs

- "Bluemoon," a **multi-thousand-core**, high-performance computing cluster, supporting large-scale computation, low-latency networking for MPI workloads, large memory systems, and high-performance parallel file systems.
- "Big Green," a **massively parallel cluster composed of over80 GPUs** capable of over 8 petaflops of mixed precision calculations based on the NVIDIA Tesla V100 architecture. Its hybrid design and parallelism can expedite and support high-throughput artificial intelligence and machine learning workflows.

- “Black Diamond,” a HPC built using **AMD's 2nd Gen AMD EPYC processor**, which pushes the boundaries for x86 performance, efficiency, security features, and overall system throughput.