ROSWELL PARK
COMPREHENSIVE CANCER CENTER

Shared RESOURCES GUIDEBOOK 2025

ROSWELL PARK MISSION

To eliminate cancer's grip on humanity by unlocking its secrets through personalized approaches and unleashing the healing power of hope.

A MESSAGE FROM OUR DEPUTY DIRECTOR

Roswell Park Comprehensive Cancer Center currently supports 15+ scientific shared resources that provide our investigators with access to a broad range of sophisticated scientific instrumentation, cutting edge technical and analytical applications, comprehensive sample biorepositories and more. Our shared resources perform a highly valuable role in facilitating basic, clinical and translational scientific research at Roswell Park and are critical elements in accelerating the progress of our researchers and allowing them to successfully compete for peer-reviewed grant funding in an increasingly competitive scientific funding environment.

The primary objectives of the Roswell Park shared resources are as follows:

- Provide institutional and regional access to high-end shared instrumentation.
- Provide technical services, which vary in degree of sophistication, but which usually cannot be readily performed in the investigators laboratory in a timely and cost-effective manner.
- Assist staff in understanding the applications and limitations of various techniques to their research through consultation and discussion.
- Provide expertise toward the development of pilot feasibility studies, and referral to more capable or authoritative sources of information.
- Assess the technical needs of the staff in the context of the services offered by the resource, and develop the resource to assist investigators in accomplishing their research goals.
- Through surveys, research and staff requests, our resources work to anticipate future needs and help establish institutional directions for expanded technical and analytical services.

The Shared Resources Guidebook at Roswell Park is intended to orient institute faculty to the currently available scientific shared resources at Roswell Park. The services outlined are financially supported by a variety of mechanisms including an NCI Cancer Center Support Grant, chargebacks and importantly, significant institutional support. This guide is updated regularly as new technologies and applications are introduced within the existing resources, and also as new resources are established to meet and address the changing needs of scientific and clinical research at the Institute. Our ultimate goal in providing access and necessary support to our institutional shared resources is to facilitate the natural progression of increased scientific interactions and accomplishments, enhanced peer-reviewed funding, and professional collaborations and partnerships among our scientific and clinical investigators.

Renier Brentjens, MD, PhD

Deputy Director & Chair, Department of Medicine
The Katherine Anne Gioia Endowed Chair in Cancer Medicine

Shared RESOURCES BUILDING/LOCATIONS 2025

#	Building Name	Shared RESOURCES	Floor
9	Basic Science Building (BSB)	BioRepository & Laboratory Services Nicotine & Tobacco Product Assessment	6 3
	Grace Cancer Drug Center (GCDC)	Investigational Drug Services	5
5	Research Studies Center (RSC)	Shared Resources Management Office Bioinformatics Biomedical Research Informatics Biostatistics & Statistical Genomics	2 4 4 4
7	Medical Research Complex (MRC)	Advanced Tissue Imaging Comparative Oncology Gene Targeting & Transgenic	3 2 3
3	Center for Genetics & Pharmacology (CGP)	Bioanalytics, Metabolomics & Pharamacokinetics Gene Modulation Genomics Onsite Research Supply Center	1 2 1 1
8	Cancer Cell Center (CCC)	cGMP Engineering & Cell Manufacturing Facility Flow & Immune Analysis Translational Imaging	2 3 1
6	Carlton House (CH)	Health Communications	2

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OVERVIEW

The Shared Resource Management Office (SRMO) provides comprehensive oversight for all Roswell Park Comprehensive Cancer Center shared resources that provide our investigators with access to a broad range of sophisticated scientific instrumentation, cutting-edge technical and analytical applications, comprehensive sample biorepositories and more. The SRMO effectively manages administration, equipment, marketing and human resource needs for all our shared resources. We also engage with shared resource leaders and invest in service delivery and enhancement, and purchase new equipment.

Roswell Park places a strong focus on advanced technologies to maintain our status as leaders in cancer research and patient care. This can only be accomplished with the proper tools, staffing, and management. In support of our strategic plan, the SRMO will continue to support our existing shared resources and facilitate the development of new shared resources and services.

The Value of Our Shared RESOURCES (SRs)

SRs are Force Multipliers

Enable strategic planning at an institutional level

Enhance access to high-end equipment for investigators

Drive research efficiency through diversifying & centralizing the scope and scale of technology investments

Forward Looking

SRs Increase Efficiencies: A Concrete Example

One piece of high-end instrumentation in a SR vs. a single lab:

- Serves 10x the users per square foot of space
- Serves 10x the number of users
- Supports 150x the number of research dollars making it more cost effective

Efficient

SRs are Collaboration Hubs

SRs bring together researchers from diverse fields to tackle complex scientific challenges.

- Foster innovation
- Accelerate technology development
- Provide expertise
- Collaboration between SRs
- Projects flow through multiple SRs at a lower cost

Propel Science

SRs are Leaders in Domain Expertise

Improve research outcomes, reproducibility and reliability

Provide users educational resources, consultation, and training to increase their ability to more effectively utilize technologies in their research programs.

Ensure Rigor

Shared RESOURCES TABLE OF CONTENTS 2025

ADVANCED TISSUE IMAGING (ATISR)
Shared Resource

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OVERVIEW

The Advanced Tissue Imaging Shared Resource (ATISR) uses complex biomarker panels to elucidate the tumor microenvironment (TME) in various forms of cancer by employing TSA Opal multiplex immunofluorescent staining (mIF). This process allows us to produce data with both qualitative and quantitative veracity; we deliver phenotype counts without losing their morphological context in the TME. This is possible due to the unique mIF method paired with the power of AKOYA's inForm quantitative phenotyping software. We have recently acquired the Leica DMi8 inverted microscope to enable affordable brightfield, immunofluorescent, and confocal microscopy to complement our multispectral capabilities. Additionally, our new acquisition of the NanoString GeoMX Digital Spatial Profiler expands our research opportunities to the novel field of spatial genomics, offering whole transcriptome and RNA sequencing while preserving the morphological integrity of the sample, enabling multiplexed analyses.

We provide services to Investigators at Roswell Park Comprehensive Cancer Center, as well as other cancer centers, academic institutions, and industry. Investigators are encouraged to consult with our staff as early as possible during the planning phases of their project or grant development. Proper slide preparation is vital to successful outcomes. By starting discussions early, ATISR can advise on proper sample preparation and handling prior to any requests for cutting slides.

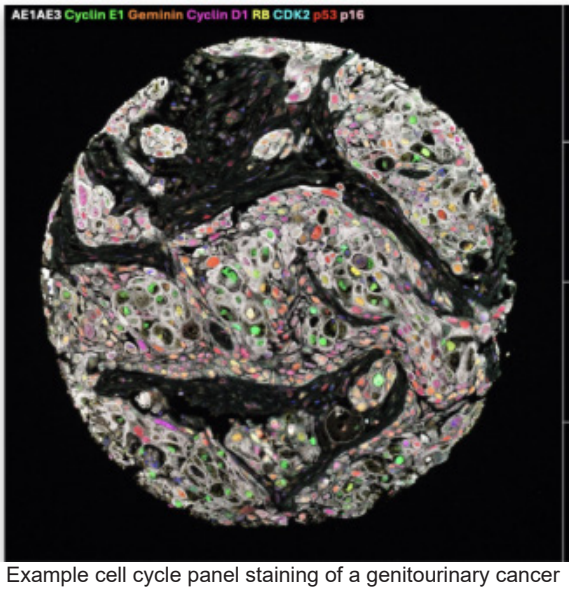
USING THE RESOURCE

For all new requests, please complete the Initial Inquiry Form and submit to ATISR@RoswellPark.org. ATISR will contact you to schedule a consultation to discuss your project.

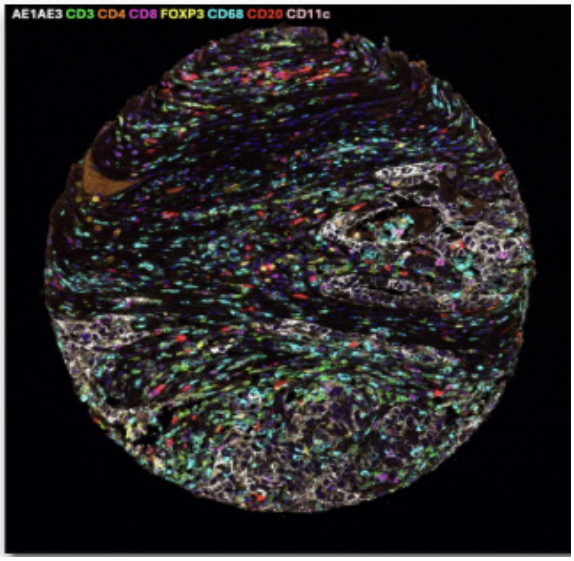
SERVICES

Multispectral Immunofluoroescence (mIF)

We offer a wide array of optimized cell cycle and immune panels. Custom panels are also available upon request. ATISR requires any biomarkers to have a commercially available IHC validated antibody for panel inclusion. Panels can consist of six (6) or eight (8) biomarkers plus DAPI.

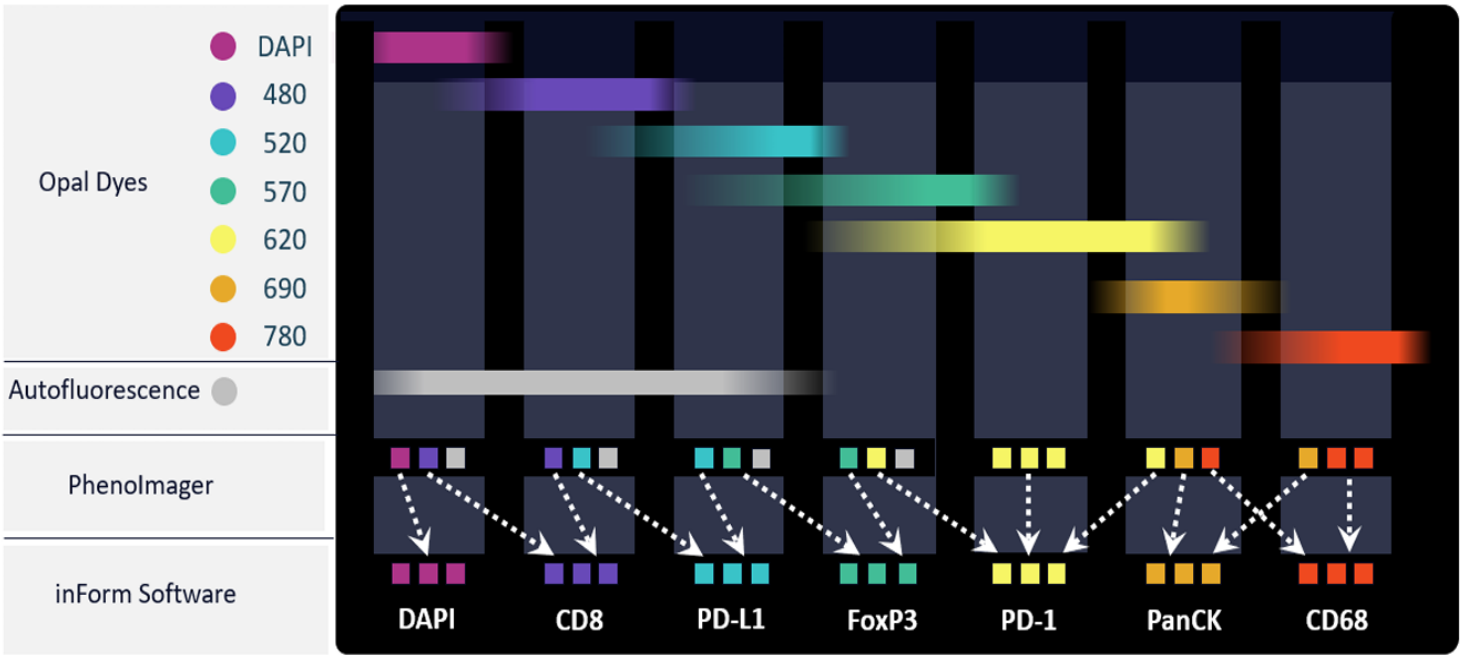


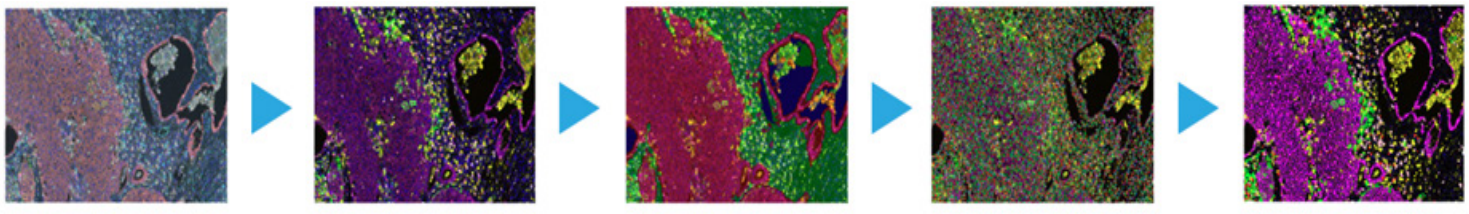
Example cell cycle panel staining of a genitourinary cancer tissue microarray.



Example immune panel staining of a gynecological cancer tissue microarray.

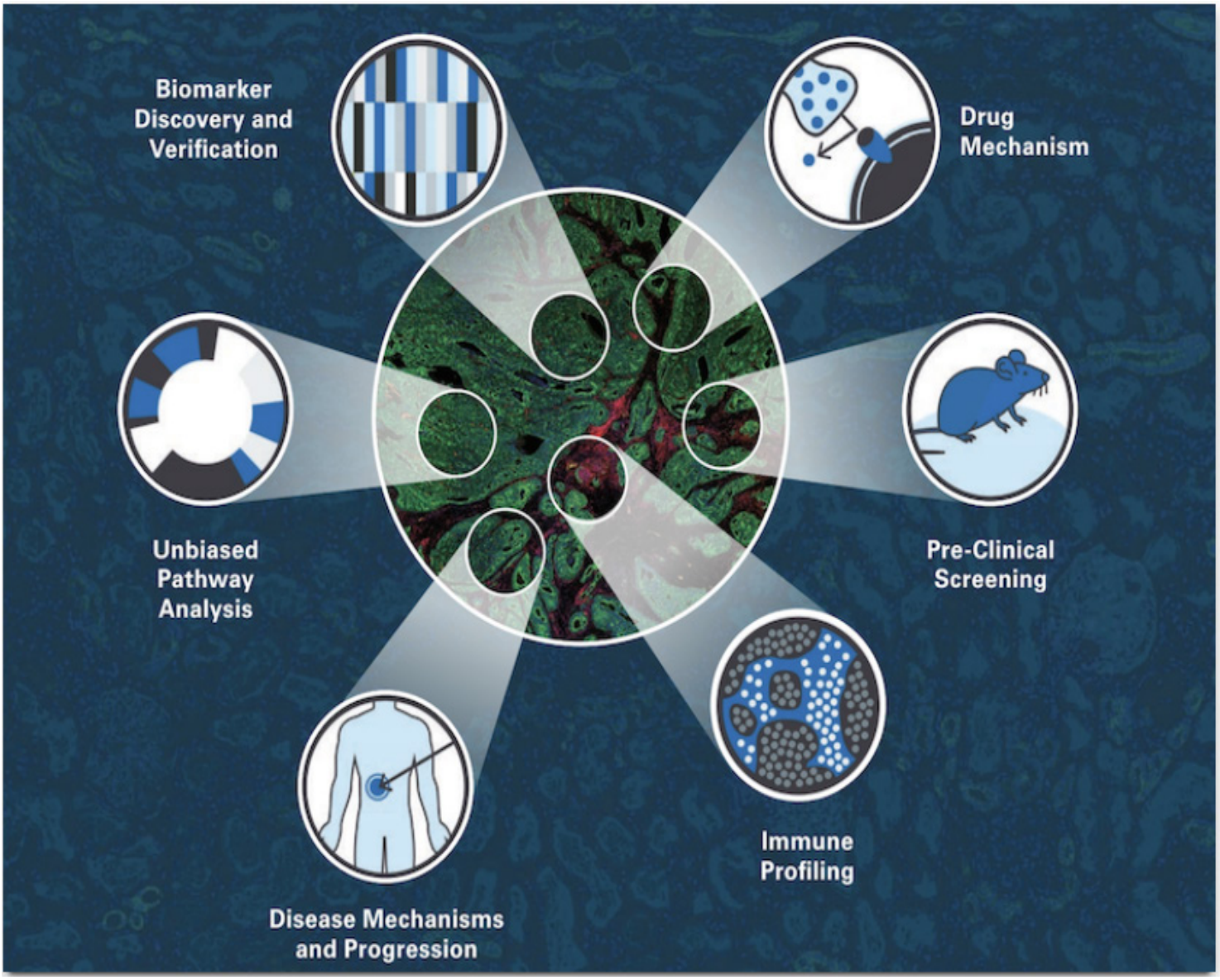
WORKFLOW





Spatial Transcriptomics

We deliver whole transcriptome analysis of your FFPE or fresh frozen tissues while preserving the morphological integrity of your sample to enable multiplexed analysis with our multispectral immunofluorescence (mIF) pipeline if desired.



WORKFLOW

1

Sample Prep

Provide your FFPE or fresh frozen sample.

2

Profile

Profile spatial RNA with GeoMX DSP.

3

Count

Use nCounter Analysis System to count RNA barcodes.

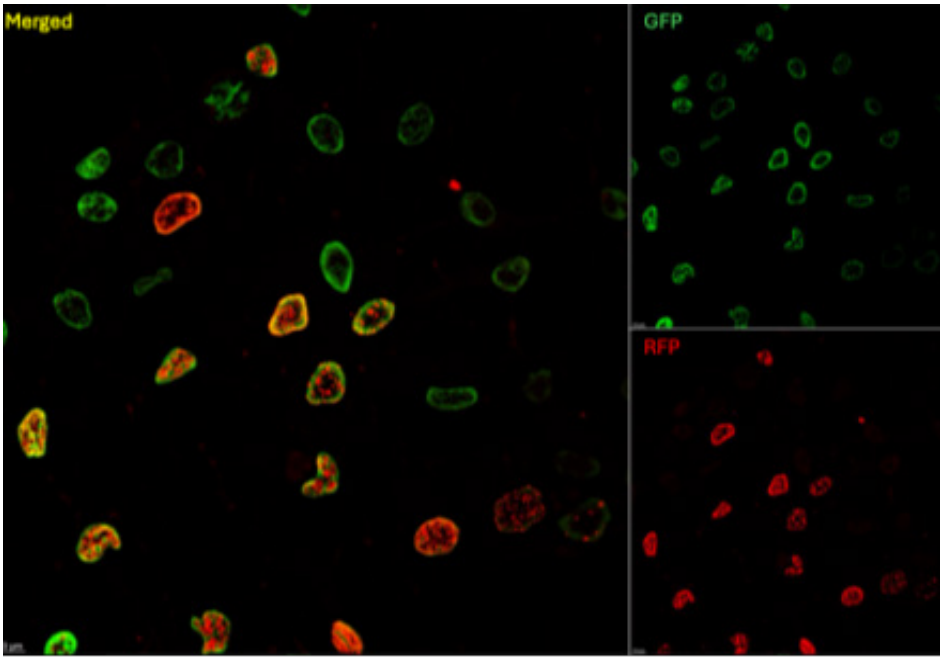
4

Analyze & interpret

Our data processing pipelines digest your data into meaningful biological insights.

High-Resolution Microscopy

Our recently acquired Leica DMi8 inverted microscope with the THUNDER technology suite that enables computational clearing provides you with the sharpest images possible. Capable of both high-resolution sub-cellular imaging and fast low-magnification slide scanning. Additionally, the Leica DMi8 can perform confocal 3D imaging to get in-depth spatial information on your samples.



Sub-nuclear image captured with 60x lens on Leica DMi8 inverted microscope of PCNA foci (red) with nuclear GFP staining in T47D breast cancer cells.

Live-cell Imaging

Use our high-throughput IncuCyte live-cell imaging system to automate cell proliferation tracking around the clock as you assess the impact of treatment on your cell and organoid cultures.

INSTRUMENTATION & SOFTWARE

Leica BOND RX^{m} Fully Automated Stainer

This fully automated slide stainer allows ATISR to run conventional DAB IHC, as well as complex multiplex fluorescent staining in a timely and highly reproducible manner.

BOND RXm IHC Academic Research Stainer (leicabiosystems.com)

AKOYA PhenoImager HT

This automated slide scanner delivers high throughput images from both brightfield and multispectral fluorescent staining. It allows for unmixed annotated regions of interest for panels of eight biomarkers and full slide unmixed images for panels of six biomarkers.

The accompanying inForm and phenoptr software enables rapid turnaround of spatial analysis and biomarker quantification of your samples.

PhenoImager HT | Akoya Biosciences

NanoString GeoMX Digital Spatial Profiler (DSP)

This spatial profiler can run both mouse and human whole transcriptome assays (WTA) or the human cancer transcriptome assay (CTA) on your samples. The tissue is initially stained to identify tumor and stroma and then ROIs are selected by the investigator, with guidance from our pathologist. UV cleavable tags from the ROIs are finally retrieved, sequenced, mapped, and reported as read counts.

GeoMx DSP Spatial Genomics | NanoString

Leica THUNDER DMi8 Inverted Microscope

The newly acquired high-resolution Leica DMi8 inverted microscope with the advanced Leica THUNDER technology suite, enabling 3D imaging and Computational Clearing that can produce both high magnification sub-cellular immunofluorescent images of the highest quality or crisp low magnification images of entire tumor microarrays.

DMi8 Inverted Microscope I Leica Microsystems

Sartorius Incucyte S3

The fully automated IncuCyte S3 live-cell imaging system for multi-condition cellular proliferation analysis with red/green fluorescence channels and phase contrast imaging at 4, 10, and 20X around the clock. Capable of assessing six microplates, dishes, flasks, or slides simultaneously.

Sartorius Incucyte S3

NOTABLE PROJECTS

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BIOANALYTICS, METABOLOMICS & PHARMACOKINETICS (BMPK)

Shared Resource

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OVERVIEW

The mission of the Bioanalytics, Metabolomics and Pharmacokinetics Shared Resource (BMPK) is to support basic research, pre-clinical and clinical sample metabolic assessment and pre-clinical/clinical drug development by providing broad-based bioanalytical analyses, PK/PD modeling, metabolomics and consultation services to Roswell Park investigators and other academic institutions, cancer centers, and industry. The BMPK works closely with investigators at each stage of their project to provide feedback on study design, timing of sample collections, sample handling, use of enzymatic inhibitors and other parameters to help optimize observations, data correlations and therapeutic outcomes. The BMPK offers a wide array of analytical methods along with capabilities to develop and validate new assay methods to help achieve the required objectives from studies of pharmacological mechanisms, cancer therapeutics, and preventive agents, alongside advanced metabolomics measurements and tracing. Using state-of-the-art techniques like LC-MS/MS and high-resolution LC-MS the BMPK provides highly sensitive measurements for chemotherapeutic agents and their metabolites, biomarkers, other endogenous compounds, and targeted metabolomic pathways. Investigators are encouraged to consult with the BMPK as early as possible during the planning phases of their project or grant development to obtain a comprehensive understanding of the time commitment and cost associated with each phase of their project.

USING THE RESOURCE

Investigators who are interested in using the BMPK facility and its services should contact Joshua Prey and Dr. Spencer Rosario to discuss shared resource capabilities, scheduling and pricing.

SERVICES

The BMPK provides comprehensive services to investigators and sponsors ranging from study design consultation to analytical method development, assay validation/qualification, sample preparation, sample storage, analysis of study samples, and PK/PD data analysis. The services provided by BMPK are guided by more than 45 standard operating procedures, which are the framework for our resource policies, staff orientation and training, quality audits, metrology program, and bioanalytical guidelines. Routine preventative maintenance and calibration programs are in place to ensure the proper performance and functioning of laboratory equipment.

Bioanalytical / Metabolomic Services

In addition to our existing methodologies, BMPK will develop new assay methods as needed by investigators to generate highly sensitive analytical measurements to meet their intended objectives in their in vitro, preclinical or clinical studies. To contain costs for investigators, the development and performance testing of analytical methods can range from simple, basic testing for a discovery method to much more thorough testing following the FDA Guidance, which is done for validated methods and required for all clinical trials. These methods have been developed for a wide range of matrices including, but not limited to plasma, serum, whole blood, a large variety of tissue samples, tumors, xenografts, bronchial alveolar lavage, cell pellets and media.

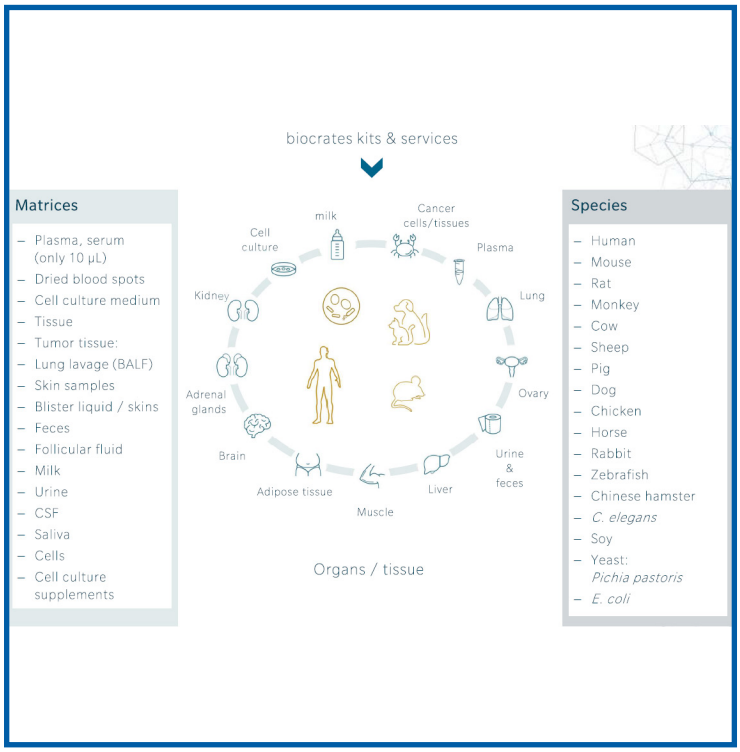
Examples of assays the BMPK provides include:

- **Hormones:** Testosterone, dihydrotestosterone, androstenedione, dehydroepiandrosterone (DHEA), and androsterone (LC-MS/MS), and estrone and estradiol (LC-MS/MS)
- **Antimetabolites:** Gemcitabine and dFdU (LC-MS/MS), capecitabine (LC-MS/MS), and 5-fluorouracil (LC-MS/MS)
- **Taxanes:** Docetaxel (LC-MS/MS) and paclitaxel (LC-MS/MS)
- **Topoisomerase Agents:** Irinotecan (CPT-11), SN-38, SN-38G (UPLC and LC-MS/MS)
- **Anthracyclines:** Doxorubicin (UPLC) and daunorubicin (UPLC)
- **Targeted Agents:** Tivozanib (LC-MS/MS), enzalutamide and N-desmethylenzalutamide (LC-MS/MS), sorafenib and sorafenib-N-oxide (LC-MS/MS), carfilzomib (LC-MS/MS), and sunitinib (LC-MS/MS)
- **Targeted Major Energetic Pathway Assays:** TCA/Glycolytic Intermediates, Nucleotides (LC-MS/MS)
- **Platinum Based Compounds:** Oxaliplatin (atomic absorption), cisplatin (atomic absorption), and carboplatin (atomic absorption)
- **Selenium Based Compounds:** Selenomethionine and methylselenocysteine (atomic absorption)
- **Others:** Tryptophan/kynurenine (LC-MS/MS), sex hormone binding globulin (SHBG; CMIA), VEGFR2 (ELISA), lignans (enterodiol and enterolactone; LC-MS/MS) and eicosanoids (LC-MS/MS)

For a complete listing of our assays and additional details, please visit our website.

Biocrates

Roswell Park's BMPK currently serves as one of two certified Biocrates labs in North America, with the capability of assessing large numbers of known metabolites in these assays. We are currently running the Biocrates MxP Quant 500 kit, which covers 630 metabolites spanning 26 biochemical classes including all amino acids, extensive lipidomics panels, and key metabolites from many major pathways. In 2023, we are expanding to the Biocrates MxP Quant 500 XL kit, which will cover up to 1018 metabolites spanning 38 biochemical classes, including more extensive coverage of lipids. These assays utilize a combined flow injection analysis (FIA) and liquid chromatography (LC) approach with multiplexed mass spectrometry (MS/MS) to allow for high-throughput assessment of the key metabolites of many metabolic pathways, using limited sample volume. These assays have been utilized for metabolomics assessment of both pre-clinical (cell line, media, tissue, serum) and clinical samples (tissue, ascites, serum, plasma, urine, and feces), with high levels of reproducibility. Further, to facilitate investigator understanding of these results, we've developed and implemented advanced bioinformatics approaches for differential abundance analysis, metabolic modeling, and multi-omics data integration, which has aided in quick grant and publication quality results and figures.



SERVICES (cont'd)

Data Analysis and PK/PD Modeling

PK/PD modeling of bioanalytical results in conjunction with demographic and longitudinal data is used to characterize relationships between the time course of drug concentrations and pharmacological effects. The BMPK is available to assist investigators in the design of preclinical and clinical studies which incorporate clinical pharmacology and PK/PD objectives. Our support for preclinical studies includes providing recommendations on study design and PK sampling schedules, and non-compartmental analysis for rapid characterization of key PK parameters, such as clearance, area under the curve, and half-life. Population PK/PD modeling and simulations are performed to gain insight into the mechanism of action of drugs, or combinations of drugs, and to assess inter-individual and random variability within a population. This information is crucial for optimal design of various aspects of a clinical trial, including dosing strategy and the selection of patient populations. The software utilized is dependent on the information available and the type of modeling being requested. Dataset assembly and graphics are performed in a variety of ways to meet the needs of the investigator. Non-compartmental analyses are performed using Phoenix WinNonlin, whereas NONMEM is typically utilized for population PK/PD modeling and simulations. Dataset assembly and graphics are performed in a variety of ways to meet the needs of the investigator.

Proteomics Services

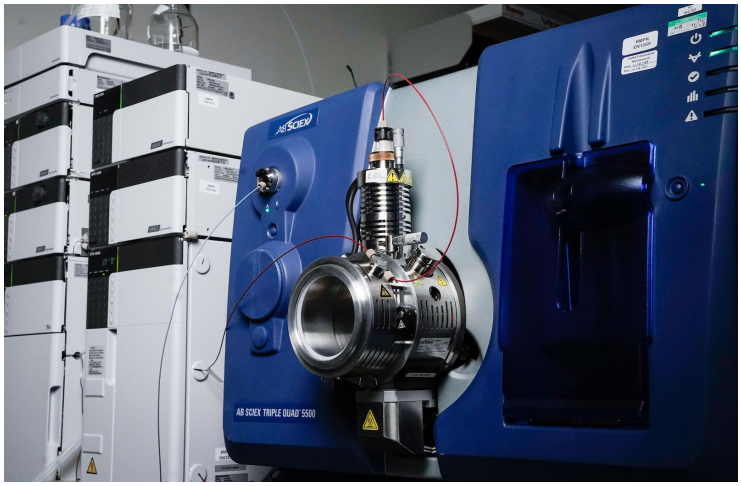
BMPK has recently acquired an Olink Q100, which allows us to quantify up to 92 proteins in up to 88 samples, from 5 uL of sample. These pre-prescribed panels provide coverage for 1000s of proteins including those associated with immunology, inflammation, oncology, cardiovascular health, neurology, organ damage, and other disease states. Chose from 15 different available panels, or let us help you design a custom panel to best support your proteomics needs. For a full list of available panels, please visit the company website.

INSTRUMENTATION

The BMPK is equipped with state of the art instrumentation and PK/PD modeling software.

Instrumentation:

- Applied Biosystems 5500 QTrap triple quadrupole (ESI/APCI-LC/MS/MS)
- Applied Biosystems 5500 triple quadrupole (ESI/APCI-LC/MS/MS)
- Thermo Scientific TSQ Vantage triple quadrupole (ESI/APCI-LC/MS/MS)
- Applied Biosystems API3000 triple quadrupole (ESI LC/MS/MS)
- Agilent 6545B LC/Q-TOF MS system
- Olink Signature Q100



SOFTWARE

Modeling Software:

- Phoenix WinNonlin: Noncompartmental and compartmental modeling
- ADAPT 5 and S ADAPT: Individual compartmental PK and PK/PD modeling
- NONMEM: Nonlinear mixed effect modeling software for population analysis to determine sources of variability in the PK and PD of a drug
- SAS 9.3: Used to manage and clean databases, and create graphics and tables

NOTABLE PROJECTS

Rosario SR, Long MD, Chilakapati S, Gomez EC, Battaglia S, Singh PK, Wang J, Wang K, Attwood K, Hess SM, McGray AJR, Odunsi K, Segal BH, Paragh G, Liu S, Wargo JA, Zsiros E. Integrative multi-omics analysis uncovers tumor-immune-gut axis influencing immunotherapy outcomes in ovarian cancer. Nat Comm. 2024 Dec 5;15(1):10609. PMCID: PMC11621351.

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Harding JJ, Kelley RK, Tan B, Capanu M, Do GK, Shia J, Chou JF, Ferrer CS, Boussayoud C, Muenkel K, Yarmohammadi H, El Dika I, Khalil DN, Ruiz C, Rodriguez-Lee M, Kuhn P, Wilton J, Iyer R, Abou-Alfa GK. Phase Ib Study of Enzalutamide with or Without Sorafenib in Patients with Advanced Hepatocellular Carcinoma. Oncologist. 2020 Dec;25(12):e1825-e1836. PMID: 32548867.

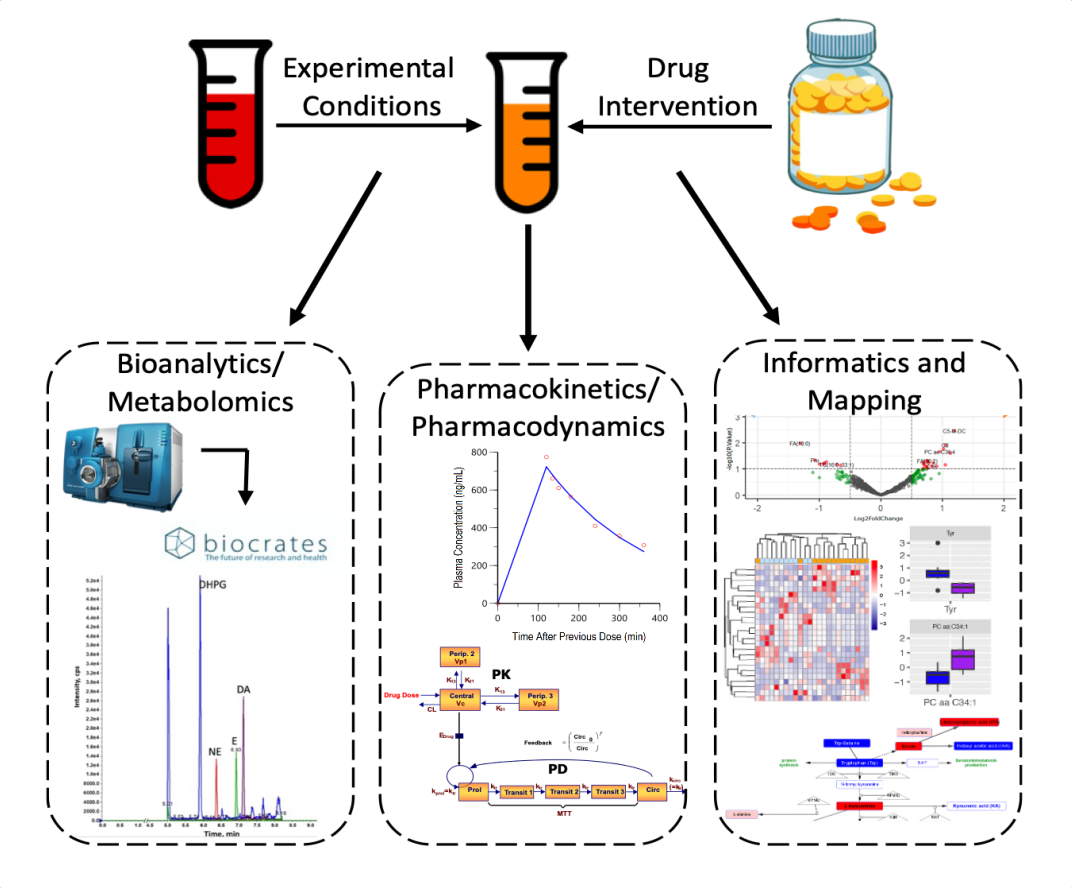
NOTABLE PROJECTS

Iyer RV, Konda B, Fountzilas C, Mukherjee S, Owen D, Attwood K, Wang C, Maguire O, Minderman H, Suffren SA, Hicks K, Wilton J, Bies R, Casucci D, Reidy-Lagunes D, Shah M. Multicenter phase 2 trial of nintedanib in advanced nonpancreatic neuroendocrine tumors. Cancer. 2020 Aug 15;126(16):3689-3697. PMID: 32525561.

Fountzilas C, Gupta M, Lee S, Krishnamurthi S, Estfan B, Wang K, Attwood K, Wilton J, Bies R, Bshara W, Iyer R. A multicentre phase 1b/2 study of tivozanib in patients with advanced inoperable hepatocellular carcinoma. Br J Cancer. 2020 Mar;122(7):963-970. PMCID: PMC7109127.

Affronti HC, Rowsam A, Pellerite AJ, Rosario S, Long M, Jacobi J, Bianchi-Smiraglia A, Boerlin CS, Gillard B, Karasik E, Foster B, Moser M, Wilton J, Attwood K, Nikiforov MA, Azabdaftari G, Pili R, Phillips JG, Casero RA Jr, Smiraglia D. Pharmacological polyamine catabolism upregulation with methionine salvage pathway inhibition as an effective prostate cancer therapy. Nat Commun. 2020 Jan 7;11(1):52. PMCID: PMC6946658.

WHAT WE DO



BIOINFORMATICS (BIOINF) Shared Resource

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OVERVIEW

The mission of the Bioinformatics Shared Resource (BIOINF) is to provide exceptional bioinformatics expertise for the design, analysis, and interpretation of genomics, proteomics, and other high-resolution, high-throughput studies to better understand cancer biology and translate cancer omics discoveries to cancer treatment. BIOINF's strategy is to lower the barriers to accessing analytic expertise, maintain high standards for data collection and management, design and perform rigorous analytical strategies, provide training in all aspects of design and analysis, and foster a collaborative and supportive research community.

Services include: directing the design of high-throughput experiments; data processing, data analysis and interpretation; data mining and integration; assisting the design and deployment of appropriate informatics infrastructure for data sharing and management; reviewing and preparing grants and manuscripts; software evaluating, new methods and databases; and providing education and training.

The BIOINF ensures that CCSG investigators have ready access to expert bioinformatics support and services to carry out basic, translational, clinical, and population science research. BIOINF staff maintain regular contact with CCSG investigators to ensure the consistency and efficiency of procedures that will ultimately generate high-quality data and reproducible analytic results. Bioinformatics expertise provided by BIOINF personnel ensures that the yield of useful information from the scientific studies conducted is maximized while costs are minimized.

USING THE RESOURCE

To use the core service, users should first contact the listed core staff members or submit a job request via the LIMS system at https://rpcilims.roswellpark.org. The users will then be contacted by core staff regarding the project details and feasibility. Hours of operation are weekdays 8 AM-5 PM.

BIOINF is located on the fourth floor of the Research Studies Center. Approximately 1,300 sq. ft. of space consisting of offices, storage space, and general secure areas equipped with filing cabinets. Geographic proximity to the Genomics Shared Resource (GSR), located in an adjoining building allows for daily interactions among members of both Shared Resources. Data produced at GSR are transferred easily to the BIOINF High Performance Computing infrastructure for analysis via secure File Transfer Protocol. BIOINF offices are located in close proximity to many research laboratories, which facilitates research collaboration and communication.

SERVICES

The BIOINF offers CCSG investigators a full spectrum of services. These include:

- **Project Design:** Resource personnel work closely with principal investigators and other members of the research team to define the nature and scope of relevant bioinformatics needs, as well as the type(s) of omics data to be collected and analyzed to achieve the study objectives.
- **Grant Development:** Resource personnel provide exploratory data-mining support for the development of the preliminary data section. They review--and, in general, develop--the bioinformatics analysis plan for the majority of CCSG and Roswell Park grant applications.
- **Data Processing, Integration and Interpretation:** Resource personnel perform bioinformatics analysis and data mining of various omics and other biological datasets. They implement well-established data processing, visualization and analysis pipelines and workflows for various multi-omics and imaging applications at both single cell and cells in bulk levels. They assist investigators with the integration of omics data with clinical information; develop analytical models for these data based on the hypothesis of interest, and assist investigators with finding plausible biological and/or clinical interpretations of their respective results.
- **Manuscript Preparation:** Resource personnel, serving as scientific collaborators, review and write the bioinformatics analysis section of the manuscript of interest, and provide the relevant interpretation of the data models as they relate to the conclusions presented in the given manuscript.
- **Education & Training:** Resource personnel provide consultation, assistance, and hands-on training, when necessary, for investigators on the bioinformatics tools and resources needed to analyze their own data. Details regarding educational efforts are contained in the body of the text below.
- **Infrastructure Development:** In order to provide data warehousing and computing resources access for CCSG investigators for storing, managing, analyzing and sharing omics data and other types of data, the Resource contributes to the development of the underlying informatics infrastructure in close collaboration with the IT department.
- **Software Evaluation:** Resource personnel collect and test available bioinformatics products in order to help investigators select the appropriate tools for their specific studies.
- **Tool, Database, and Web Development:** Resource personnel develop customized bioinformatics tools, interactive web applications and underlying back-end databases, as necessary, when existing products are unavailable or do not meet the customized needs of CCSG investigators relative to answering specific study objectives. Whenever possible, we make these tools available to the broader community.

In addition to providing general collaborative and consulting services necessary for CCSG research and operations, the BIOINF provides unique and specialized services via its methodological research. As an example, the Bioconductor, for which Dr. Martin Morgan serves on the Scientific Advisory Board and leads its Roswell Park team, is an open-source, open-development software project for the analysis and comprehension of high-throughput data in omics. Bioconductor is essential in cancer research - it is highly successful (>2,100 software packages), widely used (>3/4 million downloads annually), highly cited (>44,000 citations), and well respected (>1,200 developers worldwide).

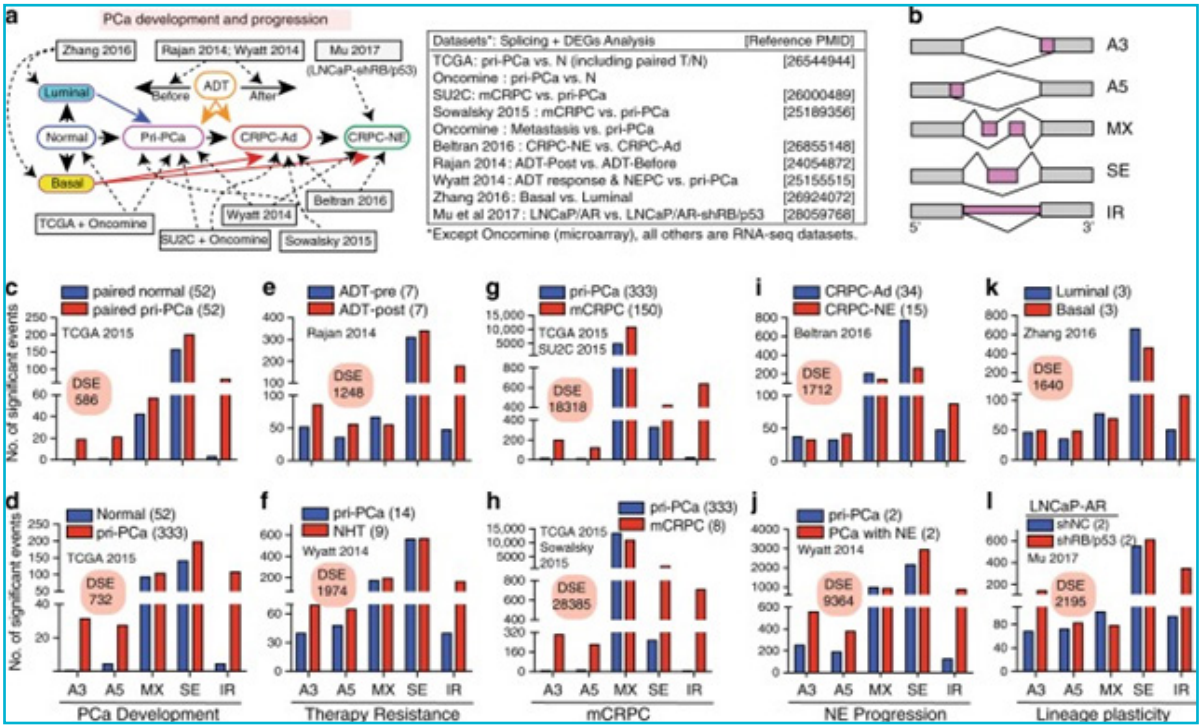
INSTRUMENTATION / SOFTWARE / EQUIPMENT

Each member of the BIOINF is equipped with state-of-the-art workstations loaded with general and specialized analytics software packages. Frequently used bioinformatics software includes R/Bioconductor, CellProfiler, Cell Ranger, BWA, Bowtie, GATK, Tophat, STAR, Cufflinks, RSEM, DESeq2, edgeR, MACS, GSEA and SingleR.

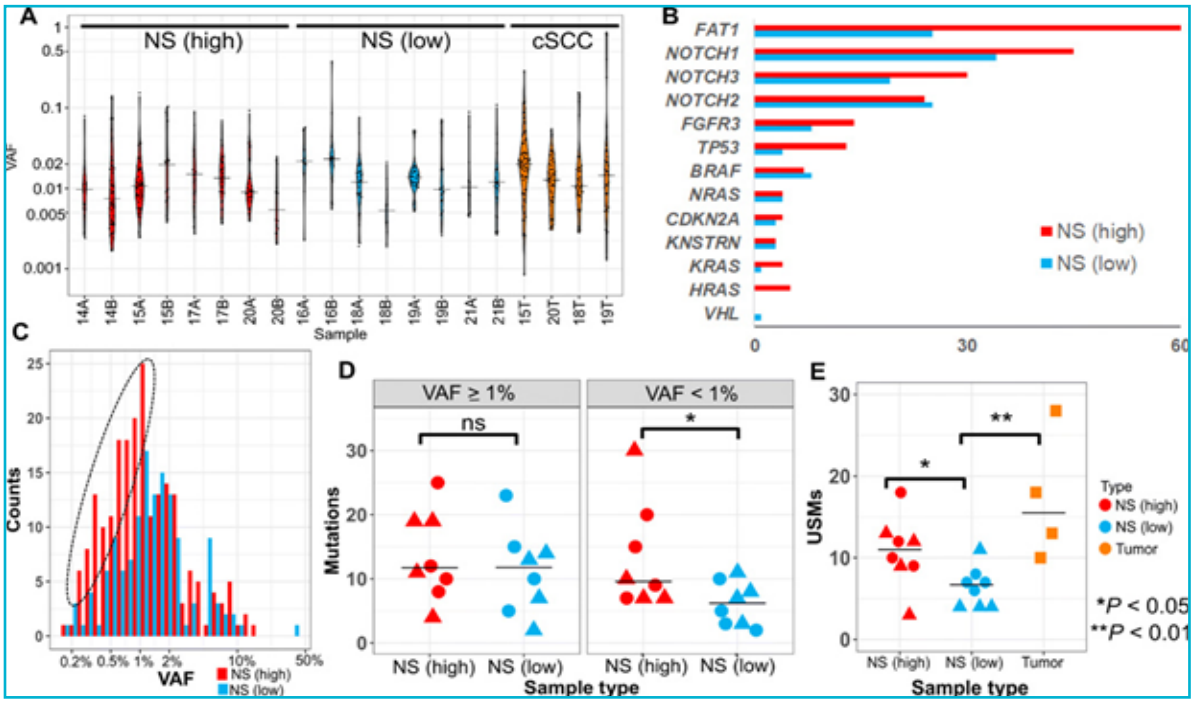
The BIOINF team has ready access to high-performance computing and dedicated high-performance storage provided by the University at Buffalo Center for Computational Research (CCR), a leading academic supercomputing facility with more than 2 PFlop/s of peak performance compute capacity, to ensure that computing capacity and required data storage continue to meet the demands of the BIOINF user base while maintaining cost-effectiveness.

NOTABLE PROJECTS

Dr. Dean Tang (R01 CA240290) worked with Drs. Liu and Wang to perform a comprehensive analysis of the global alternative splicing (AS) landscape during prostate cancer development and progression and upon treatment failure. This big data-driven study established aberrant AS landscape as a hallmark of prostate cancer aggressiveness and the spliceosome as a therapeutic vulnerability for prostate cancer (Publication: Zhang et al., Nat Commun., 2020).



Dr. Gyorgy Paragh (R01 CA255242) and Dr. Wei developed an ultradeep sequencing–based method to investigate the relationship between UV light exposure and the accumulation of clonal mutations, as well as the relationship between clonal mutations and skin cancer risk. Findings from this study shed light on UV's carcinogenic effect and pave the way for future quantitative assessment of subclinical UV damage and skin cancer risk (Publication: Wei et al., Sci Adv., 2021).



BIOMEDICAL RESEARCH INFORMATICS (BRISR)
Shared Resource

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OVERVIEW

The Biomedical Research Informatics Shared Resource (BRISR) provides data services to investigators in support of translational research at Roswell Park.

BRISR provides structured access to real-time reliable clinical data for the advancement of non-interventional studies at Roswell Park. Data is delivered in a HIPAA-compliant manner, and we ensure that all regulations and data safety standards are met to ensure our patient's privacy.

We offer the infrastructure and processes to establish and monitor data standards, quality, integration, and distribution across Roswell Park. BRISR's highly trained staff support translational, clinical, and basic science researchers by making Roswell Park research data persistently findable, accessible, interoperable, and reusable (FAIR) using cutting-edge informatics technology and methods. We work to train and assist researchers in using current informatics tools available and continually research new tools that may benefit our customers. BRISR staff are also able to develop and implement custom tools and methods to streamline the collection, storage, processing, and distribution of data to researchers.

Mission

The mission of BRISR is to advance the Roswell Park Comprehensive Cancer Center Data Science Strategic Plan, in alignment with the NIH Data Science Strategic Plan published in 2018.
These goals include:

- Facilitate data accessibility and sharing to maximize data standardization, use and re-use
- Enable high quality data capture and management through project-appropriate software development
- Provide highest quality data to biostatisticians for analytics
- Provide grant application co-authorship and support to increase Roswell Park grant funding

USING THE RESOURCE

Investigators may request BRISR support via email: BRISR@roswellpark.org

SERVICES

Clinical data requests

BRISR works with investigators to provide clinical data for non-interventional studies. Data Managers can integrate clinical data from multiple sources to best serve investigators' studies. Data requests can be sample based or data only.

Software Research and Development

The BRISR team will research software to be used by research projects (commercial and custom) and develop custom open-source software (database, web applications) to support data capture, management and reporting for research protocols. Engineering of protocol processes, a critical step to ensure highest quality data capture, is part of this service.

REDCap survey/database design and development

BRISR will work with investigators and clinicians to design, build and administer REDCap surveys and databases. Data managers can also assist in data abstraction into any database.

Cohort selection

BRISR utilizes available clinical data to assist the biobanks with cohort selection based on project needs.

REDCap support

BRISR provides Roswell Park investigators with REDCap training and support.

Honest Broker services

BRISR data managers are certified Honest Brokers and can provide de-identification services for your research projects

Grant application support

BRISR will provide reports for potential sample/patient numbers needed for grant applications, contribute to grant text, recommend required computing resources, provide budgets for informatics and data management.

NOTABLE PROJECTS

Visualization Portal (visPortal)

BRISR provides an advanced platform streamlining genomics research by promoting effective data visualization, sharing, and exploration among Roswell Park investigators.

BioRepository & Laboratory Services (BLS) Shared Resource

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OVERVIEW

The Biorepository and Laboratory Services Shared Resource (BLS) is a comprehensive data and biospecimen bank (malignant and normal tissue and their derivatives, blood and bone marrow) for research along with a range of services that accompany biospecimens. The overall mission of BLS is to facilitate access to human tissue, blood and bone marrow for investigators with Institutional Review Board (IRB) approved protocols emphasizing translational research. BLS plays an essential role at Roswell Park, helping investigators to establish Biospecimen and Data Research (BDR) protocols and supporting the submission of grants by providing feasibility analysis, cost estimates and letters of support.

USING THE RESOURCE

BLS Laboratory and Biospecimen Storage facilities are in the Gratwick Basic Science Building. Hours of operation are weekdays, 7:00 AM – 5:30 PM. BLS Recruitment is located in the Main Hospital lobby and the Request Management Office is located in Carlton House.

Investigators interested in the use of the facility should contact BLSAdmin@RoswellPark.org to discuss scheduling and procedures for placing a work request.

SERVICES

Biospecimens, Procurement & Banking

The BLS functions to assist investigators with translational research by providing a variety of biospecimens.

Banked Samples

The focus of this shared resource is to collect blood, bone marrow, remnant tissue, and other sample types from patients with a variety of solid and hematologic malignancies ideally at time of diagnosis and prior to any therapeutic intervention. Patients provide informed consent on an IRB approved non-interventional clinical protocol. All samples are collected at the same time as other existing clinical laboratory orders and procedures.

We strive to provide specimens that are rigorously collected, processed, and stored so that the integrity of potential analytes will be consistent across all patients and controls. Samples are drawn and sent to the BLS laboratory for processing into serum, plasma, buffy coat, peripheral blood mononuclear cells (PBMC), bone marrow mononuclear cells (BMMCs) and genomic DNA.

Samples are processed following stringent standard operating procedures and stored in barcoded containers that are linked and managed in our Laboratory Information Management System (LIMS). Requests for samples are guided by the LIMS and can be integrated with other shared resources facilities (e.g. Genomics Shared Resource). The liquid bank has more than 1.3 million blood and/or other sample types banked from more than 43,000 patients and healthy controls. This includes more than 220,000 cryopreserved marrow and blood samples from patients with hematological malignancies dating back to 1991. Banking of blood specimens from patients with solid tumors started in 2003. All samples have related clinical data available.

Tissue

Formalin-Fixed Paraffin-Embedded (FFPE) Tissue

Formalin-fixed paraffin-embedded blocks from surgical pathology tissues are archived and can be accessed for research purposes. The archive of paraffin tissues is extensive, having more than 200,000 cases that can be electronically searched and used for research purposes.

Fresh & Frozen Tissue

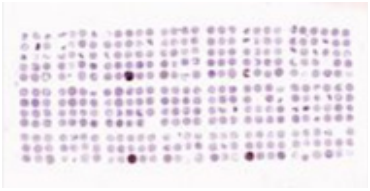
Fresh and frozen remnant tissues are banked from surgical specimens and distributed for research purposes. Our biospecimens are procured by certified Pathologist Assistants and then stored in -80ºC freezers that are protected 24/7 by state-of-the-art monitoring systems. The number of biospecimens available in the biobank varies by disease site and utilization.

DNA and RNA

DNA and RNA are isolated from tumor and matching non-tumor tissues in the biobank. DNA and RNA are primarily extracted from frozen tissue samples, but DBA can be extracted from FFPE tissue as well. All samples are Quality Controlled (QC) after extraction to confirm the DNA is of high quality.

Services (cont'd)

Tissue Microarrays



Tissue microarrays (TMAs) are constructed by using a hollow needle to remove very small tissue cores from multiple tumors of interest which are then inserted into a recipient paraffin block in an arrayed fashion. This format permits the screening of a large number of patient samples on a single slide. TMAs are an efficient and effective way to screen potential biomarkers and are typically used in conjunction with immunohistochemical (IHC) staining or fluorescent in situ hybridization.

BLS has constructed more than 200 different TMAs representing a wide variety of disease and tissue types from more than 16,000 patients. BLS has a large collection of assembled TMA blocks available representing a diverse selection of disease and tissue types. Currently, our TMA library contains over 60 breast TMAs, 42 TMAs from gastrointestinal tissue, and 73 with prostate tissue. Several other tissue types for which TMAs are constructed include lung, head and neck cancers, gynecological cancers, brain cancers and melanoma.

Aperio Scanning & image Analysis

Successful digital pathology depends upon the effective and timely creation of high-quality digitized glass slides. The Aperio Imaging and Analysis lab uses The Aperio AT2 slide scanner, an ultra-fast, high-capacity scanning system with powerful 400-slide capacity. This system creates digital images from glass slides with superior image quality and includes the following features:

- 20X and 40X scanning magnification capabilities
- Create digital slides in multiple formats (SVS, JPEG, TIFF, composite web slide)
- View and edit digital slides with the user-friendly and freely downloadable ImageScope viewing software
- Connect multiple, remote parties through digital slide conferences.

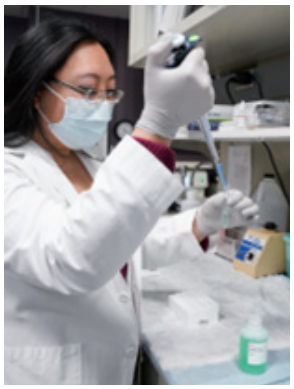
Aperio slide scanning permits investigators to easily access digital images of slides from anywhere using Leica eSlide Manager, a web-based digital pathology information management system. Annotation of the digital slides can be conducted via a digital platform, **Aperio® ImageScope**. This allows researchers to create digital images for publication as well as facilitate inter-institutional collaboration by providing rapid and easy sharing of digital image information.

Digital slide scanning also permits **automated image analysis**, a service also provided by BLS. **Aperio® algorithms** can be tailored to fine tune the cellular, nuclear, and stain parameters, creating an optimized algorithm macro for each antibody target and tissue type to select the cells of interest. The original digital slide image is never modified. Rather, an annotation layer with the markup image and quantitative data is created and linked to the digital image.

Services (cont'd)

Histology Services

The Histology Facility is a centralized lab that provides histology service for human and mouse tissue. Services include standard tissue processing and embedding, cryotomy, microtomy, special staining, antibody optimization, and immunohistochemistry (IHC). The Histology team also performs special procedures such as sterile needle coring to isolate DNA from tumor samples, tissue prep for Phenocycler, and histology preparation for Visium Spatial Gene Expression. Histology staff work closely with the Biomedical Research Informatics Shared Resource (BRISR) and other shared resource labs to identify samples sets, and then perform the required staining for research studies that use IHC. The lab uses several auto stainers for consistent and high-throughput IHC staining. Antibody staining procedures and IHC slides are regularly reviewed by a pathologist for quality control.

Study Specific Procurement

BLS can prospectively collect material in a custom format at single or multiple time points. These samples can be prospectively banked under our IRB consent and obtained for future research following approval of study-specific biological data review and/or IRB protocols. BLS is more than happy to provide letters of support and can perform feasibility studies as needed in support of current and/or pending grant proposals.

Clinical Data

Each sample collected from patients has clinical data available. The clinical data is available from disease specific data managers, BRISR, and BLS data managers. Available data includes:

- Roswell Park Cancer Registry data with basic tumor information, treatment and first recurrence details. Data collected includes: diagnosis date, laterality, histology, behavior, grade, tumor size, clinical and pathological stage, distant sites, tumor markers, surgery date, pathology and recurrence (as of the sample collection date).
- Electronic health record: Includes drug treatment, patient information (height, weight, BMI, blood pressure, etc.), visits, orders (scans, scopes, tests, procedures, etc.), comorbidities, family history, karyotype, mutational profile, and outcome.
- Additional medical record abstraction
- Honest broker services
- Linking and de-identifying data and study data file storage

Services (cont'd)

Epidemiological Data

At the time of consent, participants (patient or non-patient/control) are asked to complete a self-administered epidemiological questionnaire available online or paper version. The questionnaire contains more than 1,100 items including:

- Demographics and background
- Personal and family history of cancer and other conditions
- Medical and cancer screening histories
- Lifestyle (smoking, diet, physical activity, alcohol, cannabis)
- Supplement and medication use

The questionnaire data dictionary and codebooks are available to investigators for research planning and analysis.

BLS Recruitment

BLS has a team devoted to participant recruitment, located at registration area in the main hospital lobby in downtown Buffalo and throughout hospital clinics. Their focus is to perform informed consent on patients and healthy controls. The Universal consent includes questions for approval for biospecimen procurement including blood collections, bone marrow and remnant tissue along with access to clinical data, and permission to recontact for additional research opportunities and/or additional collections. Once consented, recruitment staff can order blood samples and track for serial samples to be collected alongside existing clinical laboratory orders and drawn by the phlebotomy service at Roswell Park. Bone marrow and tissue collections are part of routine clinical collections and surgery.

Family members and friends accompanying patients, as well as other visitors to Roswell Park, also are asked to donate samples as controls. Control samples follow the same sample procurement and processing procedures as patient samples.

Roswell Park staff may reach BLS Recruitment Coordinators for recruitment issues by paging "Biorepository Consent" from inside the hospital. Recruitment staff may also be reached for questionnaire issues by telephone at **716-845-7774** or please email BLSRecruitment@RoswellPark.org.

BIOSTATISTICS & STATISTICAL GENOMICS (BSGSR)
Shared Resource

LEADERS

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OVERVIEW

The Biostatistics and Statistical Genomics Resource (BSGSR) offers collaborative and consulting services at the interface of biology, medicine, statistics, mathematics, and computer science. The staff has experience and expertise in the theory and application of biostatistics, biomathematics, statistical genetics, and computer simulation to all aspects of cancer research. Specialties include clinical trial design and analysis, statistical genetics modeling, including the analysis of microarray data and other high-throughput approaches, and epidemiological statistical methods. The resource has the ability to develop customized software and algorithms for specialized data analysis problems.

The BSGSR provides well-planned designs and data collection instruments that are ethical, do not waste resources, and are cost-effective. The biostatistics component of the resource provides statistical support for pre-clinical experiments, clinical trials, and observational studies. Clinical trials are monitored for data collection and study conduct to help ensure patient safety. For all open and recently closed studies, written interim reports are provided to the PI and, if required, the Data and Safety Monitoring Committee (DSMC). Additionally, ClinicalTrials.gov reports are generated for all Phase I and II clinical trials where Roswell Park is responsible for the data and analysis; and other NIH or NCI funded intervention/non-intervention trials. The Statistical Genomics component of the resource applies and develops statistical and computational methods to address biological questions on human diseases and traits from genetics and genomics data. The data dealt by the team includes but not limited to candidate-gene studies, genome-wide association studies (GWAS), and next-generation sequencing (NGS) studies. The resource as a whole can provide support for the entire life-cycle of a project: from grant/proposal development, to data analysis, and through presentation of results (i.e. biostatistical sections of abstracts and manuscripts, and graphics development).

There are no formal direct charges for the services provided by the BSGSR to internal users. Projects requiring extensive use of resource services may require a charge-back of a flat project fee. External services are available at an hourly rate. Collaborative joint grant proposals are encouraged. Funding for biostatistical support must be included in grant proposals.

USING THE RESOURCE

Investigators may contact Drs. Yu and Zhu for further information and details. Requests for collaboration should be made in our project tracking system, LIMS, at rpcilims.roswellpark.org

Priority is given to Cancer Center Support Grant members versus non-members, and investigators who have outside funding, an approved clinical trial, or are preparing protocols and/or grant applications. Statistical sections for abstracts and special presentations should be received at least two weeks in advance of a submission deadline. The BSGSR is located in the Research Studies Center R-420. Hours of operations are weekdays, 8:30 AM-5 PM.

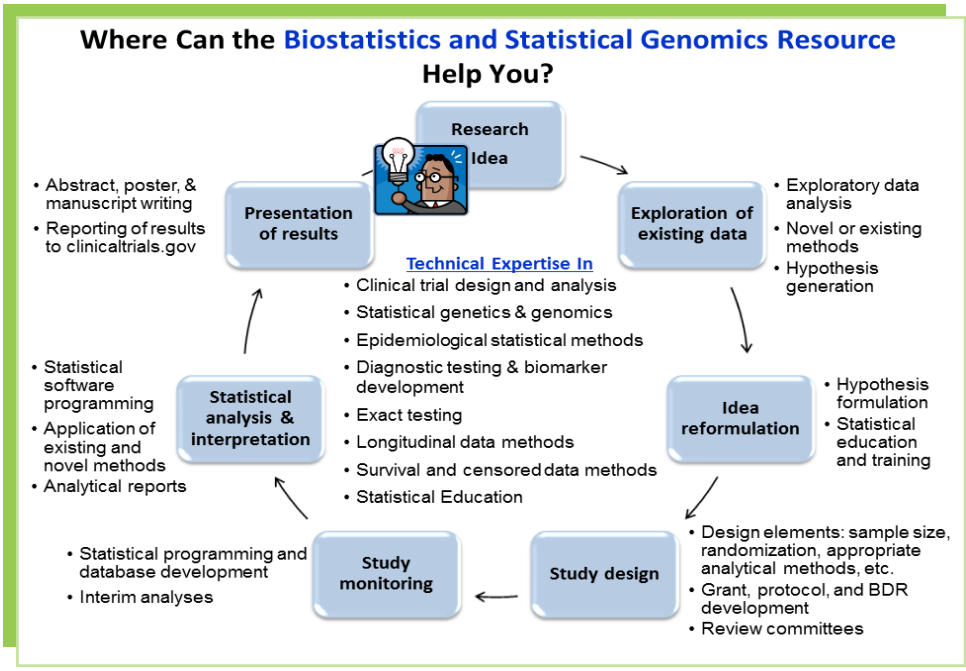
SERVICES

- Provide biostatistical support to basic, clinical, and population-oriented Roswell Park collaborators
- Exploratory data analysis
- Statistical methods sections for grants
- Protocol development (close working relationships with IT, CRS, and BRISR)
- Study design (pre-clinical experiments, observational studies, and clinical trials)
- Fitting models to data (model rational, development, and fitting)
- Simulating data from models
- Developing customized data mining software and novel methods based on emerging technologies
- Statistical software development: developing novel statistical methodologies, software applications, quality control metrics, custom visualizations and custom diagnostics for high throughput technologies utilized at Roswell Park
- Statistical training and education
- Assistance in abstract and manuscript writing
- Statistical reviews across several Roswell Park committees (SRC, IRB, DSMC, Alliance Foundation)
- Machine Learning
- Provides statistical expertise in proteomics, genomics, and epidemiology research within Roswell Park
- Statistical Genetics and Genomics
    - Research study design consultation, applying preprocessing methods to eliminate quality issues and account for inherent biases, deriving and applying statistical and machine learning algorithms for discoveries in genetics, genomics and proteomics experiments, and employing disease related gene/ pathway/network/system-biology analysis.

SOFTWARE

The team at the BSGSR utilize a variety of software packages in order to provide effective analytical support. Some of these packages include:

- SAS
- R
- PASS
- SEER-Stat
- PLINK
- GATK



NOTABLE PROJECTS

- NCI funded (R01CA262899) multi-ethnic high-throughput study to identify novel non-HLA genetic contributors to mortality after blood and marrow transplantation. Dr. Qianqian Zhu is a co-PI of the project. She leads data management and analysis, including data QC, single-variant and gene-level association tests, candidate causal variant identification, gene network analysis, and designing the clinical-genomic prognostic models.

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- Odunsi K, Qian F, Lugade AA, Yu H, Geller MA, Fling SP, Kaiser JC, Lacroix AM, D'Amico L, Ramchurren N, Morishima C, Disis ML, Dennis L, Danaher P, Warren S, Nguyen VA, Ravi S, Tsuji T, Rosario S, Zha W, Hutson A, Liu S, Lele S, Zsiros E, McGray AJR, Chiello J, Koya R, Chodon T, Morrison CD, Putluri V, Putluri N, Mager DE, Gunawan R, Cheever MA, Battaglia S, Matsuzaki J. Metabolic adaptation of ovarian tumors in patients treated with an IDO1 inhibitor constrains antitumor immune responses. Sci Transl Med. 2022 Mar 16;14(636):eabg8402. doi: 10.1126/scitranslmed.abg8402. Epub 2022 Mar 16. PMCID: PMC9311231.

COMMUNITY OUTREACH & ENGAGEMENT (CER)
Shared Resource

LEADERS

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OVERVIEW

The Community Engagement Resource (CER) directly supports Roswell Park's commitment to conduct research that meaningfully integrates information gained through bi-directional community engagement to answer important questions in our catchment area. One of the core initiatives within the CER is the Research Oncology Community Knowledge (ROCKstars) program, which is an initiative developed in collaboration with Roswell's Community Outreach and Engagement team, cancer survivors, caregivers and community stakeholders from Roswell Park's catchment area. The ROCKstars program conducts training for both advocates and investigators, assists with the recruitment and retention of patients into clinical trials, provides specific consultation to investigators on engaging participants in research and assists with lay abstracts and letters of support for grant submissions.

Example Research Studies with ROCKstars Advocates

CCSG Program	Project	PIs and Advocates
PS	R01CA247281 - Tumor Immune Contexture and Breast Cancer Disparities	Ambrosone (PS), Abrams (TII), Community Advocate Focus Group Participants
TII	W81XWH2110059 - Inhibiting MDSC Biogenesis to Augment Immunotherapy Efficacy in Triple-Negative Breast Cancer	Abrams (TII), Nemeth (TII), Colden (Advocate)
CSB	NCCN/AstraZeneca - Utilizing Patient Reported Q0L to Inform Decision Making in Early-Stage Lung Cancer	Singh (CSB), Yendamuri (PS), Bouchard (PS), Dexter, Study CAB Members
DT	W81XWH1910111 - Estrogen Receptor Beta-p53 Signaling Axis: A New Therapeutic Target in Triple-Negative Breast Cancer	Das (DT), Peters (Advocate)

Annette Colden
Cancer Survivor

Donald Lee
Cancer Survivor

Vickie Sailor
Cancer Survivor

Dr. Gandhi (TII) &
Rob Jones, Cancer Advocate

Breast Cancer Network of
Western New York (BCNWNY)

We R As 1 Breast Cancer
Support Group

SERVICES

In addition, CER also provides research infrastructure and facilitates our established **Roswell Park Community Advisory Board (CAB), and newly formed Rural Equity and Cancer Health Community Advisory Board (REACH CAB)**. The mission statement for our CABs states that: "We will recommend best practices related to cultural competency, education, awareness and access and treatment services to eliminate/reduce cancer inequities for the medically under served." The CAB includes representation from many diverse communities including but not limited to African American, Hispanic/Latino, Native American, Rural, immigrant and refugee, as well as cancer survivors and caregiver populations in the WNY area.

COMPARATIVE ONCOLOGY (COSR)
Shared Resource

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LEADERSHIP

The daily operations of the COSR are managed by a team led by the Directors, Dr. Leslie Curtin, who is responsible for the veterinary program and regulatory compliance of the resource and Dr. Emily Mackey who oversees the histopathology, cytology and PDX procurement among other services as well. They are supported in the management of administrative matters by the COSR Administrator, Justin Hartley, and with facilities environmental controls and personnel by Raymond Young, COSR Manager.

OVERVIEW

The Comparative Oncology Shared Resource (recently known as the Laboratory Animal Shared Resource) is one of Roswell Park's Scientific shared resources available to our investigators to facilitate basic, clinical and translational scientific research. The mission of COSR is to promote the humane and responsible care and use of laboratory animals, to provide full-service support for animal studies to investigators that will take original ideas from hopes to treatments and cures. The facilities and veterinary program are both accredited by AAALAC International demonstrating commitment to humane and responsible animal research and dedication to good science. COSR is designed to offer the highest standards of animal care, with an expert technical staff performing ALL aspects of study execution including small animal surgery (castration, tumor resection, tumor inoculation - SQ, orthotopic, sub renal, tumor measurement, therapeutic treatments such as injection (IP, IV, sub-Q,), oral gavage, dietary manipulation, tissue procurement, tissue microdissection and histopathology comprehensive services.

All aspects of daily health observations, veterinary medical care, facility and equipment maintenance and surgical and technical services. The resource staff includes specialized veterinarians, specialized veterinary pathologist, surgical research specialist, senior research specialists, licensed veterinary technicians (serving in different capacities within the resources) and a dedicated group of staff (many certified by the American Association of Laboratory Animal Science AALAS)) that take pride in offering professional, timely and high-quality service to support the research projects of cancer center members.

USING THE RESOURCE

Principal Investigators are encouraged to consult with Drs. Curtin and Mackey to review experimental design, select appropriate animal models, and plan procedures to be performed by COSR staff—including surgeries, treatments, data collection, and histopathology/cytology services. The first step in initiating a project is submitting a protocol to the Institutional Animal Care and Use Committee (IACUC). Adding COSR staff to protocols is streamlined through a simple request form that outlines the required services.

COSR also maintains service protocols for toxicological evaluations of test articles, which can be amended as needed to meet specific research requirements. Additional steps may include establishing and maintaining a breeding colony managed by COSR, transferring animals to the experimental protocol, assigning staff, and supporting animal procedures in accordance with standard barrier guidelines to ensure research quality.

COSR prioritizes service requests in the following order: 1) CCSG members with peer-reviewed funding; 2) CCSG members with non-peer-reviewed funding; 3) Non-CCSG members; 4) External academic collaborators; 5) External industry collaborators.

Research model orders from approved commercial vendors are placed through Workday and processed by our research service associate. To request animals from COSR's in-house mouse production colonies, investigators should submit the I**n-House Mouse Colony Purchase Requisition Form** available on i2.

Before starting any laboratory animal research project, investigators are strongly encouraged to meet with COSR staff to ensure that an appropriate animal care and health surveillance plan is in place.

SERVICES

The COSR offices are in the Medical Research Complex, M260. The laboratory animal housing facilities are located in the Medical Research Complex (MRC) and Cancer Cell Center (CCC) buildings. Hours of operation are weekdays 7:30 AM – 4:00 PM. Drs. Curtin and Mackey are on call for veterinary services during the weekend and holidays.

Services include:

- ***Veterinary and Surgical Services:*** Study design and budget preparation. Surgical procedures including orthotopic implantation (pancreas, prostate, cecal) sub-renal implantation, intra femoral, SQ and IV tumor inoculation, castration, ovariectomies, grafting clinical tissues. Data collection and record keeping, tumor measurements, diagnostic services, animal treatments, clinical pathology, necropsy, and histopathology, are available to investigators. Other research support related to specialized techniques and procedures, as well as specialized surgical and microsurgical techniques, anesthesia, analgesia, and euthanasia are available. **For information - Contact Dr. Leslie Curtin (ext.7621) or Dr. Minhyung Kim (ext. 2974).**

SERVICES (cont'd)

- ***Veterinary Pathology Services:*** Histopathology and cytology services including paraffin processing and embedding (single/multi-chamber cassette), cryosectioning, facing blocks, cutting slides (FFPE & OTC, H&E staining, IHC and specialized stains, gross necropsies, standard and comprehensive necropsy, tissue collection and trimming, histopathology processing and interpretation. **For information- Contact Dr. Mackey (ext.4370).**

- ***Education and Training:*** COSR conducts an IACUC approved "Training Course in Responsible Care and Use of Animals in Research". This course is mandatory for individuals who wish to work with animals. "The principles of Rodent Surgery" course is mandatory for those researchers performing surgical procedures in their laboratory rodents. **Contact IACUC office at ext. 8853 for course schedule.**

- ***Good Laboratory Practices (GLP):*** The recognized need to facilitate the FDA applications for test articles being developed at Roswell Park has given rise to an initiative to provide pre-clinical toxicologic testing non-GLP in the COSR and establishment of preferred provider agreements with GLP compliant providers for Roswell Park PI's.

- ***Husbandry:*** Special arrangements can be made for most species, including large animals. All work involving animals must be approved by the IACUC. Care and use programs are developed to ensure that space, appropriate housing, nutrition, macro and micro environmental conditions, veterinary care procedures, decontamination and technical procedures are suited to the study. Barrier and isolation maintenance of rodents is provided for immune-deficient animals and *in vivo* use of Biohazardous agents.

- ***Animal Imports/Exports:*** COSR has developed specialized standard operating procedures to expedite researcher needs for animal transfer between institutions, nationally and internationally. **Contact Dr. Curtin at ext. 7621 or Justin Hartley, Administrator and Import/Export Coordinator, at ext. 5732 for required procedures.**

- ***Animal Receiving:*** All orders for animals from external sources must be processed through COSR. Please submit purchase requisitions on Workday and the research models will be ordered by **Wendie Siminski (ext. 3397).**

- ***Mouse Production:*** COSR supervisors will manage mouse strains that cannot be purchased through commercial vendors for Principal Investigators. All Principal Investigators must have an approved protocol on file with the IACUC office justifying the requested breeding program. To set up a COSR managed mouse breeding colony contact the floor supervisor.

- COSR manages breeding colonies of immune competent strains (SCID's and NSG's). **For information on any of these models, contact Venessa Bazinet (ext. 2368).**

- COSR maintains a unique colony of the animal model for liver cancer, the Woodchuck *(Marmota monax)*. **For information, please contact Dr. Curtin (ext. 7621).**

SERVICES (cont'd)

- ***Hematology Services:*** COSR offers in house hematology services for laboratory animals.
  - *ProCyte Dx® Hematology Analyzer* - Delivers an advanced five-part white blood cell differential, absolute reticulocyte count, and band neutrophil and nucleated red blood cell (nRBC) parameters.
  - *Catalyst Dx® Chemistry Analyzer* - Run the tests you need with complete testing flexibility. Preloaded CLIPs and 26 different tests. LAR offers renal panels, liver panels, and comprehensive panels according to the researcher's needs.

- ***Tissues/Blood:*** Various tissues, blood and serum products from several species of laboratory animals may be available through COSR. **Contact Dr. Curtin (ext. 7621) for information.**

INSTRUMENTATION & EQUIPMENT

- State-of-the-art Rodent Micro isolation racks with individually ventilated cage system
- Reverse osmosis, computer-controlled, self-flushing, water distribution system
- 75 biosafety cabinets (BSCs) Class II Type II
- Isolation Cubicles
- The COSR houses an irradiation suite with Gamma and X-Ray irradiators.
- A state-of-the-art necropsy suite with CO2 systems and downdraft dissection tables
- Two fully equipped large animals OR suites with an additional anesthesia system for large animals.
- Two large Bulk autoclaves to process ~ 10,000 cages/week.
- IDEXX Hematology and Clinical Chemistry analyzers for diagnostics in multiple species.
- ABSL2/3 Suites
- Bio Bubble® Clean Rooms
- Histology equipment (Tissue processor, microtome, cryostat, DAKO immunostainer, freezers for controlled cryopreservation of tissues.

NOTABLE PROJECTS & CAPABILITIES

COSR supports scientists that conduct *in vivo* studies in an AAALAC International accredited barrier facility. To further the success of the research programs at Roswell Park, COSR is actively involved in refinement of procedures that usually become new methods or innovations to accomplish the goals of proposed animal studies. COSR also actively participates in meetings focused on correlative sciences related to clinical trials and multi-PI program grants using laboratory animal models and tumor specific initiatives. International import and export of animals have broadened the scope of cancer research at Roswell Park.

At an institutional level, COSR interacts with other shared resources that are also dedicated to providing specific services using laboratory animals including the Translational Imaging Shared Resource (TISR), and the Gene Targeting and Transgenic Shared Resource (GeTT). This interaction streamlines the management of the members' projects and promotes centralization of services.

As of June 30, 2025, the Experimental Tumor Shared Resource has been officially consolidated into the Comparative Oncology Shared Resource (COSR). This integration enhances our ability to provide comprehensive, expert support for all aspects of animal research, while improving efficiency and streamlining services for our investigators.

COSR meet rigorous standards that demonstrate our commitment to humane and responsible animal research and our dedication to good science.

Dedication & Commitment to Science

- COSR is a central resource for preclinical research, offering CCSG investigators access to advanced facilities, expert guidance on animal model usage, and skilled personnel to support all aspects of study execution.
- COSR veterinary services staff has expertise in advanced technical procedures for generation, monitoring and testing of PDX models and provides training and surgical support for both small and large animal models.
- COSR staff manage breeding colonies of C57BL/6, SCID, NSG, and SGM3 mice, which are maintained by COSR and available to CCSG members.
- COSR now provides comprehensive histology and comparative pathology services to support disease research using animal models.

FLOW & IMMUNE ANALYSIS (FIASR)
Shared Resource

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OVERVIEW

The mission of the Flow and Immune Analysis Shared Resource (FIASR) is to provide exceptional and comprehensive advanced cytometry services in a cost-effective, user-friendly, and scientifically rigorous environment for the support of translational, basic science, and clinical research programs at Roswell Park, with a strong focus on technologies relevant to immunotherapy and immune monitoring. The FIASR consults with investigators about these technologies and maintains an active program to educate scientific professionals, graduate and undergraduate students, as well as lay audiences regarding cutting-edge cytometry applications. The resource provides scientists access to a variety of state-of-the-art cytometry platforms and laboratory services for their research, including conventional, full spectrum, and mass flow cytometry; imaging flow cytometry; immunoassays such as ELISA and ELISPOT; small particle detection including extracellular vesicles and nanoparticles; proteomic and metabolomic analyses, with spatial multi-omic options; immunophenotyping of the tumor microenvironment; confocal microscopy; Luminex multiplex bead assays; and single-cell secretome profiling. Sample preparation and data analysis support are available for all procedures.

USING THE RESOURCE

Investigators are encouraged to contact FIASR (the general research lab number: 845-3470) prior to initiating a project for appropriate training, to establish an account and to obtain access to instrumentation. FIASR is located in the Cancer Cell Center, 3rd Floor. Following the appropriate training, users have access to the research equipment 24/7. Regular hours of operation are weekdays, 8:00 AM - 6:00 PM

SERVICES

(1) Experimental design consultations; (2) sample preparation and staining; (3) conventional, full spectrum, and mass flow cytometry; (4) imaging flow cytometry; (5) cell sorting; (6) live cell imaging; (7) assays for cellular viability and metabolic function, including label-free options; (8) immunoassays including ELISA and ELISPOT; (9) small particle detection including extracellular vesicles and nanoparticles; (10) proteomic and metabolomic analyses, with spatial multi-omic options; (11) spatial immunophenotyping of the tumor microenvironment; (12) confocal microscopy; (13) Luminex multiplex bead assays; (14) single-cell secretome profiling; (15) data analysis; (16) education and training on all procedures.

EQUIPMENT

Available equipment is listed in the table below. In addition to equipment data acquisition software, the following analysis software packages are available to users free of charge: FCSExpress (DeNovo); IDEAS (Amnis); AMNIS-AI; WinList and ModFit (Verity); FlowJo (BD Bioscience); OMIQ; VisioPharm; WAVE (Agilent) and ImagePro (MediaCybernetics).

TYPE	MODEL
Conventional flow cytometers*	BD LSR Fortessas (3)
Full spectrum flow cytometer	Cytek Aurora
Flow cytometry sorters*	BD FACSAria, SONY MA900
Imaging flow cytometers	AMNIS-MKII analyzers (2)
Mass cytometry analyzer	Fluidigm Helios CyTOF
Tumor microenvironment imagers	Fluidigm Hyperion, Akoya Phenocycler-Fusion
Proteomic analyzers	IsoLight, ELLA, Luminex 200, CTL-Immunospot
Metabolic analyzers	Seahorse XFe96
Live cell imaging instruments	xCelligence-MP, Bio-Tek Cytation 5
Small particle analyzer	ZetaView
Microplate readers	BioTek Synergy H1 with fluorescence detection

NOTABLE PROJECTS

Recent examples of FIASR contributions include:

1. Applications of imaging flow cytometry to identify circulating Dentric cell/Tcell conjugates (Oba T et al, Nat Commun. 2020;11(1):5415. PMCID: PMC7592056 **(Figure 1)**
2. Development of high dimensional full spectrum phenotyping panels such as applied to study immune infiltration of renal cell carcinoma (Chow J, et al, J Immunother Cancer. 2023;11(4). PMCID: PMC10124322
3. Use of multiplexed Imaging Mass Cytometry to exaine spatial relationship of immune cells within the tumor microenvironment (TME) (Odunsi K et al., Sci Transl Med. 2022 Mar 16. PMCID: PMC9311231 **(Figure 5)**

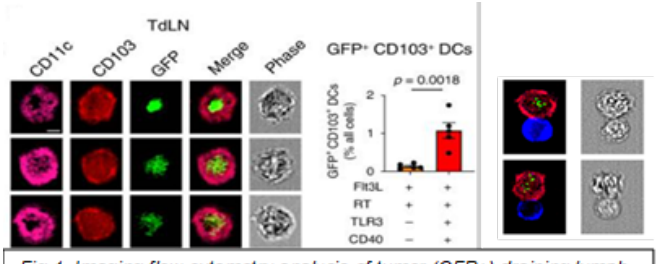

Fig 1. Imaging flow cytometry analysis of tumor (GFP+) draining lymph nodes (TdLN) following in situ immunomodulation with Flt3L, radiotherapy (RT), and TLR3/CD40 revealed increased numbers of GFP+ CD103+ DCs in treated mice compared to the PBS controls, consistent with efficient trafficking of tumor-associated antigen (TAA)-loaded cDC1s to TdLN by TLR3/CD40 stimulation. Moreover, an increased presence of GFP+ CD103+ DC/CD8+ T cell doublets (CD8+ cells are colored blue) was observed, suggesting a cross-talk between TAA-loaded cDC1s and CD8+ T cells

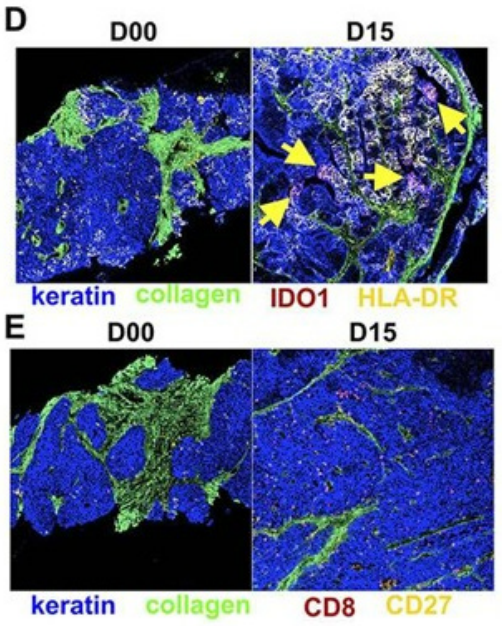

Figure 5. Spatial relationship of immune cells within TME. (D) IMC images highlighting IDO1 and HLA-DR expression and changes between two timepoint collections, Day 0 (D00,left) and Day 15 (D15,right). Yellow arrows indicate focal points of co-localization. **(E)** IMC analyses indicating CD8 and CD27 co-expression in samples at D00 (left) and D15 (right).

NOTABLE PROJECTS (cont'd)

4. Metabolic pathway testing investigating myeloid-derived suppressor cell function within the TME (Mohammadpour H et al., Cell Rep. 2021 Oct 26. PMCID: PMC8601406 **(Figure 2)**

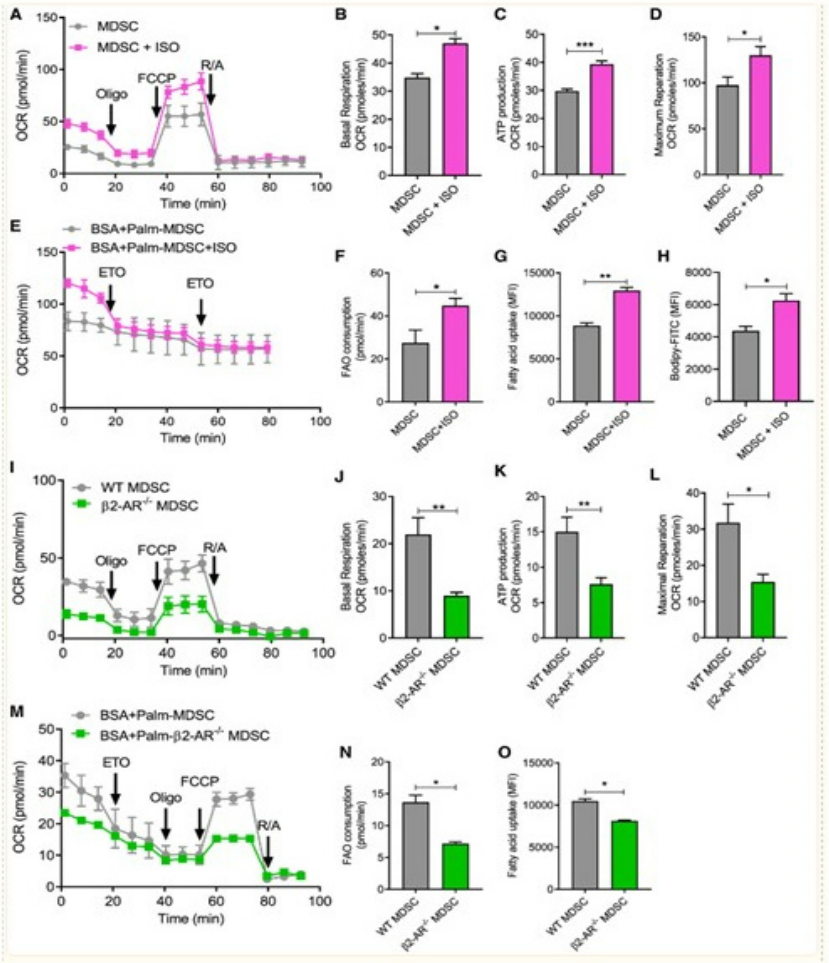

Figure 2. β-AR signaling in MDSCs decreases glycolysis and enhances oxidative phosphorylation

(A-H) MDSCs in the presence of GM-CSF and IL-6, with or without isoproterenol (ISO). (I)O) WT and β2-AR-/- mice orthotopically implanted with 4T1 tumor cells.

The following measurements were performed using a Seahorse Extracellular Flux Analyzer: (A) Mitochondrial respiration. (B) Basal respiration levels. (C) ATP production. (D) Maximum respiration. (E) FAO measured in media in which palmitate was the only fatty acid source. (F) FAO consumption. (I-L) Oxidative phosphorylation. (M-N) FAO. (O) Fatty Acid uptake.

FIASR also serves as one of the central flow cytometry facilities for the National Marrow and Donor Program research consortium.

ADDITIONAL KEY INFORMATION

FIASR is one of 14 worldwide shared resource laboratories recognized by the International Society for the Advancement of Cytometry (ISAC) for operational excellence and adherence to best practices. Best practice are outlined in Barsky LW et al, International Society for Advancement of Cytometry (ISAC) flow cytometry shared resource laboratory (SRL) best practices. Cytometry A. 2016 Nov;89(11):1017-1030.

GENE MODULATION SERVICES (GMSR)
Shared Resource

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OVERVIEW

The Roswell Park/University at Buffalo (UB) Gene Modulation Services Shared Resource (GMSR) serves as the focal point of RNA interference and CRISPR (clustered regularly interspaced short palindromic repeat) repression and activation expertise for the Roswell Park and UB research communities. Researchers have access to a whole genome resource of individual shRNA constructs, pooled shRNA libraries, and the newly acquired CRISPRi and CRISPRa pooled libraries.

The GMSR can also help with retroviral and lentiviral packaging of constructs provided by researchers and the subsequent infection and selection of target cells. The resource also houses the ORFeome 8.1 library that contains ~13,000 full length human gene cDNAs in a Gateway-adapted lentivirus vector, originally produced by the Center for Cancer Systems Biology at Dana-Farber Cancer Institute. The resource also makes available plasmids with gene markers (drug selection markers: G418, hygromycin, puromycin, bleomycin; cell markers: GFP, RPF, mCherry, luciferase, etc.), immortalization constructs (SV40-Tag, HPV16- E6, E7, hTERT), and various regulated expression vector systems (e.g., tetracycline-regulated).

In this way, the resource provides a centralized service from which investigators interested in gene transfer or modulation, cell selection or immortalization, using viral vector technologies can order packaged, infectious yet replication-defective lenti- or retrovirus in a rapid and cost-efficient manner.

USING THE RESOURCE

Investigators interested in the use of the facility should contact Renae Holtz to discuss available products, scheduling, procedures, or to obtain an order form. You may also contact Irwin Gelman for questions regarding experimental design. The GMSR is located in the CGP, 2nd Floor, L2-135. Hours of operation are weekdays, 8:30 AM - 5:00 PM

SERVICES

Individual shRNA constructs

The GE Dharmacon/Open Biosystems Expression Arrest™ Human pGIPZ lentiviral shRNAmir library and Expression Arrest™ Human and Mouse pSM2 retroviral shRNAmir library.

These libraries are available as renewable bacterial stocks, plasmid DNA, or infectious, replication-incompetent viral supernatants. The researcher's chosen target cells can also be infected and selected for antibiotic-resistant colonies in our BSLC2+ approved facility. After expansion, these cells will be provided back to the researcher and can be safely maintained following regular BSL2 guidelines.

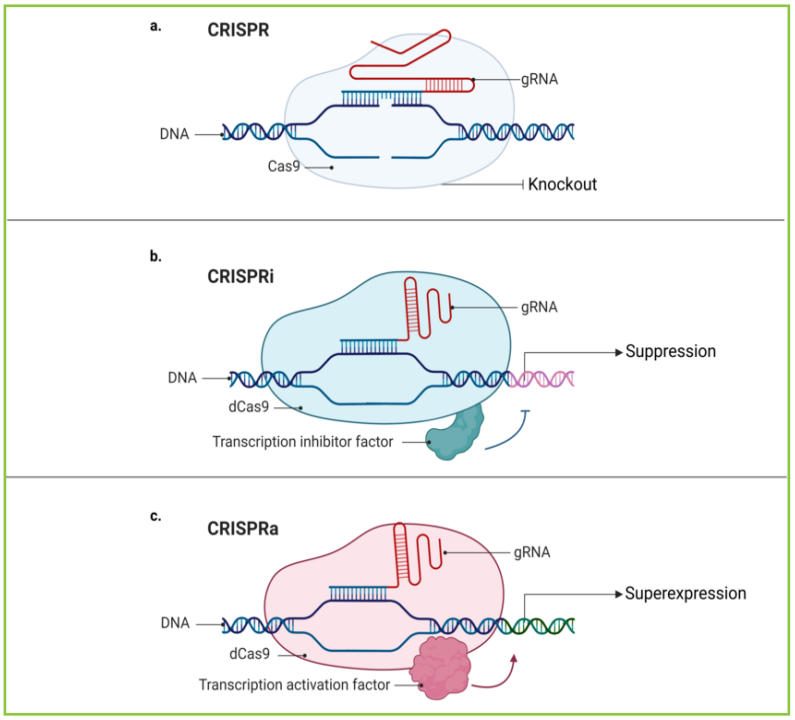
SERVICES (cont'd)

Pooled shRNA libraries

GE Dharmacon/Open Biosystems Decode™ Human RNAi Viral Screening Library and the CELLECTA DECIPHER™ Pooled shRNA Human and Mouse Lentiviral Libraries.

The pooled format of both screening libraries follow a simple protocol that does not require access to expensive high-throughput arrayed screen equipment and infrastructure, putting the genome-wide shRNA knockdown screens within reach of any researcher.

Both the Decode™ and DECIPHER™ libraries are bar-coded lentiviral shRNA libraries optimized for RNAi Genetic Screens and are available as plasmid DNA or packaged infectious lentivirus.



Genomic Screens with CRISPR Pooled Libraries (targets human genes)

Activate or repress gene expression using the recently acquired CRISPRi and CRISPRa pooled libraries developed by Jonathon Weissman and made available through Addgene.

The libraries use inactive dCas9 to activate (CRISPRa) or inhibit (CRISPRi) gene transcription in human cells. The CRISPRa sgRNA library uses the sunCas9 system and contains 10 sgRNAs for each transcription start site in 15,977 human genes, and a set of 5,968 control sgRNAs for a total of 198,810 sgRNAs. The CRISPRi library contains 10 sgRNAs for each transcription start site in 15,977 human genes, and a set of 11,219 control sgRNAs for a total of 206,421 sgRNAs.

Please visit the following website for more information: addgene.org/crispr/libraries/

Individual cDNA constructs and pooled cDNA screening library

The hORFeome 8.1 cDNA library from Broad Institute contains individual annotated 13.5K full-length human cDNAs in lentivirus vectors with protein products fused to the V5 epitope tag, as described in the 2011 Nature Methods paper: "A public genome-scale lentiviral expression library of human ORFs." (DOI: 10.1038/nmeth.1638). A pooled version of the library is also available for screening purposes.

Additional Services

Packaging of researcher supplied retro- or lentiviral constructs

The Roswell Park/UB shRNA Resource can help with all your retro- and lentivirus packaging. Viral supernatants can be produced from ecotropic, amphotropic, or polytropic retro- or lentiviral DNA constructs provided by the researcher.

Mycoplasma detection testing:

PCR based Mycoplasma testing using the Agilent Mycoplasma Plus PCR Primer Set is available for monitoring of cell cultures. The presence of contaminant mycoplasma can be detected accurately and rapidly in a cost-effective manner.

GENE TARGETING & TRANSGENIC (GeTT) Shared Resource

LEADER

Aimee Stablewski, PhD
Director
Medical Research Complex M-312A
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aimee.stablewski@roswellpark.org

OVERVIEW

The mission of the Gene Targeting and Transgenic Shared Resource (GeTT) at Roswell Park Comprehensive Cancer Center is to ensure investigators can mimic and analyze disease in vivo by creating genetically modified mouse models. These models allow investigators to conduct research that can lead to new discoveries and treatments against cancer. To obtain these mouse models, our team uses highly specialized instrumentation and expertise not available in most labs.

Dr. Stablewski provides guidance to investigators from the earliest planning stages of the project when constructs or guide RNAs are designed to advanced stages of the project during phenotype analysis. Resource staff members perform the specialized mouse embryonic stem cell and/or embryo manipulation methods to generate the genetically modified models.

During the past 24 years, the facility has provided more than 1,500 novel genetically engineered mouse models as well as human and mouse cell lines for faculty members. Our services created novel mutants through gene knockouts and transgenics through various strategies, including those via embryonic stem (ES) cell modification and pronuclear injection, as well as more recently established CRISPR/Cas9-, adeno-associated virus (AAV)- and lentivirus-mediated technologies. The GeTT has assisted in the development of unique mouse models in the areas of prostate, breast, bladder, and pancreatic cancers, which has significantly facilitated mechanistic studies of tumor development and progression.

Use of the resource continues to increase with the ongoing recruitment into the Tumor Immunology and Immunotherapy, Cancer Stress Biology, and Developmental Therapeutics programs. Projects requiring the development of genetically modified mouse models increasingly are becoming relevant to validate in vitro findings, especially considering high- throughput clinical-based findings.

As such, the GeTT observed an increasing trend in the use of the resource by clinical researchers as well as basic scientists.

USING THE RESOURCE

Please contact Aimee Stablewski at 716-845-5843 or Aimee.Stablewski@RoswellPark.org for a project specific cost estimate.

SERVICES

Transgenics

Transgenic injection (various strain backgrounds)

The GeTT will harvest and inject the pronuclei of oocytes with DNA prepared and purified by the investigator or the GeTT (whichever is chosen). Surviving eggs will be implanted in pseudopregnant females, and pups born will

SERVICES (cont'd)

undergo tail biopsy for isolation of DNA and will also be identified by an ear tag. The GeTT guarantees that at least 100 eggs will be surgically transferred, or three transgenic offspring will be produced (whichever comes first).
Note: The expression of your gene is not guaranteed.

Gene Targeting

Upon receiving your lab's DNA construct, the GeTT will perform an electroporation of your DNA into W4 (129S6/SVEvTac), G4 (129/B6) or JM8A3.N1 (C57BL/6Tac) mouse embryonic stem cells. Colonies will be selected with the appropriate drug, depending on your positive selectable marker. Colonies also can be negatively selected for enrichment purposes. Selection methods should be discussed with the resource prior to the electroporation date to prepare the necessary feeder cells.

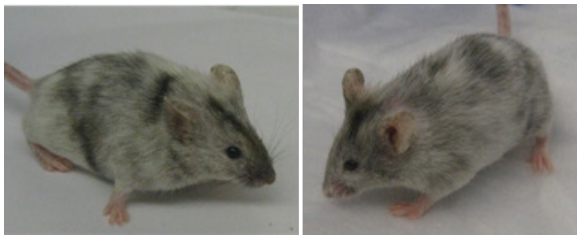
The resource will pick and freeze ~240 colonies, of which we will give the investigator's lab ~200 DNA preps. The investigator will screen these clones by Southern analysis and/or PCR and notify the resource of the positives for homologous recombination. The facility will expand five of these clones and give the investigator DNA again to reconfirm positives. When reconfirmed, the resource can begin blastocyst microinjections for the investigator's laboratory.

The entire electroporation process takes approximately one month, and the resource expects the investigator's lab to perform the positive confirmations in a timely fashion.

Chimeric Mice

Blastocyst microinjection with your ES cells generated in-house or by a collaborator
The GeTT will harvest blastocysts from C57BL/6 mice (currently C57BL/6 albino mice from the Jackson Laboratory) and inject the appropriate number of ES cells/blastocyst (either provided by the investigator or generated in our facility (If not generated in our resource, you must submit a Mycoplasma Pathology Report and IMPACT testing from IDEXX RADIL with your cell line or we can submit your cell line for testing, which will incur additional charges).

Injected blastocysts will then be implanted into pseudopregnant females. The GeTT guarantees that at least 20 blastocysts will be successfully injected and implanted into foster mice or three chimeric pups will be produced, whichever comes first.



Blastocyst microinjection with KOMP/EUCOMM ES cells
The procedure will be similar as aforementioned.

Rederivation to generate specific pathogen free mice

Frozen or fresh embryos
The GeTT will rederive strains from fresh or frozen embryos at the request of an investigator. The resource will also work with investigators to rederive lines from dirty facilities into the clean facilities here at Roswell Park. In this situation, arrangements will need to be made with the resource regarding where the mice are currently housed and how the resource will receive embryos for transfer.

In vitro fertilization
Embryos will be created and then rederived as above. Please see IVF for details.

Embryo and sperm cryopreservation

Cryopreservation of sperm
Two male mice between the ages of 10-16 weeks are needed to perform this service. We will freeze down 20 straws worth of sperm and will store them in liquid nitrogen. A post-thaw viability check and an in vitro fertilization (IVF) to the 2-cell stage will be performed on one of the straws to determine fertilization rate.

Sperm cryopreservation presents several important benefits:

- Substantially reduce the number of mice in an investigator's colony.
- Sperm collected from a single male can potentially give rise to large numbers of offspring following IVF of oocytes. A large cohort of mice via IVF can give an investigator age-matched and sex-matched progeny that are

SERVICES (cont'd)

sometimes needed for experimental cohorts and can help to generate the number of mice needed when there are multiple alleles needed in the mouse.

- The disadvantage of sperm cryopreservation is that monoploid genome is preserved. The sperm cryopreservation service does not guarantee recovery to live born by IVF, and for some strains ICSI is required for recovery. Sperm counts, motility and morphology will be analyzed before cryopreservation.

Cryopreservation of embryos

Our professional staff will determine the quantity of embryos to cryopreserve and the most efficient procedure for embryo collections. In vitro quality control to indicate the success of cryopreservation is performed on every batch of embryos.

Embryo collections can be done in one of two ways:

- Traditional mating, collection and freezing: Specifically, stud males are mated weekly with egg donors per cryopreservation session to produce embryos for cryopreservation. On average, it takes two to four embryo collection sessions to freeze down enough embryos to guarantee recovery in this traditional way. If using homozygous mutant males, fewer sessions will be needed. However, it may take more sessions if the mouse strain has a low superovulation rate, the stud males have low fertility, or males are too old. Some strains cannot be successfully cryopreserved. The investigator is responsible for providing all stud males, embryo donors and per diem costs for these animals. Females will be superovulated by the GeTT facility and mated with males, and the resulting embryos will be harvested and cryopreserved. This procedure will be repeated until a sufficient number of embryos are cryopreserved. Embryos are isolated and cryopreserved in straws and stored in liquid nitrogen.

- IVF, collection and freezing: Females will be superovulated by the GeTT, and embryos will be created through IVF with frozen or fresh sperm. Embryos will be cryopreserved at the 2-cell stage. This procedure will be repeated until a sufficient number of embryos are cryopreserved. This usually should only take one session, but sometimes a second is needed. Embryos are cryopreserved in straws and stored in liquid nitrogen.

In Vitro Fertilization

Mouse in Vitro Fertilization (IVF)

This procedure can be used to rapidly expand lines from as little as one male that carries the desired genotype or to maintain strains with poor breeding efficiency. The GeTT will superovulate egg donors per session. We will perform IVF with sperm from your male and egg donors.

After overnight culture, two-cell embryos will be transferred to pseudopregnant females the following day (unless specified for freezing). All weaned pups will be transferred to the investigator. We expect the investigator to genotype the pups and determine which pups have the desired genotype(s). IVF results vary according to genotype, strain background and the quality of individual males used for IVF. Thus, we cannot offer a guarantee that any given IVF procedure will produce large number of pups.

The GeTT has three sizes of IVF: small, medium and large. We are able to produce up to 100 or more animals at a time if needed.

New ES cell derivation

The GeTT will prepare new mouse ES cell lines from blastocysts or mice provided by investigators. Standard methods employing serum-containing medium and MEK1 inhibitor are used. The success rate of this procedure is high provided blastocysts can be obtained from the strain in question. ES cells provide an endless supply of cells for in vitro studies because ES cells do not undergo senescence and cease division as do other cell types (e.g., fibroblasts).

Advance notice should be given, preferably when the future blastocyst donors are obtained. The ideal age for in-house blastocyst donors for superovulation response is 24-28 days for C57BL/6 background.

SERVICES (cont'd)

Karyotyping

The GeTT can provide basic chromosome counting. Mouse ES cells, from either your lab or purchased, will be expanded in our facility, frozen down and screened for chromosomal abnormalities via karyotyping.

Subcloning

In certain instances, mouse embryonic stem cells are found to be aneuploid (greater than or less than 40 chromosomes). Aneuploid ES cells might generate chimeras; however, they will never be transmitted through the germline. If you have an aneuploid ES cell clone, it may be possible to rescue that clone by plating it at a low density and picking subclones that would be diploid, and thus transmit through the germline.

CRISPR/Cas9-based genome editing

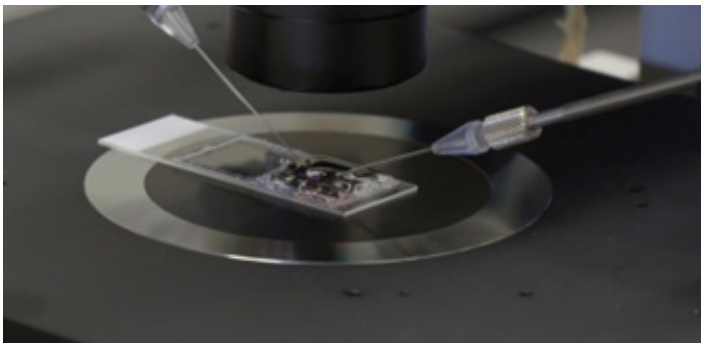
CRISPR genome editing in animals

CRISPR/Cas9 is a powerful genome-editing tool that is redefining the boundaries of biological research. The GeTT is pleased to introduce a full CRISPR-based gene-editing platform to modify your mouse genome to introduce global knockouts, small amino acid substitutions or other small tag knockins as well as larger gene fusions, reporter mice and conditional allele knockins. We have had more than 200 projects since 2013.

Design and production of your guide RNA and oligos: The GeTT will work with you to design the reagents needed for a successful project or design the entire project for you.

CRISPR electroporation used for global knockouts, small DNA deletions/insertions/replacements for base changes amino acid substitutions, and etc. (≤200bp), large chromosomal deletions, inversions and translocations): The GeTT will harvest and electroporate fertilized oocytes with CRISPR reagents. The RNA/protein complex (called an RNP complex) with or without donor DNA are concurrently electroporated and handled with the utmost care to prevent degradation. DNA and RNA are prepared and purified by the GeTT. Surviving eggs will be implanted in pseudopregnant females, and pups born will undergo tail biopsy for isolation of DNA and will also be identified by an ear tag.

CRISPR one-cell injection (used for larger DNA insertions (>500bp): The GeTT will harvest and inject fertilized oocytes with CRISPR reagents. The RNA/protein complex (called an RNP complex) with or without donor DNA are concurrently injected into one-cell embryos and handled with the utmost care to prevent degradation.



Targeting DNA with homologous arms can be co-injected to direct integration/homologous recombination to that site. DNA and RNA are prepared and purified by the GeTT. Surviving eggs will be implanted in pseudopregnant females, and pups born will undergo tail biopsy for isolation of DNA and will also be identified by an ear tag.

The GeTT highly suggests getting targeted next-generation sequencing (NGS) done on the founder and F1 animals resulting from CRISPR injections/electroporations, as mosaicism is always a concern.

CRISPR genome editing in cells

The GeTT provides services to investigators interested in CRISPR-mediated genome editing of cultured cells to generate cellular models as research tools. Our facility possesses the extensive expertise and technologies for such tasks. The types of genetic alterations we can generate include null alleles (KO) and insertion of a reporter cassette (KI), as well as correction of mutations, which can be particularly useful for developing isogenic control cells. We have established an efficient and full-service protocol for these types of need. We will provide free consultation at the beginning of a project. An outline of the experimental steps and the associated cost will then be emailed to the PI before initiation of the experiment. Afterwards, the PI will receive genetically modified polyclonal cells or individually cloned cells.

GENOMICS (GSR)
Shared Resource

LEADERS

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TECHNICAL CONTACTS

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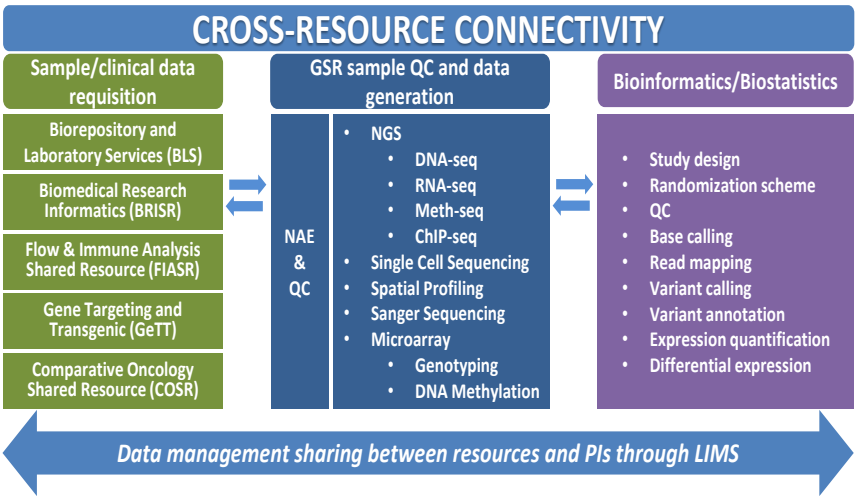
OVERVIEW

The Genomics Shared Resource (GSR) offers sample-to-data genomics services, with expert technical staff performing all aspects of sample preparation, quality control, assay design, and analysis. Our long-standing history and contribution to the Human Genome Program through clone generation, high throughput mapping, array technology development, and distribution of these resources worldwide provides a track record documenting our expertise. The GSR is a state-of-the-art facility that utilizes a variety of genomic platforms to accommodate any size request, and all processes are monitored using a Laboratory Information Management System (LIMS) to ensure high-quality reproducible data. The GSR offers a full spectrum of services, including Next Generation Sequencing (NGS), single-cell sequencing, spatial transcriptomics, Genome-wide SNP and copy number analysis, DNA methylation, and Sanger sequencing. We currently house state-of-the-art Illumina NovaSeq 6000, NextSeq500, NextSeq 2000 and MiSeq sequencers necessary for carrying out NGS projects. The GSR has extensive collaborations with investigators at Roswell Park as well as external users carrying out projects using NGS as well as other companion technologies such as Illumina Microarrays, Sanger sequencing, and 10X Genomics platform for single cell sequencing and spatial profiling.

At the institutional level, the GSR interacts with other shared resources such as the Biostatistics and Bioinformatics Shared Resource and the Biorepository and Laboratory Services Shared Resource facilitate the high-throughput sample-to-data pipelines with archival samples and prospective cohorts for investigator-initiated projects. Fundamentally, this synergy of GSR and other shared resources has created a streamlined full-service approach for projects conceptualized by the investigators regarding experimental design, sample preparation, library construction, data analysis and interpretation, integration, and storage, as well as the pursuit of follow-up validation experiments to confirm novel scientific findings.



USING THE RESOURCE

Investigators interested in using the facility that would like to discuss scheduling, procedures, quotes, and pricing should contact Dr. Prashant Singh or call 716-845-3869. The GSR is located in the CGP, first floor, L1-120. Hours of operation are weekdays, 8:00 AM – 5:00 PM.

SERVICES

The GSR offers investigators a full spectrum of genomics services. These include:

- Project consultation: Experimental design, platform, budgeting, and bioinformatics analysis are discussed.
- Sample preparation: DNA/RNA extraction from various sample types including cells, tissue, formalin-fixed, paraffin-embedded (FFPE) samples, saliva, blood, peripheral blood mononuclear cells (PBMC), cell-free DNA (cfDNA), plasma, fecal samples, etc. DNA/RNA QC using Qubit and Agilent TapeStation/Bioanalyzer.
- Next-generation sequencing (NGS): Whole genome sequencing (WGS), whole-exome-seq (WES), RNA-seq, Whole Genome Bisulfite Sequencing (WGBS), Reduced Representation Bisulfite Sequencing (RRBS), Chromatin Immunoprecipitation sequencing (ChIP-Seq), ATAC-seq (Assay of Transposase Accessible Chromatin sequencing), small RNA-seq (miRNA), microbiome (16S, 18S, meta-genome, and meta-transcriptome), immune profiling (TCR and BCR), as well as a myriad of boutique techniques to support various types of investigator driven initiatives.
- Illumina Infinium SNP and methylation arrays: Single-nucleotide polymorphism (SNP)/copy umber variation (CNV) and methylation arrays (human and mouse) using Illumina BeadChip technology on Illumina iScan.
- Single-cell sequencing and spatial profiling: The GSR uses the 10x Genomics Chromium X and Parse Biosciences to support different types of scRNA-seq assays (3' and 5' gene expression, immune profiling, multiomics, ATAC-seq, and CRISPR screens). Spatial profiling applications are performed using 10X Visium.
- Validation technologies: qPCR, Cell Line Authentication, and Sanger sequencing.

EQUIPMENT & TECHNOLOGIES

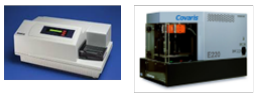
Next-generation sequencing (NGS): NovaSeq 6000, NextSeq 500, and MiSeq; Microarray: Illumina iScan; Single-cell RNA sequencing (scRNA-seq): 10X Genomics Chromium X; Targeted validation technologies: ABI 3500 sanger sequencers; ABI QuantStudio 6 Flex Real-Time PCR System; Ancillary Equipment: Qubit, Spectrophotometer, TapeStation 4200, Covaris E220; Lab Automation: Agilent Bravo, Tecan Infinium Automation system, Caliper Sciclone NGS workstation, Opentrons OT-2 Lab Robot, QIAcube Connect.

Nucleic Acid Extraction & QC

DNA/RNA extraction
-Tissue, FFPE, Cells, blood, plasma (cfDNA), saliva, buccal swabs etc.
Microbiome
-Feces, tissue, and saliva
Quality Control
-Qubit, TapeStation

Bioanalyzer TapeStation Qubit

Spextromax Covaris

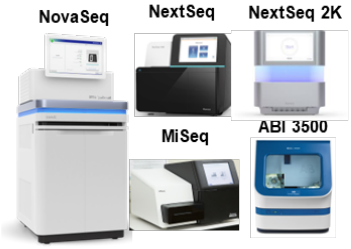


Sequencing

Next Generation Sequencing
- RNA-seq
- Whole Genome (WGS)
- Whole Exome (WES)
- Methylation (WGBS, RRBS)
- Metagenome (16s, meta-GEX, meta-genome)

-EpiGen: ChIP, ATAC, cut&run
Sanger Sequencing
- Sanger Sequencing
- Fragment Analysis

NovaSeq NextSeq NextSeq 2K MiSeq ABI 3500

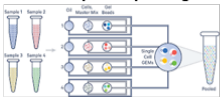


Single cell and spatial profiling

Single cell transcriptomics
-Gene Expression Profiling
-CRISPR Screening
-Gene & Cell Surface Protein
-Immune Profiling
-On-Chip Multiplexing (OCM)
Single cell epigenomics
-Chromatin Accessibility (ATAC-seq)
-Multiome - GEX+ATAC-seq
Spatial transcriptomics
-10x Visium

Chromium X 10X Visium

On-Chip Multiplexing



Companion Technologies

Illumina iScan
-SNP arrays
-Methylation arrays
Real time PCR
-TaqMan: GEX, SNP
-SYBR GEX
Lab Automation
-Agilent Bravo
-Tecan Infinium System
-QIACube

iScan Quant 6

QIACube Bravo

cGMP ENGINEERING & MANUFACTURING FACILITY (GEM)
Shared Resource

LEADERS

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Senior Vice President, Industry Partnerships
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Brian Betts, MD
Medical Director
Vice Chair of Strategic Initiatives
Cancer Cell Center C-521C
Ph: 716-845-5525
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OVERVIEW

The mission of cGMP Engineering and Cell Manufacturing Facility (GEM) is to enable scientific innovation from research to development through the finest talent & technology. Established to address the growing demand for Good Manufacturing Practice (GMP) manufacturing of cell and gene therapies, our state-of-the-art facility continues to evolve to meet the needs of this rapidly expanding field.

To support this mission, we have expanded our infrastructure from six clean rooms to a total of 20, providing the capacity to manage not only academic investigator-initiated projects but also collaborative research, development, and manufacturing partnerships with industry leaders. These enhanced capabilities allow us to support the entire spectrum of cell therapy research and clinical trials, from early-phase discovery to late-stage clinical development.

Our vision is to be leaders in developing and manufacturing innovative processes for curative therapies. By building strategic partnerships with innovators in the cell and gene therapy field, we aim to enhance the impact of our work on Roswell Park's research and clinical trials. We are committed to continuous investment in infrastructure and expertise to deliver exceptional results for clinical trials at all stages.

Through these efforts, the GEM Facility strives to be a global leader in developing and manufacturing cell therapies, positively transforming patients' lives locally and worldwide.

USING THE RESOURCE

Clients interested in collaborating with Roswell Park and using the facility should contact Dr. Choi to discuss the business process and scheduling. The cGMP facility is in the Cancer Cell Center, 5th floor, Room C-521D. General hours of operation are weekdays, 8:00 AM – 5:00 PM.

SERVICES

At Roswell Park, we pride ourselves in providing high-quality clinical-grade cell therapy and viral vector manufacturing services for phase I and II clinical trials. Our state-of-the-art facilities have the latest technology and infrastructure for tech transfer, manufacturing, storage, warehousing, analytical method development, quality control testing, and more. Our experienced team of experts ensures that all quality systems and procedures are in place to deliver clinical-grade material and meet regulatory compliance requirements.

We have deep expertise and specialize in the development, scale-up, and manufacturing of cell and gene therapies, including CAR-T, engineered TCRs, Dendritic Cell Vaccines, TILs, and viral vectors. As a full-service one-stop-shop for research, development, and manufacturing facility, we are committed to delivering innovative solutions and providing a comprehensive cell therapy portfolio to meet the unique needs of our clients.

SERVICES (cont'd)

With a local network of dedicated, clinical GMP manufacturing facilities located at Roswell Park in Buffalo, NY, we are poised to meet the demands of our clients and the rapidly expanding cell and gene therapy market. Choose Roswell Park GMP facility as your innovative and reliable partner in advanced therapeutics.

INSTRUMENTATION / SOFTWARE / EQUIPMENT

We are procuring equipment, and the equipment that is in the procurement process is listed below.

Cell Fractionation Equipment

1. CliniMACS Plus by Miltenyi Biotec
2. Prodigy by Miltenyi Biotec
3. CTS Dynamag Magnet by Fisher Scientific

CliniMACS Plus

Prodigy

CTS Dynamag

Gene Engineering Equipment

1. MaxCyte GTx

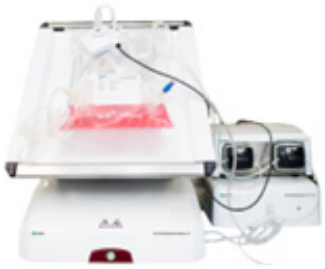
MaxCyte

Cell Expansion Equipment

1. Prodigy by Miltenyi Biotec
2. Cocoon Platform by Lonza
3. Cytiva Xuri by Cytiva
4. TSCD II Sterile Tube Welder by Thermo Fisher Scientific

Prodigy

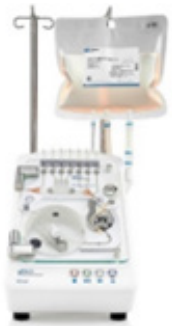
Cocoon



Xuri

Cell Wash / Volume Reduction Equipment

1. CTS Rotea from Thermo Fisher Scientific
2. Automated Cell Processing System (wash and volume reduction) from Lovo
3. Sepax from Cytiva



CTS Rotea

Lovo

Sepax

HEALTH COMMUNICATIONS (HCR)
Shared Resource

LEADERS

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Rodney C. Haring, PhD, MSW
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OVERVIEW

The Health Communications Resource (HCR) is a full-service video and media production unit specializing in health communications. Our work extends both locally, nationally and internationally. HCR is based out of Roswell Park Comprehensive Cancer Center, a National Cancer Institute-designated cancer center, and helps investigators, institutions, community health advocates and non-governmental organizations educate the public about important health-related matters. One area of focus is motivating target audiences to advocate for their health, by creating effective, salient and emotive media and creating a shift in attitudes and behaviors to help promote healthier communities.

LEADERSHIP

Paul Hage, MFA serves as Lead Project Manager and Co-Director of the Health Communications Resource (HCR) since it was established in 2009. He has Master of Fine Arts degree in Documentary Film/Digital Media from at University at Buffalo, and a BSc degree in Television, Radio, Film production from Newhouse Communications School, Syracuse University, and has been a Roswell employee since 2008. He also holds an adjunct faculty position at the University at Buffalo Department of Community Health & Health Behavior, and SUNY Fredonia Department of Communications.

Rodney Haring, PhD, MSW serves as Co-Director of Health Communications Resource (2023) and Director of the Roswell Park Center for Indigenous Cancer Research and Services. He holds a PhD in Social Welfare and a Master's in Social Work. Film production and directing background includes support from NIH, foundations, and the private sector for health communication media film, vignettes, and video shorts. Mainstream media collaborations in film and TV include "the War that Made America" a PBS – docudrama, and collaborative effort with the award-winning Tribeca Film titled, "Catch the Fair One" (2021)- a movie on Murdered and Missing Indigenous Women and Children. He has also partnered with Indigenous dance theatre companies in areas of health, wellness, trauma, and resilience. Dr. Haring is a master wood carver with Indigenous art displays featured at the Buffalo Museum of Science, Seneca-Iroquois National Museum, and the University of California, Fullerton.

USING THE RESOURCE

Investigators interested using the facility should contact HCR's Executive Secretary, Linda Thompson, to schedule an appointment with our Co-Directors to discuss quotes, pricing, and inquiries.
Ph: 716-845-8130
Email: linda.thompson@roswellpark.org
Website: https://vimeo.com/channels/healthcommunications

SERVICES

Services are designed for inter-departmental and inter-center collaborations and externally for universities, cancer centers, health centers and community-based health organizations. We can create research/study highlight reels, service vignettes, facility overview videos, cancer prevention and public outreach campaigns, full documentary films, health conference media, recruitment and dissemination videos, translational science videos and other health science-related digital media. As a non-profit entity, HCR can provide exceptional, professional media services that can accommodate most budgets.

Pre-Production

- Subject matter expertise in cancer and health-related topics
- Health media campaign planning and assistance
- Housed in Roswell Park Comprehensive Cancer Center, an NCI-designated cancer center
- Scriptwriting and creative direction and assistance
- Storyboarding
- Location scouting, research and coordination
- Consultation and direction on all aspects of desired media products

Production

- 4K or higher video production
- Conduct interviews, and record narration
- Multi-camera studio and field production
- Professional lighting and audio
- Coordination of production personnel anywhere geographically
- Studio-staging area for production
- Green screen, multiple backdrops

Post-Production

- Editing of video footage into a professional finalized media product
- Full audio and narration recording, plus cinematic sound design when applicable
- Custom and original music composition and arrangement available
- Social media assistance by providing multiple file formats for uploading

NOTABLE PROJECTS

HCR has created videos utilized by the World Health Organization, Native American Indian Education Association of New York, World Cardiology Congress, University of British Columbia, International Tobacco Control Project, Global Smokefree Partnership, NCI SPRINT Initiative, NY State Department of Health, NY State Smokefree Coalitions, Roswell Park Cessation Services, NY State Smokers Quitline, Flight Attendant Medical Research Foundation, and Americans for Non-Smokers Rights Foundation, Roswell Park Center for Indigenous Cancer Research.

- Haring, R, & Hage, P (Videographer/Producer/Editor). (2024) Films for Indigenous Cancer Health: Films for Indigenous Cancer Health. Roswell Park Comprehensive Cancer Center.
- Hage, P (Producer) & PhD, Haring, R (Producer) (2023) Colonoscopy Screening PSA: video research study. In collaboration with the University at Buffalo. PIs are Heather Orom, PhD, and Natasha Allard.
- Haring, R, & Hage, P (Videographer/Producer/Editor). (2023) NAIEA/NY 2023: Native American Indian Education Association. Roswell Park Comprehensive Cancer Center.
- Hage, P & Haring, R (Videographer/Producer/Editor). (2023) ARCH/CICR High School Summer Internship: ARCH Summer Internship Program. Roswell Park Comprehensive Cancer Center.
- Haring, R (Producer) (2023) & Hage, P (Producer). The Silent Genomes Project: research study video. HCR was hired by the University of British Columbia, Dr. Laura Arbour PI (Principal Investigator) to create this video.
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INVESTIGATIONAL DRUG SERVICE (IDS)
Shared Resource

LEADER

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OVERVIEW

The Investigational Drug Service (IDS) plays a critical role in Roswell Park research. IDS staff members are responsible for all aspects of investigational drug management, including accountability, ordering, receiving, destruction, returns, proper storage and dispensing. IDS pharmacists provide medication counseling for patients enrolled in clinical research studies. They also provide medication reconciliation for patients in screening for a research study, and this is documented in the electronic medical record (EMR). The number and complexity of research studies, especially Phase I studies, were the driving forces behind the creation of IDS by the Department of Pharmacy and the Clinical Protocol and Data Management (CPDM) office.

Responsibilities of IDS staff include study review for SRC and IRB submission, review of amendments and amended investigator brochures, study implementation, dispensing and sterile products preparation, and clinical services such as medication review and patient counseling. An IDS staff member is also involved with implementation of Investigator-Initiated studies in the Roswell Park Clinical Research Network. IDS staff members provide expert consultation for each clinical research study utilizing pharmaceutical products.

USING THE RESOURCE

Investigators should contact Kathy Galus for details. Utilization of IDS resources is prioritized as follows: First priority for use is given to peer-review-funded Roswell Park CCSG members; second priority to non-peer-review-funded CCSG members; third priority to non-members and academic collaborators; and last priority to external users. The IDS is located in the Grace Cancer Drug Center. Hours of operations are weekdays, 7:30 AM – 4:30 PM.

SERVICES

- Medication reconciliation for study eligibility
- Medication review for possible interactions with study drug
- Patient counseling
- Inventory control and maintenance
- Review of proposed investigator initiated study prior to submission to ensure medication section is appropriate for implementation

nSight™ & Imagine™ Data Discovery Resource

LEADERS

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OVERVIEW

nSight™ is a data discovery platform provided by the Research Information Technology department. This powerful system is made available for complimentary use by all Roswell Park staff who possess the requisite CITI training certifications. The core mission of the nSight™ initiative is to enable Roswell researchers with real-time access to vital clinical, research, and regulatory data, thereby facilitating their research endeavors. With its diverse range of capabilities, the platform serves various purposes, including research feasibility assessment, grant proposal preparation, poster creation, and clinical trial population design, among others. Imagine™ is an advanced add-on to the nSight™ suite, designed to empower users in exploring radiographic imaging data for machine learning experiments. The product features integrated DICOM viewing capabilities and robust image segmentation pipelines, streamlining workflows for research and analysis.

SERVICES

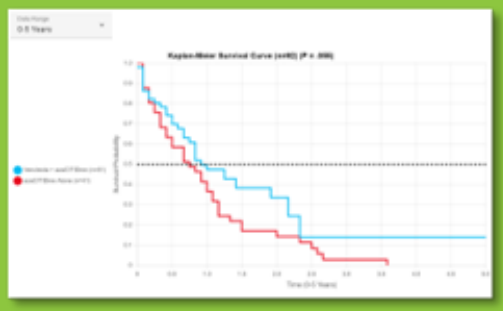
All services are provided via the power of the remarkable nSight™ data portal, where all services are conveniently consolidated for seamless accessibility. Within this cutting-edge platform, users are empowered to conduct targeted searches for desired cases, utilizing a wide range of factors such as disease type, treatment modality, and biospecimen characteristics. The Imagine™ add-on enhances the nSight™ suite by enabling users to effortlessly examine CT scans associated with queries, create tailored image cohorts, execute advanced segmentation routines, and explore detailed radiomic statistical outputs using pyradiomics – all within a unified, intuitive platform. Unlocking a world of advanced analysis possibilities, nSight™ equips users with the ability to delve deeper into their research by facilitating the exploration of comparison groups. With user-friendly features and comprehensive statistical outputs, including characteristic tables with p-values and captivating Kaplan Meier survival curves, researchers can unravel invaluable insights and glean meaningful conclusions from their data.

USING THE RESOURCE

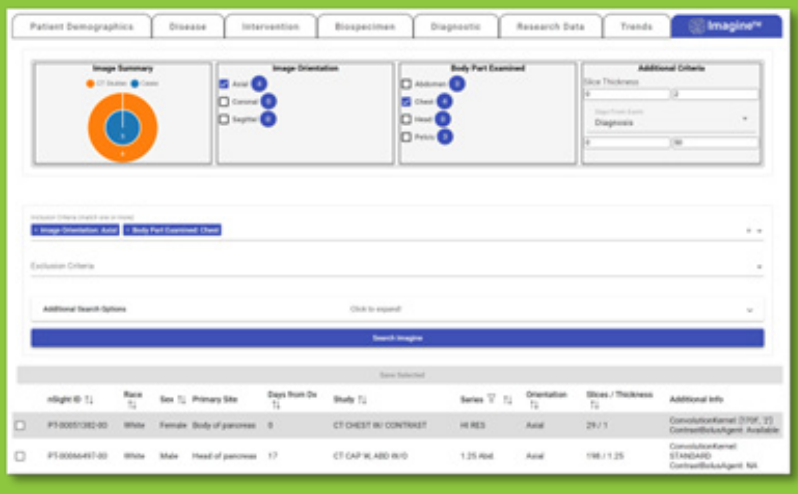
Investigators may request access to nSight™ via the following link: page: nSight Access Request (roswellpark.org)

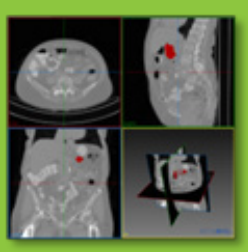
Once access is gained, users can access the resource via: nSight ™ (roswellpark.org)


Patient Demographics
Disease
Intervention
Biospecimen
Diagnostic
Research Data
Trends
Sex
Hispanic
Treated at Roswell
Alcohol Use
Tobacco Use
Race
Patient Status
Age at Diagnosis




Case Trends


Patient Demographics
Disease
Intervention
Biospecimen
Diagnostic
Research Data
Trends
Imagine™
Image Summary
Image Orientation
Body Part Examined
Additional Criteria
Exclusion Criteria
Additional Search Options
Search Imagine



NICOTINE & TOBACCO PRODUCT ASSESSMENT (NICOTAR)
Shared Resource

LEADERS

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OVERVIEW

The Nicotine and Tobacco Product Assessment Resource (NicoTAR) provides comprehensive testing of tobacco, nicotine-containing, and cannabis products to determine the concentration of nicotine, THC, CBD, and various additives, toxicants, and carcinogens. In addition to product testing, NicoTAR provides analysis of biomarkers of tobacco and cannabis use and exposure to second- and third-hand tobacco and cannabis smoke, along with monitoring of indoor air pollution. The NicoTAR facility is equipped with systems for controlled exposure of cells and living tissue to tobacco and cannabis smoke and emissions from vaping devices. Facility personnel also provide NicoTAR services such as user training, data acquisition, processing, and interpretation.

USING THE RESOURCE

For those who wish to learn to run their own samples, training classes are available on an as-needed basis and can be arranged by contacting facility personnel (845-8603; NicoTAR@RoswellPark.org). To operate the instruments, a candidate will be instructed over several sessions by one of our operators. The successful candidate will then be allowed to operate under supervision until the operator deems him/her qualified to collect data alone.

NicoTAR director offices are located in Carlton House. Laboratory facilities are located in the Gratwick Basic Science Building. Hours of operation are weekdays 7:00 AM-4:00 PM.

SERVICES

NicoTAR provides a full spectrum of services for analyses of tobacco and cannabis products.
This resource provides biomarker and product testing as a paid service, as well as access to state of the art instrumentation. Investigators are encouraged to consult NicoTAR for pricing, grant documents and manuscript material.

LC-MS/MS Assays:

NicoTAR offers analysis of biomarkers of tobacco exposure from urine, serum, plasma, and saliva samples.

- Cotinine and other nicotine metabolites
- THC and CBD and their metabolites
- NNAL – a tobacco-specific biomarker
- Metabolites of VOCs – biomarkers of exposure to toxic combustion byproducts
- TSNAs – tobacco-specific nitrosamines in tobacco products

GC-Q-TOF Assays:

- Identification and quantification of flavorings used in various tobacco products
- Identification and quantification of terpenes present in various cannabis products

SERVICES (cont'd)

GC-MS Assays:

- Propylene glycol (PG) and Vegetable Glycerin (VG) quantification
- Identification of additives used in various tobacco products
- Quantification of cannabinoids in cannabis products (THC, CBD etc)

GC-NPD Assays:

- Nicotine content in tobacco products
- Nicotine yields in Mainstream (MS) and Sidestream (SS) smoke
- Nicotine in environmental samples (secondhand exposure from air and thirdhand exposure from surfaces)

Atomic Absorption Spectroscopy (AAS):

- Analysis of metal content in tobacco and cannabis products as well as urine for the following metals.
- Cadmium
- Chromium
- Lead
- Nickle

Analysis of combustible tobacco and cannabis products, e-cigarettes, vaping devices, smokeless tobacco products, shisha, and Nicotine Replacement Therapy (NRT) products:

- Generation of emissions using smoking machines under standardized or customized puffing testing regiments
- Measuring of cigarette filter ventilation, pressure drop and cigarette paper porosity

In vitro and In vivo Exposure Models:

- Cytotoxicity assays using air liquid interface (ALI) and established cell lines
- Inhalation toxicity of tobacco and cannabis products using small animal exposure models

NicoTAR uses standardized methods (ISO, CORESTA) but we are fully prepared to adapt our routines to accommodate requests of our clients.

INSTRUMENTATION

- Agilent 6495 Tandem Mass Spectrometer with 1290 Chromatography System (LC-MS/MS)
- Sciex 6500+ Tandem Mass Spectrometer with Shimadzu LC-30 Chromatography System (LC-MS/MS)
- Waters Xevo TQ-XS Tandem Mass Spectrometer with ACQUITY UPLC I-Class Chromatography System (LC-MS/MS)
- Agilent Technologies 7890B Gas Chromatograph/ 7250 Quadrupole Time-of-Flight Mass Spectrometry (GC-QTOF)
- Agilent Technologies 7890B Gas Chromatograph/ 5977A Mass Spectrometer (GC-MS)
- Agilent Technologies 7890B Gas Chromatograph equipped with nitrogen-phosphorous detector (GC-NPD)
- Perkin-Elmer PinAAcle 900Z Graphite Furnace Atomic Absorption Spectrometer (AAS)
- Borgwaldt LX1 Single-Port Smoking Machines
- Borgwaldt S1000 Shisha Smoker
- Borgwaldt PV10 and KC-3 ventilation and pressure drop tester
- Cerulean PPM-1000 paper porosity tester
- 30-Port Automatic Cigarette and E-Cigarette Smoking Machine JB2090
- E-Cigarette Aerosol Generator ECAG

Please see our website for a full list of instrumentation.

ONSITE RESEARCH SUPPLY CENTER (ORSC) Shared Resource

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OVERVIEW

The Onsite Supply Center Shared Resource (ORSC) at Roswell Park offers everyone the opportunity to get the best pricing and turnaround time on products required for their research. There are no shipping or dry ice charges when ordering through the ORSC. The Supply Center Technician will track your orders upon request. There is a substantial amount of products on site, but non-stocked items may be ordered as well.

The ORSC carries commonly used products from Bio Rad, Integrated DNA Technologies, Invitrogen, Thermo Fischer Scientific, Gold Biotechnology, New England BioLabs, Krackeler Scientific, Sigma Aldrich, Corning and Qiagen. Providing these supplies and reagents on site saves time, reduces shipping costs and increases production in your lab.

USING THE RESOURCE

Investigators or lab leads should contact Gina Blasko at the above number or email her to establish a user account. The ordering procedure is easy. Hours of operations are weekdays, 7:30 AM – 4:30 PM. The ORSC is located in the Center for Genetics and Pharmacology (CGP) L1-218.

TRANSLATIONAL IMAGING (TISR)
Shared Resource

LEADERS

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OVERVIEW

The overall mission of the Translational Imaging Shared Resource (TISR) is to provide state-of-the-art preclinical and translational imaging services to investigators at Roswell Park Comprehensive Cancer Center in a time-efficient and cost-effective manner. The resource provides users access to advanced, non-invasive imaging modalities including magnetic resonance imaging (MRI), ultrasound (US), photoacoustic imaging (PAI), fluorescence and bioluminescence imaging (FI/BLI). The resource is led by two PhD faculty with extensive experience in preclinical and clinical imaging, and is the only shared resource within 200 miles of Buffalo that allows for multimodal anatomic and functional imaging of small and large animal models of disease.

TISR currently supports the research of over 50 Roswell Park and University at Buffalo (UB) faculty who are conducting basic and translational investigations in oncology, radiology, tumor biology and cancer therapeutics.

The objectives of TISR are to:
Aim 1: Provide Roswell Park investigators with access to state-of-the-art in vivo imaging technologies.
Aim 2: Develop customized imaging protocols and quantitative image analysis schemes to conduct preclinical trials of experimental therapeutics in small and large animal models of cancer.
Aim 3: Establish a technology platform that facilitates clinical translation of imaging methods for improved disease detection and therapy monitoring in patients.

These objectives are accomplished through formal policies that have been established within the resource to create a structured environment that ensures prioritization of projects while providing equitable access to cancer center members. TISR staff members closely interact with investigators from the planning stages of projects to provide input into study design and provide continuous feedback during the conduct of research studies to ensure that reliable, high-quality scientific data is generated in a timely manner. The resource provides cancer center members 24/7 access to and training in the application of non-invasive imaging technologies for their research needs.

USING THE RESOURCE

TISR directors meet with interested faculty, free of charge, to discuss project objectives. This consultation helps assure the use of appropriate imaging modalities, proper study design, and cost-effective use of resources.

The operational work flow for investigators interested in utilizing TISR services is as follows: The investigator (or the personnel from his/her lab) directs initial inquiries to either Dr. Seshadri or Dr. Spernyak. A brief summary of the research goals of the project are provided for review. An initial meeting is held with the investigator during which the feasibility of the project and the overall research plan are discussed. The investigator is also notified of the resource service charges associated with the use the imaging instrumentation. Once deemed feasible, a formal service request form that includes all pertinent information (animal protocols, laboratory personnel dedicated for the project, grant/funding) is completed by the investigator. The investigator is requested to amend his/her IACUC protocol to include the resource service protocol for imaging procedures. Following IACUC approval, users are

provided access (swipe card access to the resource, resource user account; access to resource schedule) to the resource and added to the user base. Lab personnel will undergo training on use of the instrumentation prior to the start of the actual experimental study. Protocols on data acquisition, SOPs on instrumentation and additional training modules are provided to users. Resource members interact closely with investigator/lab personnel throughout this process to ensure smooth and efficient workflow.

Investigators interested in exploring the use of imaging for their research should direct their inquiries to Dr. Seshadri or Dr. Spernyak by email or phone.

SERVICES

Imaging Services

Services provided by TISR to cancer center members can briefly be summarized as follows:

- Access to imaging technology
- Expert consultation for study design and execution of preclinical imaging studies
- Multimodal image acquisition and analysis
- Development of customized image analysis, image co-registration and visualization schemes
- Assistance with manuscript and grant preparation
- Assistance with IACUC protocol submission and approval
- Training and education.

Anatomic Imaging

- Multimodality imaging of tumor growth in vivo (MRI, BLI, FI, µCT)
- Evaluation of metastatic tumors in vivo (liver, lungs, brain, spleen) (MRI, µCT, BLI, FI)
- Assessment of chemotherapeutic efficacy (MRI, US, BLI)
- Genetic phenotyping (MRI, µCT)
-

Functional Imaging

- Dynamic contrast enhanced (DCE) and macromolecular contrast media (MMCM) imaging for assessment of relative tumor vascular volume and permeability (MRI)
- Microbubble-enabled tumor/tissue blood flow (US)
- Tumor/tissue oxygenation and hemoglobin content (PAI)
- Cardiac Function (US, MRI, µCT)
- Diffusion-weighted MR imaging of tumor cell kill following treatment (MRI)
- Heteronuclear in vivo MR spectroscopy and chemical shift imaging (MRI)
- Angiography and quantitative flow measurements (MRI, US)
- Genetic expression via use of marker proteins, e.g. luciferase (BLI, FI)

Additional services

- Development of labeled therapeutic and/or diagnostic agents (Gd-based, iron-based agents; CEST imaging; 19F labeled as well as fluorescent probes)
- Physiologic monitoring of cardiac ECG signal
- Customized image processing and quantitative analysis of digital data

IMAGING TECHNOLOGIES / INSTRUMENTATION

Presently, TISR's imaging armamentarium includes a 7T MR scanner (obtained through a $2 million S10 award in 2021), an ultrasound/photoacoustic imaging system (obtained through an S10 award in 2012), a Xenogen Spectrum bioluminescence and fluorescence imaging system (obtained through an S10 award in 2013), a IVIS 50 bioluminescence imaging system, and a cabinet X-ray system.

- **Magnetic Resonance Imaging:** The "workhorse" for TISR is a 7 Tesla preclinical MRI scanner operating on the latest ParaVision 360 acquisition platform. It features a fixed gradient set (112 mm ID) for whole body mouse or rat imaging with upgraded 300A amplifiers for sub-second echo planer imaging or <50 µM planer resolution.

There are 4 parallel receive channels for accelerated 1H imaging and a broadband transmit/receive RF channel for X-nuclei spectroscopy/imaging. TISR has several body volume coils ranging from 23-86mm ID, mouse and rat brain arrays and several surface coils for high SNR localized imaging.

- **An MR compatible animal monitoring & gating system** (Model 1030, SAII Instruments, Stony Brook, NY), which allows for the monitoring of body temperature, ECG signal, and respiratory rate of anesthetized animals, as well as providing warm air heating for anesthetized animals undergoing MR imaging.

- **Optical imaging systems:** TISR currently operates multiple Xenogen systems for bioluminescence imaging of small animals. In 2013, an S10 Shared Instrumentation grant was awarded to TISR to an IVIS Spectrum, dual bioluminescence/fluorescence imaging system (Perkin-Elmer). The Spectrum system features a thermoelectrically-cooled charge-coupled device (CCD) camera capable of simultaneous imaging of 5 mice. A 24-position filter wheel featuring 18 emission filters (500-840 nm, 20 nm band pass) is situated in front of the camera for spectral unmixing capabilities. A laser galvanometer provides surface topography and alignment capabilities. An older IVIS-50 capable of imaging 3 mice simultaneously is available for select studies as well.

- **A preclinical µCT system (Quantum GXII, Perkin-Elmer):** with adjustable physical magnification for both large FOV and/or high resolution imaging and support for imaging medium sized animals (e.g. rabbit, guinea pig. The system features a micro-focus X-Ray source: 90 kVp, 8W, a CMOS based flat panel detector: 50 µm pixel pitch with high readout speed, 14-bit range and GPU accelerated image reconstruction. These allow low-dose and high-throughput with scan times as low as 8s. Alternatively, high-resolution, ex-vivo images with voxel sizes down to 4.5 µm are achievable. Intrinsic, retrospective dual phase respiratory and cardiac gating is available, as is turn-key co-registration with datasets acquired on the IVIS® Spectrum optical imaging system.

- **Ultrasound/Photoacoustic Imaging system:** The US/Photoacoustic Micro Imaging system (VevoLAZR; VisualSonics Inc. Toronto, Ontario) system is based on linear array technology developed by VisualSonics and enables collection of photoacoustic and ultrasound imaging datasets on the same plane, thereby enabling co-registration of structural and functional information on the tissues of interest. The VevoLAZR system provides an integrated, compact and safe platform for in vivo imaging of morphology and microvascular dynamics of tumors in 2D and 3D. Combined use of PA mode imaging along with B-mode imaging gives both structural information on tumor morphology and functional information on tumor blood flow and oxygenation. Studies routinely utilize US for monitoring tumor growth and for image-guided interventional procedures to establish tumors in orthotopic sites (e.g. lungs, salivary glands, prostate).

- **Software/Computational resources:** The resource has numerous 64-bit multicore/multi-processor Windows-based graphics workstations all featuring at least 8 GB memory, including a workstation with 16 GB RAM for processing of large datasets. The resource maintains 5 network licenses of Analyze 14.0 (biomedical image processing software) that provides a versatile tool chest of medical image processing modules including: volumetric and intensity quantification of 2D/3D/4D image datasets, three-dimensional volume rendering, and object/cell counting. It also maintains an annual service contract for MATLAB (Mathworks) including the Image Processing and 6 additional toolboxes for programming of customized image processing routines, available on every computer within the facility. Lastly, the facility maintains 1 fixed-node license of visualization software Amira installed on a graphics workstation for 2D/3D quantification, visualization & animation. Additional open-source analysis packages such as 3D Slicer and Python are also available.

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- Bolookat ER, Vincent-Chong VK, Rich LJ, Singh AK, Seshadri M. Ultrasound-Guided Photoacoustic Imaging of Salivary Gland Hemodynamics in Rabbits. Photonics. 2024;11(3):273. PMID: doi:10.3390/photonics11030273.
- Benzekry S, Mastri M, Nicolo C, Ebos JML. Machine-learning and mechanistic modeling of metastatic breast cancer after neoadjuvant treatment. PLoS Comput Biol. 2024;20(5):e1012088. PMID: 38701089; PMCID:PMC11095706.
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- Yan L, Su Y, Hsia I, Xu Y, Vincent-Chong VK, Mojica W, Seshadri M, Zhao R, Wu Y. Delivery of anti-microRNA-21 by lung-targeted liposomes for pulmonary fibrosis treatment. Mol Ther Nucleic Acids. 2023 Jun 13;32:36-47.. PMID: 36919116; PMCID: PMC9972768.
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