ROSWELL PARK
COMPREHENSIVE CANCER CENTER

Shared RESOURCES GUIDEBOOK 2023

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 22 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.

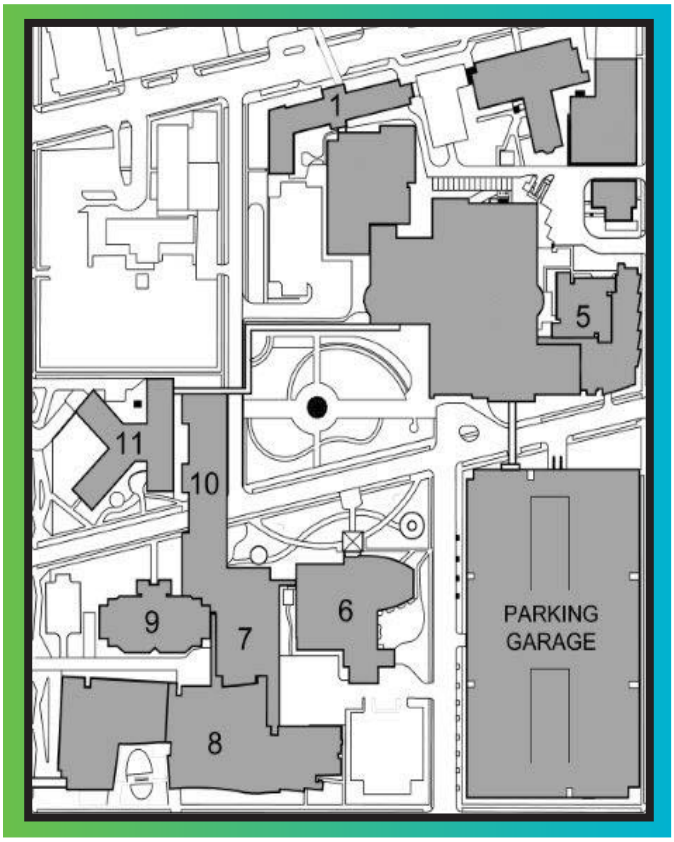
The Shared Resources Guidebook at Roswell Park is intended to orient institute faculty to the currently available scientific shared resources at Roswell Park. The services outlined are financially supported by a variety of mechanisms including an NCI Cancer Center Support Grant, chargebacks and importantly, 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

2023



#	Building Name	Shared RESOURCES	Floor
1	Gratwick Basic Science Building (GBSB)	Hematologic Procurement Pathology Network Clinical Research Laboratory Services Nicotine & Tobacco Product Assessment Data Bank & BioRepository Translational Immuno-Oncology • Vector Development Production Facility	6 6 6 3 7 6
5	Grace Cancer Drug Center (GCDC)	Investigational Drug Services	4
6	Research Studies Center (RSC)	Shared Resources Management Office Bioinformatics Biomedical Research Informatics Biostatistics & Statistical Genomics Scientific Editing & Research Communications Core	2 4 4 4 3
7/10	Medical Research Complex (MRC)	Advanced Tissue Imaging Comparative Oncology Experimental Tumor Models Gene Targeting & Transgenic	3 2 4 3
8	Center for Genetics & Pharmacology (CGP)	Bioanalytics, Metabolomics & Pharamacokinetics Gene Modulation Genomics Onsite Research Supply Center Drug Development Core	1 2 1 1 1
9	Cancer Cell Center (CCC)	cGMP Facility - Center for Immunotherapy Flow & Immune Analysis Translational Immuno-Oncology • Therapeutic Cell Production Facility Translational Imaging	2 & 5 3 4 1
11	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.

Shared RESOURCES TABLE OF CONTENTS 2023

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. Additionally, our new acquisition of the NanoString GeoMX Digital Spatial Profiler expands our research opportunities to the novel field of spatial genomics, offering whole transcriptum and RNA sequencing while preserving the morphological integrity.

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.

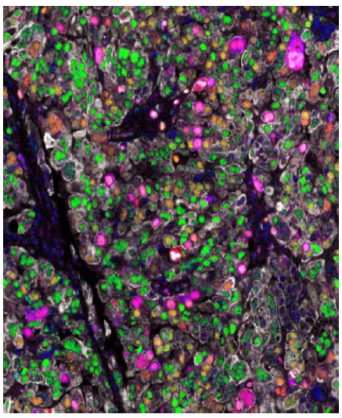
USING THE RESOURCE

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

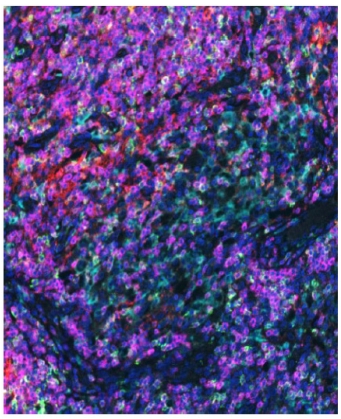
SERVICES

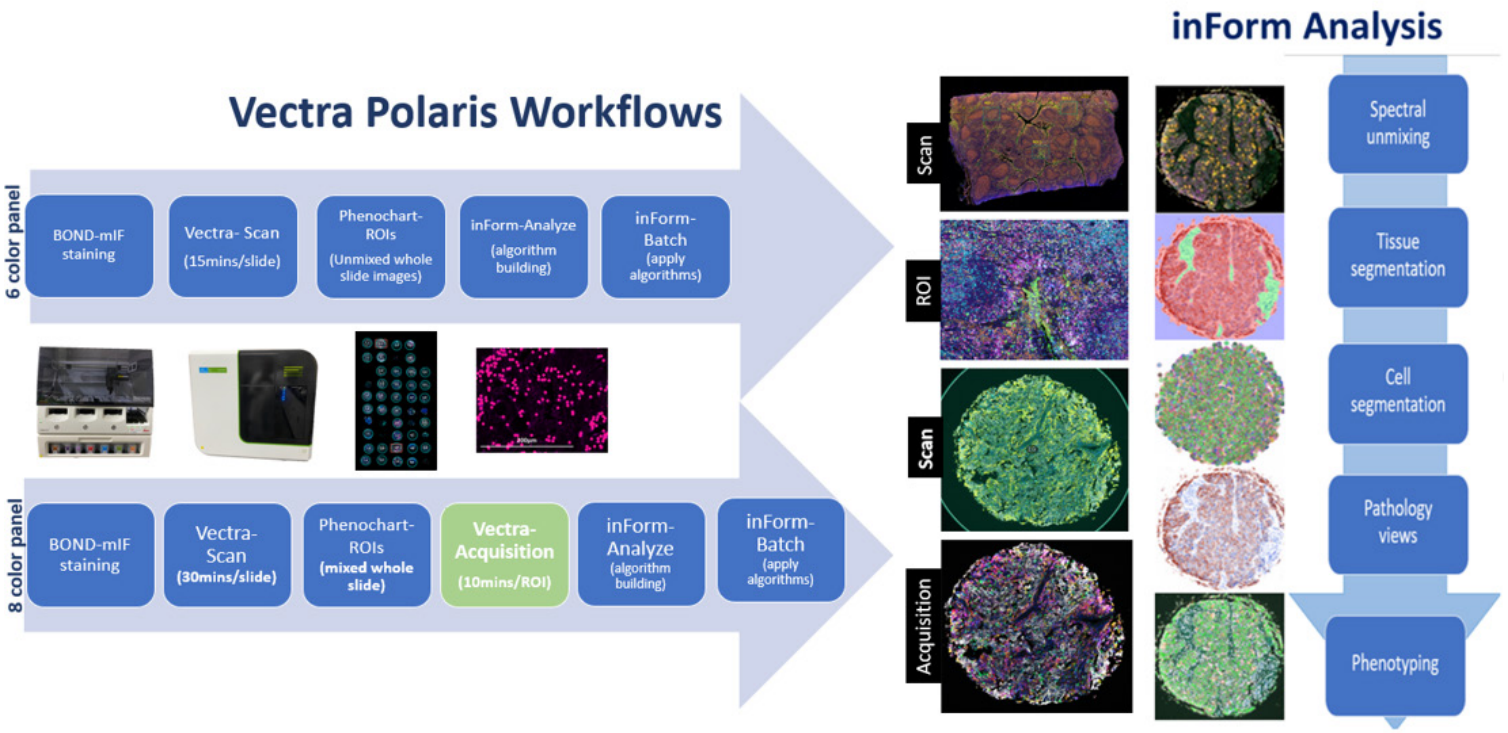
Custom panels are available upon request. ATISR requires any biomarkers to have a commercially available IHC validated antibody for panel inclusion. Panels can consist of six (6) or eight (8) biomarkers plus DAPI.

Hu Cell Cycle
MCM2
pRB
RB
CCNA
CCND1
CCNE
pHH3
AE1AE3



Hu Immune
CD3
CD8
CD163
PD-1
PD-L1
OX40
FOXP3
AE1AE3





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. This resource is used in the optimization and staining of vectra panels, as well as the initial staining step of the RNA assays used for the NanoString DSP.

BOND RXm IHC Academic Research Stainer (leicabiosystems.com)

AKOYA PhenoImager HT (formerly Vectra Polaris)

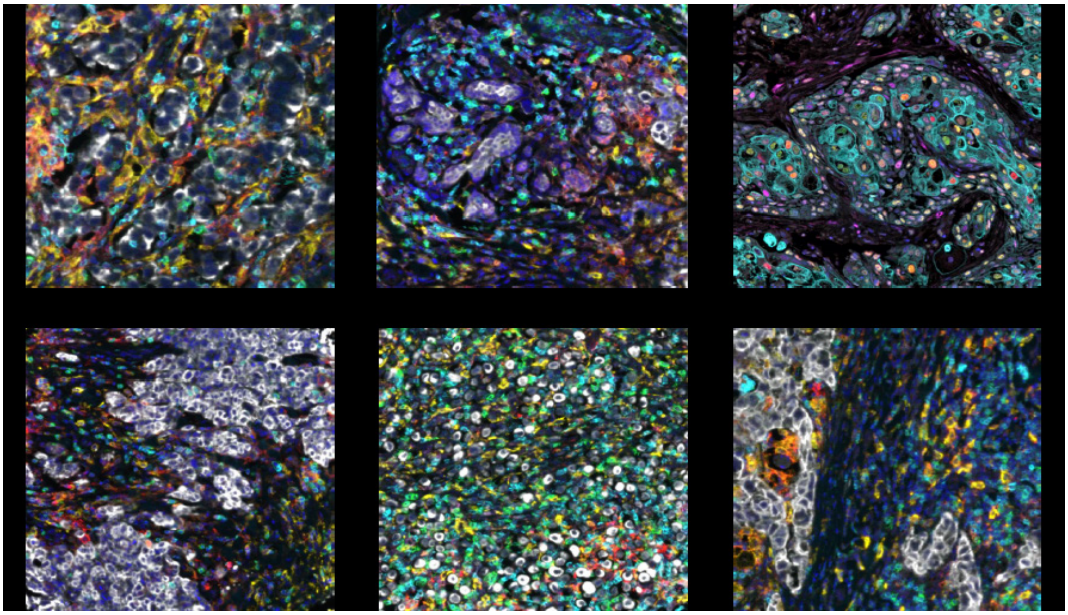
This anatomical scanner delivers high throughput images from both brightfield and multispectral fluorescent staining. It allows for full slide unmixed images for 6 plex fluorescent panels. In addition, we can expand panels to 8 plex and deliver unmixed annotated regions of interest (ROI).

PhenoImager HT | Akoya Biosciences

NanoString GeoMX Digital Spatial Profiler (DSP)

This digital spatial profiler has the capability to run both mouse and human whole transcriptome assays (WTA) or human cancer transcriptome assay (CTA) on FFPE tissue, while retaining morphological context of the tissue. Tissue is stained with basic morphology markers to identify tumor and stroma and then ROIs are selected by the investigator, with guidance from our pathologist. Once the UV cleavable tags have been retrieved from the ROI and sequenced read counts from that specific ROI are available for analysis.

GeoMx DSP Spatial Genomics Overview | NanoString



Representative images from optimized panels

NOTABLE PROJECTS

1. Knudsen ES, Kumarasamy V, Chung S, Ruiz A, Vail P, Tzetzo S, Wu J, Nambiar R, Sivinski J, Chauhan SS, Seshadri M, Abrams SI, Wang J, Witkiewicz AK. Targeting dual signaling pathways in concert with immune checkpoints for the treatment of pancreatic cancer. Gut. 2021 Jan;70(1):127-138. doi: 10.1136/gutjnl-2020-321000. Epub 2020 May 18. PMID: 32424005; PMCID: PMC7671951.
2. Gandhi S, Pandey MR, Attwood K, Ji W, Witkiewicz AK, Knudsen ES, Allen C, Tario JD, Wallace PK, Cedeno CD, Levis M, Stack S, Funchain P, Drabick JJ, Bucsek MJ, Puzanov I, Mohammadpour H, Repasky EA, Ernstoff MS. Phase I Clinical Trial of Combination Propranolol and Pembrolizumab in Locally Advanced and Metastatic Melanoma: Safety, Tolerability, and Preliminary Evidence of Antitumor Activity. Clin Cancer Res. 2021 Jan 1;27(1):87-95. doi: 10.1158/1078-0432.CCR-20-2381. Epub 2020 Oct 30. PMID: 33127652; PMCID: PMC7785669.
3. Kumarasamy V, Vail P, Nambiar R, Witkiewicz AK, Knudsen ES. Functional Determinants of Cell Cycle Plasticity and Sensitivity to CDK4/6 Inhibition. Cancer Res. 2021;81(5):1347-60 PMID: 33323381; PMCID: PMC8026500.
4. Fountzilas C, Bajor DL, Mukherjee S, Saltzman J, Witkiewicz AK, Maguire O, Minderman H, Nambiar R, Rosenheck HR, Knudsen ES, Muhitch JB, Abrams SI, Wang C, Hutson AD, Attwood K, Hicks KA, Jurcevic JA, Kalinski P, Iyer R, Boland PM. Phase Ib/II Study of Cetuximab plus Pembrolizumab in Patients with Advanced RAS Wild-Type Colorectal Cancer. Clin Cancer Res. 2021 Dec 15;27(24):6726-6736. doi: 10.1158/1078-0432.CCR-21-1650. Epub 2021 Oct 13. PMID: 34645646.
5. Pearson JD, Huang K, Pacal M, McCurdy SR, Lu S, Aubry A, Yu T, Wadosky KM, Zhang L, Wang T, Gregorieff A, Ahmad M, Dimaras H, Langille E, Cole SPC, Monnier PP, Lok BH, Tsao MS, Akeno N, Schramek D, Wikenheiser-Brokamp KA, Knudsen ES, Witkiewicz AK, Wrana JL, Goodrich DW, Bremner R. Binary pancancer classes with distinct vulnerabilities defined by pro- or anti-cancer YAP/TEAD activity. Cancer Cell. 2021;39(8):1115-34 e12. PMID: 34270926; PMCID: PMC8981970.
6. Kumarasamy V, Nambiar R, Wang J, Rosenheck H, Witkiewicz AK, Knudsen ES. RB loss determines selective resistance and novel vulnerabilities in ER-positive breast cancer models. Oncogene. 2022 Jul;41(27):3524-3538. doi: 10.1038/s41388-022-02362-2. Epub 2022 Jun 9. PMID: 35676324.
7. Knudsen ES, Kumarasamy V, Nambiar R, Pearson JD, Vail P, Rosenheck H, Wang J, Eng K, Bremner R, Schramek D, Rubin SM, Welm AL, Witkiewicz AK. CDK/cyclin dependencies define extreme cancer cell-cycle heterogeneity and collateral vulnerabilities. Cell Rep. 2022 Mar 1;38(9):110448. doi: 10.1016/j.celrep.2022.110448. PMID: 35235778; PMCID: PMC9022184.
8. Hamad SH, Montgomery SA, Simon JM, Bowman BM, Spainhower KB, Murphy RM, Knudsen ES, Fenton SE, Randell SH, Holt JR, Hayes DN, Witkiewicz AK, Oliver TG, Major MB, Weissman BE. TP53, CDKN2A/P16, and NFE2L2/NRF2 regulate the incidence of pure- and combined-small cell lung cancer in mice. Oncogene. 2022 Jun;41(25):3423-3432. doi: 10.1038/s41388-022-02348-0. Epub 2022 May 16. Erratum in: Oncogene. 2022 Sep;41(39):4485. PMID: 35577980.
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10. Mohammadpour H, Tsuji T, MacDonald CR, Sarow JL, Rosenheck H, Daneshmandi S, Choi JE, Qiu J, Matsuzaki J, Witkiewicz AK, Attwood K, Blazar BR, Odunsi K, Repasky EA, McCarthy PL. Galectin-3 expression in donor T cells reduces GvHD severity and lethality after allogeneic hematopoietic cell transplantation. Cell Rep. 2023 Mar 15;42(3):112250. doi: 10.1016/j.celrep.2023.112250. Epub ahead of print. PMID: 36924493.
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12. Shipra Gandhi, Mateusz Opyrchal, Melissa J. Grimm, Ronald T. Slomba, Kathleen M. Kokolus, Agnieszka Witkiewicz, Kristopher M. Attwood, Adrienne Groman, Lauren Williams, Mary Lynne Tarquini, Paul K. Wallace, Kah Teong Soh, Hans Minderman, Orla Maguire, Tracey L. O'Connor, Amy P. Early, Ellis G. Levine, and Pawel Kalinski. Systemic Infusion of TLR3-Ligand and IFNα Reprograms Local Breast Tumor Microenvironments for Selective CTL Influx, in submission.

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.

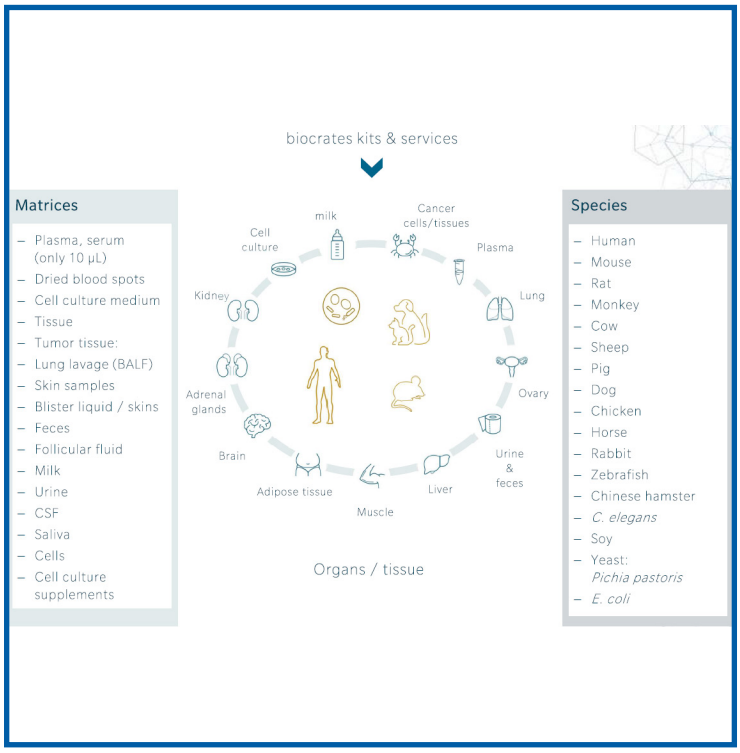
Examples of assays the BMPK provides include:

- **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.



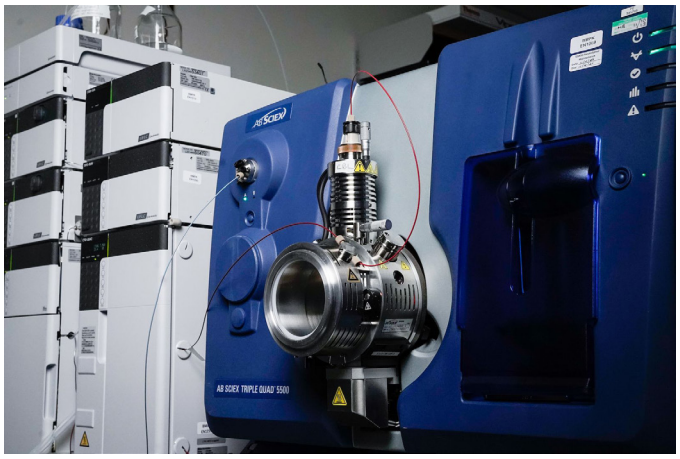
SERVICES (cont'd)

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.

INSTRUMENTATION & SOFTWARE

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

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, Jacobi JJ, Long MD, Affronti HC, Rowsam AM, Smiraglia DJ. JAZF1: A Metabolic Regulator of Sensitivity to a Polyamine-Targeted Therapy. Mol Cancer Res. 2023 Jan 3;21(1):24-35. PMCID: PMC9808368.

Dai T, Rosario SR, Katsuta E, Sawant Dessai A, Paterson EJ, Novickis AT, Cortes Gomez E, Zhu B, Liu S, Wang H, Abrams SI, Seshadri M, Bshara W, Dasgupta S. Hypoxic activation of PFKFB4 in breast tumor microenvironment shapes metabolic and cellular plasticity to accentuate metastatic competence. Cell Rep. 2022 Dec 6;41(10):111756. PMCID: PMC9807018.

Rosario SR, Smith RJ Jr, Patnaik SK, Liu S, Barbi J, Yendamuri S. Altered acetyl-CoA metabolism presents a new potential immunotherapy target in the obese lung microenvironment. Cancer Metab. 2022 Oct 26;10(1):17. PMCID: PMC9598035.

Jin R, Forbes C, Miller NL, Strand D, Case T, Cates JM, Kim HH, Wages P, Porter NA, Mantione KM, Burke S, Mohler JL, Matusik RJ. Glucocorticoids are induced while dihydrotestosterone levels are suppressed in 5-alpha reductase inhibitor treated human benign prostate hyperplasia patients. Prostate. 2022 Oct;82(14):1378-1388. Epub 2022 Jul 12. PMCID: PMC9427722.

NOTABLE PROJECTS (cont'd)

Fountzilas C, Adjei A, Opyrchal M, Evans R, Ghasemi M, Attwood K, Groman A, Bshara W, Goey AKL, Wilton J, Ma WW, Iyer R. A phase 1 study of the ALK inhibitor ceritinib in combination with gemcitabine-based chemotherapy in patients with advanced solid tumors. Int J Cancer. 2021 Dec 15;149(12):2063-2074. PMID: 34319586.

Burke SM, Kamal M, Goey AKL. Development and Validation of a Quantitative LC-MS/MS Method for CDK4/6 Inhibitors Palbociclib, Ribociclib, Abemaciclib, and Abemaciclib-M2 in Human Plasma. Ther Drug Monit. 2023 Jun 1;45(3):327–336. PMCID: PMC10175095.

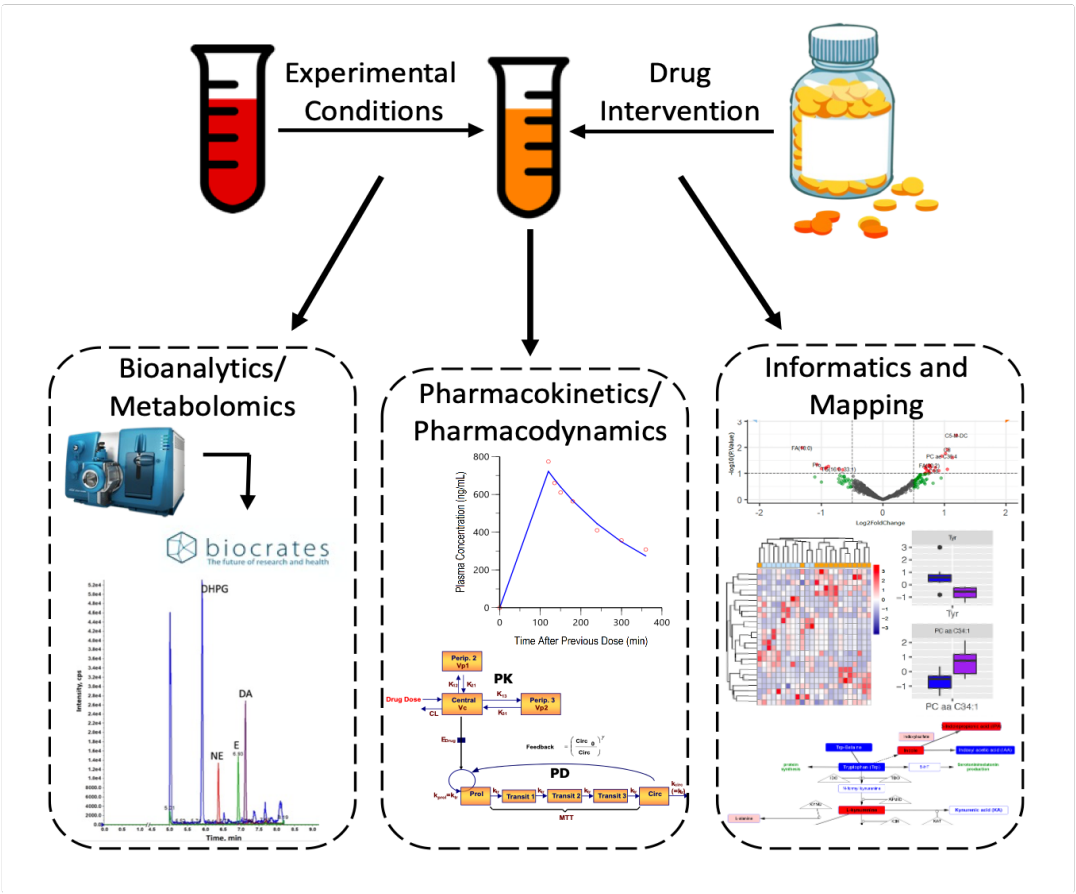
Harding JJ, Kelley RK, Tan B, Capanu M, Do GK, Shia J, Chou JF, Ferrer CS, Boussayoud C, Muenkel K, Yarmohammadi H, El Dika I, Khalil DN, Ruiz C, Rodriguez-Lee M, Kuhn P, Wilton J, Iyer R, Abou-Alfa GK. Phase Ib Study of Enzalutamide with or Without Sorafenib in Patients with Advanced Hepatocellular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

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

LEADERS

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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).

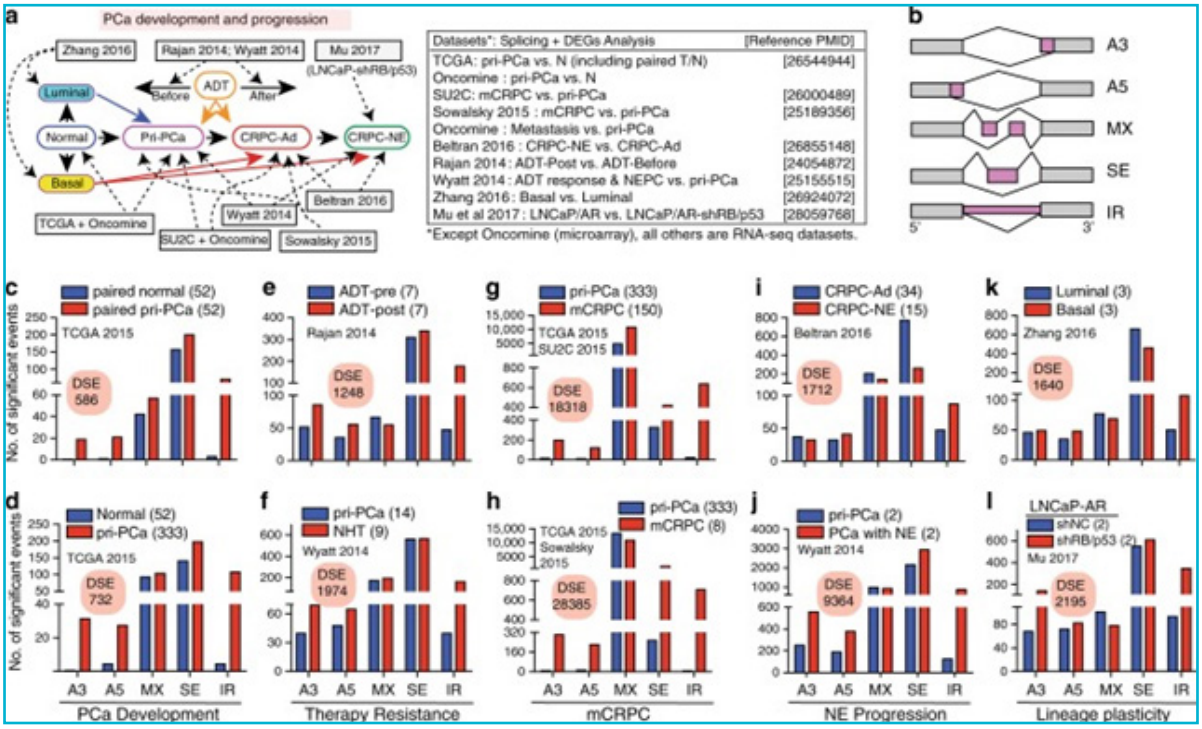
INSTRUMENTATION / SOFTWARE / EQUIPMENT

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.

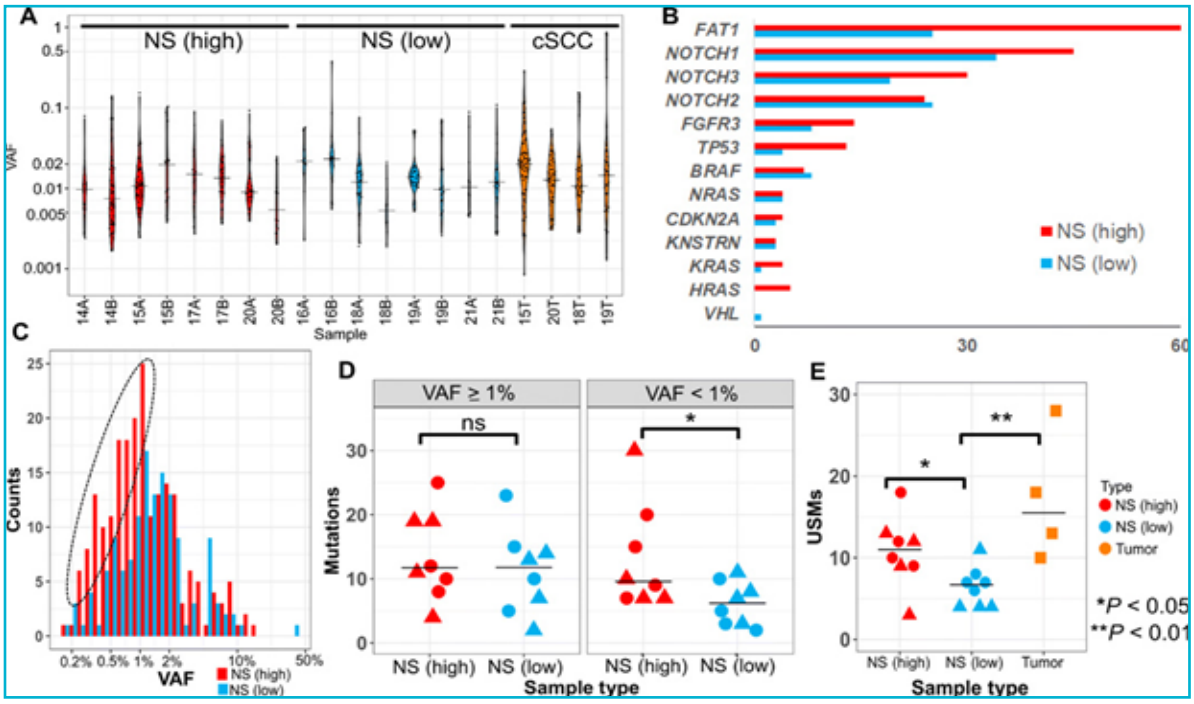
The BIOINF team has ready access to high-performance computing and dedicated high-performance storage provided by the University at Buffalo Center for Computational Research (CCR), a leading academic supercomputing facility with more than 2 PFlop/s of peak performance compute capacity, to ensure that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

BIOSTATISTICAL & 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. Attwood 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

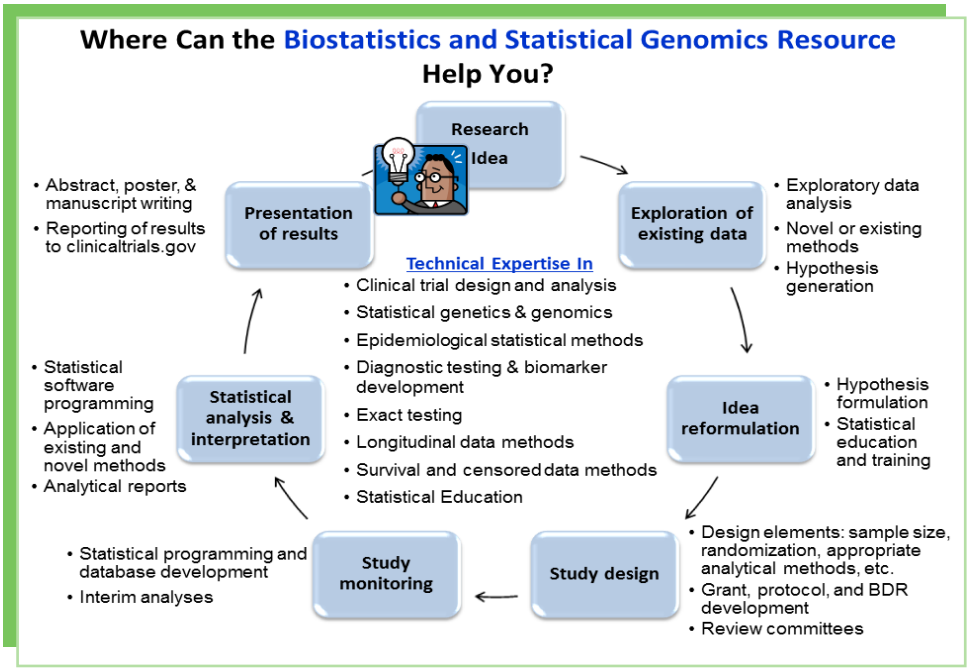
- Provide biostatistical support to basic, clinical, and population-oriented Roswell Park collaborators
- Exploratory data analysis
- Statistical methods sections for grants
- Protocol development (close working relationships with IT, CRS, and BRISR)
- Study design (pre-clinical experiments, observational 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 (R01CA267690) clinical trial of APL-2 in combination with both Bevacizumab and Pembrolizumab in patients with recurrent ovarian cancer and symptomatic malignant effusion. The trial investigators include Drs. Zsiros (Chair, Department of Gynecology) and Segal (Chair, Department of Internal Medicine). Dr. Attwood provided the novel study design (utilizing randomized safety lead-ins and imbalanced cohorts) and analytical plan for the grant submission and subsequent protocol.

NCI funded (R01CA262899) multi-ethnic high-throughput study to identify novel non-HLA genetic contributors to mortality after blood and marrow transplantation. Dr. 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.

COMPARATIVE ONCOLOGY (COSR)
Shared Resource

LEADERS

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ADMINISTRATIVE & TECHNICAL CONTACTS

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OVERVIEW

The Comparative Oncology Shared Resource (COSR [recently known as the Laboratory Animal Shared Resource]) facilitates basic, clinical and translational scientific research to all our investigators. Our mission is to promote the humane, responsible care and use of laboratory animals, that will take original scientific ideas from hopes, to treatments and cures. COSR is accredited by AAALAC International for both our program and facilities, demonstrating the 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 daily health observations, veterinary medical care, facility and equipment maintenance and surgical and technical services. The resource staff includes specialized veterinarians, 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) that take pride in offering professional, timely and high-quality service to support the research projects of cancer center members.

USING THE RESOURCE

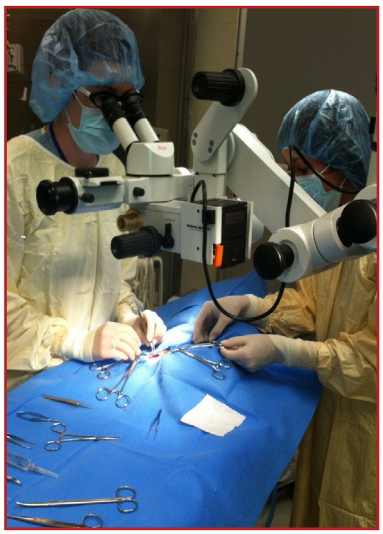
Services by COSR to investigators are prioritized in the following order: 1) CCSG members with peer-reviewed funding; 2) CCSG members with non-peer-reviewed funding; 3) Non-CCSG members; 4) External academic collaborators; and 5) External industry collaborators. Principal Investigators are encouraged to contact Dr. Sexton or Ms. Spierto for operational information and are advised on the process to use the COSR. The submission of a protocol to the Institute Animal Care and Use Committee (IACUC) is the first step in the process followed by staff training and assistance with the animal procedures following standard barrier guidelines to ensure the quality of the research. Research model orders from approved commercial vendors are placed on Workday and processed by our research service associate. To obtain mice from COSR mouse production colonies IN -House mouse colony purchase requisition form available on i2 should be submitted to COSR. Prior to initiating a lab animal research project, investigators are encouraged to discuss plans with COSR staff so that an appropriate animal care program, including suitable health surveillance, can be planned.

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

SERVICES

Services include:

- 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.
- Veterinary and Surgical Services: Diagnostic services such as health surveillance and animal health profile, 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. Sexton ext. 4463, Dr. Curtin ext.7621 or Dr. Minhyung Kim ext. 2974.**



- 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 principal investigators.

- Animal Imports/Exports: COSR has developed specialized standard operating procedures to expedite researcher needs for animal transfer between institutions, nationally and internationally. **Contact Dr. Sexton ext. 4463 or Robyn Wilkins, Import/Export Coordinator, ext. 5914 for required procedures.**
- Animal Receiving: All orders for animals from external sources must be processed through COSR. **Please submit purchase requisitions on Workday and research models will be ordered by Wendie Siminski ext. 3397.**
- Mouse Production: 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 managed mouse breeding colony contact the floor supervisor.

- COSR manages breeding colonies of immune competent strains (SCID's and NSG's) in addition COSR maintains an aging colony of C57BL/6 and BALB/c mice. **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. Sexton ext. 4463.**

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. COSR offers renal panels, liver panels, and comprehensive panels according to the researcher's needs.
- Tissues/Blood: Various tissues, blood and serum products from a number of species of laboratory animals may be available through COSR. **Contact Dr. Sexton at ext. 4463 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 animal 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

NOTABLE PROJECTS & CAPABILITIES

The 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, the COSR is actively involved in refinement of procedures that usually become new methods or innovations to accomplish the goals of proposed animal studies. The 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, the COSR interacts with other shared resources that are also dedicated to providing specific services using laboratory animals including the Translational Imaging Shared Resource (TISR), the Gene Targeting and Transgenic Shared Resource (GeTT), and the Experimental Tumor Model Shared Resource (ETM). This interaction streamlines the management of the member's projects and promotes centralization of services.

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

DATA BANK & BIOREPOSITORY (DBBR)
Shared Resource

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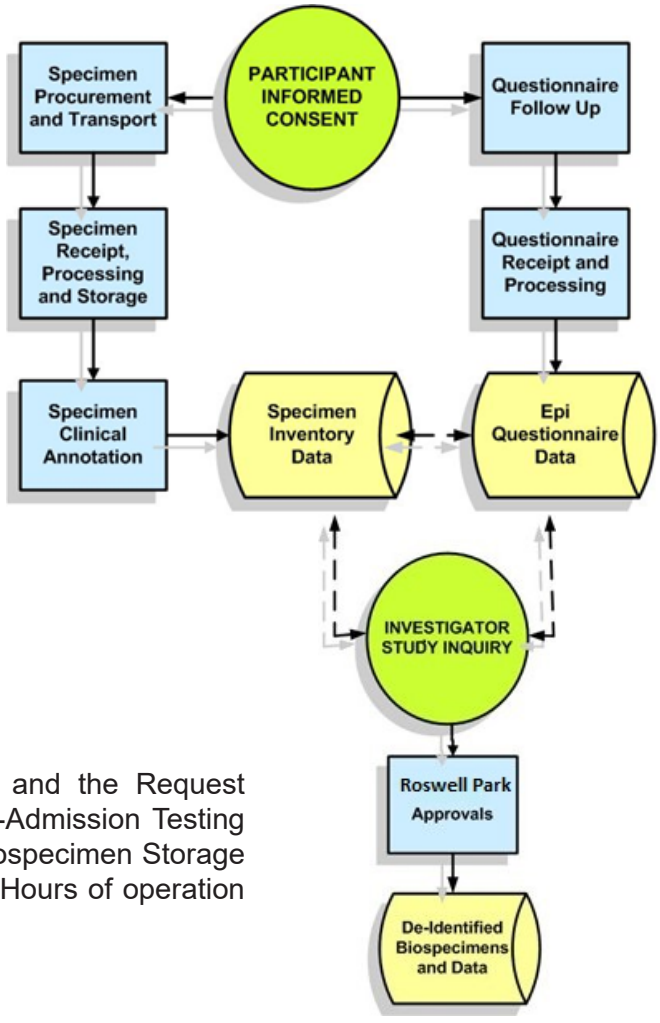
OVERVIEW

The mission of the Data Bank & BioRepository (DBBR) is to reduce the burden for Investigators conducting translational research by providing a comprehensive bank of biospecimens and data. Services include biospecimen inventory evaluation and study feasibility, incorporation of DBBR services in grants, protocols and publications, and associated study data management services.

Data and biospecimens (primarily serum, plasma, DNA, PBMC, buffy coat and whole blood) are donated by Roswell Park patients who have cancer or who are at risk for cancer. Non-patients are also welcome to volunteer as healthy controls. Data and samples are made available to investigators with protocols approved by the Roswell Park Institutional Review Board (IRB) for studies related to cancer prevention, etiology, detection, treatment and prognosis.



USING THE RESOURCE

DBBR Recruitment is located in the Main Hospital lobby and the Request Management Office is located in Carlton House. DBBR Pre-Admission Testing Services are located in the Main Hospital. Laboratory and Biospecimen Storage facilities are located in the Gratwick Basic Science Building. Hours of operation are weekdays 7:00 AM-5:30 PM.

USING THE RESOURCE

1. At the time of initial inquiry, investigators are asked to meet with or arrange a telephone call with DBBR Operations Director, Annmarie Nowak to:
- Review existing inventory or determine need for study specific collection
- Determine project time frame and develop cost estimate.

2. Submit a Biospecimen and Data Research (BDR) Protocol Application for the use of specimens and data.
- All samples and data provided by the DBBR are de-identified prior to release.
- The DBBR maintains the link between participants and their samples and data
- Roswell Park Cancer Center Support Grant Members with peer-reviewed funding are given top priority for requests, followed by Roswell Park investigators with newly developing programs, then external academic investigators with federal funding and finally commercial investigators. Cost recovery fees are tiered for these different groups of investigators.

SERVICES

Banked Biospecimens

The focus of the prospective bank is to collect blood samples from newly diagnosed patients prior to surgery or cytotoxic treatment. Patients who are post-treatment are also asked to participate based on identified future research needs. The DBBR recruitment staff work with outpatient clinical staff to identify and consent patients and coordinate sample collection for the bank. Blood samples are collected alongside existing clinical laboratory orders, and drawn by the phlebotomy service at Roswell Park. Family members and friends accompanying patients, as well as other visitors to Roswell Park are also asked to donate samples as controls. Control samples follow the same sample procurement and processing procedures as patient samples.

Every participant is asked to donate 30 mL of blood: one 10-ml non-heparinized red top tube (for serum and clot), and one 10-ml EDTA lavender top tube for plasma and buffy coat, and a second 10-ml EDTA lavender top tube (whole blood for DNA). The phlebotomist prints sample barcode labels for the blood collection tubes using the Roswell Park laboratory management system. This procedure produces an alert signaling the pending arrival of specimens for processing in the biorepository processing laboratory. Samples are sent from phlebotomy to the sample processing laboratory via pneumatic tube delivery system. **The standard time from collection to freeze for DBBR blood samples is one hour.**

Specimens are centrifuged and the supernatant is aliquoted into 2D barcoded Matrix tubes or cryovials. Aliquots include serum, plasma, and buffy coat (0.5 mL each) which are stored in a liquid nitrogen vapor. In addition, whole blood is aliquoted in 2 ml barcoded cryovials and stored at -80oC.

For specific studies and/or populations, blood is processed with density gradient separation techniques using SepMate Tubes (Stem Cell Inc). These cells are aliquoted into 2D barcoded matrix tubes and slow frozen before transferring to liquid nitrogen vapor for long term storage.

Genomic DNA is readily available from the extracted blood using Autogen XTRACT 16+ nucleic extractor which allows rapid extraction from up to 48 samples per day, a Qubit fluorometer from Thermofisher that facilitates accurate quantification and evaluation of double stranded DNA and a Janus liquid handling system from Perkin Elmer Life Sciences which is used to automate DNA quantification and distribution.

Study-Specific Procurement

The DBBR can prospectively collect material in a custom format at single or multiple time. Procurement, processing, and storage of additional sample type (PBMC, stool, urine, and other biospecimens) by request. Specific collection requests are carefully evaluated for feasibility and reviewed for approval by the DBBR Advisory Board and Translational Research Groups (TRGs).

Clinical and Epidemiological Data

Clinical data from the Rowell Park Cancer Registry are reviewed against the donor's Electronic Medical Record (EMR) for context, and linked to each qualifying biospecimen donated by cancer patients where applicable, in

SERVICES (cont'd)

addition to EMR abstraction for samples from high risk and benign patients. This efficient annotation approach minimizes duplication of effort and allows the clinical data to be associated to the original sample collection and each individual aliquot and to any derivative material from that sample in the biorepository.

Basic Sample Annotation (Linked from Cancer Registry and Abstracted by the DBBR)

- Demographics – participant age, sex, race, ethnicity
- Personal History of Cancer – status and sites
- Diagnosis – site, topography, morphology, tumor size, nodes
- Staging – Collaborative Stage, AJCC Stage, SEER Stage
- Surgery – procedure of the primary site
- Benign diagnoses (for benign-only patients) at the time of sample collection
- Prior history of cancer at the time of sample collection
- Treatment status at the time of sample collection

Extended Sample Annotation (Extracted from Cancer Registry at the Time of Request to Ensure Timeliness)

- Site Specific Factors (tumor markers)
- Treatment history (chemotherapy, radiation, immunotherapy, hormone, hematologic/endocrine) and reason (first course, progression, recurrence, subsequent)
- Recurrence (type of recurrence, distant sites)
- Survival time
- Cancer status at follow up
- Patient status at follow up

Study Specific Data Collection (Abstracted from Medical Records by Request Only)

- Comorbidities at the time of sample collection
- Medications at the time of sample collection
- Other Data as designated by the Investigator

Epidemiologic Questionnaire Data: At the time of consent, all participants are asked to complete and return a self-administered scannable questionnaire (over 1,100 items). A five-point follow up schedule is used for missing surveys, participants are re-contacted to clarify inconsistencies, and customized data quality software is used for error checking. There is an overall 75% response rate and a complete data dictionary is available by request.

- Demographics
- Family history of cancer
- Medical history (screening, prior history of cancer, comorbidities, BMI history)
- Tobacco use history (lifetime)
- Medication use history (lifetime)
- Women's health history (lifetime)
- Food habits and food/beverages and alcohol frequency (last year)
- Exercise (past 10 years)
- Multivitamins, vitamins, supplements (past 10 years)
- Common supplements (lifetime)

Linkage to Investigator Patient Data – With IRB approval and Data Use/Destruction Agreement, the DBBR will coordinate and link DBBR specimens and data to other data provided by Investigators. All final data sets are rendered to Investigators de-identified.

Variable and Analytic Data File Construction – The DBBR will construct variables needed for analysis by request (i.e., Age at Sample Collection, Time from Diagnosis to Sample Collection, Time from Sample Collection to Death, etc).

DBBR samples and data can also be paired with tumor tissue from the Pathology Network Shared Resource and clinical data abstraction from the Biomedical Research Informatics Shared Resource.

DRUG DISCOVERY CORE (DDCSR)
Shared Resource

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OVERVIEW

The Drug Discovery Core Shared Resource (DDCSR) (formerly the Small Molecule Screening Shared Resource) at Roswell Park, provides investigators with the possibility of working on drug discovery and development within an academic institution. We provide guidance, expertise and technical support to investigators with all level of experience in drug development at all steps of the process, from target identification, through assay development, small molecule screenings and hit validation.

We also provide our customers with access to more advanced stages of drug development such as structure activity relationship studies (SAR), hit to lead optimization (H2L), and animal testing in partnership with other expert resources. We work with our clients to make the development process a clear and efficient one.

Researchers at Roswell Park and outside biomedical institutions can receive assistance with the design and execution of chemical screenings in a variety of readout systems and assistance with pre-screening and post-screening steps of drug discovery and development. Located on the Roswell Park campus, the DDCSR provides easy access to local investigators during all stages of discovery and development including:

- Target identification (assessment of target "drugability," development of strategies to overcome undruggable targets, phenotype-based screening to find chemical probes for target discovery)
- Target validation (generation of tools to modulate target genetically including design and generation of genetic vectors: shRNA, CRISPR/Cas9, inducible, degradation based, etc; generation of cells with modified expression/activity of target; running of assays to monitor target and phenotypic effects)
- Assay design and optimization (assay selection: biochemical, cell based or in silico [partnership/collaboration], generation of cell lines, generation of cell-free biochemical assays, selection of appropriate controls)
- High throughput screening and automation of custom assays (providing access to a variety of in-house standard screening libraries or screening of client provided libraries along with access to high throughput assay automation services)
- Hit selection and confirmation Hit characterization
- Help with preclinical drug evaluation via partnership with Experimental Tumor Model (ETM) shared resource at Roswell and Buffalo Biolabs
- Help with selection of a strategy for drug discovery and development, submission of grants, patent applications and understanding of the regulatory process

OVERVIEW (cont'd)

- Non-screening projects (genetic modification of cell lines, reporter cell line generation, cell characterization, storage and expansion, 2D and 3D cell culture, cell imaging, time lapse movies, cell migration, invasion experiments, fluorescent cell labeling, label-free cell counting etc)
- Experiment automation using our equipment (training required)
- The collection of chemicals at the DDCSR totals more than 110,000 compounds. Sophisticated automated liquid handling equipment is used to ensure accurate delivery of this library in both the 96- and 384-well format, and our detection equipment allows for screening using either cell based or biochemical assays.

The DDCSR capabilities are not only limited to screening related projects. We have significant experience with analysis of the activity of individual bioactive compounds (IC50/CC50 experiments) and co-treatment experiments in different biological systems.

With the facility's recent addition of the BioTek Cytation 5, we have begun working with 3D cell culture models and live cell assays. This new technology allows for researchers to investigate wound healing, cell proliferation and mobility, and the levels and localization of fluorescent molecules in individual cells.

USING THE RESOURCE

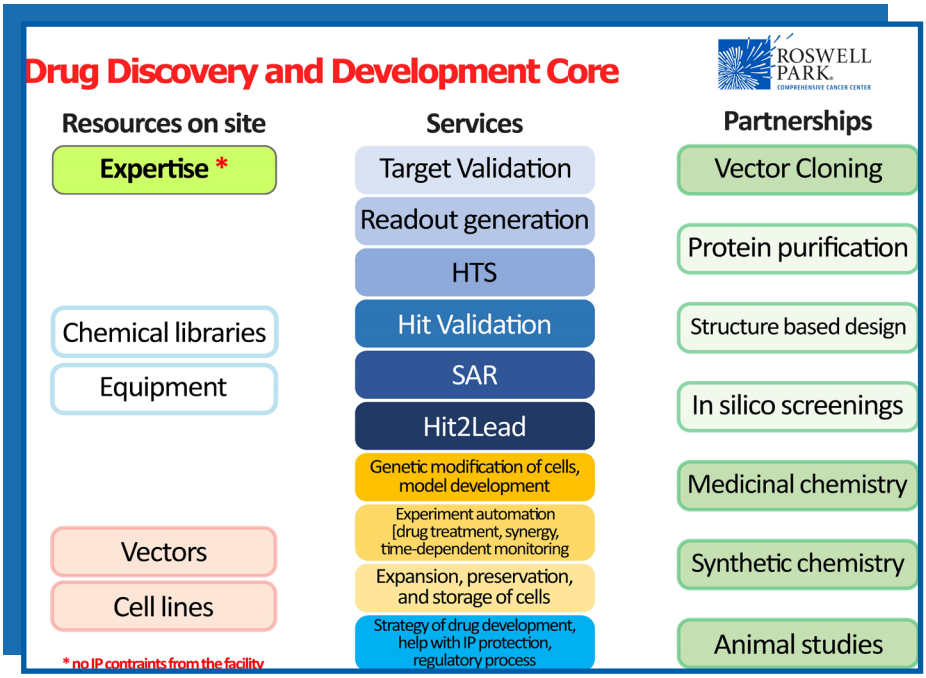
Investigators interested in the use of the facility should contact Dr. Gurova or Brian Buckley to discuss scheduling and procedures. The DDCSR is located in the CGP, first floor, L1-215. Hours of operation are weekdays, 9 AM – 5 PM.

SERVICES

The Service Structure flowchart illustrates the timeline of a typical chemical library screening project. It can be roughly divided into three phases: preparation, library screening, and data analysis/hit selection/pickup.

We recommend scheduling a preliminary meeting early during the planning phase of your project to discuss estimated costs, assay requirements, detection methods and controls for the high throughput format. By doing this early, you will save time and cost by avoiding unnecessary and repeated experiments later on. Core personnel will provide you general information about chemical screenings; requirements and evaluation of readouts to be used in high throughput screening and information about statistical analysis of readouts and HTS data. This information can be very helpful at the early stage of screening project planning.

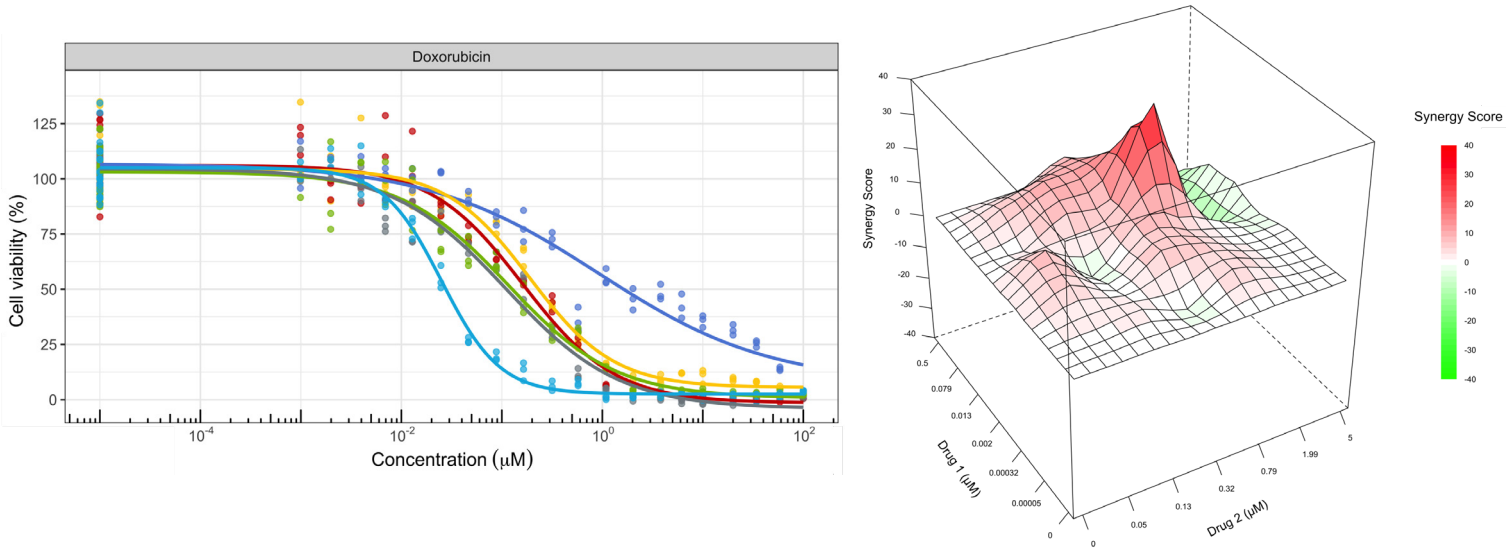
The DDCSR's liquid handling and detection equipment can be used for non-screening projects by Roswell Park researchers for a minimal hourly fee. Our equipment is capable of running assays in high density format allowing investigators to minimize the use of rare or expensive reagents. Contact us for more details. Please note, that screening projects will have a priority in equipment use, so check the availability before planning your experiments.



Data analyses and integration services

The DDCSR provides high level capabilities in the design, execution, and interpretation for a variety of drug discovery projects. Expertise includes preliminary public database queries to generate supporting data for grant submissions, cell line selection, assay optimization, and experimental design. Analyses of high throughput drug library screening data include quality control assessment, normalization, hit selection/categorization, and characterization of common drug targets. Follow-up, multi-dose hit validation is performed for selected compounds of interest. Generation of dose response curves utilizing 4-parameter log-logistic modeling to determine effective concentrations (EC50) is available along with comprehensive synergy modeling for studies investigating the action of multiple compounds in combination. Custom publication quality images are provided for all analyses. Additionally, data can be integrated with client-provided or publicly available omics-level datasets.

Examples dose response curve and synergy modeling:



CHEMICAL LIBRARIES & INSTRUMENTATION

The three main components of the chemical screening facility are: chemical libraries, liquid handling equipment, and detection equipment.

Libraries

The DDCSR owns three historical libraries created based on two different principles:

- EXPRESS-Pick ™ by ChemBridge Corporation (San Diego, CA) – a diverse library of 55,230 compounds. This library consists of organic molecules with molecular weight in a range of 250 – 550, dissolved in DMSO at concentration 5mg/ml or 10-20 mM.
- HitDiscover by Maybridge (Part of Thermo Fisher) – 52,160 compounds dissolved in DMSO at 10mM concentration.
- LOPAC1280 by Sigma (1280 compounds), Spectrum by MDS, Inc (2000 compounds), Tocriscreen Total (1120 compounds), Tocriscreen Kinase Inhibitor Toolbox (80 kinase inhibitors) by Tocris Bioscience and FDA-approved Drugs Library (1508 compounds) by Selleckchem.com are the libraries of pharmacological compounds dissolved in DMSO, in 10 mM concentration (MW is < 500). These libraries include FDA and internationally approved drugs, bioactive and natural compounds with described biological activity.

Library Format - all libraries are available in both the 96- and 384-well format. Screening in the 384-well format is faster and less expensive, but some of the assays are incompatible with this high density format.

Liquid handling equipment - equipment used for automated the delivery of liquid reagents and the transfer of compounds from the library to the assay plates in multi-well format.

Automated Liquid Handling Workstation JANUS by PerkinElmer
Using two pin-tools, library compounds can be delivered to 96- and 384-well plates in nl volumes.

Compact automated reagent dispensers
Compact automated reagent dispensers, such as MicroFill and MicroFlo by BioTek, are designed for accurate and fast distribution of solutions to 96- and 384-well plates.

Tecan D300e Digital Dispenser by Tecan
The D300 is a digital drug dispenser based on HP's ink jet technology. The D300 allows direct addition of liquids from compounds in DMSO to biomolecules in surfactant-containing aqueous solutions in picoliter-microliter range. It uses disposable dispensing chips in order to minimize dead volumes of these liquids. The D300 is perfect for setting up your PCR and qPCR reactions, generating enzyme profiles, drug combinatorial experiments, and dose response curves.

Detection equipment

Envision Excite multi label reader by PerkinElmer
This reader can be used for a wide range of fluorescence, luminescence and photometry based detection technologies:

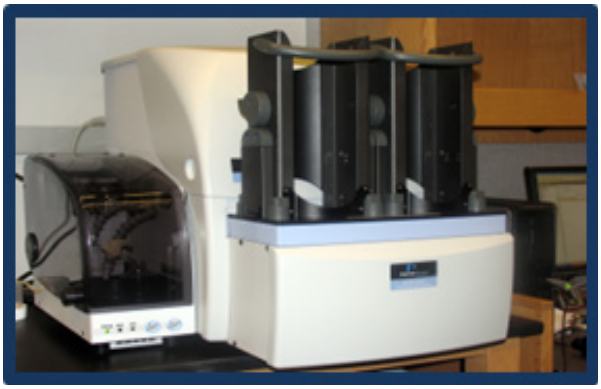
- Fluorescence Intensity
- Fluorescence Polarization
- TRF – time-resolved fluorescence
- FRET – fluorescence resonance energy transfer
- Luminescence and enhanced luminescence
- Absorbance
- AlphaScreen

Cytation™ 5 Cell Imaging Multi-Mode Reader with automated mini incubator BioSpa manufactured by BioTek

- Cytation™ 5 Cell Imaging Multi-Mode Reader manufactured in combination with the automated mini incubator BioSpa 8 by BioTek provides the unique opportunity to capture, store and analyze live cell images in bright field and fluorescence. Below are just a few examples of biological assays that can be performed using this equipment.
- Label-free imaging and quantification of 3D spheroid-based tumor invasion assays
- Live cell imaging of multi-parametric cell death using high contrast bright field and fluorescence imaging
- Label-free imaging of 2D scratch wound healing assays
- Imaging and cellular analysis of 2D and 3D T cell mediated cytotoxicity assays
- Automated immunofluorescent imaging and dual-mask spot counting of γH2AX Foci to determine DNA damage
- Cell cycle analysis using DNA content and protein expression

TC complex

Dedicated tissue culture equipment simplifies the procedure of cell preparation for cell based readout systems and the plating of the cells in multi-well format.



EXPERIMENTAL TUMOR MODELS (ETM)
Shared Resource

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OVERVIEW

The Experimental Tumor Model Resource (ETM) was established to facilitate investigators in conducting preclinical animal studies. The staff of the ETM are highly trained and experienced in a wide range of small animal surgeries, procedures, and techniques in addition to histology processing and staining. The goal of the ETM is to provide full service support for animal studies to investigators. Services provided by ETM include in vivo experimental design for animal studies, treatment of animals, tissue procurement and processing, histological processing and animal colony management. The services available through the ETM include but are not limited to small animal surgery, castration, tumor resection, tumor inoculation (SQ, orthotopic, subrenal), tumor measurement, therapeutic treatments such as injection (IP, IV, sub-Q,), oral gavage, dietary manipulation, tissue procurement, tissue microdissection. ETM provides tissue processing services including: formalin fixed/paraffin embedding, cryofrozen in OCT, LN2 flash frozen, cryopreservation in DMSO and primary cell culture. Longitudinal animal studies can be conducted including tumor measurement, blood draw, and bioluminescent imaging. The ETM can manage your mouse colony including breeding, PCR screening and culling the colony for cost effective colony management. Specialized services include embryonic dissections, tissue recombinations, subrenal grafting and xenografting of human clinical samples into immunocompromised hosts. ETM also maintains several tumor models that are available to researchers for their studies. Tumor models available through the ETM or in development include: TRAMP, CWR22, PB-Cre-4/Pten knockout, and PDX models of lung, bladder, colon, pancreas, sarcoma, pediatric, ovarian, prostate, melanoma, head & neck, esophagus, mesothelioma, liver and kidney. Immune intact syngeneic mouse models are available for bladder, pancreas, and prostate. Experimental animals as well as flash frozen tissue and histological slides are available in the tumor bank. Tissue samples are available for disease progression (multiple timepoints and castration recurrent disease) for many of the models. The expertise of the ETM is available to assist with all of your preclinical animal studies.

USING THE RESOURCE

To initiate a project, investigators should contact Drs. Moser and Foster to obtain a description of the services offered and an explanation of the models available. Investigators meet with ETM personnel to discuss experimental design, treatment strategies, endpoints and data collection. The goal of these discussions is to develop an experimental plan with animal numbers and ages designated for all experiments. Next, the investigator needs to complete material transfer agreements, obtain IACUC approval or have the ETM added to the protocol as personnel, and

provide a charge source.

If the investigator contracts with ETM to maintain and provide experimental treatment, as well as, monitor and collect tissues and data, then ETM will be added to the investigators Roswell Park IACUC protocol or the experiment will be performed under an ETM IACUC Core Protocol.

If the PI only needs the ETM to provide the animals needed for the experiments then the ETM initiates a breeding plan to obtain the needed number of animals. At weaning the experimental animals are transferred to the investigator's IACUC protocol and the animals are the responsibility of the investigator and all treatment and monitoring of the animals is performed under the investigator's approved IACUC protocol. At the time of tissue procurement, the ETM can assist with microdissection and tissue collection. This service is scheduled at the time of breeding so that scheduling of ETM personnel can be taken into account for the breeding strategy. Investigators using the Tumor Tissue Bank are required to schedule an initial meeting, complete MTAs and provide a charge source. Tumor models, PDX lines or cell lines are provided to investigators after MTAs are completed. Investigators are expected to expand the cell lines in their laboratories and freeze down sufficient aliquots for all necessary experiments.

The ETM is located in the Medical Research Complex, Room 452. Hours of operation are weekdays, 7:00AM – 6:00 PM, and by appointment.

SERVICES

Mouse models available:
- CWR22
- CWR22R
- Pten null
- NSG
- NSG-SGM3
- PbCre4+
- Allograft immune intact tumor lines:
  - bladder (BURP)
  - pancreas (KPC)
  - TRAMP (prostate)

Surgical Procedures:
- orthotopic implantation
- sub-renal implantation
- intrafemoral
- SQ and IV
- intrafemoral

Other procedures:
- serial and terminal blood collection
- tissue microdissection
- gavage
- changing medicated or treated feed and water
- serial animal weights
- data collection and records maintenance
- primary cell culture
- tissue procurement
- snap freezing
- teratoma assay
- bioluminescence imaging
- high resolution X-ray
- embryonic dissection
- daily health monitoring
- tumor volume measurements
- organoid culture
- spheroid culture

Histological procedures & services:
- paraffin processing and embedding (single/multi-chamber cassette)
- cryosectioning
- facing blocks
- cutting slides (FFPE & OTC)
- H&E staining
- IHC
- Specialized stains

Customized Protocol Development

The ETM provides scientific consultation/expertise on appropriate use of the models (strengths & limitations), experimental design (cohort design, timing, end-points and parameters) and tissue procurement. Additionally, for the tumor models available through the core the ETM maintains a tumor tissue bank representing tumor progression and corresponding normal tissues. The tissue bank contains the following types of samples: paraffin embedded, cryo-embedded and snap frozen. Contact Dr. Moser for a full list of samples available through the ETM tissue bank

SERVICES (cont'd)

and the models currently supported through the ETM. Currently the ETM has established tumor banks for the following mouse models: TRAMP, CWR22 and CWR22R (castration recurrence), Pten null, KPC, Myc, and various PDX models within the ETM.

The purpose for the ETM arises from the multitude of animal models of cancer that have been established and characterized. Genetically modified mouse models of human cancers are increasingly being utilized for the study of cancer. These models have been used to identify molecular mechanisms of cancer initiation and progression, as well as for preclinical testing of new therapeutic compounds and approaches for the prevention and treatment of cancer. The appropriate use of transgenic and xenograft models require an in-depth working knowledge of the strengths and limitation of individual models. While such expertise is not readily available in all laboratories, this expertise is available within ETM for some of the widely used mouse tumor models. ETM provides a consolidated resource for maintenance of necessary breeding colonies, collection and archival of tumor samples in a tissue bank, consultation with experimental design, appropriateness of the model, breeding strategies and logistics, and technical expertise in tissue procurement. The shared costs for services provided by the ETM results in reduced costs to the individual investigators at Roswell Park resulting from the resources conserved by maintaining only one colony per animal model, one maintenance xenograft line as well as capitalizing on the ETM technical and scientific expertise. The resulting savings are passed on to the Roswell Park investigator as reduced animal related costs for their research as well as access to mouse models that they would not normally have the technical and scientific expertise to utilize.

The ETM maintains homozygous breeding colonies of TRAMP animals (C57BL/6 & FVB) and provides experimental animals for investigators. Dr. Barbara Foster is the ETM's scientific consultant for investigators using the transgenic prostate models in their research. The ETM maintains the pten null model and TRAMP models of prostate cancer. In addition, the ETM maintains a tissue bank representative of disease progression for many of the models in ETM including TRAMP, Pten, HiMyc, CWR22, KPC and BURP. The tumor bank consists of tissues for histology (paraffin embedded and cryosections), snap frozen tissue samples for molecular analysis and serum samples. The TRAMP tissue bank consists of prostates from at least 50 paraffin embedded prostates and associated tissues and controls (liver, kidney, lymph node, seminal vesicle and metastatic lesions; included in a 9 chamber cassette with the 4 lobes of the prostate), 50 specimens of snap-frozen prostate and associated tissue, 50 cryopreserved prostates for cryosectioning for each of the following stages of disease as well as matching serum samples. Banked tissue of the progression of the disease includes prostate and associated tissues from animals at 6, 8, 10, 12, 15, 20-25, and >35 weeks of age, castration recurrent disease and metastasis. Prostates from wildtype mice at similar time points are also available within the resource. The ETM also serves as a resource to Roswell Park investigators for stocks of parental and clonal cell lines established from the TRAMP tumor model. For all TRAMP mice, TRAMP tissue, and cell lines ETM requires that the PI obtain a material transfer agreement (MTA).

The CWR22 and CWR22R xenograft models maintained by ETM were a gift from their originator, Dr. Thomas G. Pretlow at Case Western Reserve University School of Medicine, hence the name of the xenografts. The ETM maintains by animal passage the CWR22 and CWR22R human xenograft lines in order to provide xenograft implanted mice and primary cells to Roswell Park investigators in a timely and efficient manner. ETM also maintains a tumor bank of CWR22 and CWR22R tumors (paraffin embedded, snap frozen, cryopreserved and matched serum) for use in preliminary studies by Roswell Park investigators.

The full resources and specialized technical expertise of the ETM are available to Roswell Park investigators. This includes providing transgenic mice from the various models, aged matched wildtype mice, xenograft bearing experimental animals, and cell line implanted animals for projects as well as technical expertise in experimental design and appropriate use of these models. Technical services available through the ETM include subrenal grafting and orthotopic grafting of tissues. ETM routinely implants human clinical samples into NSG and NSG-SGM3 mice subcutaneously and orthotopically. The success rate for ETM subcutaneous grafting of human tumor tissue ranges from <10% up to >80%. Take-rates for establishing PDX lines vary widely by the cancer type being grafted. In addition to establishing PDX models, ETM has experience establishing organoid and spheroid tissues from clinical

SERVICES (cont'd)

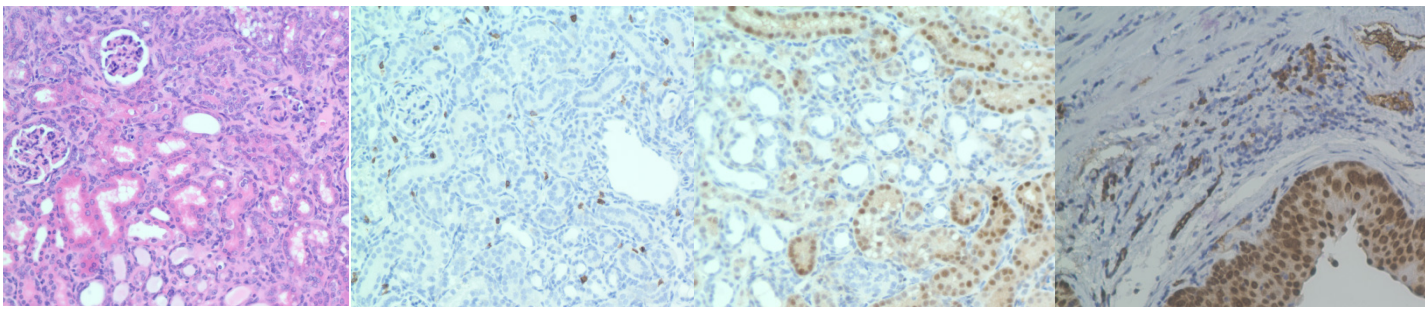
samples. The ETM is also able to perform the embryonic dissection and tissue recombination allowing for rescue of tissue from embryonic lethal transgenic lines. Additional surgical services provided by the ETM include castration, subcutaneous and orthotopic implantation of xenografts and surgical samples, subcutaneous implantation of cells and tissues, intra femoral implantation, and implantation of testosterone and other drug impregnated implants. Other services provided include collection of animal related data such as high resolution X-ray (Faxitron), in vitro imaging of luciferase using the Xenogen IVIS 50, bigenic breeding and screening, biweekly measurement of tumors, daily monitoring of health, serial blood sampling, and harvesting of tissue. ETM routinely performs tissue processing of formalin fixed tissues, paraffin embedding, and sectioning of paraffin and OTC fixed tissues. ETM also provides H&E staining and immunohistochemical (IHC) staining for select markers. On request ETM can provide specialized biochemical and IHC staining of tissues. The ETM is dynamic and expands its models and technical services to accommodate the growing needs of investigators of the Institute.

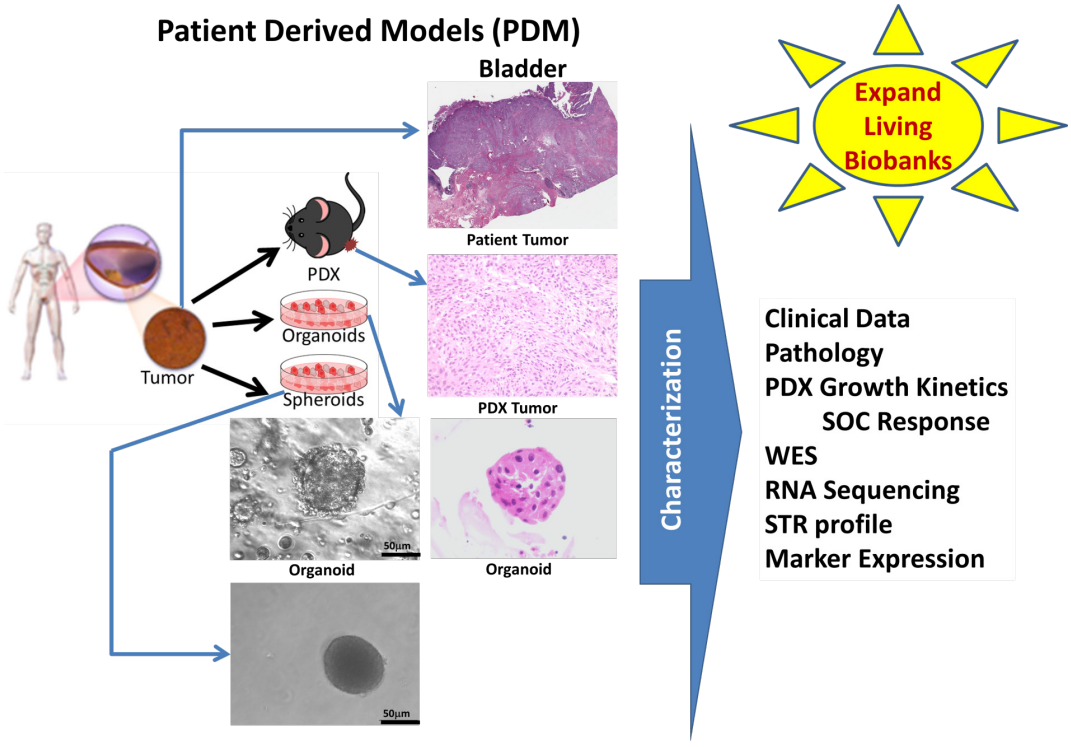
The ETM provides "fee for services" for specialized techniques as well provides personnel efforts for larger experiments that require extensive labor and considerable technically demanding procedures.

EQUIPMENT

The ETM has a Leica Tissue Processor (ASP300), a Leica microtome, cryostat, dissecting scope with image capturing capability, DAKO immunostainer (Autostainer Plus), 2 liquid nitrogen cryostorage system, ultralow freezers (Sanyo) and step-down freezer for controlled cryopreservation of living samples.

IHC STAINING OF MOUSE TUMORS





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 the Shared Resource (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
Confocal microscope	Leica TCS SP8

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)**

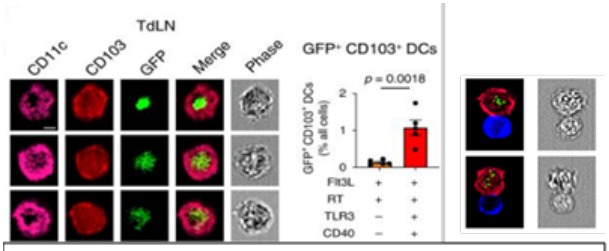

Fig 1. Imaging flow cytometry analysis of tumor (GFP+) draining lymph nodes (TdLN) following in situ immunomodulation with Flt3L, radiotherapy (RT), and TLR3/CD40 revealed increased numbers of GFP+ CD103+ DCs in treated mice compared to the PBS controls, consistent with efficient trafficking of tumor-associated 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

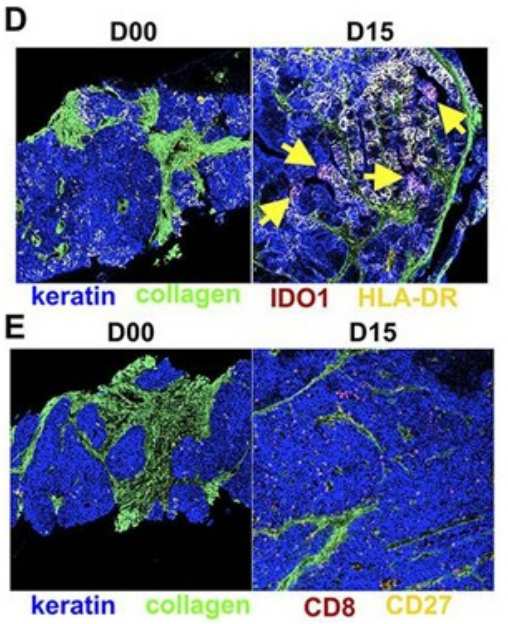

Figure 5. Spatial relationship of immune cells within TME. (D) IMC images highlighting IDO1 and HLA-DR expression and changes between two timepoint collections, Day 0 (D00,left) and Day 15 (D15,right). Yellow arrows indicate focal points of co-localization. **(E)** IMC analyses indicating CD8 and CD27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

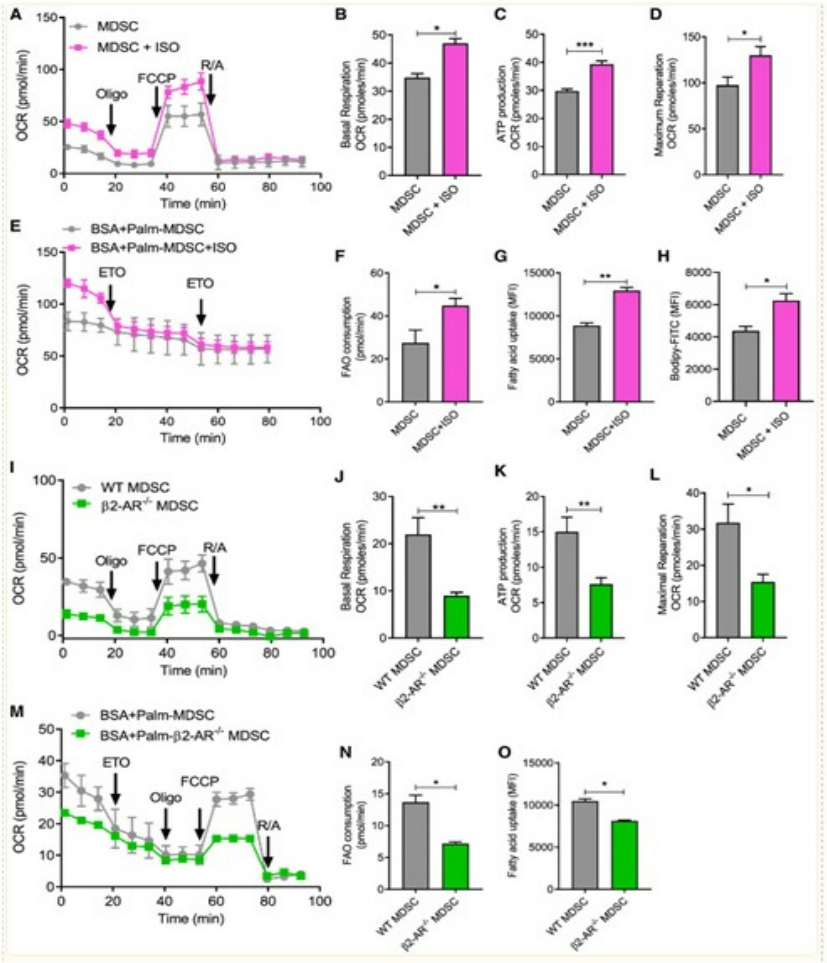

Figure 2. β-AR signaling in MDSCs decreases glycolysis and enhances oxidative phosphorylation
(A-H) MDSCs in the presence of GM-CSF and IL-6, with or without isoproterenol (ISO). (I)O) WT and β2-AR-/- mice orthotopically implanted with 4T1 tumor cells.

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.

The 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

LEADER

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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.

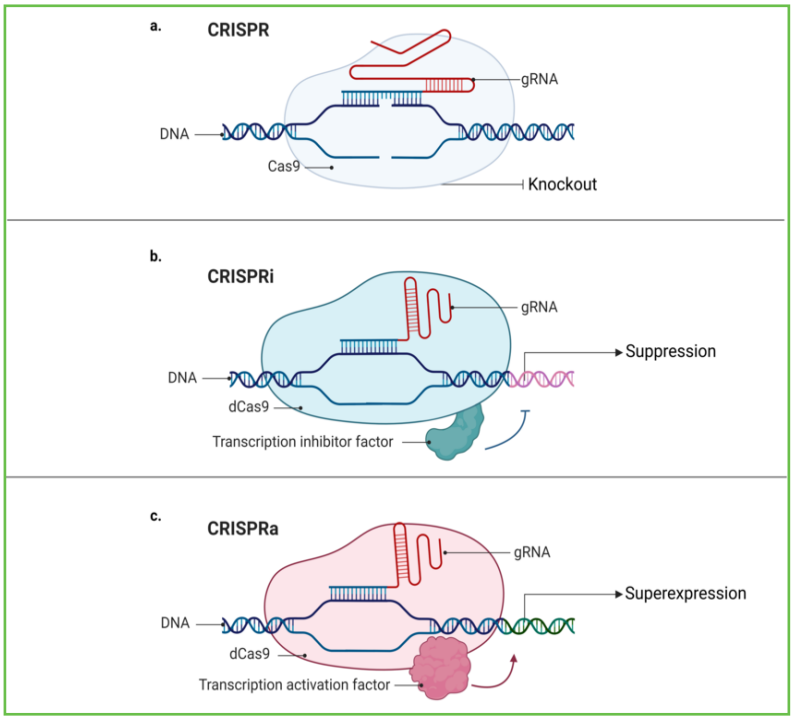
SERVICES (cont'd)

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

LEADERS

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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.

The Resource Co-Directors provide 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.

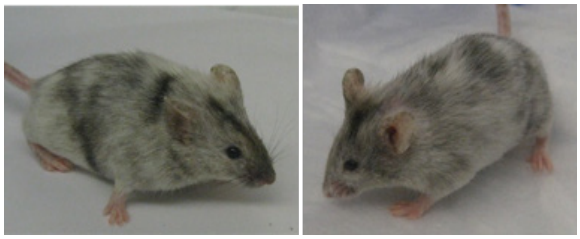
The entire electroporation process takes approximately one month, and the resource expects the investigator's lab to perform the positive confirmations in a timely fashion.

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

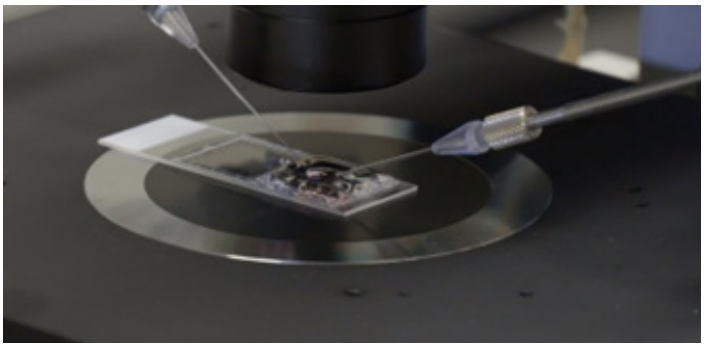
CRISPR genome editing in animals

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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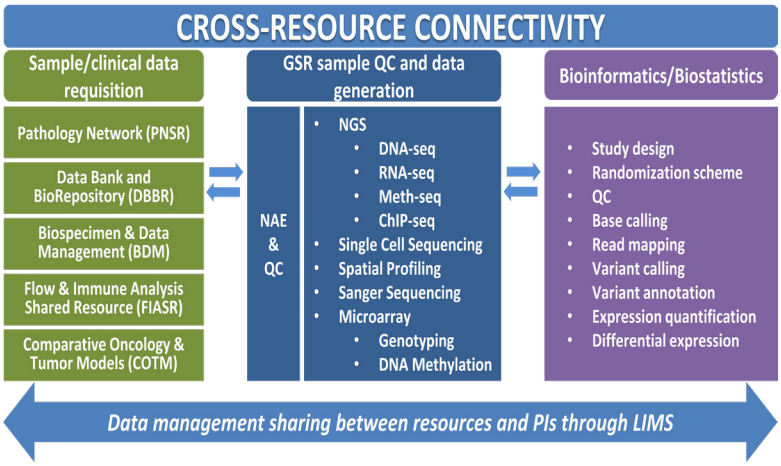
OVERVIEW

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 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 Nanostring nCounter, 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 Biospecimen and Data Management Shared Resource to 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.



GENOMICS (GSR)
Shared Resource

LEADERS

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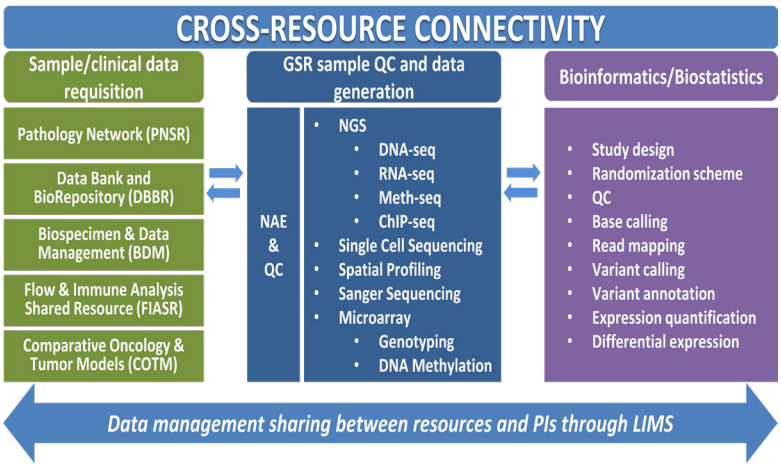


USING THE RESOURCE

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. Additionally, the we provide support for library preparation and sequencing for the NanoString GeoMx system housed within the Multiscale Bio-Imaging Shared Resource (MBISR).
- Validation technologies: NanoString nCounter, qPCR, Cell Line Authentication, Sanger sequencing, and Optical Genome mapping using Bionano Saphyr.

EQUIPMENT & TECHNOLOGIES

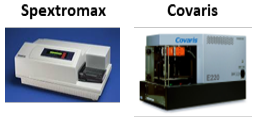
Next-generation sequencing (NGS): NovaSeq 6000, NextSeq 500, and MiSeq; Bionano Saphyr optical mapping; Microarray: Illumina iScan; Single-cell RNA sequencing (scRNA-seq): 10X Genomics Chromium X; Targeted validation technologies: ABI 3500 sanger sequencers; NanoString nCounter, ABI QuantStudio 6 Flex Real-Time PCR System; Ancillary Equipment: Qubit, Spectrophotometer, Agilent Bioanalyzer and TapeStation 4200, Covaris E220; Lab Automation: 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

Bioanalyzer TapeStation Qubit

Spextromax Covaris

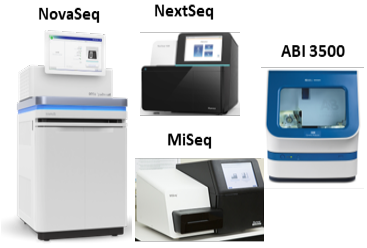


Sequencing

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 ABI 3500 MiSeq



Single cell and spatial profiling

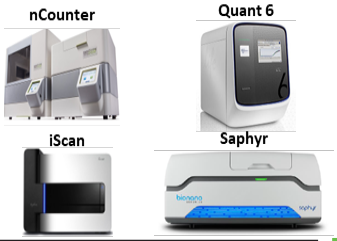
Single cell transcriptomics
-Gene Expression Profiling
-CRISPR Screening
-Gene & Cell Surface Protein
-Immune Profiling
Single cell epigenomics
-Chromatin Accessibility (ATAC-seq)
-Multiome - GEX+ATAC-seq
Spatial transcriptomics
-10x Visium

Chromium X 10X Visium

Companion Technologies

Illumina iScan
-SNP arrays
-Methylation arrays
NanoString nCounter
-Gene expression panels
-CNV
Real time PCR
-TaqMan: GEX, SNP
-SYBR GEX
Bionano Optical mapping
-Structural Variation

nCounter Quant 6 iScan Saphyr



HEALTH COMMUNICATIONS (HCR)
Shared Resource

LEADERS

Paul Hage, MFA
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Rodney Haring, PhD, MSW
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OVERVIEW

The Health Communications Shared Resource (HCR), is a full service video and media production center, specializing in health communications locally, regionally, nationally, and internationally. Based out a NCI-Designated Cancer Center, HCR helps investigators, institutions, community health advocates, and NGO's educate the public about important health-related matters, and promotion of health services. One area of focus is on understanding the many determinants that influence health behaviors, in order to reduce the burden of illness, and create effective, salient, and emotive media.

LEADERSHIP

Paul J. Hage, MFA serves as Lead Project Manager and Co-Director of the Health Communications Shared 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 C. Haring, PhD, MSW serves as co-Director of Health Communications Shared 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 organization, we can provide exceptional, professional media services that can accommodate most budgets.

Pre-Production

- Health media campaign planning and assistance
- Housed in Roswell Park Comprehensive Cancer Center, an NCI-Designated Cancer Center
- Subject matter expertise in cancer health related topics
- Scriptwriting or assistance
- Storyboarding

Production

- 4K UHD Video Production
- Coordination of production crews anywhere in the world
- Conduct interviews, and record narration.
- TV Studio-staging area for production
- Green screen, multiple backdrops

Post-Production

- Editing: Adobe Premiere Pro, Apple Final Cut Pro
- Full Audio and Narration recording, Pro-Tools, Apple Logic Pro
- Custom Music Composition and Arrangement
- Digital Social Media assistance with multiple file conversion and 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.

HEMATOLOGIC PROCUREMENT (HPSR)
Shared Resource

LEADERS

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ADMINISTRATIVE CONTACT

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OVERVIEW

The Hematologic Procurement Shared Resource (HPSR) serves two key functions at our institute: (1) procurement of hematologic samples for future research projects and (2) processing of correlative hematology samples from patients with any cancer enrolled on therapeutic cancer clinical trials.

In its first role, the HPSR successfully facilitates translation of basic research in hematological cancers to the clinical setting by providing basic researchers and clinical investigators with appropriately procured and cryopreserved samples of bone marrow and peripheral blood. This includes mononuclear cells, serum, and plasma samples from individual patients treated at our institute with hematological and other cancers. Currently the procurement bank contains a total of over 100,000 cryopreserved samples dating from the present back to 1991 and linked to a clinical database. On an annual basis, the resource procures over 5000 samples from patients with myeloid malignancies, acute and chronic leukemias, lymphoproliferative diseases, multiple myeloma, and other hematological disorders. Prior academic and grant funded research collaborations have included projects with the Dana Farber Cancer Institute, Washington University, and University of Chicago.

In addition, the HPSR staff also promote cutting edge innovative clinical and translational research by providing around the clock (24/7) collection of samples from patients with any type of cancer enrolled on clinical trials at Roswell Park. A technician for sample processing is available nights, weekends and holidays on call to process patient samples. We support the Roswell Park Clinical Research Service (CRS) by accurately processing PBMC/BMMC, serum, plasma, urine, and other samples based on individual protocol specifications from individuals with all cancer types receiving experimental therapy on clinical trials at our center. These correlative pharmacodynamic and pharmacokinetic samples are typically batch stored and shipped both to individual investigators and central laboratories dry ice for further analysis. The availability of technical staff to receive, process, and store peripheral blood and other samples from patients on a 24/7 basis (including after hours and on weekends) is essential to the institute's commitment both to investigator initiated clinical research as well as our early phase clinical trials requiring intensive pharmacokinetic testing. The ability of laboratory staff to custom process and store samples ensures these valuable samples are not missed and ensures that patients can receive therapy in a timely fashion any day of the week. As an example, In calendar year 2022, the HPSR processed correlative samples for patients enrolled on at total of over 150 clinical trials, including 50 investigator initiated, 15 cooperative studies and 90 pharmaceutical sponsored studies at Roswell Park. Pharmaceutical sponsors have included Astex Pharmaceuticals, Amgen, Sanofi-Aventis, Astellas, Pfizer, Harpoon Therapeutics and many other large and small companies involved in phase 1 through 3 cancer studies.

Current laboratory personnel include a physician-scientist facility director, a laboratory supervisor, two full-time technicians and a clinical database manager. The square footage of the procurement lab where primary patient samples are being processed encompasses approximately 800 square feet. The core laboratory contains sixteen large LN2 freezers, four -80° stand up freezers, one -20° stand up freezer, and one fridge/freezer. All freezers are monitored 24/7. The core also has one 6-foot hoods, one 4-foot hood, a Beckman Multisizer 4e cell counter, three refrigerated swing rotor centrifuges, and two non-refrigerated centrifuges. The core also has a cytospin, water bath and micro-centrifuge as well as desk space, computers, and monitors for all staff members. De-identified sample information is entered into an institute-wide LIMS system.

USING THE RESOURCE

Individuals interested in the use of the facility should first contact Linda Lutgen to discuss scheduling, procedures, pricing and other inquiries.

Discussion of research proposals including requests for letters of support for grant applications should be directed to Dr. Eunice Wang (Director).

SERVICES

Banked Samples

The main focus of this shared resource is to collect blood and bone marrow samples on patients at time of diagnosis of hematologic malignancies ideally prior to any therapeutic intervention as well as throughout the entire course of their disease. Patients must 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.

In general, samples from normal donors, patients with hematological malignancies and other malignancies, as well as other sources are processed by density ficoll gradient centrifugation for isolation of viable peripheral blood and/or bone marrow mononuclear cells. Peripheral blood samples are also centrifuged for collection of plasma and serum samples. Viable cells can also be processed for RNA and DNA extraction as requested by individual investigators. Additional samples processing for research purposes may also be possible following discussion with resource staff.

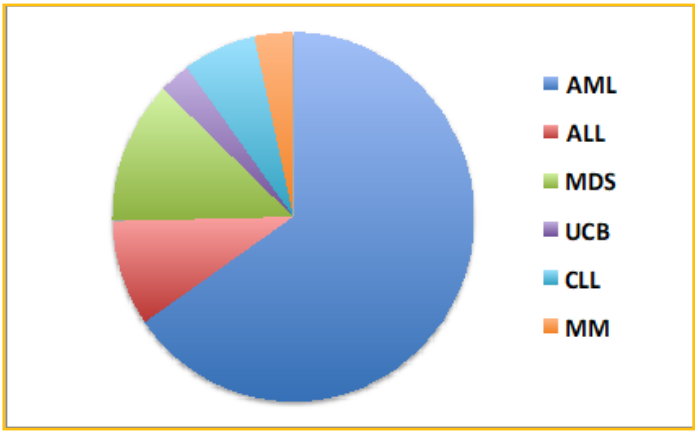

Figure: Diagnoses of >100,000 patient samples currently stored in HPSR

Study Specific Procurement

If a project can be accommodated within standard banking operations, the HPSR will prospectively collect samples at single or multiple time points for a limited amount of time. 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. The HPSR 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 after discussion with the HPSR director and laboratory manager and appropriate budgeting for services.

Clinical Data

We maintain an extensive clinical database linked to stored HPSR samples for certain hematological malignancies. Currently, the HPSR employs a full-time dedicated clinical data manager who is tasked with abstraction of clinically relevant diagnostic, treatment, and pathological information from patients' medical records after informed consent. All samples are de-identified at the time of processing. Clinical data are handled by a dedicated data manager who functions in an honest broker capacity for all requests. Relevant information may include, but is not limited to, demographics such as age, sex, race and ethnicity, prior history of cancer, treatment history, comorbidities, medications, cytogenetics and molecular diagnostic findings. Other relevant patient data as designated by the Investigator can be obtained upon request and discussion with resource staff with appropriate resource allocation. Researchers are responsible for procuring and providing appropriate IRB-approved protocols in order for HPSR staff to release specimens linked to clinical data. Assistance with this process and discussion of construction of custom data sets can be provided upon request. All final data sets are distributed to Investigators de-identified.

INVESTIGATIONAL DRUG SERVICE (IDS)
Shared Resource

LEADER

Barbara Todaro, PharmD
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barbara.todaro@roswellpark.org

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 Barbara Todaro 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™ 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.

USING THE RESOURCE

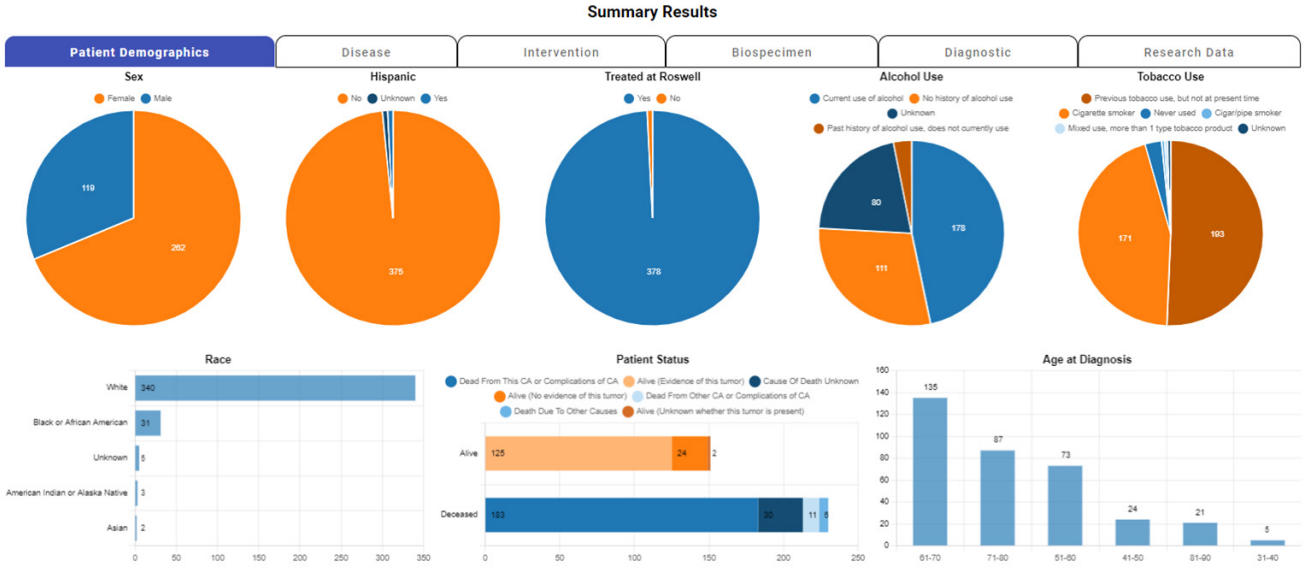
Investigators may request access to nSight™ via the following link: nSight Access Request

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

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.

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.



NICOTINE & TOBACCO PRODUCT ASSESSMENT (NICOTAR)

Shared Resource

LEADERS

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Richard O'Connor, PhD
Co-Director
Carlton House 428
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richard.o'connor@roswellpark.org

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

LEADERS

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Center for Genetics & Pharmacology
L1-218
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gina.blasko@roswellpark.org

Kevin McGinley
Shared Resource Business Administrator
Research Studies Center R-232
Ph: 716-845-1534
kevin.mcginley@roswellpark.org

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.

IDT INTEGRATED DNA TECHNOLOGIES

GOLDBIO®

KRACKELER Scientific

Mediatech, Inc.

QIAGEN

life invitrogen by life technologies

CORNING

PATHOLOGY NETWORK (PNSR)
Shared Resource

LEADERS

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OVERVIEW

The Pathology Network Shared Resource (PNSR) provides human specimens and laboratory services for basic and translational research to further the understanding of the cellular and molecular pathogenesis of human cancers. The overall mission of the PNSR is to facilitate access to human tissue for investigators with IRB approved protocols that have an emphasis on translational efforts.

USING THE RESOURCE

PNSR is located in the Gratwick Basic Science Building, 6th floor. Hours of operation are weekdays, 7:00 AM – 4:30 PM. Investigators interested in the use of the facility should contact PCFAdmin@RoswellPark.org to discuss scheduling and procedures for placing a work request.

SERVICES

Aperio Scanning and 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.

Analysis 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.

PNSR performs image analysis for slides stained by IHC only. Nuclear, cytoplasmic and membranous expression can be scored individually or in any combination. Vascular analysis can be performed and tailored to calculate specific vessels by tweaking vessel size parameters.

PATHOLOGY NETWORK (PNSR)
Shared Resource

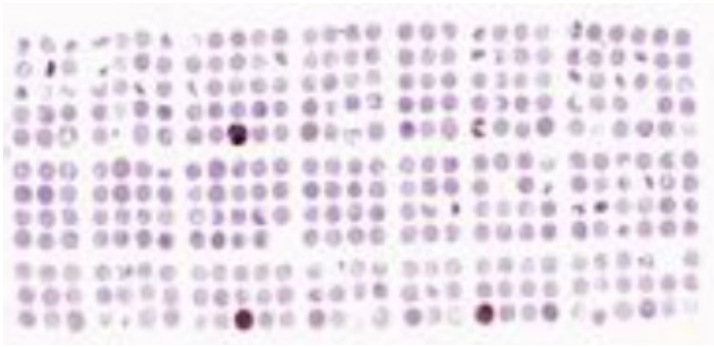
SERVICES (cont'd)
Biospecimens and Tissue Services
The PNSR functions to assist investigators with translational research by providing a variety of biospecimens.

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. All samples are Quality Controlled (QC) after extraction to confirm that high quality DNA and RNA is delivered. DNA and RNA isolation from formalin-fixed paraffin-embedded tissue can be performed at the Genomic Shared Resource (GSR). PNSR can provide FFPE tissue to investigators and facilitate submission to GSR for the extraction.

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 and 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. Requests for fresh or frozen tissues are guided by the Laboratory Information Management System (LIMS) and can be integrated with other shared resource facilities (e.g., GSR). The number of biospecimens available in the biobank varies by disease site and utilization, which is subject to Translational Research Groups (TRGs) approval and prioritization.

Tissue Microarrays (TMAs)
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.



PNSR 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.

Please contact PCFAdmin@RoswellPark.org to inquire about the availability of biospecimens or for a list of available TMAs or to inquire about constructing a TMA from cases of special interest to your research.

PATHOLOGY NETWORK (PNSR)
Shared Resource

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 laser microdissection, sterile needle coring to isolate DNA from tumor samples, and histology preparation for Visium Spatial Gene Expression. Histology staff work closely with the Biomedical Research Informatics Shared Resource and other core labs within the PNSR to identify samples sets, and then perform the required staining for research studies that use IHC. The lab uses state-of-the-art autostainer for consistent and high-throughput IHC staining. Antibody staining procedures and IHC slides are regularly reviewed by a pathologist for quality control.

Clinical Research Laboratory Services

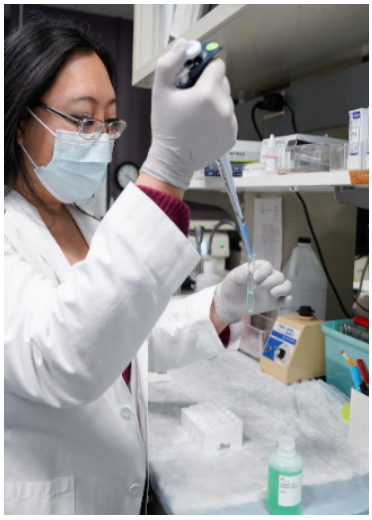
The Clinical Research Laboratory Services (CRLS) consists of a team of laboratory professionals dedicated to managing all aspects of biospecimen pre-analytical activities related to clinical trials. CRLS coordinates tissue feasibility for clinical trials and provides services for processing, storing, and the shipment of specimens for clinical trials.

All staff members are International Air Transport Association certified to ship biological specimens and function as a point of contact for addressing laboratory specimen related concerns for clinical trials. Team members function in lab and office areas dedicated to performing clinical research activities. Additionally, CRLS staff are involved with protocol and budget development, review of clinical trials for operational and scientific review for lab implementation at Roswell Park.

The CRLS team is comprised of two labs. The labs are dedicated to anatomic pathology material management and manage all other biospecimen types.

CRLS performs the following tasks:

- Processing of various specimen types, i.e., blood, urine, body fluids and bone marrow
- Storage of specimens
- Shipment of specimens (same day and/or batch)
- Specimen transport
- Tissue feasibility determination
- Form and specimen requisition completion
- Facilitate specimen testing and reporting
- Facilitate budget completion
- Study reviews for lab implementation
- Protocol development and editing



Please contact CRSLabAdminTeam@RoswellPark.org for a project specific cost estimate.

SCIENTIFIC EDITING & RESEARCH COMMUNICATIONS CORE (SERCC)

Shared Resource

LEADERS

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Mukund Seshadri, DDS, PhD
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Jamie L. Brooks, MBA
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OVERVIEW

The Scientific Editing and Research Communications Core (SERCC) provides scientific editing services to faculty and trainees at Roswell Park Comprehensive Cancer Center and the State University of New York at Buffalo (UB) with the goal of helping them succeed in their pursuit of grant funding and publication of high-impact research.

Services provided by the resource range from quick copy edits to detailed, substantive editing support to maximize clarity and enhance the overall quality of written documents. The resource also provides educational materials on scientific communication to all faculty and trainees at the cancer center on a regular basis.

SERCC can edit projects on all topics related to cancer research and the biomedical sciences. All requests for reviews of scientific documents are handled with confidentiality, professionalism, and respect.

USING THE RESOURCE

Please review the information on fees and turn-around times on SERCC's website prior to submitting a request. To submit a request for editing support, use the submission buttons on the SERCC website or email us at editing@roswellpark.org. In your email, include the document type, any deadline information (requested or external due date), and type of service(s) requested. You may submit a request for editing support approximately one month prior to the projected start date for your project. The editing resource is free for Roswell Park Assistant Professors with active mentoring committees.

SERVICES

Content editing (substantive editing); Copy editing (light editing for grammar, spelling, and punctuation); Multiple-round editing (rapid rework following author revisions); Preparation support for responses to reviewers' comments; Journal formatting; Cover letter preparation

SOFTWARE & INSTRUMENTATION

Microsoft Office (Word, Excel, Powerpoint, Teams, Forms); TexMaker (for working with LaTeX files); Adobe Acrobat Pro

NOTABLE PROJECTS

Clients have secured funding from a variety of organizations including the Roswell Park Alliance Foundation, National Institutes of Health, U.S. Department of Defense, Hyundai Hope on Wheels, and Susan G. Komen Breast Cancer Foundation. Clients have published papers in various journals including JAMA Oncology, Genes, The American Statistician, and Photochemistry and Photobiology.

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

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)
- 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.

- **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).

- **A fully digital, cabinet X-ray radiography system** TISR also oversees a cabinet digital X-ray radiography system (Faxitron MX-20) for animal imaging. This system allows for high-throughput monitoring animal models efficiently and affordably. X-RAY is the optimal imaging modality for bone-related studies such as osteoporosis, phenotyping and detection of bone metastases.

- **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.

RECENT PUBLICATIONS

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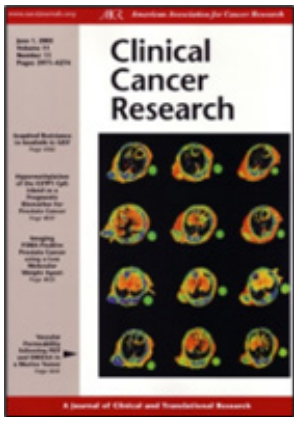
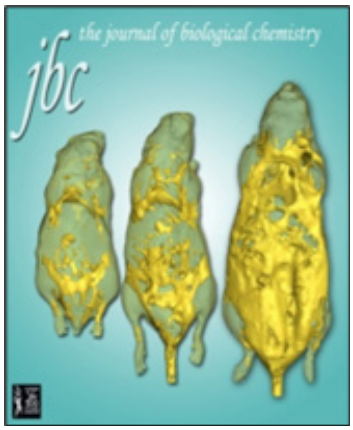
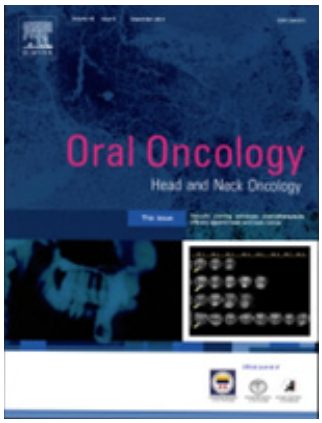
COVER ART


Clinical
Cancer
Research


the journal of biological chemistry
jbc


Journal of
Cerebral Blood Flow
& Metabolism


AngioGENESIS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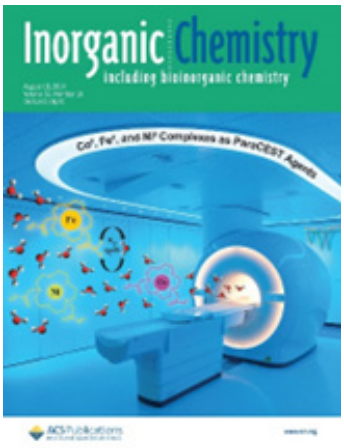
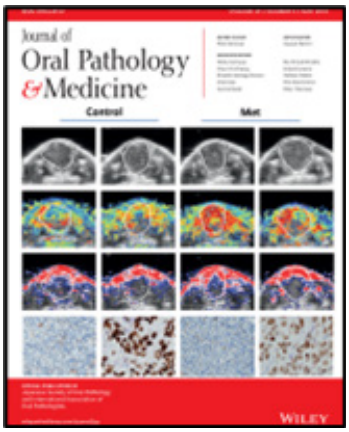
Head and Neck Oncology


Inorganic Chemistry
including bioinorganic chemistry


Cancer
Prevention
Research
AACR


Journal of
Oral Pathology
& Medicine
WILEY

TRANSLATIONAL IMMUNO-ONCOLOGY (TIOSR)
Shared Resource

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THERAPEUTIC CELL PRODUCTION FACILITY

OVERVIEW

The Therapeutic Cell Production Facility (TCPF) at the Translational Immuno-Oncology Shared Resource (TIOSR) started with a single processing room cGMP facility in 2012. With increasing demand, the current 2,574 sq. ft. cGMP facility with four ISO7 processing rooms was built in 2014. With a proven track record, including active participation in internally developed, industry-sponsored, and collaborative group cell therapy trials, the TCPF is well established to support investigators from academia and industry in the development and execution of Phase I and II cell therapy product manufacturing. TCPF received the initial FACT accreditation (Nov 5, 2018) for cellular therapy product processing with more than minimal manipulation. The mission of TCPF is to provide manufacturing support for type 351 biologic and cell therapy products, where we have established a core expertise to efficiently and cost-effectively translate novel and often complex laboratory processes to cGMP-compatible processes.

USING THE RESOURCE

Investigators interested in using the facility should contact Joanna Stanson to discuss scheduling and procedures. The TCPF cGMP facility is located in the Cancer Cell Center building, 4th floor. General hours of operation are weekdays, 8:00 AM – 5:00 PM.

SERVICES

The TCPF provides a full spectrum of services to support investigators in manufacturing clinical cellular therapy products for phase I and II clinical trials and works closely with the Transplant and Cellular Therapy (TCT) team at Roswell. Services range from protocol-specific complete manufacturing of the cellular product starting from scheduling/communication with the clinical research coordinators/physicians, pick up of the apheresis product, cell purification/modification/expansion, cryopreservation or fresh, and the delivery of the cellular product to the bedside for administration, to simply shipping the starter product to the sponsor's central manufacturing site and receiving/storage of the cellular product until administration including any thawing/reconstitution/dilution required in preparation for administration (for company-sponsored studies where the product is manufactured at the sponsor's central manufacturing site). TCPF also provides help during clinical protocol development, CMC section for IND preparation, and IND-enabling runs.

SERVICES CONT'D

Cell Processing-related Services

- Cell (bone marrow mobilized and MNC apheresis products) purification/selection (Ficoll, Percoll, CliniMACS Plus, CliniMACS Prodigy)
- Retro- and Lentiviral vector transduction of T cells
- Dendritic cell culture, alpha DC1 vaccine
- Others (protocol specific per request)

Shipping/Receipt-related Services

- Media preparation (study specific) for specimen collection
- Shipment of tumor/apheresis product (domestic/international)
- Receipt/storage of cellular therapy product
- Receipt/storage of study-specific reagents

Cellular Product Administration-related Services

- Fresh product transport to bedside
- Cryopreserved product thaw/wash/dilute and transport to bedside
- Cryopreserved product, bedside thaw

Quality Control-related Services

- QC/QA/chain of custody
- In-process and release tests (in-house and outsourced, including Endotoxin, Mycoplasma, Gram stain, bacteria, and fungal culture, cell identity/enumeration/transduction efficiency using flow cytometry)

INSTRUMENTATION

Each key card entry restricted Production room is equipped with the essential tools:

- 6 ft and 4 ft Class II biological safety cabinets
- Under-the-counter 4º C refrigerator and -20 º C freezer
- Tabletop refrigerated centrifuge(s),
- Double stacked CO2 incubators
- Water bath, Plasmatherm-dry bath microscope, balance, Terumo sterile connecting device, tube sealer, vortex, DxH 520 hematology analyzer, NucleoCunter NC-200, Vi-Cell Blu cell viability analyzer

Specialized equipment:

- Miltenyi CliniMACS Plus
- Miltenyi CliniMACS Prodigy
- LOVO cell washer
- Anteroom, Quarantine room:
- 4º C refrigerators
- -20º C freezer
- -80º C freezers

Freezer room:

- Controlled Rate Freezer (CRF)
- LN2 freezer

INSTRUMENTATION CONT'D

QC /PD room:

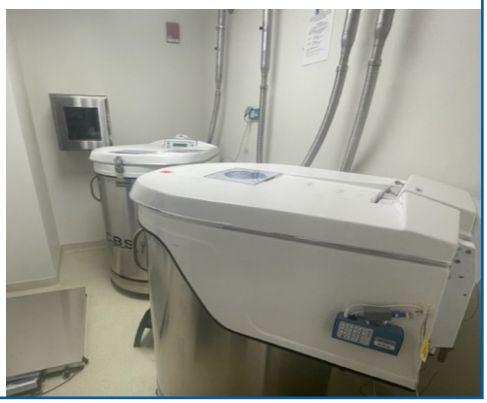
- Endosafe-PTS machine
- MycoAlert reader
- 3 ft Class II biological safety cabinet
- Quant Studio 6 PCR System
- MaxCyte Electroporator

Facility and equipment 24/7 monitoring:

- Isensix Guardian System
- Magnahelic gauges

Controlled-Rate Freezer Room

Production Room



VECTOR PRODUCTION FACILITY

OVERVIEW

The Vector Development and Production Facility (VDPF) occupies 1331 sq. ft. of space on the 6th floor of Gratwick Basic Science Building (GBSB) and is part of the Translational Immuno-Oncoloy Shared Resource (TIOSR) at Roswell Park Comprehensive Cancer Center. VDPF is a cGMP (current Good Manufacturing Procedure) facility dedicated to manufacturing clinical-grade lentiviral and retroviral vectors to be utilized to genetically modify cells from patients enrolled in clinical trials.

The facility follows cGMP, i.e., manufacturing products that meet specific requirements for identity, strength, quality, and purity in the pharmaceutical field, ensuring that the generated viral vector product is suitable for clinical trial use and compliant with FDA guidelines. Research and Clinical Grade viral vectors are tested in-house to include bioburden, transduction efficiency by flow cytometry, vector copy number by ddPCR, biological titer, and ELISAs for cytokines and protein assessments. The VDPF can assist with developing the assays required for lot release testing and characterization of viral vectors and cell lines.

The VDPF is equipped to manufacture large-scale viral vectors. The facility includes two class 10,000 cell-processing clean rooms. It has a unidirectional design with gown-in, ante-room, production rooms, post-ante-room, and gown-out. The facility also has a QC room for lot release tests, storage room, and freezer rooms.

VDPF was designed following discussions with the FDA (Type C meeting). The clean room area has pre- and terminal HEPA filtration with air changes/hour meeting the ISO7 requirements (>50 changes/hour) in the two production rooms and ante-room one and ISO 8 requirements (>20 changes/hour) in the gown-in, ante-2 and gown out rooms. The biosafety cabinets are equipped with terminal HEPA filters. It has a uni-directional flow design to avoid contamination. cGMP Suite and entry to production rooms are controlled via an electronic card access security system, and air and equipment are monitored continuously by a centralized system. Refrigerators and suites are always locked with access to only designated VDPF personnel. Vector manufacture is only performed by trained personnel following SOPs and using appropriate PPEs, including cleanroom coverall suits, booties, hair covers, masks, sterile sleeve covers, and nitrile gloves. All procedures are performed inside the biosafety cabinet or using closed-system bioreactors. Closed system filtration (Tangential Flow Filtration system) will be used to concentrate the vector when required.

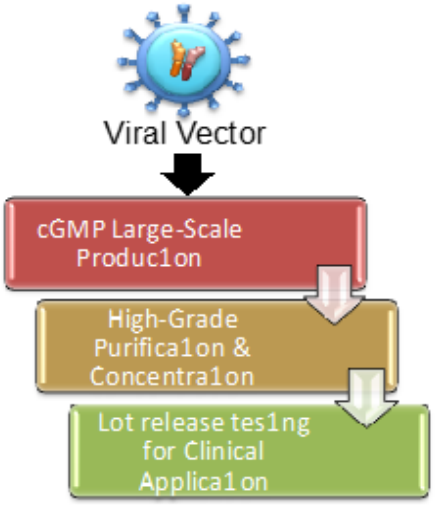
Vector Development and Production Facility (VDPF) Manufacturing

The VDPF manufactures clinical-grade retroviral and lentiviral vectors for Phase I and II studies. Manufacture of every batch of viral vector comprises three phases:

1. Phase 1: Assessment (sponsor requests and confirmation of plasmid identity)
2. Phase 2: Small-scale manufacturing, testing, and optimization
3. Phase 3: Final product manufacture and release

Retroviral Vector Manufacturing Process

1. Establishing a master cell bank (MCB).
2. Master Cell bank certification.
3. Manufacture of cGMP retroviral vector supernatant.
4. Vector supernatant harvest and filtration.
5. Vialing and Storage.
6. Certification of final product.



Lentiviral Vector Manufacturing Process

1. Cell Plating of Certified 293T cells.
2. Transfection.
3. Transfection media removal.
4. Vector supernatant harvest.
5. Purification and concentration
6. Vialing and Storage.
7. Certification of final product.

USING THE RESOURCE

Investigators interested in using the facility should contact Joanna Stanson to discuss the project and services. For quotes, pricing, and inquiries, please contact Joanna Stanson or Cindy Bonura or call 716-845-1300 ext. 6580. The VDPF is located in the GBSB, sixth floor. Hours of operation are weekdays, 9:00 AM – 5:30 PM.

SERVICES

The VDPF provides comprehensive services for developing and producing large-scale lentiviral and retroviral vector products suitable for clinical trials. Since each vector is a custom project, prospective customers should discuss their project with Joanna Stanson for consultation on services and scale of production.

INSTRUMENTATION

- Tangential flow filtration and Diafiltration System (KMPI KROSFLO M.KROS and KROSFLO R IIii)
- Automated Hollow Fiber Bioreactor System
- BIORAD digital Droplet PCR system
- Gell Electrophoresis and Restriction Digestion Palsmid Testing Systems
- Automated Thawing and Couting Instrumentation
- Endosafe Endotoxin Instrument
- Synergy HTX Microplate absorbance reader
- PCR cycler instruments
- 6-foot Class II biosafety cabinets
- Double stacked CO2 Heracell incubators
- SORVALL centrifuges
- Liquid Nitrogen storage containers
- -80 C, -20 C freezers
- Inverted Phase Contrast Microscope
- Terumo Sterile Connecting Device
- Tube Sealer
- Electronic Key Card Access system
- ISENSIX Advanced Remote Monitoring System
- Magnahelic Gauges

UNDER DEVELOPMENT...

COMMUNITY OUTREACH & ENGAGEMENT (CER)
Shared Resource

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OVERVIEW

The CER provides the infrastructure to support CCSG faculty integrating community engagement in their research projects, as well as intervention and implementation mapping to promote successful execution and dissemination. Specifically, the CER: 1) will provide a formal infrastructure to facilitate collaborations between scientists and community stakeholders, 2) offer trainings and professional development opportunities to enhance Roswell Park scientists' skills in community engagement science, and 3) provide consultation and support regarding study design and grant development. Importantly, the CER will facilitate opportunities for bi-directional communication and collaboration among community stakeholders and CCSG scientists. The CER has developed the Research Oncology Community Knowledge (ROCKstars) program which has paired 60 Roswell Park scientists with ROCKstars patient advocates across each of the CCSG programs. We will utilize SRM Developmental Funds to continue recruiting and training cancer survivors, caregivers, and lay individuals from the community who are interested in serving as advocates on scientific research projects. Further, we will continue training Roswell Park scientists how to integrate and collaborate with community scientists as research partners.

UNDER DEVELOPMENT...

cGMP FACILITY - CENTER FOR IMMUNOTHERAPY (CFI)
Shared Resource

LEADERS

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OVERVIEW

The facility is involved in product development, product optimization, large scale viral vector and cell production for clinical trials, as well as consulting and advisory projects for our intramural projects with Roswell Park faculty in addition to our external academic and biotech/pharma partners. We are currently building a new facility with 14 new clean rooms to accommodate the growing number of intramural products and clinical trials involved in our federal-, state- and philanthropy-funded projects in cancer immunotherapy, as well as the growing number of external academic and biotech collaborations. The cost of this project is estimated at $132.6M, which includes $32.6M in capital costs funded through a combination of an Empire State Development grant ($30M), Roswell Park Alliance Foundation funds ($10M), and institutional support ($92.6M). As part of this effort, Roswell Park is establishing a consortium of cancer centers across New York state (Empire State Cell Therapy Consortium) to rapidly recruit patients for future clinical trials.