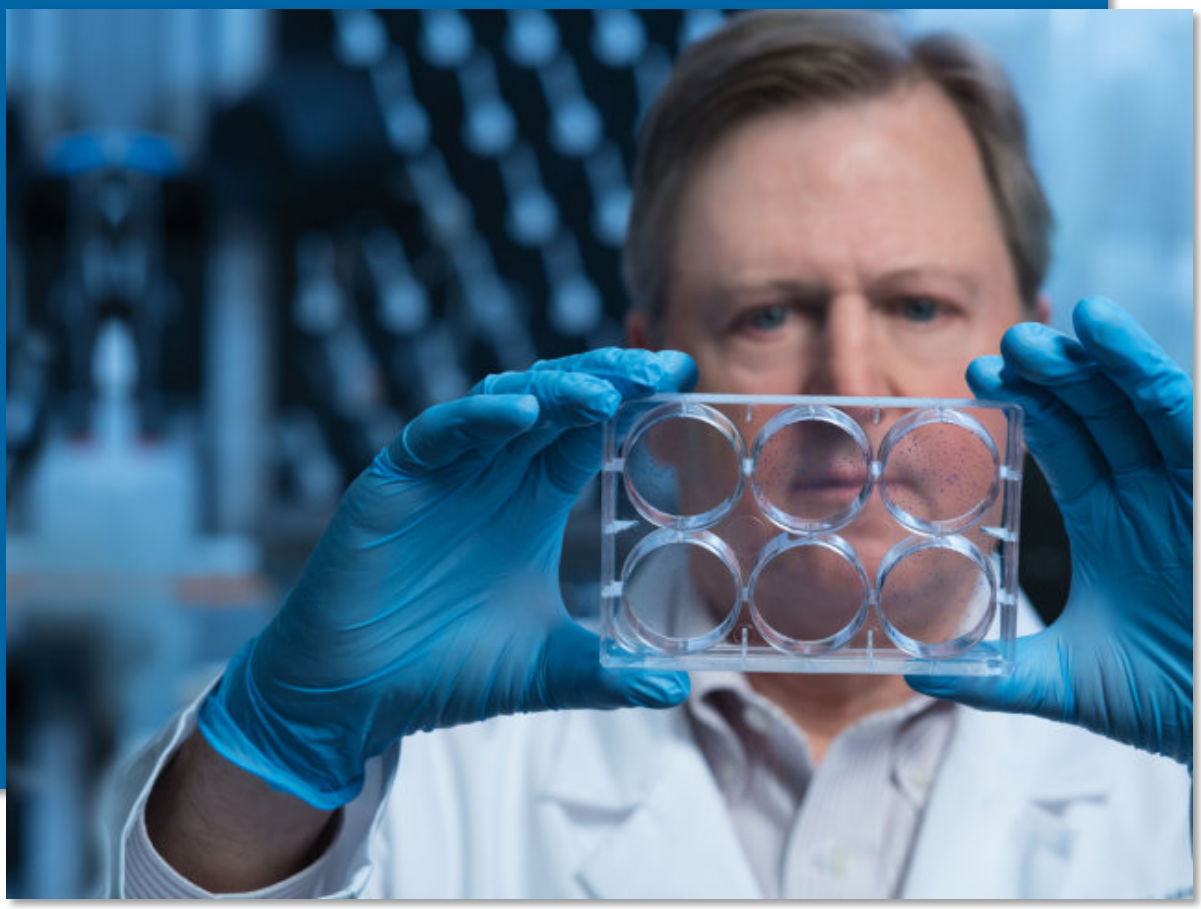


Karmanos Cancer Institute Shared Resources

BARBARA ANN Karmanos
CANCER INSTITUTE
Wayne State University

Karmanos Cancer Institute
4100 John R
Detroit, MI 48201
800-KARMANOS

NCI Comprehensive Cancer Center
A Cancer Center Designated by the National Cancer Institute

TABLE OF CONTENTS

INTRODUCTION

Karmanos Cancer Institute, headquartered in Detroit, is the largest cancer research and provider network in Michigan and has 15 treatment locations. Cancer patients have increased access to advanced cancer care in communities throughout the state. This provides an extra level of comfort and peace of mind to patients and their families, knowing they can receive the best care locally.

Caring for approximately 14,000 new patients annually and conducting more than 800 cancer-specific scientific investigation programs and clinical trials, Karmanos is among the nation's best cancer centers. Karmanos offers one of the largest clinical trials programs in the nation, giving patients access to more than 100 promising new treatments often available only at Karmanos.

Through the commitment of 1,000 staff, including nearly 300 faculty members, and supported by thousands of volunteer and financial donors, Karmanos strives to lead in transformative cancer care, research and education through courage, commitment and compassion. Our long-term partnership with the Wayne State University School of Medicine enhances the collaboration of critical research and academics related to cancer care.

As a leader in cancer research, Karmanos is able to offer patients access to innovative treatments and clinical trials that are not available anywhere else. More than $60 million is invested each year into cancer research with a level of commitment and expertise that cannot be duplicated at local hospitals.

We believe that our total focus on cancer ensures we will always be the best in developing and applying maximally effective treatment options. Our energy and resources are never diverted to other pursuits.

"A world free of cancer."

SHARED RESOURCES AND NIH PUBLIC ACCESS

The Shared Resources (Cores) at the Karmanos Cancer Institute, in partnership with Wayne State University, provide access to specialized technologies, services, and expertise that enhance scientific interaction and productivity. These Cores are supported, in part, through a NIH/NCI Cancer Center Support Grant (CCSG), P30 CA022453 (PI: Bepler). *As such, any peer-reviewed manuscript that includes results from these Cores must adhere to the NIH Public Access Policy, which states:*

The NIH Public Access Policy (https://publicaccess.nih.gov/policy.htm) applies to any manuscript that:

- Is peer-reviewed;
- And, is accepted for publication in a journal on or after April 7, 2008;
- And, arises from:
    - Any direct funding from an NIH grant or cooperative agreement active in Fiscal Year 2008 or beyond, or;
    - Any direct funding from an NIH contract signed on or after April 7, 2008, or;
    - Any direct funding from the NIH Intramural Program, or;
    - An NIH employee.

Compliance is evidenced by the presence of a PubMed Central ID (PMCID) number. You are required to provide the PMCID number when citing your papers in biosketches, NIH applications, proposals, and reports.

Some journals automatically deposit all NIH-funded final published articles in PubMed Central, to be made publicly available within 12 months of publication, without author involvement. Alternatively, articles can be submitted by the author or designee through the NIHMS system (https://www.nihms.nih.gov). KCI Research Administration acts as the designee on behalf of KCI members.

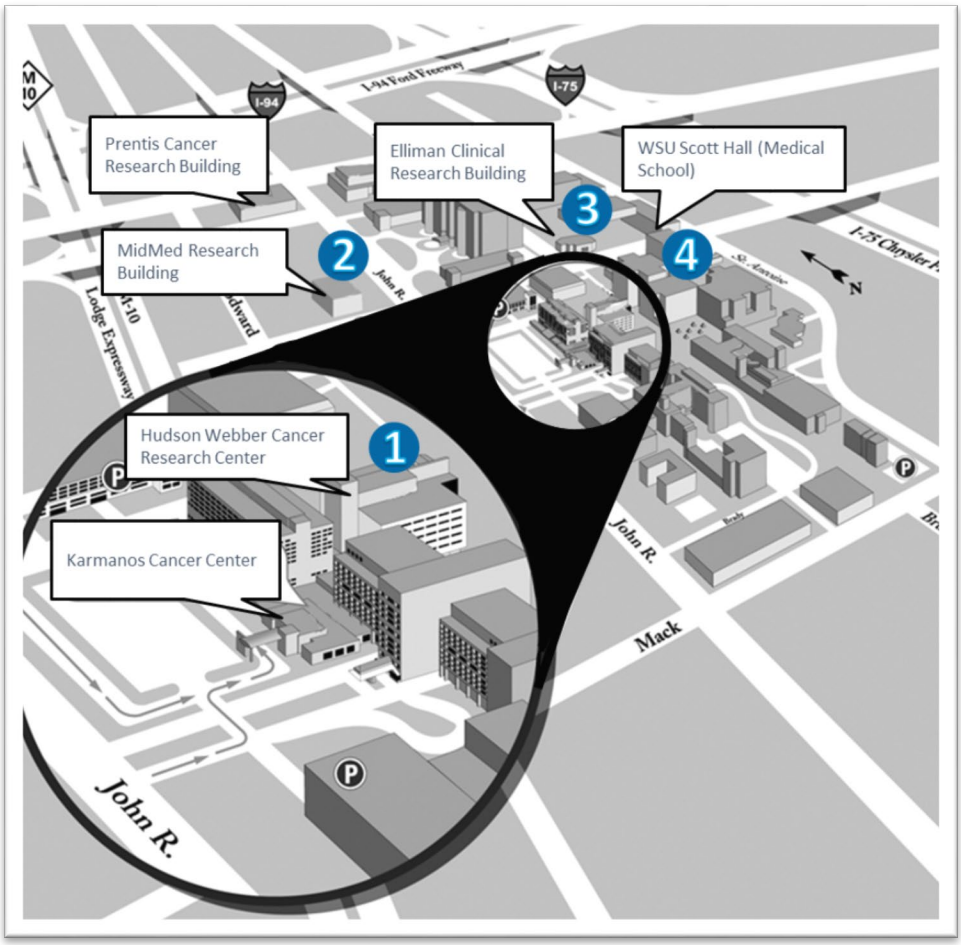
The NIH Public Access Policy applies to all publications that are funded directly through the P30 Cancer Center Support Grant (CCSG) via CCSG-supported Shared Resources, Developmental Funds, or Early Phase Clinical Research Support (EPCRS) funds.

Additionally, when a publication results from use of a KCI Shared Resource, it is essential that the CCSG be listed in the funding acknowledgements section of the published article. This helps identify research supported by the NIH. Specifically,

"The (Insert Name) Core is supported, in part, by NIH Center grant P30 CA022453 to the Karmanos Cancer Institute at Wayne State University."

Questions? researchadmin@karmanos.org

LOCATION OF SHARED RESOURCES



1 Hudson Webber Cancer Research Center

- Biobanking and Correlative Sciences (BCS) Core
- Microscopy, Imaging, and Cytometry Resources (MICR) Core-Cytometry Division
- Pharmacology and Metabolomics Core (PMC)

2 Mid Med Research Building

- Behavioral and Field Research Core (BFRC)
- Biostatistics and Bioinformatics Core (BBC)
- Clinical Trials Office
- Epidemiology Research Core (ERC)

3 Elliman Clinical Research Building

- Animal Model and Therapeutics Evaluation Core (AMTEC)
- Microscopy, Imaging, and Cytometry Resources (MICR) Core-Imaging Division

4 Scott Hall – WSU School of Medicine

- Microscopy, Imaging, and Cytometry Resources (MICR) Core-Imaging Division
- Proteomics Core

DIRECTORY OF SHARED RESOURCES

Animal Model and Therapeutics Evaluation Core (AMTEC)
Director: Lisa Polin, PhD (313) 578-4270 polinl@karmanos.org

Behavioral and Field Research Core (BFRC)
Director: Felicity Harper, PhD (313) 576-8763 harperf@karmanos.org

Biobanking and Correlative Sciences (BCS) Core
Director: Julie Boerner, PhD (313) 576-8351 boernerj@karmanos.org


Biostatistics and Bioinformatics Core (BBC)
Director: Judith Abrams, PhD (313) 576-8651 abramsj@karmanos.org
Co-Director: Sorin Draghici, PhD (313) 577-2162 sorin@wayne.edu

Epidemiology Research Core (ERC)
Director: Jennifer Beebe-Dimmer, PhD (313) 578-4209 dimmerj@karmanos.org

Microscopy, Imaging, and Cytometry Resources (MICR) Core
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Pharmacology and Metabolomics Core (PMC)
Director: Jing Li, PhD (313) 576-8258 lijin@karmanos.org

Proteomics Core
Director: Paul Stemmer, PhD (313) 577-6536 pmstemmer@wayne.edu

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Director, Research Administration:
Ben Herring, MA (313) 578-4408 herringb@karmanos.org

Animal Model and Therapeutics Evaluation Core (AMTEC)

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Assistant Director: Sijana Dzinic, PhD
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Email: polinl@karmanos.org

Web: https://www.karmanos.org/AMTEC

Mission of the Core:

The purpose of the Animal Model and Therapeutics Evaluation Core (AMTEC) is to enhance the peer reviewed funded research activities of KCI members whose research needs involve the use of animal models. Our goal is to provide expert scientific consultation, technical expertise and access to a wide breadth of relevant tumor models and associated animal-related services.

Core Services Available:

- Animal Study Technical Support
- Tumor Models and Cell Lines (Mouse and Human – Syngeneic, Transgenic, GEMM, Xenograft and PDX)
- In Vivo Orthotopic Tumor and Metastasis Models
- In Vivo Therapeutic Evaluation: Consultation, Study Design, Implementation and Analysis
- In Vivo Training/Teaching for researchers, staff and students
- Consultation and Assistance: Grant, manuscript and IACUC submissions
- In Vivo Study Sampling: pK analysis treatment and time point collections; treatment and harvest of tumor and/or tissue specimens at endpoint or during Rx regimens for further analyses (e.g. to BCS, Proteomics, Pharmacology Cores as well as for genomics, metabolomics and veterinary pathological examination).

Resources:

- Two ultracold units (-80ºC & -150ºC) connected to the Public Safety monitoring system
- New dedicated cell culture room w/BSL2 laminar flow hood
- Table top refrigerated centrifuge
- Two Panasonic incubators equipped with germicidal & UV sterilization
- New BSL2 flow hood (animal suite)
- Eight liquid nitrogen dewars
- Somno suite and SurgiSuite surgical platforms for surgical procedures
- Techniplast environmental chamber
- Excelsior AS Tissue Processor and HistoStar Instrument Embedding Center

Research:

Patient Derived Xenograft (PDX) In House Development

Metastatic hormone resistant prostate PDX: 3 models (KCI-PR022 (shown in right panel, established from patient bone biopsy)**, KCI-PR035 and 18-016 in current development):**

Metastatic lung PDX:
20 metastatic lung models established and undergoing characterization: Utilization: Part of an R01 submission to assess USP10's role in platinum response in NSCLC patients. Drs. Bepler (MT) and Zhang (MT)

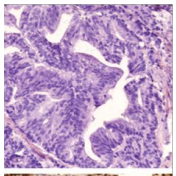
samples	Date*	Lab ID	USP10 level	p53 status
1	12/9/2014	14-049 M2	0.12	wt
2	12/18/2014	14-055 M7	0.23	mut
3	2/10/2015	14-065 M7	0.43	wt
4	2/10/2015	14-068 M12	2.25	mut
5	6/23/2015	14-012 M8	1.51	wt
6	6/3/2015	14-113 M6	3.37	mut
7	6/23/2015	14-023 M8	7.91	wt
8	7/2/2015	15-002 M7	0.22	wt
9	10/13/2015	15-009 M7	0.94	mut
10	8/27/2015	14-110 M3	0.97	mut
11	8/27/2015	15-030 M3	2.66	wt
12	10/9/2015	15-028 M8	2.06	mut
13	10/20/2015	15-001 M5	0.96	mut
14	10/27/2015	14-097 M4	1.93	mut
15	11/11/2015	14-114 M4	1.52	wt
16	10/20/2015	15-033 M3	0.07	wt
17	3/22/2016	14-112S M6	0.65	mut
18	3/31/2016	15-016 M8	1.34	wt
19	9/20/2016	15-022 M7	0.13	wt
20	10/25/2016	15-018 M5	1.44	mut

*dates on which tumors were harvested

WT-p53 USP10-Low
WT-p53 USP10-High
Mut-p53 USP10-Low
Mut-p53 USP10-High

KCI-PR-022 PDX

H&E



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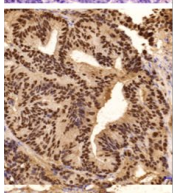
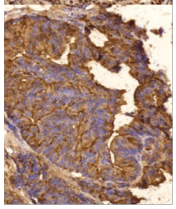


PSA



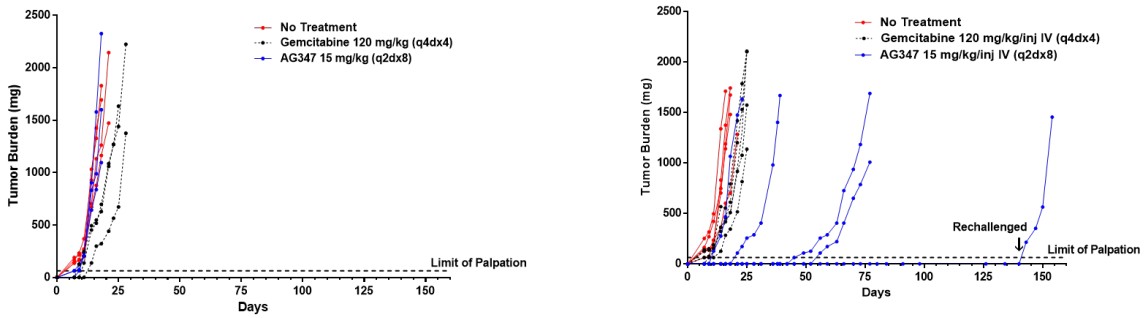
Prostate PDX:
AMTEC with Drs. Elisabeth Heath (MT) and Julie Boerner (MT)

Metastatic Lung PDX:
AMTEC with Drs. Sandeep Mittal (MT) and Sharon Michelhaugh

AGF-347 - A Novel Therapy for Pancreatic Cancer: In Vivo Study with MiaPaCa-2 in SCID Mice

Goal: Develop a new class of antifolates: Multi-targeted cytosolic and mitochondrial C1 metabolism inhibitors that are efficacious against lung, colon and pancreatic cancer.

Genes encoding one-carbon (C1) metabolism enzymes in the mitochondria and cytosol are consistently upregulated across multiple cancer types. Dr Matherly and collaborators have designed and evaluated AGF-347 as one such prototype multi-targeted small molecule inhibitor of mitochondrial C1 metabolism at serine hydroxymethyltransferase (SHMT) 2, and cytosolic C1-dependent purine biosynthesis (β-glycinamide ribonucleotide formyltransferase and 5-aminoimidazole-4-carboxamide ribonucleotide formyltransferase). *In vivo* proof of principle study shown below: MiaPaCa-2 xenografts with WT multi C1 targets: Left panel (standard diet) vs Right panel (folate depleted diet):



Supported in part by R01 CA53535 and R44 221543 from the National Institutes of Health. The Animal Model and Therapeutics Evaluation Core was supported, in part, by NIH Center grant P30 CA022453 to the Karmanos Cancer Institute and Wayne State University.

Acknowledgement Text:

Publications that result from Core involvement should include following statement:

> ***"The Animal Model and Therapeutics Evaluation Core is supported, in part, by NIH Center grant P30 CA022453 to the Karmanos Cancer Institute at Wayne State University."***

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Scientific Director: Felicity Harper, PhD
Director: Tanina Foster Moore, PhD
Phone: (313) 576-8763
Email: harperf@karmanos.org

Web: https://www.karmanos.org/BFRC

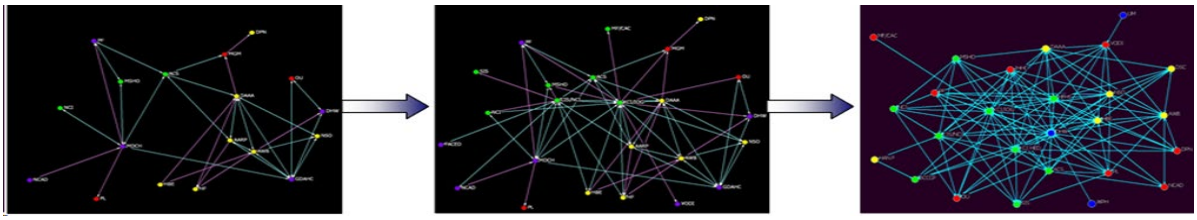
Mission of the Core:

The Behavioral and Field Research Core (BFRC) is designed to facilitate the integration of communication and behavioral research across KCI's Programs, including studies involving epidemiology, cancer prevention, clinical and developmental therapeutics, palliative care, and genetics. The Core translates research findings from the behavioral sciences into formats that are useful to investigators trying to understand the impact of human behavior on the clinical or research problem at hand.

Core Services Available:

Project Design/Analysis

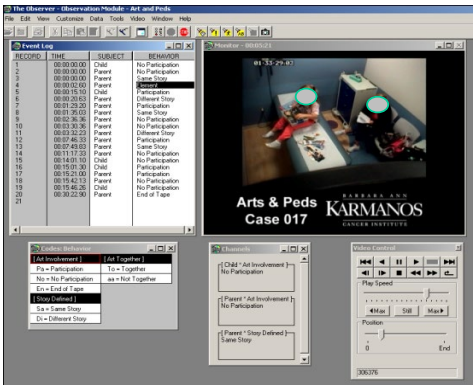
- Expertise in designing research protocols for studies involving behavioral aspects of cancer health disparities; behavioral and communication theory; social network methods and analysis, social marketing approaches and strategies for behavior change; social network analysis and community based participatory research methods
- Training for junior investigators utilizing data archives (Medical Interaction Research Archives)
- Expertise in health education program design and evaluation
- Expertise in post-production design
- Expertise in professional intervention – focus group moderation, motivational interviewing, ethnographic interviewing
- Expertise in data management and analysis

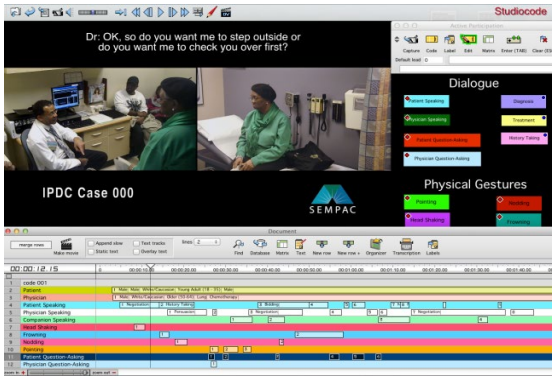


Social Network Analysis

Clinic Liaison, Community Liaison, Advanced Management

- Expertise in all regulatory preparation, submission – PRMC, IRB, WSU, McLaren
- Training for new project team members
- Expertise in clinic liaison services: Mosaic, Cerner/Citrix, CIS; participation in MDT meetings
- Expertise in codebook development
- Expertise in post-production editing
- Expertise in advanced coding
- Expertise in developing and maintaining community partnerships
- Expertise in longitudinal and multi-site project management





Observer and StudioCode

Project Management

- Oversight of behavioral and communication research studies by highly skilled and experienced Core staff, such as quality of life data collection, video capture, and community-based studies
- Expertise in real time video capture (KCC Wertz, Walt, ROC, Flint ROC, Weisberg)
- Expertise in medical chart abstraction
- Expertise in participant interviewing
- Expertise in coding verbal statements in video and audio interactions

Video Recording and Capture

Technical Operations

- Audio/video technical support
- Transcription services
- Data collection via hardcopy or electronic formats
- Consenting participants to research studies and clinical trials

Operations

- Recruitment and retention of study participants (from clinical and community-based research sites) through maintenance of a community participant registry that includes more than 1,000 names and contact information of persons who are willing to be contacted for possible research participation
- General operations and administration of research projects
- Data entry
- Coding discreet data (e.g. who/what is in the exam room)

Resources:

Resources available through the BFRC include real-time video recording and coding of clinical interactions, access to an extensive video archive for communication and behavioral studies, patient and community research participant registries, as well as an extensive bank of clinical and social/behavioral instruments and measures; a community based research registry populated by adults from within the catchment area who have consented to be contacted for research participation; expertise in Qualtrics, Observer, StudioCode, Final Cut, SPSS and data management, and access to comprehensive national datasets (e.g., HINTS), geographical and population tracking/mapping capabilities.

Research:

The Influence of Affective Behavior on Impression Formation in Interactions Between Black Cancer Patients and Their Oncologists.
Senft, et al. Social Science and Medicine, 2018 1U54CA153606-01, 1R03CA195147, and P30CA022453

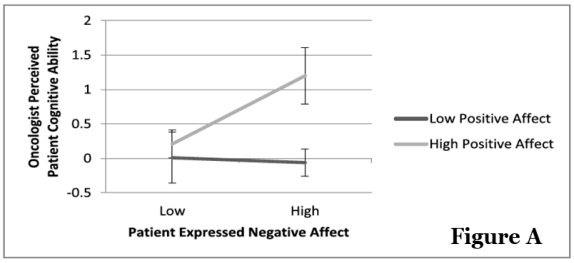


Figure A

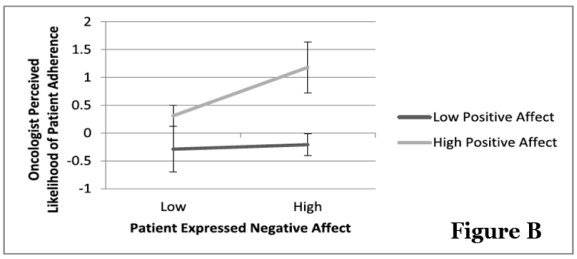


Figure B

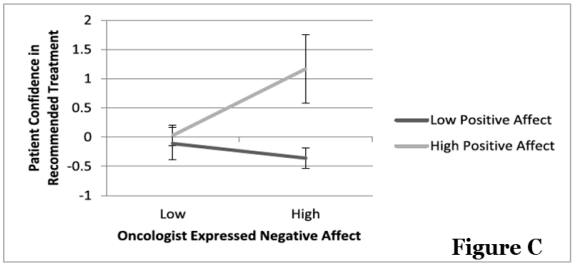


Figure C

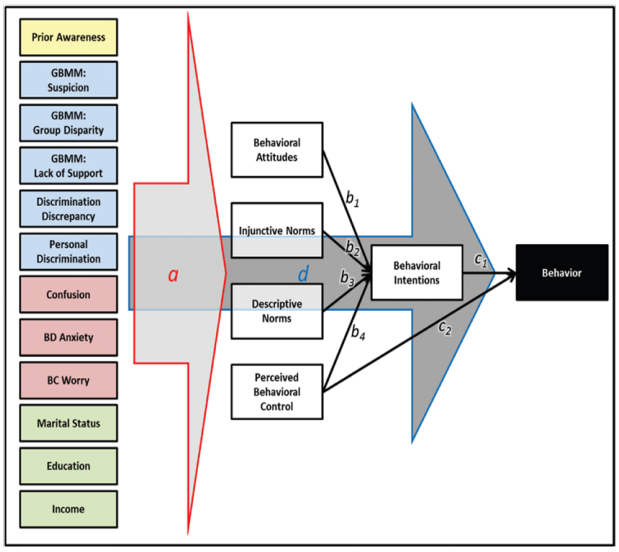
Figure A shows the impact of patient positive (**+**) and negative (**-**) affect on oncologist perceived patient cognitive ability. When patients expressed lower levels of **+** affect, their expression of **-** affect had little effect on oncologists' perceptions of cognitive ability. However, when patients expressed higher levels of **+** affect, higher levels of **-** affect were associated with more positive perceptions.

Figure B shows the impact of patient **+** and **-** affect on oncologist perceived likelihood of patient adherence to treatment. When patients expressed lower levels of **+** affect, their expression of **-** affect had no effect on oncologists' perceptions. In contrast, when patients expressed higher levels of **+** affect, higher levels of **-** affect were associated with more positive perceptions.

Figure C shows the impact of oncologist **+** and **-** affect on patient perceived confidence in treatment. When oncologists expressed lower levels of + affect, their expression of - affect had little effect on patients' confidence in the recommended treatment. Yet, when oncologists expressed higher levels of **+** affect, higher levels of **-** affect were associated with patients' increased confidence in the recommended treatment.

This study provided further evidence of the importance of subtle nonverbal behaviors and expressions of affect in treatment related perceptions of patients and oncologist.

Explaining Between-Race Differences in Processes Predicting Physician Communication for African American and European American Recipients of Breast Density Notifications. Manning et al, Annals of Behavioral Medicine, 2018 P30CA022453



Using the theory of planned behavior (TPB) as a framework, the authors examined between-race differences in behavior after receiving breast density notifications for Caucasian American (CA) and African American (AA) women. Although no between-race differences were found in self-reported physician communication, CA women followed TPB in their decision-making process (i.e. behavioral intention, education and income). Rather, race-related medical suspicion, prior breast density awareness and emotional responses to breast density notifications predicted behavioral decision-making processes in AA women.

This study highlights the need to focus on racially distinct psychological targets when designing interventions that support behavioral decision-making among women who receive breast density notifications.

Acknowledgement Text:

Publications that result from Core involvement should include following statement:

"The Behavioral and Field Research Core is supported, in part, by NIH Center grant P30 CA022453 to the Karmanos Cancer Institute at Wayne State University."

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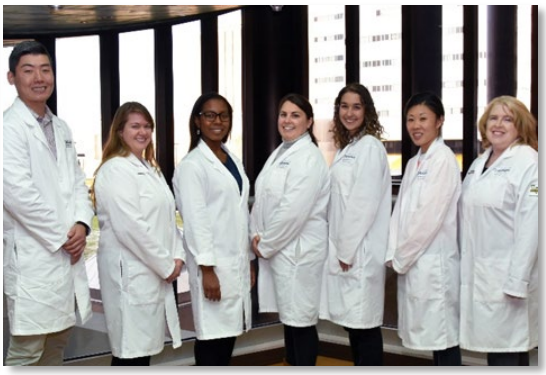
Web: https://www.karmanos.org/biobank



Mission of the Core:

The purpose of the Biobanking and Correlative Sciences (BCS) Core is three-fold: 1) the Biobank pillar facilitates peer reviewed, funded research activities requiring IRB-approved access to patient tissue, 2) the Clinical Correlates pillar facilitates clinical studies by reviewing protocols, managing tissue specimens and linking radiology and study biopsies back to CTO, and 3) the Correlative Sciences pillar assists Physicians, Epidemiologists and Basic Scientists with Preclinical Assays and study development.

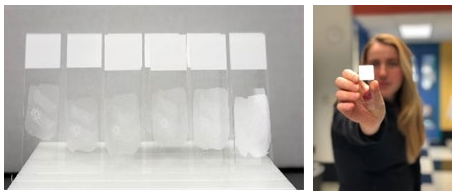
Core Services Available:

Biobanking

- Consenting patient for biobanking protocols
- Biospecimen acquisition and processing
- Biospecimen storage and quality control
- Consulting
  - Assistance with IRB protocol requirements and submission
  - Letters of support for grants
  - Annotation of biospecimens (ex. Race, ER/PR status, chemotherapy, etc.)

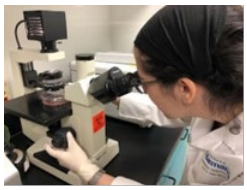
Clinical Correlates

- Protocol specific tissue retrieval for clinical trials
- Processing of tissue for clinical trials
- Pathologic verification and diagnosis of tissue
- IATA approved shipping of biospecimens
- Consulting
  - Assistance with the development of IITs
  - Flowsheet and laboratory manual (for IITs) construction based on clinical trial protocol

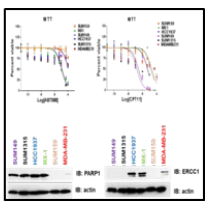


Correlative Sciences

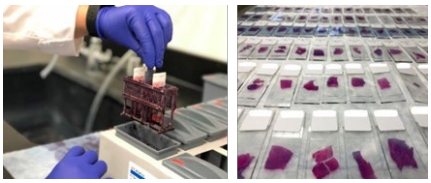
- Authentication of cell lines and xenografts models using STR profile analysis
- Signed authentication reports for journal publications and grant reviews
- Protein expression and activation assays
  - Standard viability drug treatment assays
  - Cell survival and tumorigenesis assays
  - Detection of proteins in tissues (Westerns, immunohistochemistry)



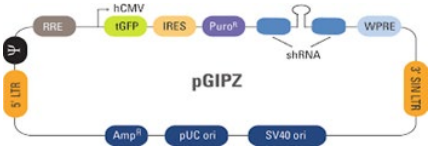
	WSU AGTC fingerprint	ATCC fingerprint
D5S818	12	12
D13S317	13	13
D7S820	9,10	9,10
D16S539	13,14	13,14
vWA	16,17	16,17
TH01	6	6
AMEL	X	X
TPOX	11	11
CSF1PO	12	12



- Histology
  - Human and animal tissue processing
  - FFPE and frozen tissue sectioning
  - H&E and specialty stains
  - Immunohistochemistry
  - Tissue microarray construction



- Distribution of shRNA clones GIPZTM lentiviral shRNA (OpenBiosystem)



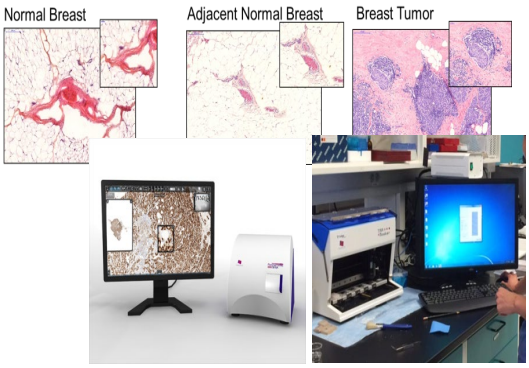
Ref: pGIPZ lentiviral vector, GE Healthcare

- Consulting
  - Assistance with protocol development
  - Letters of support of grants

Resources:

The BCS employs the following resources and instrumentation to provide quality services to KCI investigators and its affiliates:

- Growing inventory of biospecimens for research- tissue, blood, saliva, urine
  - Each specimen QC for tumor or normal tissue
  - Coming soon…. Biobank website with searchable interface and how to guides for requesting specimen tissue
  - Leica DM5500B microscopy
- Syngene PXi imaging system
- Gel Count colony analysis
- Bio-Rad and Invitrogen SDS-PAGE systems
- Perkin-Elmer TMA Master
- 3DHistech slide scanner and imaging software
- Reichert-Jung 2040 Autocut Microtome, Microm Hm 505E Cryostat, Fisher 166MP Automated Tissue Processor, Shannon Cytospin 2 Centrifuge
- The OpenBiosystems (Thermo-Fisher) human GIPZTM lentiviral shRNA library (maintained in *E.coli*), comprised of ~ 130,000 individual RNAi vectors that include 3-5 clones targeted for each human gene



Research:

BioBank

KCI downtown and network sites collect discard surgical tissue:

- Frozen and FFPE, tumor and normal adjacent
- Blood products: plasma, PBMC, RNA
- Saliva

Community collection events: saliva from 231 people

Legacy Biobank consents: 4,011

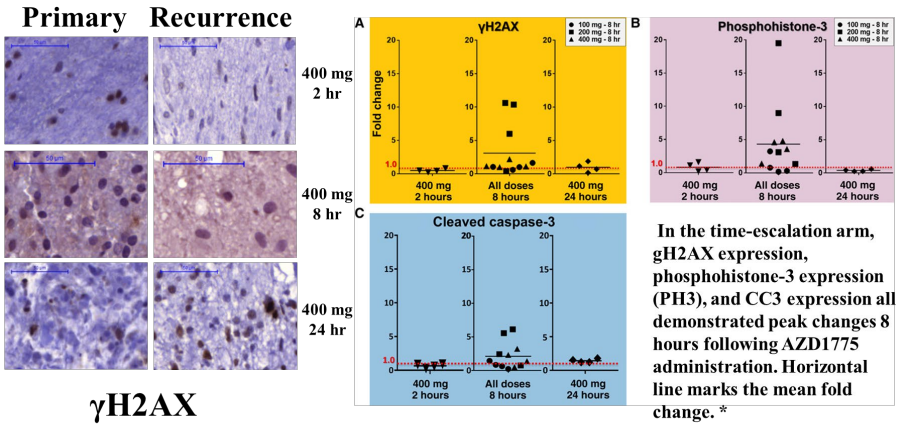
Specimens distributed in FY18: 330

Current BioBank Inventory

Diagnosis	Patients Consented	Blood	Frozen tissue	FFPE
Breast	1102	354	82	582
GI	296	189	11	532
Malignant Heme	311	222	1	71
GU	329	113	43	234
Head and Neck	570	211	60	437
Lung	2226	1764	30	503
Gyn	559	266	91	266
Other	323	78	11	332
Total	5716	3197	329	2957

Active Trials Supported:	395
Biopsies Collected:	2,187
H&E Staining:	6,315
Slide Sectioning:	28,783

Correlative Sciences



Acknowledgement Text:

Publications that result from Core involvement should include following statement:

> ***"The Biobanking and Correlative Sciences Core is supported, in part, by NIH Center grant P30 CA022453 to the Karmanos Cancer Institute at Wayne State University."***

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Biostatistics and Bioinformatics Core (BBC)

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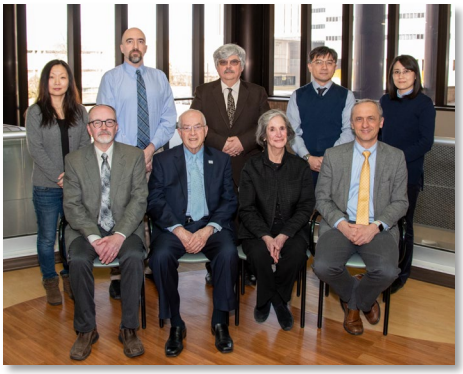
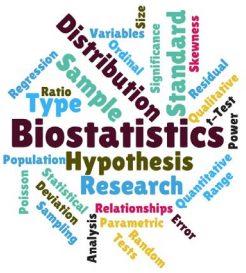


Mission of the Core:
The Biostatistics and Bioinformatics Core is a resource for KCI members in basic (*in vitro* and *in vivo*), clinical, population and translational sciences. Biostatistics is important in the design of cancer research studies to ensure that the scientific questions are framed so that they can be answered precisely and efficiently and in the analysis of these studies to ensure that the conclusions are accurate and valid. Bioinformatics is important to ensure computationally efficient and informative analyses.

Core Services Available:
The work of the Core falls into four major categories: 1) development of grant proposals for peer reviewed, external funding, 2) design and protocol development of investigator-initiated clinical trials, 3) analysis of pilot studies, and 4) statistical analysis of data for publication. Specifically, members of the Core:

- Develop experimental designs for clinical, laboratory, intervention, and observational studies
- Conduct statistical and bioinformatic analyses and collaborate on interpretation of results
- Process raw genomic data (e.g., RNA-seq, exome sequencing) for use in statistical analyses
- Conduct downstream bioinformatics analyses, including pathway, differential expression, and network analyses
- Conduct statistical analyses of *in vivo*, clinical and epidemiologic data
- Write statistical reports and make statistical presentations
- Write statistical and bioinformatic sections for grant proposals and manuscripts in collaboration with investigators
- Provide instruction in biostatistics to cancer researchers in journal clubs, seminar series and grand rounds presentations
- Evaluate new and conventional statistical and bioinformatic methodology for applicability to cancer research projects and for application or adaptation of methods as required
- When current methods are inadequate, develop biostatics and bioinformatics methods for specific cancer research projects

Resources:
Statistical applications include general-purpose software R, SAS and Stata/MP. Software for calculating statistical power includes PASS and nQuery Advisor. Bioinformatics software includes ANNOVAR, Bioconductor, GATK, Ingenuity and Oncomine among others. The Core continuously reviews and updates processes to follow and maintain best practices when designing custom computational pipelines for all stages of bioinformatic analysis from data pre-processing to variant discovery.



MS Windows based application software resides on a Dell PowerEdge 2950 III, which has two quad core Intel Xeon 5460 3.16 MHz processors, each with 2x6 MB cache, 32 GB memory and two 300 GB disk drives and a Dell R820 with 4 Xeon E5-4650 2.70GHz processors, each with 8 cores, 128 GB

memory, 4 600 GB and 2 146 GB disk drives. The back-up unit is a 4 DAT drive running Veritas Backup Exec. Incremental back up of data files is performed nightly. Full back-ups are performed weekly and the data tapes are maintained off-site in a secure, fireproof storage facility. Access to the server is restricted to members of the Biostatistics Core and authorized guests.

Linux based application software may be run on the WSU high-performance grid system. The WSU Grid is a tightly networked system of 400+ nodes and over 8000 processing cores. Integrated into the WSU high-performance grid computing facility are two PowerEdge R710 computers, each with 48 GB RAM; dual 6 core Intel Xeon X5680 3.33 GHz processors and 1 TB hard drives that run under the Linux operating system. Those computers were purchased by KCI for the use of Core members, but are accessible to other authorized KCI members whose research requires high performance computing capabilities.

The Core uses the Google Cloud Platform for computationally intensive analyses, analyses that require large memory, are highly distributed or CPU intensive, particularly pre-processing raw sequence data. Cloud resources will also be utilized for medium and long-term storage of raw data, processed data and associated procedures and pipelines. All third-party resources are HIPAA compliant.

Google Cloud Platform

Core Service Eligibility

- All KCI members
- Clinical fellows, post-doctoral fellows, residents and graduate students who conduct cancer research under the supervision of a mentor who is a KCI member

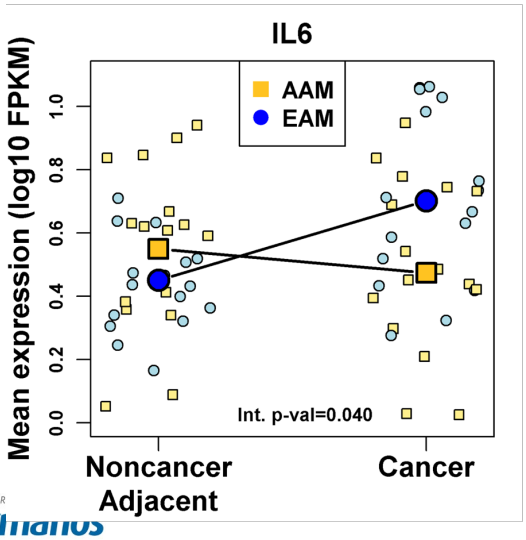
Guidelines for Lead Time

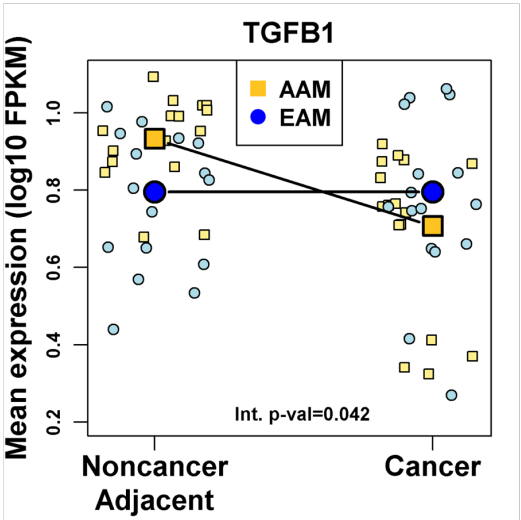
Researchers are encouraged to contact the Core early in the formulation of a research project to allow sufficient time for collaboration. Meaningful collaboration requires time for familiarization with research problems, communication, review of the literature in the particular research field, tailoring the appropriate statistical methods. Requests for statistical collaboration are addressed based on Core priorities and within a priority in the order in which they are received. Because requests for collaboration on grant proposals have the highest priority, the Core may be unable to respond immediately to other types of requests. It is recommended that researchers provide sufficient lead-time to Core members:

- **External grants**: two months before the grant is due at funding source
- **Abstracts**: one month before the abstract deadline

Research:

Teslow E et al. (2018) Exogenous IL-6 induces mRNA splice variant MBD2_v2 to promote stemness in TP53 wild-type, African American PCa cells. Mol Oncol.





Karmanos CANCER INSTITUTE Wayne State University

NCI Cancer Center
A Cancer Center Designated by the National Cancer Institute

Acknowledgement Text:

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Mission of the Core:
The Epidemiology Research Core (ERC) mission is to support population-based research by accessing Metropolitan Detroit Cancer Surveillance System (MDCSS) cancer cases and their data for use in approved research. The ERC provides epidemiology expertise and collaborates with researchers conducting investigations in cancer prevention, etiology, treatment and outcomes. This type of population-based cancer research is made possible by ERC accessing this data on behalf of researchers, which ensures confidentiality.

Core Services Available:

- Consultation. Consultation and collaborative research expertise focused on study design, proposal development, IRB applications, and interpretation of population-based local and national SEER data. ($0.00) (Free initially, but salary support for MDCSS-affiliated faculty with appropriate expertise is requested for ongoing funded projects.)
- Rapid Case Ascertainment. Rapid identification and ascertainment of eligible study participants, requiring review of all pathology reports indicating a cancer diagnosis at approximately 60 metropolitan area hospitals, clinics, pathology laboratories and radiation therapy facilities and rapid collection of patient demographic information. This speeds up case identification for population-based studies, with most cases identified within two to three months of diagnosis. ($55.00/case)
- Control Identification. Identification of population-based control groups for case-control study designs via random digit dialing, Centers for Medicaid and Medicare Services (CMS) records, Department of Motor Vehicles (DMV) records, and other mechanisms. ($36.37/hour)
- Research Support and Training: Regulatory oversight and research training support of study staff involved in studies in which participants are being contacted. ($53.43/hour)
- Collection and Abstraction of Medical Records. Collection of medical records and abstraction of study-specific data that are not available in the MDCSS registry. ($51.64/hour)
- Biospecimen Collection. Collection of biologic specimens, including blood, buccal cells, saliva, urine and spirometry, from study participants and/or diagnosing hospitals including KCI and non-KCI facilities. ($75.00/specimen)
- Tissue Retrieval. Collection of biologic tissue specimens, including tumor blocks and H&E stained slides and unstained slides from diagnosing hospitals including KCI and non-KCI facilities. Tumor Collection from KCI facilities is coordinated with the KCI Biorepository Core. ($49.51/specimen)
- Database Query: Response to requests for population-based data requiring query of the MDCSS and/or the national SEER de-identified research data files for descriptive analyses. ($49.00/hour)
- Database Linkage. Linkage of outside data sources to MDCSS data for the collection of patient demographics, treatment and survival data. Use of the linked SEER-Medicare files is included in this service line. ($49.00/hour)

Resources:

The MDCSS data system contains all cancer diagnosis and survival information for the Metropolitan Detroit area from 1973 forward, housed in the SEER Data Management System (SEER*DMS). SEER*DMS is a relational database that supports central cancer registry operations and includes features for importing, editing, consolidating, exporting and reporting on cancer-related data. This database currently houses data on in excess of 760,000 patients and 860,000 cancers. In addition, ERC analyst(s) have access to the national de-identified SEER Research data, as well as Statistical Analysis System (SAS©) and ArcGIS© softwares.

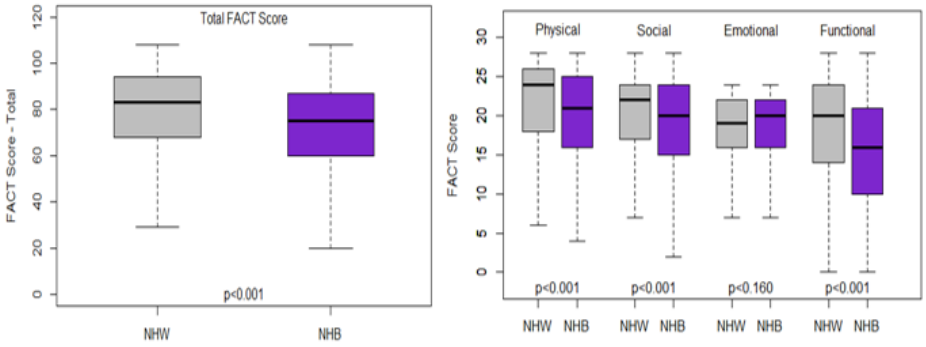
Research:

The Epidemiology Research Core (ERC) supports a broad array of research. Set forth below are selected projects currently being supported by the ERC.

The Detroit Research on Cancer Survivorship (ROCS) study PIs: Schwartz A. and Albrecht T., NCI U01 CA199240, (2/27/2017-1/31/2022)

There are an estimated 15.5 million cancer survivors in the US so that understanding the unique issues cancer survivors face is essential. African Americans (AA) with cancer experience the highest death rate and shortest survival for most cancers. The Detroit ROCS study will be the largest case cohort of AA cancer survivors with projected enrollment over 5 years to exceed 5,500 patients diagnosed with female breast, prostate, colorectal and lung cancer and about 2,750 caregivers. Participants complete a web-based survey at baseline and annually for up to 4 years. Blood and tumor specimens are collected and banked for projects focused on germline genetics, plasma biomarkers and tumor molecular profiling.
To date, 1,848 patients have been enrolled, (58% response rate*), along with 274 caregivers (88% of those nominated*). A comparison of baseline responses among the first 593 participants to a referent group of 421 non-Hispanic white patients suggests AA diagnosed with cancer experience poorer quality of life even after adjustment for the presence of comorbid conditions.

Figures 1 & 2: Racial differences in reported quality of life measured by the FACT instrument.



The Epidemiology Research Core supports this project with Rapid Case Ascertainment (RCA), Database Query, Research Support and Training (RST), Biospecimen Collection and Tissue Retrieval.

*Response rate calculated based upon those with a final participant outcome code.

Characterizing the Genetic Landscape of Prostate Cancer in Young African-American Men, a.k.a. Early Onset Prostate Cancer (EPC)
PIs: Cooney K./Beebe-Dimmer J., W81XWH-16-1-0713, Duke University/DoD, (09/30/16 - 09/29/19)

This study will collect data through a brief survey (taken online or over the phone) and DNA (via blood and/or saliva) on 750 African-American men diagnosed with prostate cancer before age 60. The study will include men diagnosed from 2009-2016 with Gleason scores of 7+. The goal of the study is to identify men who harbor germline variants that increase the risk of developing clinically significant prostate cancer. This study uses Next Generation Sequencing (NGS) approaches to analyze germline DNA from 750 African American men with clinically significant prostate cancer, focusing on genes already known to be mutated in the germline or tumor of men with prostate cancer, as well as genes in functional pathways of interest (i.e. hormone biosynthesis and signaling and DNA damage repair). To date 532 cases have enrolled with 69.9% blood consent and with 83.8% having consented to tumor retrieval. The study will enroll for approximately 2 years. The ERC supports this project with Biospecimen Collection, Tissue Retrieval and Research Support and Training.

Risk of Incident Claims for Chemotherapy-Induced Peripheral Neuropathy Among Women With Breast Cancer in a Medicare Population
PI: Beebe-Dimmer J. (12/7/2016-8/29/2018)

Chemotherapy-induced peripheral neuropathy (CIPN) is a debilitating side effect of first-line neurotoxic agents used to treat breast cancer. This study evaluated 11,149 first primary female breast cancer cases diagnosed 2007-2013 in ages 66+ that were identified from the NCI SEER-Medicare database who had received chemotherapy as first-line therapy. Cases were restricted to AJCC stage II-IV and those with preexisting neuropathy were excluded. CIPN occurred in 8.3% of cases within 1 year of commencing chemotherapy. **Significant predictors of CIPN incidence in the adjusted model included: younger age (P for trend < .0001), being married or equivalent (HR 1.30, 95% CI: 1.09-1.54), AJCC stage II (HR 1.34, 95% CI: 1.06-1.69) or stage III (HR 1.56, 95% CI:1.23-1.98).**

Paclitaxel as part of first-line chemotherapy treatment was associated with significantly higher CIPN incidence in comparison with other first-line chemotherapies. **After adjustment for age group, marital status and stage, Paclitaxel was associated with a 2.7-fold greater risk for CIPN than nonneurotoxic regimens (HR 2.69, 95% CI: 2.23-3.23)** (*Greenwald MK et al., Cancer 2018:00 1-10, released online before print).* The ERC supports this project with Database Linkage.

Acknowledgement Text:

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"The Epidemiology Research Core is supported, in part, by NIH Center grant P30 CA022453 to the Karmanos Cancer Institute at Wayne State University."

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The Team:

(Left to right starting with front, then back: Velma White, Field Interviewer/Phlebotomist; Jennifer Beebe-Dimmer, PhD, MPH; Scientific Director; Sharon Moton, MEd, Division Administrator; Arkeshia Barnes, Field Interviewer/Phlebotomist; Tricia Arballo-Spong, Manager; Fawn D. Vigneau, JD, MPH, Co-Director; Julie Ruterbusch, MPH, Analyst; Terry Smith, Research Assistant. Not pictured: Victoria Mabrey, CTR, Senior Oncology Data Analyst; Angela Piasecki, CTR, Senior Oncology Data Analyst; Terri Essex, CTR, Senior Oncology Data Analyst; Bridget Reno, Research Assistant; Amanda Reed, Research Assistant; Jasmine Brown, Field Interviewer/Phlebotomist, Shannon Johnson, Field Interviewer/Phlebotomist.

Microscopy, Imaging, and Cytometry Resources Core (MICR)

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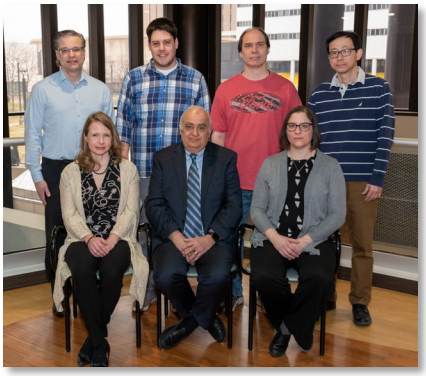
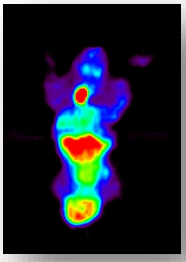


Mission of the Core:
The mission of the Microscopy, Imaging & Cytometry Resources (MICR) core is to enhance the peer reviewed funded research activities of KCI members whose research requires confocal microscopy, flow cytometry, small animal imaging and related techniques. We provide KCI members with expert scientific consultation and access to state-of-the-art instrumentation.

Core Services Available:

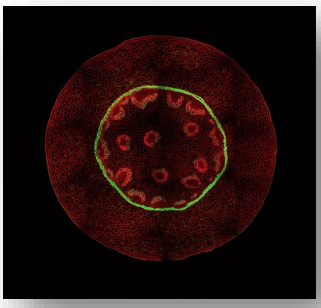
- Confocal Microscopy, including both point scanning and spinning disk technologies
- Multiphoton Microscopy, including Second Harmonic Generation imaging
- Conventional, widefield epifluorescence
- Optical sectioning using Structured Illumination (via the Zeiss ApoTome system)
- In vivo small animal SPECT/CT
- In vivo small animal and large animal PET/CT
- In vivo small animal X-Ray, fluorescence, and bioluminescence imaging
- In vitro and in vivo X-Ray Irradiation
- Multi-parameter Flow Cytometry
- Cell Sorting
- Imaging Cytometry
- Advanced Data Analysis, including 3D and 4D image reconstruction and quantitative measurements
- Expert consultation, including advice on application choice and experimental design
- Instrument-specific training for users as well as workshops on data analysis and advanced techniques
- Grant collaboration and assistance with application preparation



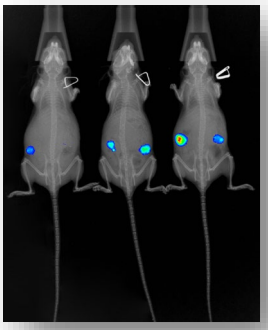
Resources:

Microscopy

- Zeiss LSM-800 Laser Scanning Confocal with Airyscan Super Resolution
- Zeiss LSM-780 Laser Scanning Confocal
- Zeiss LSM-510 META NLO MP Laser Scanning Confocal
- Leica TCS SP5 MP Laser Scanning Confocal
- Leica TCS SP8 Laser Scanning Confocal
- Zeiss Cell Observer Spinning Disk Confocal
- Zeiss LSM-410 Laser Scanning Confocal
- Zeiss ApoTome Structured Illumination Microscope (2)
- Zeiss Axiovert inverted fluorescent photomicroscope
- Atomic Force Microscope/Total Internal Reflection Fluorescence Microscope



In Vivo Imaging



- Siemens Inveon SPECT/CT
- Bruker Albira 2-ring uPET/CT
- Bruker *In Vivo* Xtreme
- Bruker MSFX Pro
- GE Discovery LS4 large animal PET/CT
- Precision X-Ray XRAD 320

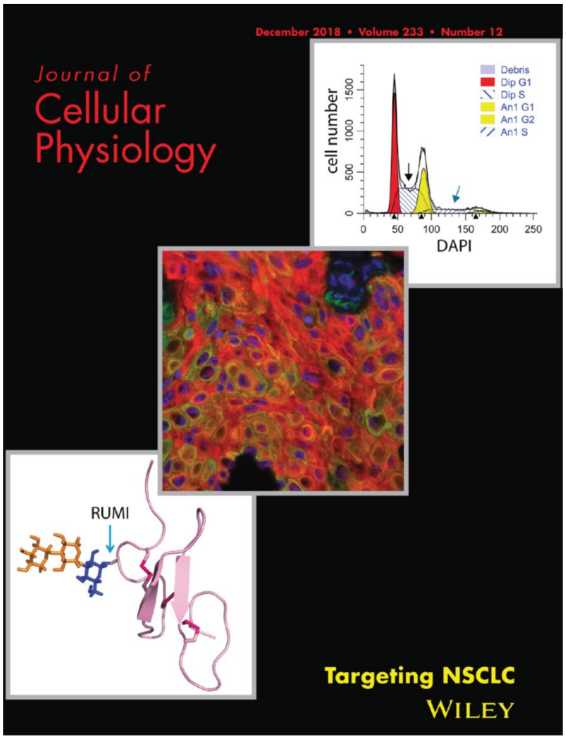
Cytometry

- BD LSR II SORP
- BD FACSCanto II
- Sony SY3200 Cell Sorter
- Sony SH800 Cell Sorter (2)
- Amnis ImageStream^{X} MarkII Imaging Cytometer

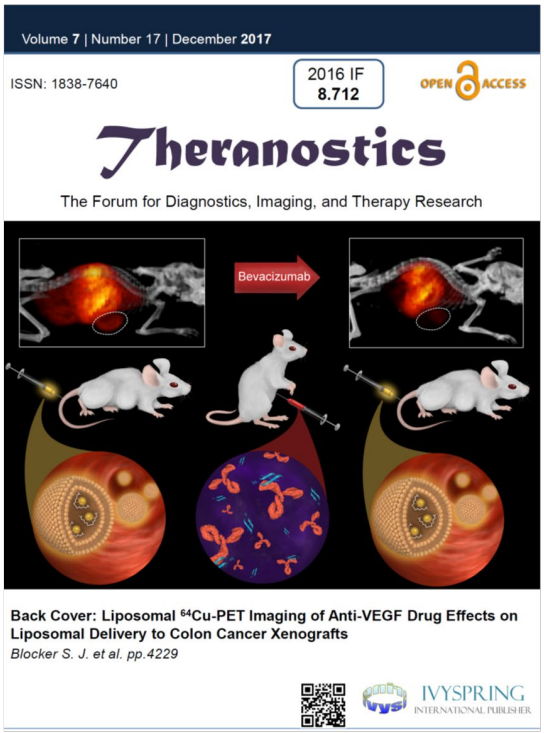
Supporting equipment

- Molecular Imaging Portal (MIP), a high capacity image server module
- Computer workstations with analytical imaging and cytometry software
- In-house cell culture facility and animal holding facility

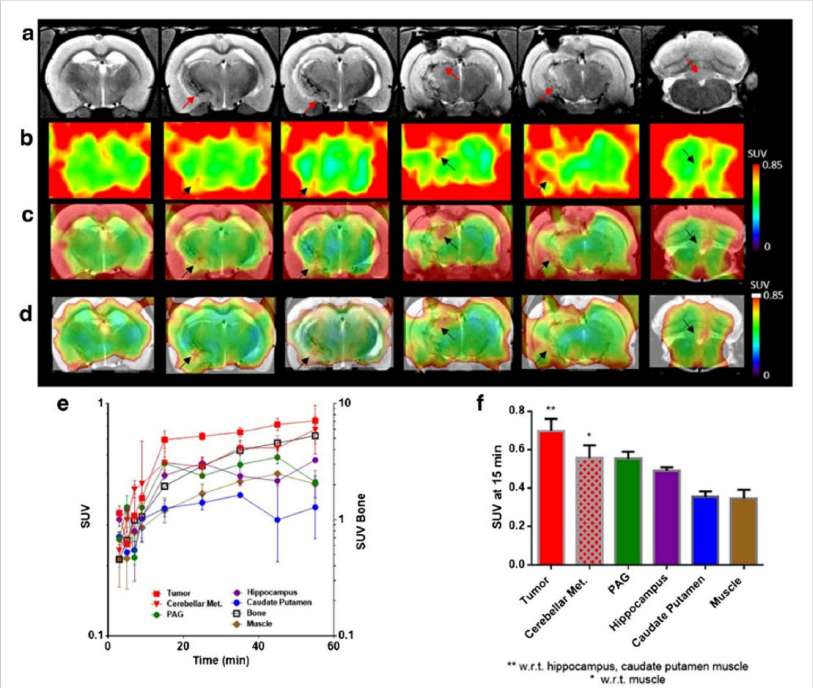
Research:



Chammaa, et al. J Cell Physiol. 2018;233:9548–9562
Funding: 11-053-01-IRG
14-238-04-IRG



Funding: T32-CA009531



a T2-weighted MR image sliced coronally through the 9L glioma lesion and hippocampus with red arrows indicating areas of tumor lesion. **b** Dynamic PET images at 15-min post administration of 12-[^{18}F]DDAHA NIH lookup table (LUT). **c** Dynamic PET images post administration of 12-[^{18}F]DDAHA overlaid onto T2-weighted MR images using the NIH LUT. **d** The same images as in **c**, but with the NIH + white LUT, to better visualize the internal structures due to the high degree of defluorination occurring, which is seen as F-18 accumulation in the bone causing a "halo" effect around the cortical region due to partial volume effect of bone signal into cortex. **e** Time activity curves for each region of interest within the brain over 60 min of dynamic PET images displayed as long (SUV) *vs* time. The error bars represent standard deviation of the voxel values within each ROI. **f** A visual representation of differential washout between tumor and other regions of the brain at 15-min post i.v. administration of 12-[^{18}F]DDAHA, where error bars represent standard deviations and * or ** represent $P<0.05$ as found from one-way ANOVA.

Bonomi, et al. Mol Imaging Biol (2018) 20:594-604

Acknowledgement Text:

Publications that result from Core involvement should include following statement:

"The Microscopy, Imaging, and Cytometry Resources Core is supported, in part, by NIH Center grant P30 CA022453 to the Karmanos Cancer Institute at Wayne State University."

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Pharmacology and Metabolomics Core (PMC)

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Mission of the Core:
To provide state-of-the-art bioanalytic technology and a broad range of pharmacology expertise to enable evaluation of critical pharmacological endpoints in clinical trials and preclinical studies.

Core Services Available:
The Pharmacology and Metabolomics Core offers the following services based on fee-for-service:

- **Biospecimen Processing** service provides a centralized resource for the acquisition, processing, and shipment of patient specimens (including blood and bone marrow samples) that are required for evaluation of pharmacokinetics or pharmacodynamics according to clinical protocol specifications. All specimens are collected from patients who provided informed consent following an Institutional Review Board approved protocol. Specimen handling, processing, and shipment are in compliance with good laboratory practice procedures, approved standard operating procedures, and regulatory requirements to ensure sample integrity and quality. A secure database that includes detailed information on the acquisition, processing, distribution of samples, along with related clinical data, is maintained.
- **Bioanalysis service** provides development, validation, and implementation of liquid chromatography coupled with tandem mass spectrometer (LC-MS/MS) based analytical methods for quantitative determination of drugs and their metabolites as well as and endogenous chemicals (metabolites) in biological samples (including biofluid, tissue, cell culture samples). Method validation is provided based on the United States Food and Drug Administration Guidance for Bioanalytical Method Validation to ensure that a particular method is specific, sensitive, reliable, reproducible, and suitable for the intended analytical use. Rigorous quality assurance and quality control are provided for the analyses of clinical and preclinical samples. The list of established LC-MS/MS methods for quantitation of drugs and their metabolites is presented in **Table 1**.
- **LC-MS/MS based targeted metabolomics** aims to measure predefined groups of metabolites that are involved in central metabolic pathways including carbohydrate, protein, and lipid metabolism. We strive to provide GLP-quality analytical service at competitive prices, and regularly customize assays to meet investigators' needs. Our services spans from initial consultation for study design and sample collection, to sample preparation and instrumental analysis, and to assistance with data analysis (**Figure 1**). **Table 2** summarizes the major metabolic pathways (classes) measured by our targeted metabolomics platform. **Table 3** lists the name of metabolites measured by our platform.

In addition, the Core provides a broad range of pharmacological support including:

- **Pharmacokinetic study design** to assist study design for pharmacokinetic evaluation in clinical and preclinical studies.
- **Pharmacokinetic data analysis and modeling** to characterize drug pharmacokinetics using traditional compartmental or non-compartmental analysis, nonlinear mixed-effect (population) pharmacokinetic modeling, or physiologically based pharmacokinetic modeling approaches.
- ***In vitro* drug metabolism studies** to determine metabolic pathways and potential drug-drug

interactions using liver microsomes, recombinant metabolizing enzymes, or cellular system.

- **Metabolite identification** to identify chemical structures of unknown metabolites using LC-MS/MS.
- **Drug plasma protein binding** to determine binding of a drug to plasma proteins, blood cells, and tissues.

Table 1 The list of established LC-MS/MS methods for quantitation of drugs and their metabolites

Assay #	Drugs, Metabolites	Assay #	Drugs, Metabolites
1	AG127	20	FAU, FMAU
2	Aminoflavone, AFP464	21	Gefitinib
3	AZD1775	22	HBC (Hydrazinobenzoylcurcumin)
4	Betulinic acid	23	Irinotecan, SN-38, SN-38G
5	Carboplatin	24	Isoflavones (Daidzein, Genistein)
6	CDF (diflourinated-curcumin)	25	Lapatinib
7	Ceritinib	26	Methotraxate, DAMPA
8	Combretastatin A4	27	Pazopanib
9	Compound #9 (Rad6 inhibitor)	28	Phenylethylamine
10	CP-1	29	Ribociclib
11	Cu27	30	RO4929097
12	CuDDSF2	31	Sertaline, Venlafaxine
13	Curcumin	32	Sorafenib
14	Decetaxel	33	Temozolomide, AIC
15	Dexamethasone	34	Thiourea
16	Hydroxyflavone (di, tri, and tetra-)	35	Tunicamycin A
17	DIM (Diindolmethane)	36	UTL-5g, DCA, ISOX
18	Erlotinib	37	Veliparib, M8
19	Everolimus		

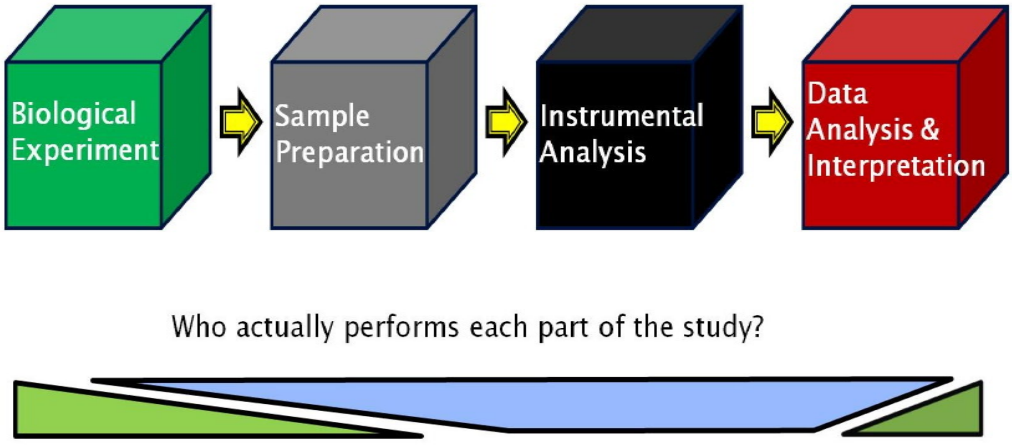


Figure 1: Workflow of the targeted metabolomics service

Table 2: Typical metabolic pathways and classes covered by the targeted metabolomics platform*

Classes or Pathways	Number of Metabolites Determined
Glycolytic, TCA cycle, and pentose phosphate pathway	25
Nucleosides, nucleotides and NAD-related metabolites	40
Amino acid and related metabolites	60
Acyl CoAs	10
Acyl Carnitines	20
Bile acids	15
Ceramides	10
Steroids	10
Short chain fatty acids	8
Phospholipids	15
Gut microbial related metabolites	15
Miscellaneous Metabolites	65
Total	293

*Typical metabolites measured are listed above but the capacity is not limited to these. Assays can be tailored to investigators' needs.

Table 3 The list of metabolites measured by the targeted metabolomics platform

ID	Metabolite name	Calibration curve range
M001	M001_Tryptophan	0.01 - 10
M002	M002_L-kynurenine	0.01 - 10
M003	M003_Serotonin	0.01 - 5
M004	M004_5-Hydroxyindoleacetic acid (5'-HIAA)	0.01 - 10
M005	M005_Kynurenic acid	0.01 - 1
M006	M006_Quinolinic aicd	0.2 - 10
M007	M007_Cis aconitic acid	0.02 - 2
M008	M008_Succinic acid	0.5 - 5
M009	M009_Fumaric acid	0.5 - 10
M010	M010_DL-isocitric acid	0.1 - 5
M012	M012_L-malic acid	0.02 - 5
M013	M013_Succinyl coenzyme A	0.01 - 10
M015	M015_Acetyl coenzyme A	0.01 - 10
M016	M016_α- ketoglutaric acid	0.1 - 10
M019	M019_fructose 6-phophate	0.01 - 2
M020	M020_D-fructose 1,6-bisphophate	0.02 - 0.5
M021	M021_D(+) 2 phosphoglyceric acid	0.01 - 10
M022	M022_Phosphoenolpyruvic acid(s)	0.2 - 10
M023	M023_DL-Valine	0.01 - 2
M024	M024_DL-Leucine (s)	0.01 - 1
M025	M025_DL-Histidine	0.01 - 1
M026	M026_DL-Phenylalanine	0.01 - 10
M027	M027_DL-Glutamine	0.02 - 10
M028	M028_DL-Tyrosine	0.01 - 10
M029	M029_DL-Isoleucine (s)	0.1 - 10
M030	M030_DL-Threonine (s)	0.05 - 1
M031	M031_DL-Glutamic acid	0.02 - 2
M032	M032_DL-Arginine	0.01 - 0.5
M033	M033_DL-Lysine(s)	0.02 - 0.5
M034	M034_S-Adenosyl-L-methionine	0.02 - 2
M035	M035_Dihydroxyacetone phosphate	0.05 - 1
M036	M036_2-Picolinic acid	0.01 - 10
M038	M038_Palmitic acid	0.5 - 5

M039	M039_NADP+ (Nicotinamide adenine dinucleotide phosphate, oxidized)	0.02 - 10
M041	M041_NAD+ (Nicotinamide adenine dinucleotide, oxidized)	0.01 - 1
M043	M043_3'-Dephosphocoenzyme A	0.05 - 10
M046	M046_DL-3-hydroxy-3- methyl glutaryl -CoA	0.01 - 10
M047	M047_Nicotinamide	0.01 - 5
M048	M048_S-Aminoimidazole-4-carboxamide 1-B-D-ribofuranosyl 5-monophosphate (Aminoimidazole-4-carboxamide)	0.01 - 5
M049	M049_S-5'-adenosyl-L- homocysteine	0.01 - 10
M050	M050_2-Deoxyribose -5-phosphate	0.01 - 2
M051	M051_Alpha D-glucose 1- phosphate	0.01 - 0.5
M052	M052_dUMP (deoxyuridine monophosphate)	0.01 - 5
M054	M054_Hypoxanthine	0.01 - 2
M055	M055_D-ribose 5- phosphate	0.01 - 2
M056	M056_Glutathione	0.01 - 10
M057	M057_D-gluconate	0.01 - 2
M058	M058_Uric acid (s)	0.01 - 2
M062	M062_1-Methyl-Histidine	0.01 - 1
M063	M063_1-Methylnicotinamide	0.01 - 2
M064	M064_2,5-dihydroxybenzoic acid (2,5-DHBA)	0.2 - 10
M065	M065_2-deoxycytidine	0.01 - 2
M068	M068_2-ketohexanoic acid	0.05 - 5
M069	M069_5-methoxytryptophan	0.01 - 10
M070	M070_Acetyl-DL-carnitine	0.01 - 10
M071	M071_Acetyllysine	0.01 - 2
M072	M072_aconitate	0.02 - 2
M073	M073_adenosine	0.01 - 1
M074	M074_adenosine-5-diphosphoribose	0.01 - 2
M075	M075_ADP (adenosine 5'-diphosphate)	0.01 - 2
M076	M076_Agmatine	0.02 -0.5
M077	M077_Aminoadipic acid	0.05 - 2
M078	M078_aminolevulinic acid	0.1 - 10
M079	M079_AMP (adenosine 5′-monophosphate)	0.01 - 10
M080	M080_Biotin	0.01 - 10
M082	M082_Butyrylcholine	0.01 - 1
M083	M083_carnitine	0.01 - 2
M084	M084_Chlorzoxazone	0.5 - 10
M085	M085_Citraconic acid	0.1 - 10
M086	M086_citrulline	0.01 - 10
M087	M087_CMP (cytidine 5′-monophosphate)	0.01 - 10
M089	M089_cytosine	0.01 - 0.5
M090	M090_dAMP (deoxyadenosine monophosphate)	0.01 - 10
M091	M091_Dehydro-L-(+)-ascorbic acid	0.5 - 5
M092	M092_deoxyinosine(s)	0.1 - 2
M093	M093_deoxyuridine	0.1 - 10
M096	M096_DL-2-Aminocaprylic acid (2-Aminooctanoic acid)	0.01 - 10
M097	M097_DL-Glyceraldehyde-3-phosphate (s)	0.05 - 2
M099	M099_FAD:flavin adenine dinucleotide	0.01 - 10
M100	M100_Flavone	0.01 - 10
M101	M101_Folic acid	0.01 - 2
M103	M103_Gluconic acid	0.05 - 1
M105	M105_glucosamine	0.02 - 2
M106	M106_glucose-6-phosphate	0.01 - 2
M107	M107_glucuronic acid	0.01 - 2
M108	M108_Glycerate	0.5 - 10

M109	M109_GMP (guanosine 5′-monophosphate)	0.05 -10
M112	M112_Guanidoacetic acid	0.05 - 5
M113	M113_guanine	0.01 - 10
M114	M114_guanosine	0.01 - 10
M117	M117_homoserine(s)	0.01 - 5
M118	M118_Hydroxyisocaproic acid	0.01 - 10
M119	M119_Hydroxyphenylacetic acid	0.2 - 10
M121	M121_Imidazole	0.02 - 2
M122	M122_Imidazoleacetic acid	0.01 - 2
M123	M123_IMP (inosine 5′-monophosphate)	0.02 - 1
M124	M124_indole	0.1 - 10
M125	M125_Indole-3-carboxylic acid	0.01 - 10
M126	M126_Indoleacrylic acid	0.01 - 10
M127	M127_lipoate	0.2 - 5
M128	M128_L-Pipecolic acid(s)	0.02 - 5
M129	M129_Methionine sulfoxide	0.01 - 10
M131	M131_N-acetyl-aspartate	0.02 - 1
M132	M132_N-acetyl-glucosamine	0.01 - 1
M133	M133_N-Acetyl-L-alanine(s)	0.02 - 10
M134	M134_N-acetyl-L-ornithine	0.01 - 2
M137	M137_Niacin (Vitamin B3)	0.01 - 2
M138	M138_NMDA (N-Methyl-D-aspartic acid)	0.05 - 1
M139	M139_O-Acetyl-L-serine	0.1 - 2
M140	M140_ornithine	0.01 - 0.5
M141	M141_Orotate	0.02 - 5
M142	M142_oxaloacetate	0.02 - 10
M143	M143_pantothenic acid	0.01 - 10
M144	M144_Perfluoroheptanoic acid	0.01 - 5
M145	M145_Phenyllactic acid	0.05 - 10
M146	M146_Phenylpropiolic acid	0.05 - 10
M147	M147_Phenylpyruvate	0.1 - 10
M149	M149_p-hydroxybenzoate (4-hydroxybenzoic acid)	0.05 - 10
M150	M150_proline	0.05 - 2
M151	M151_purine	0.01 - 10
M152	M152_pyridoxal 5′-phosphate	0.01 - 5
M153	M153_Pyridoxamine (s)	0.01 - 0.5
M154	M154_pyridoxine	0.01 - 1
M155	M155_Pyroglutamic acid(s)	0.1 - 2
M157	M157_riboflavin-5-monophosphate	0.2 - 10
M158	M158_shikimate	0.05 -5
M160	M160_sorbitol	0.1 - 5
M161	M161_taurine	0.02 - 10
M162	M162_thiamine	0.01 - 10
M163	M163_thymidine	0.01 - 1
M164	M164_thymine	0.01 - 5
M166	M166_UDP-N-acetylglucosamine (uridine diphosphate-N-acetylglucosamine)	0.01 - 10
M167	M167_UMP (uridine 5′-monophosphate)	0.01 - 2
M168	M168_uracil	0.01 - 10
M169	M169_uridine	0.01 - 2
M170	M170_xanthine	0.01 - 5
M171	M171_Xanthosine	0.01 - 5
M172	M172_Xanthosine 5'-monophosphate	0.05 - 5
M173	M173_Xanthurenic acid	0.01 - 2

M174	M174_ATP (adenosine triphosphate)	0.05 - 5
M175	M175_CTP (cytidine 5'-triphosphate) (s)	0.5 - 10
M176	M176_GTP (guanosine triphosphate)	0.05 - 5
M177	M177_UTP (uridine triphosphate)	0.02 - 5
M178	M178_dATP (deoxyadenosine triphosphate)	0.01 - 10
M179	M179_dCTP (deoxycytidine triphosphate)	0.01 - 10
M180	M180_dGTP (deoxyguanosine triphosphate)	0.05 - 2
M181	M181_dTTP (deoxythymidine triphosphate)	0.01 - 5
M182	M182_L-cysteine	0.1 -1
M183	M183_L-Alanine	0.5 - 10
M183	M183_L-Alanine(s)	0.5 - 10
M184	M184_L-Asparagine	0.1 - 10
M185	M185_Glycine	0.5 - 10
M186	M186_L-Aspartic acid	0.01 - 1
M187	M187_Argininosuccinic acid	0.01 - 2
M188	M188_Sarcosine(s)	0.2 - 10
M189	M189_Dimethylglycine+M191	0.01 - 1
M190	M190_Betaine	0.05 - 5
M191	M191_Choline	0.01 - 1
M192	M192_Cystathionine	0.01 - 1
M194	M194_Urea	0.02 - 1
M195	M195_Cytidine	0.01 - 2
M196	M196_CDP (cytidine diphosphate)	0.01 - 5
M197	M197_GDP (guanosine diphosphate)	0.02 - 10
M198	M198_UDP (uridine diphosphate)	0.01 - 10
M199	M199_5'-Deoxyadenosine+M268+M092	0.02 - 2
M200	M200_dCMP (deoxycytidine monophosphate)	0.01 - 2
M201	M201_dCDP (deoxycytidine diphosphate)	0.01 - 10
M202	M202_dGMP (deoxyguanosine monophosphate)	0.05 - 10
M203	M203_dGDP (deoxyguanosine diphosphate)	0.05 - 10
M204	M204_dTMP (deoxythymidine monophosphate)	0.01 - 5
M205	M205_dTDP (doxythymidine diphosphate)	0.01 - 10
M206	M206_UDP-glucose (uridine diphosphate-glucose)	0.01 - 2
M207	M207_ADP-glucose (adenosine 5'-diphosphate-glucose)	0.01 - 1
M211	M211_Maleic acid	0.1 - 10
M214	M214_Methylmalonic acid	0.1 - 2
M216	M216_Anthranilic acid	0.01 - 10
M217	M217_4-Aminobenzoic acid	0.01 - 5
M219	M219_a-keto-4-methylthio-2-oxobutanoate	0.02 - 10
M220	M220_2,3-Dihydroxybenzoic acid	0.01 - 10
M221	M221_DL-Dihydroorotic acid	0.01 - 2
M224	M224_4-Pyridoxic acid	0.01 - 1
M225	M225_2-keto-D-gluconic acid	0.01 - 2
M226	M226_D-Erythrose 4-phosphate	0.01 - 2
M227	M227_D-Glucarate	0.05 - 2
M228	M228_Inosine	0.01 - 2
M229	M229_D-Sedoheptulose-1-7-phosphate	0.01 - 1
M230	M230_N-Acetyl-glucosamine-1-phosphate	0.01 - 2
M231	M231_Cyclic AMP (cyclic adenosine monophosphate)	0.01 - 2
M232	M232_Sucrose	0.01 - 5
M238	M238_Thiamine diphosphate	0.05 - 10
M239	M239_Adenosine 5'-phosphosulfate	0.01 - 10
M241	M241_Cholesteryl sulfate	0.01 - 10
M242	M242_Cytidine-5'-diphosphocholine	0.01 - 10

M243	M243_Taurodexoycholate	0.01 - 2
M245	M245_Coenzyme A	0.1 - 10
M246	M246_n-Propionyl Coenzyme A	0.01 - 10
M247	M247_DL-3-hydroxybutyryl CoA	0.01 - 5
M248	M248_L-alpha-hydroxyglutaric acid	0.01 - 2
M249	M249_Ethanlamine	0.01 - 1
M251	M251_4-Aminobutyric acid	0.01 - 2
M254	M254_Creatinine	0.01 - 1
M255	M255_Creatine(s)	0.01 - 1
M256	M256_N-Acetylputrescine	0.01 - 1
M257	M257_Trans-4-hydroxy-L-proline(s)	0.02 - 5
M258	M258_Adenine	0.02 - 10
M259	M259_L-homocysteine	0.05 - 2
M260	M260_L-histidinol	0.01 - 1
M262	M262_Phosphocholine	0.02 - 1
M263	M263_3-Phospho-L-serine	0.5 - 10
M264	M264_N-Acetyl L-glutamine	0.01 - 2
M265	M265_N-Acetyl L-glutamic acid	0.01 - 5
M266	M266_N^G, N^G-Dimethyl arginine	0.01 - 2
M267	M267_L-Cystine	0.02 - 1
M268	M268_2'-Deoxyadenosine(s)	0.01 - 1
M269	M269_Acadesine	0.01 - 10
M271	M271_7-Methylguanosine	0.01 - 1
M272	M272_Beta-nicotinamide mononuceotide	0.01 - 5
M273	M273_Riboflavin	0.01 - 10
M276	M276_3,5-Diiodo-L-thyronine	0.01 - 2
M277	M277_Putrescine	0.01 - 0.5
M278	M278_Spermidine	0.01 - 0.5
M279	M279_Spermine	0.01 - 1
M280	M280_Acetone	0.2 - 10
M281	M281_Alpha-Hydroxyisobutyric acid	0.01 -10
M282	M282_4-Hydroxyphenyl acetic acid	0.01 -10
M283	M283_APCI_7-Dehydrocholesterol	0.01 - 10
M284	M284_Chenodeoxycholic acid as M294 Hyodeoxycholic acid M303	0.02 - 1
M285	M285_APCI_Cholestanol	
M286	M286_APCI_Cholesterol	0.01 - 10
M287	M287_APCI_Coprostan-3-ol	
M288	M288_APCI_Desmosterol	0.01 - 10
M289	M289_Dimethylamine	0.05 - 2
M290	M290_Glycocholic acid	0.01 - 10
M291	M291_Glycoursodeoxycholic acid +M297 Glycodeoxycolic acid+M313 Glycochendeoxychlate	0.01 - 10
M293	M293_Hippurate	0.01 - 10
M294	M294_Hyodeoxycholic acid same as M284_Chenodeoxycholic acid M303	0.02 - 1
M295	M295_APCI_Lanosterol	0.01 - 10
M296	M296_APCI_Lathosterol	
M297	M297 Glycodeoxycolic acid+M313 Glycochendeoxychlate	0.01 - 10
M298	M298_Stigmasterol	0.01 - 10
M299	M299_Taurochenodesoxycholic acid	0.01 - 10
M300	M300_Taurocholic acid	0.01 - 10
M302	M302_Taurolithocholic acid	0.01 - 10
M303	M303_Ursodeoxycholic acid_ss	0.01 - 10
M304	M304_Campesterol	0.01 - 5
M305	M305_3-Phosphoglyceric acid	0.01 - 10

M306	M306_Thiamine monophosphate	0.01 - 10
M307	M307_2'-Deoxyguanosine	0.01 - 10
M308	M308_Malonyl CoA	0.05 - 1
M309	M309_R-2-Hydroxy-2-phenylpropionic acid	0.2 - 10
M310	M310_D-Citramalic acid	0.01 - 2
M311	M311_L-Homocysteic acid	0.01 - 2
M312	M312_Serine	0.02 - 10
M313	M313 Glycochendeoxychlate + M297 Glycodeoxycolic acid	0.01 - 10
M314	M314_CDP-ethanolamine	0.01 - 10
M315	M315_p-cresyl sulfate	0.01 - 10
M316	M316_Glycolithocholic acid	0.01 - 10
M317	M317_Dihydro thymine	0.01 - 0.2
M318	M318_Alpha-N-Phenylacetyl- L-glutamine	0.01 - 10
M319	M319_N-Phenylacetylglycine	0.01 - 10
M322	M322_06:0 Lyso PC	0.01 -10
M323	M323_14:0 Lyso PC	0.01 -10
M324	M324_16:0 Lyso PC	0.01 -10
M325	M325_18:0 Lyso PC	0.01 -10
M327	M327_Lithocholic acid	0.01 -10
M328	M328_ Linoleyl Carnitine	0.01 -10
M329	M329_C5:0 Carnitine (Valeryl-L carnitine)	0.01 -10
M330	M330_C12:0 Carnitine (Lauroyl-L carnitine)	0.01 -10
M331	M331_C16:0 Carnitine (Palmitoyl-L carnitine)	0.01 -10
M332	M332_18:1 Lyso PC	0.01 -10
M333	M333_17:0 Lyso PC	0.01 -10
M335	M335_26:0 Lyso PC	0.01 -10
M336	M336_18:1 SM	0.01 -10
M337	M337_24:1 SM	0.01 - 5
M338	M338_16:0 SM	0.01 - 5
M339	M339_18:0 SM	0.01 - 2
M340	M340_24:0 SM	0.01 - 10
M341	M341_C14 Carnitine (Myristoyl-L-carnitine)	0.01 - 5
M342	M342_C3 Carnitine (Propionyl-L-carnitine)	0.01 - 10
M343	M343_C8 Carnitine (Octanoyl-L-carnitine)	0.01 - 10
M344	M344_C10 Carnitine (Decanoyl-L-carnitine)	0.01 - 5
M345	M345_C4-OH Carnitine (Malonyl-L-carnitine)	0.01 - 5
M346	M346_C18 Carnitine (Stearoyl-L-carnitine)	0.01 - 5

Resources:

Major analytical instrumentation includes:

- AB SCIEX QTRAP 6500 LC-MS/MS system: Consisting of an enhanced high performance hybrid triple quadrupole/linear ion trap mass spectrometer, interfaced with a SHIMADZU Nexera UPLC system, and associated software for operation and data analysis (AnalystTM for system control and data acquisition/processing; LightSightTM for metabolite identification).
- Waters Xevo TQ-XS LC-MS/MS system: Consisting of a Waters AQUITY UPLC system coupled with a Waters Xevo TQ-XS triple quadrupole mass spectrometer, and associated software for operation and data analysis (MassLynx™ for system control and data acquisition and processing).

Major instrumentation for sample processing and storage includes:

- Revco -300C and -800C freezers with liquid nitrogen have alarms and temperature chart recorders for the proper documentation of storage conditions
- SpeedVac vacuum concentrator (Thermo Fisher Scientific)
- Centrifuges include 1 Beckman Coulter GS-15R, 1 Beckman Allegra 21, and 2 Beckman Allegra X-22R
- Other instrumentation includes homogenizers, sonicators, incubators, shakers, water bath

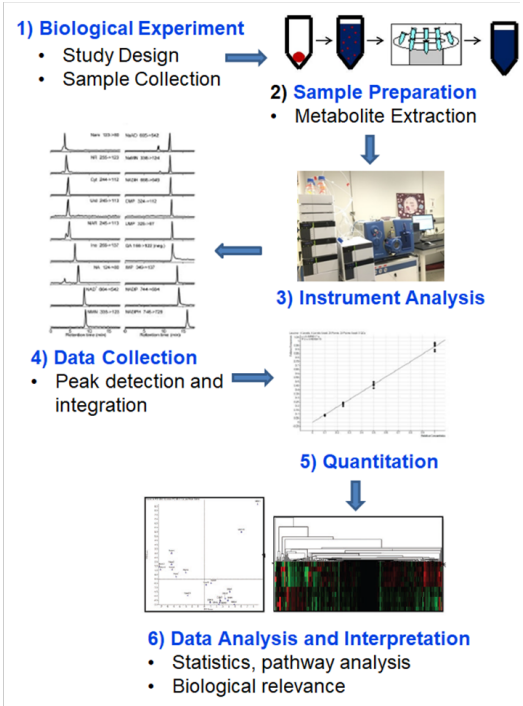
Software for pharmacokinetic data analysis and metabolomics data analysis:

- WinNonlin (Pharsight Corp., Mountain View, CA)
- NONMEM (ICON Development Solutions, Ellicott City, MD)
- Simcyp® Physiologically based pharmacokinetic modeling software (Simcyp Limited, United Kingdom)
- On-line free software for metabolomics data analysis: MetaboAnalyst (http://www.metaboanalyst.ca/)

Research:

❑ Apply targeted metabolomics as a tool to understand the mechanism of drug action, biochemical basis for drug response, and mechanisms of tumor progression.

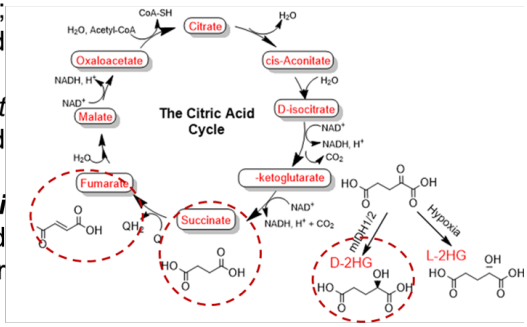
- NIH 5R01CA053535-26, ***Matherly*** *and* ***Hou*** *(Co-PI)*, 02/1993 – 02/2020 "Molecular Regulation of Folate and Antifolate Transport"
- CDMRP OC160543, ***Rattan*** *(PI)*, 05/2017 – 04/2020, "AMPK as a Novel Host Factor Regulating Ovarian Cancer Progression"
- NCI7977: A Phase I Dose-Escalation Study of Oral ABT-888 Plus Intravenous Irinotecan in Patients with Advanced Solid Tumors (*PI,* ***LoRusso***)
- Phase 0/II Study of Ribociclib in Rb-Positive Recurrent High-Grade Glioma and Meningioma Patients (*PI,* ***Sanai***)
- Phase I trial of Cytoreductive Surgery and Heated Intraperitoneal Chemotherapy with Nanoliposomal Irinotecan in Patients with Peritoneal Surface Cancers (*PI,* ***Choi***)
- PRIME trial: Phase I/II Study of Olaparib in IDH mutant Acute Myeloid Leukemia and Myelodysplastic Syndrome (*PI,* ***Prebet***)
- Bao X…LoRusso P, and **Li J**. Pharmacometabolomics reveals irinotecan mechanism of action in cancer patients. J Clin Pharmacol. 2018 Jul 27. doi: 10.1002/jcph.1275.
- Dekhne A…**Li J**, **Hou Z**…**Matherly LH**. Novel pyrrolopyrimidine compounds inhibit mitochondrial and cytosolic one-carbon metabolism with broad-spectrum anti-tumor efficacy, PNAS 2018 (under review)

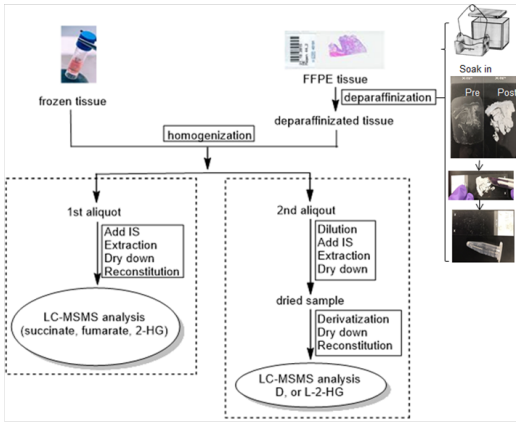


LC-MS/MS Based Targeted Metabolomics Workflow

❑ **Explore oncometabolites as potential biomarkers for DNA repair defects and tumor sensitivity to PARP inhibitors** (Collaboration with Yale Cancer Center)

- NIH 1R01 CA215453-01A1, ***Bindra*** *(PI)*, ***Li*** *(subcontract PI)*; 07/2017 – 06/2022 "Exploiting Mutant IDH1/2-Induced Homologous Recombination Defects in Cancer"
- CureSearch Catapult Impact Fund, ***Bindra*** *(PI)*, ***Li*** *(subcontract PI)* ; 08/2018 – 07/2021 "Exploiting Mutant IDH1/2-induced DNA Repair Defects in a Pediatric Glioma Phase I Trial"
- SWOG/Hope Foundation Impact Award, ***Shuch*** *(PI)*, ***Li*** *(subcontract PI)*; 07/2018 – 06/2020 "Identification and Characterization of Oncometabolite-induced DNA Repair Defects in Sporadic Papillary Kidney Cancer"
- NCI10129: A Phase 2 Study of the PARP Inhibitor Olaparib (AZD2281) in IDH1 and IDH2 mutant Advanced Solid Tumors, ***LoRusso*** *(PI)*
- NCI10222: A Phase II Study of Olaparib and AZD6738 in Isocitrate Dehydrogenase (IDH) Mutant Solid Tumors, ***LoRusso*** *(PI)*
- PNOC017: Phase1 Study of BGB-290 in Combination with Temozolomide in Adolescent and Young Adult IDH1/2 Newly Diagnosed and Recurrent Mutant Gliomas, ***Bindra*** *(PI)*
- PRIME trial: A Phase I/II Study of Olaparib in Isocitrate Dehydrogenase Relapsed/ Refractory (IDH) mutant Acute Myeloid Leukemia and Myelodysplastic Syndrome, ***Prebet*** *(PI)*
- Parker L… **Li J**… **Glazer PM**. Oncometabolite-producing hereditary cancer syndromes are defined by homologous recombination DNA repair defects. Nature Genetics. 2018 Aug;50(8):1086-1092





Multiplex LC-MS/MS Platform for Oncometabolite Profiling

Acknowledgement Text:

Publications that result from Core involvement should include following statement:

> ***"The Pharmacology and Metabolomics Core is supported, in part, by NIH Center grant P30 CA022453 to the Karmanos Cancer Institute at Wayne State University."***

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Proteomics Core

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Web: http://research.wayne.edu/proteomics
https://www.karmanos.org/Proteomics

Mission of the Core:
The mission of the Proteomics Core is to enhance research productivity of WSU/KCI researchers by providing the equipment and expertise necessary for analysis of cellular protein composition and protein-protein interactions. These two objectives require different instrumentation, but they both rely on expertise in protein chemistry, separation and analysis.

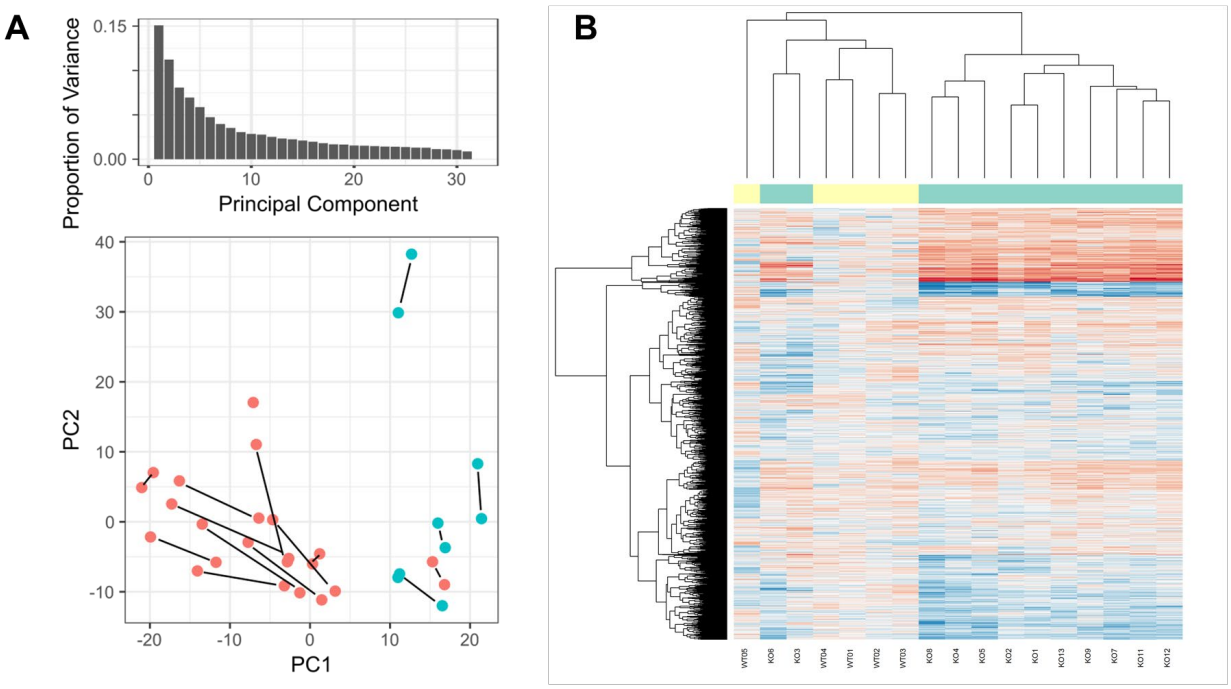
Core Services Available:

- Protein identification using nano-LC/MS/MS instruments
- Protein quantitation using spectral counting or isobaric tags with data acquired on the Orbitrap Fusion and Orbitrap QExactive systems and the Multiple Reaction Monitoring strategy using the TSQ Vantage system.
- Proteomic profiling using two-dimensional chromatographic separations or MuDPIT technologies
- Analysis of post translational modifications using nano-LC/MS/MS with fragmentation by CID, HCD and ETD
- Robotic sample preparation using the AssayMap Bravo robot.
- Sample fractionation Alkaline Reversed Phase spin columns.
- Peptide labeling and purification using an HPLC with UV and Fluorescence Detectors
- Surface Plasmon Resonance (SPR) using a Biacore 3000. Investigators performing SPR analysis must have appropriately trained personnel
- Biolayer Interferometry (BLI) for molecular interaction analysis using an Octet Red96.
- Data Analysis using MaxQuant, Mascot, Sequest, X!tandem and Peaks algorithms with data compilation and secondary analysis using Scaffold.

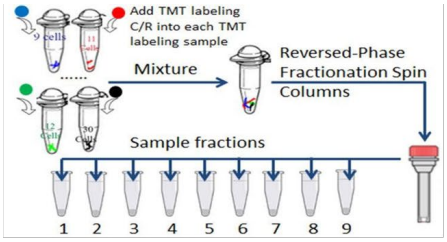
Resources:

- Thermo Orbitrap Fusion nano-LC/MS/MS with ETD
- Thermo Orbitrap QExactive nano-LC/MS/MS
- Thermo Finnigan TSQ Vantage triple quadrupol nano-LC/MS/MS
- AssayMap Bravo sample preparation robot
- HPLC system for peptide purification, which includes UV and Fluorescence Detectors
- Biacore 3000 for molecular interaction analysis by Surface Plasmon Resonance
- Octet Red96 for molecular interaction analysis by Biolayer Interferometry

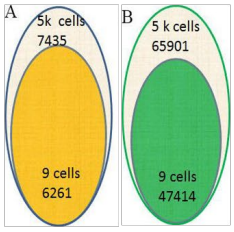
Research:



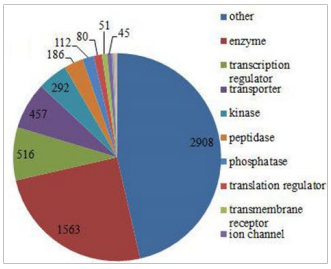
Project 1. Evaluation of mDig CRISPR-Cas9 KO clones. Proteome profiling of 12 KO and 5 control clones in duplicate to a depth of greater than 5,000 proteins demonstrates that mDig KO has consistent as well as variable effects on the proteome. Panel A shows the PCA analysis and panel B the heat map grouping the clones by protein abundance. PI: Fei Chen. R01 ES028263 & R01 ES028335.



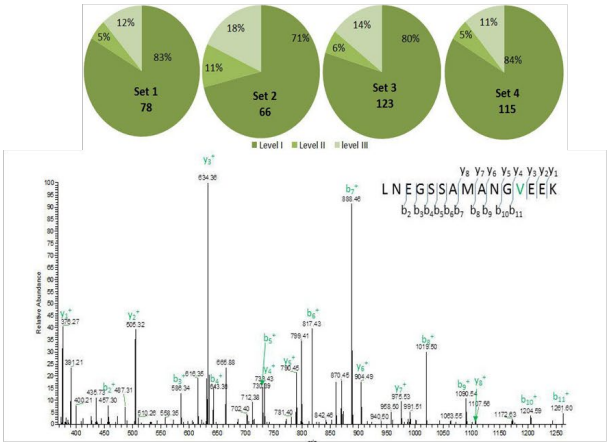
1. The Carrier/Reference Strategy for micro sample proteomics.



2. Protein (A) and peptide (B) coverage for Panc1 cells.



3. GO analysis demonstrates coverage of regulatory proteins.



4. Single Amino Acid Variant (SAAV) identification in samples of 9 cells, (upper panel). Spectrum of SAAV peptide from Septin 9, (lower panel).

Project 2. The carrier/reference (C/R) proteome allowed us to detect 47,414 unique peptides derived from 6,261 proteins in as few as 9 cells providing sufficient coverage to search for single amino acid variants (SAAVs) related to cancer. Tan Z, Yi X, Carruthers NJ, Stemmer PM, Lubman DM. J Proteome Res. 2018 Nov 7. doi: 10.1021/acs.jproteome.8b00694. [Epub ahead of print] PubMed PMID: 30404448.

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Clinical Trials Office

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Mission of the Clinical Trials Office:
The mission of the Clinical Trials Office (CTO) is to provide outstanding support to clinical trials at the Karmanos Cancer Institute (KCI) with the goal of improving cancer therapy and patient quality of life through research.

Goals and Services Available:

- Ensure that all clinical trials conducted at KCI are managed in strict compliance with the Code of Federal Regulations (CFR) and in accordance with International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines.
  - Coordinating and managing all clinical trials conducted at KCI and affiliates in strict compliance with the CFR, ICH GCP standards and internal policy and regulations
  - Ensuring the safety of patients participating in clinical trials
  - Coordinating and tracking National Cancer Institute registrations and annual updates for KCI investigators
  - Coordinating registration and maintenance of all therapeutic clinical trials to ClinicalTrials.gov and the NCI's Clinical Trials Reporting Program (CTRP)
- Facilitate and optimize accrual to clinical trials by providing well-qualified, specifically trained data management and research nurse support to KCI physicians and clinical support staff.
  - Facilitating increasing accrual to clinical trials
  - Maintaining protocol registry and accrual data utilizing OnCore®
- Ensure research coordination by facilitating and optimizing physician-patient-CTO staff interaction, communication and collaboration.
  - Increasing awareness and education of all KCI and affiliate institution staff in the clinical trials arena
  - Providing high quality research coordination and data management to KCI, affiliate institutions and external institutions participating in KCI investigator-initiated clinical trials
- Facilitate regulatory approval and oversight to rapidly review and activate appropriate trials.
  - Serving as an interface with the Institutional Review Board (IRB) Wayne State University Human Investigation Committee (WSU HIC) and NCI Central IRB to facilitate preparation of the required consent and HIPAA forms and other regulatory documents necessary to expedite effective and timely approval of KCI protocols

Research Administration

Vice President and Associate Center Director, Research Administration
Evano Piasentin, MBA
Phone: (313) 578-4400
Email: piasenti@karmanos.org

Mission of Research Administration

The mission of Research Administration is to reliably and consistently provide cost-effective administrative services that further the conduct of efficient and effective research efforts.

Services Available:

Research Administration strives to provide the best support to the researchers of the Karmanos Cancer Institute by providing expert assistance in the following areas:

- **Pre-Award Services** – Research Administration has staff members with decades of experience in meeting the requirements of funding agencies and navigating the intricacies of the submission process through Wayne State University. Research Administration staff members review and provide the final polish to grant applications for Cancer Center members, provide regular reports to senior leadership on the health of our funding portfolio, and play a vital role in the administration of the Cancer Center Support Grant (CCSG).

- **Post-Award/Billing**
  - Research Administration plays an ongoing role in assisting researchers to maximize the use of their grant funding, long after the original award date. Post award staff provide monthly reports on spending, ensure correct distribution of effort for researcher salaries, meet regularly with faculty and staff to answer questions, and play an active role in the final closeout of grant funding.
  - Billing specialists review the charges of all patients enrolled on clinical trials at KCI and bill the appropriate healthcare payer, whether insurance, government program, or the clinical trial itself. These staff are more than typical medical billers. They possess the knowledge of current CPT coding practices along with a deep understanding of clinical trial budgeting and reimbursement. No other team could perform this task for the Cancer Center.

- **CCSG Administration** – Research Administration plays a pivotal role in coordinating the various components of the CCSG application itself along with the day-to-day activities that support the Cancer Center structure: program meetings and retreats, Core business operations, institutional support for new initiatives, space allocation, and working closely with the Development and Marketing departments to increase awareness of and enthusiasm for cancer research.

- **Research Finance** – Research Administration employs dedicated accountants and budget specialists to keep a careful eye on the precious financial resources for research. Developing and managing budgets within both KCI and WSU, these financial managers develop a strategy for making the best use of available funding and provide a valuable service in purchasing and financial reporting for Cancer Center members. The finance team of Research Administration plays a critical role in the overall strategy of the Institute and provides direct support to senior leaders in their decision-making.