



2017
CASE COMPREHENSIVE
CANCER CENTER
ANNUAL REPORT



FROM THE DIRECTOR

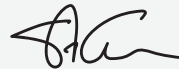
Our mission is simple: To apply scientific discoveries in human cancers to improve lives in our community and beyond through cancer prevention, detection, treatment, cure and survivorship. How we accomplish this mission and benefit patients and populations is the focus of our collective efforts.

The Case Comprehensive Cancer Center is a National Cancer Institute-designated consortium cancer center. We bring together University Hospitals, Cleveland Clinic and their networks with Case Western Reserve University. Together, we forge a remarkable effort in cancer research generating considerable community benefit. Our research programs, clinical trials, training efforts and community engagement and outreach link investigators, organizations and investments that are aligned with the strategic plan of the center and are supported by the partner institutions. The synergies and synthesis of this effort combines for a powerful demonstration of the impact of cross-institutional teamwork.

The Case CCC directly serves an area comprised of 15 counties in Northeast Ohio with a population

of 4.2 million. The area surrounding our center is culturally rich and unique. However, in our local community of Cleveland — where the obesity rate is 35 percent, smoking rates are 240 percent above the national average and the poverty rate is 285 percent above — we are concerned about the extraordinary cancer risks of our population. As a result of these factors, our population suffers a higher mortality from four common cancers: breast, prostate, lung and colon. Our investigators are examining each of these diseases to reduce cancer risk, increase prevention efforts, understand their cancer biology and improve treatments.

This report showcases our many efforts to understand, manage and support the population in our consortium through research and clinical care. I am proud to lead this impressive center, as we continue to focus on our mission and flourish as THE comprehensive cancer center serving the population of Northeast Ohio and impacting the nation at large.



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ON THE COVER: Expression of TLE3 (red), a transcriptional repressor with potential roles in regulating breast cancer, in the normal mammary gland. Myoepithelial cells are stained in green (alpha-smooth muscle actin) and DNA is stained with DAPI (blue).

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CASE
COMPREHENSIVE
CANCER CENTER

Gastrointestinal Cancer Genetics

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Sanford D. Markowitz, MD, PhD
Zhenghe John Wang, PhD

These seven programs lie at the heart of the cancer center's mission to move cancer research forward

Case Comprehensive Cancer Center is comprised of seven interdisciplinary research programs that include more than 370 members across its affiliated institutions: Case Western Reserve University, University Hospitals and Cleveland Clinic. Through collaborative efforts within and across these programs, investigators are at the cutting edge of basic science, translational and clinical research in oncology. Here, we highlight the impact each program is having on the region and beyond.



This program is dedicated to translating basic science discoveries of genetic and epigenetic causes of GI cancers into novel approaches for risk assessment, detection, prevention and treatment.

The program's ability to continue the advancement of GI cancer research is made possible through its internationally renowned, multi-investigator teams who have gained program project grants from the National Cancer Institute, including GI Specialized Programs of Research Excellence (SPORE), Barrett's Esophagus Translational Research Network (BETRNet) and Early Detection Research Network (EDRN). Notably, Dr. Markowitz received a coveted NCI Outstanding Investigator award, and Dr. Wang won a prestigious Stand Up to Cancer Colorectal Cancer Dream Team award.

INNOVATIVE DISCOVERIES: Program investigators have made multiple seminal observations and discoveries, including finding novel therapeutic vulnerabilities in PI3K-mutant colorectal cancer (CRC); discovering the first germline mutation causative of familial Barrett's esophagus and esophageal adenocarcinomas; and demonstrating that inhibition of 15-PGDH potentiates tissue regeneration and has potential as a therapeutic option in multiple cancer settings.

The research on PI3K mutants in CRC eloquently illustrates the achievements of the program in advancing basic science discoveries to the clinical setting. Investigators found that CRC tumor cells harboring PIK3CA mutations are sensitive to drugs that block glutamine metabolism. A clinical trial – the first of its kind in GI cancers – is ongoing to test this proof of principle. The trial is investigating the combination of the glutamase inhibitor CB-839 with capacitabine in the genetic subset of CRC patients whose cancers express PIK3CA mutations.

COMMUNITY IMPACT: Investigators discovered mutations in 15 genes that typify colon cancers arising in African-Americans and are associated with adverse outcomes. Studies are ongoing to identify gene-environment interactions that contribute to racial disparities in CRC, with the goal of improving risk assessment, detection and treatment of this underserved patient population.

RESEARCH PROGRAMS DRIVE New Discoveries

Molecular Oncology

LEADERS

Alexandru Almasan, PhD
Bingcheng Wang, PhD

As the central basic science research and intellectual catalyst for foundational discovery, the Molecular Oncology Program aims to elucidate the mechanisms of oncogenesis, with a concentrated focus on translating basic science discoveries in cancer stem cell (CSC) regulation, DNA damage and repair, and host-tumor interactions into strategies for the prevention and treatment of cancer.

INNOVATIVE DISCOVERIES: The program's DNA damage and repair group, dedicated to identifying how defective DNA damage and repair promotes genomic instability and alters therapeutic response, has uncovered new mechanisms of DNA repair through gene regulation and proteasome degradation. These unprecedented findings were recently published in the journal *Science*.

Program members have also made key discoveries in identifying molecular processes that control CSC development and the mechanisms by which they impact the tumorigenic progression and therapeutic resistance. Researchers have demonstrated that low toll-like receptor (TLR) 4 expression on CSCs in glioblastoma facilitate their survival through immune evasion, a mechanism through which CSCs are able to persist in hostile environments because of an inability to respond to inflammatory signals. These findings shed light on important questions regarding the impact of TLR ligands on tumor progression.

COMMUNITY IMPACT: Basic research investigators discover critical pathways that provide insight with community benefit in terms of cancer risk, cancer progression and prevention. Discoveries in brain tumor stem cells and oncogenesis have resulted in the initiation of clinical trials.

Obesity pathways are being defined that will help inform studies in the Cancer Prevention, Control & Population Research Program, on obesity-associated cancer and wellness programs to reduce obesity.

Genitourinary Malignancies

LEADERS

Nima Sharifi, MD
Brian I. Rini, MD

The GU Malignancies Program explores biologic pathways involved in the development and progression of prostate, renal and bladder cancer. It also drives translational studies and multidisciplinary, investigator-initiated clinical trials to advance approaches in disease prevention, localized disease management and metastatic disease treatment, and to elucidate mechanisms of response or resistance to treatment.

INNOVATIVE DISCOVERIES: In studies led by Dr. Sharifi, the discovery of an abiraterone metabolite that is a potent androgen receptor inhibitor led to clinical studies assessing its clinical impact and modulation to optimize anti-androgen therapy. Investigators discovered a cause of prostate cancer drug resistance – and temporarily reversed the resistance – in human prostate cancer cells grown in a mouse model, findings that provide the premise for further investigations into novel approaches to therapy.

Research is also underway to ascertain the immunomodulatory environment of renal and bladder cancers, and design novel immunotherapeutic clinical trials. In renal cancers treated with sunitinib, investigations uncovering the role of myeloid-derived suppressor cells in regulating tumor immunobiology led to phase III, combination-therapy trials.

COMMUNITY IMPACT: The program has developed genomic-based risk profiles for prostate and renal cancers now used prospectively to assist decision-making on treatment options. The team addresses patient-centric questions critical to GU cancers through investigator-initiated clinical trials, with the aim of improving the quality of life and disease outcomes.

Notably, Dr. Simon Kim received funding from the National Institutes of Health to develop decision aids for men diagnosed with localized prostate cancer. African-American men experience a greater burden of prostate cancer; however, minority patients are not always given the information needed to make informed treatment decisions. Decision aids, which inform patients about their disease severity, treatment options and the quality of life implications of each treatment option, can be delivered during or prior to specialty visits. Adding these aids to clinical practice may help patients make better treatment decisions that align with individual priorities related to sexual and urinary function, as well as reduce racial disparities in the care of patients with localized prostate cancer.

Hematopoietic and Immune Cancer Biology

LEADERS

Jaroslav P. Maciejewski, MD, PhD
Marcos de Lima, MD • Alex Y. C. Huang, MD, PhD

This research program is dedicated to improving the understanding of molecular pathogenesis and characterization of hematopoietic disorders through research that investigates the evolution of hematologic neoplasms and the role of the immune system in cancer immune response. The goal is to translate laboratory findings into innovative, patient-specific approaches for diagnosis and therapy.

INNOVATIVE DISCOVERIES: Investigators led by Dr. Maciejewski have discovered novel driver genes in MDS evolution, thereby improving disease classification and revolutionizing physician assessment of prognostic factors and treatments options.

Investigators are also working to enhance the mechanistic understanding of the tumor microenvironment and its interaction with the immune system to improve the design of molecular-targeted immunotherapies. In research led by Dr. Huang and published in *Science*, a novel role for CDK5 in immune checkpoint regulation by tumor cells was elucidated.

Investigators led by Dr. de Lima are seeking to further clarify mechanisms of tumor immune surveillance and evasion to develop and apply cell-based immune therapies for patients at risk of infection after bone marrow transplant. Leveraging the anti-cancer properties of natural killer cells, researchers are working to develop new pharmacologic and cellular therapeutic strategies to restore immune cell function.

COMMUNITY IMPACT: Efforts are underway to characterize the influence of racial disparities on outcomes in African-American patients with MDS. The identification of mutations specific to the disease in African-American patients allows physicians to develop better prognostic/detection methods, with the ultimate goal of improving outcomes in this underserved patient population.

Meanwhile, Dr. Huang is studying the cellular and molecular mechanisms of metastasis, and exploring molecular and cell-based immunotherapy strategies for therapy-refractory pediatric and adolescent and young adult cancers.

Developmental Therapeutics

LEADERS

John J. Letterio, MD
Yogen Sauntharajah, MD

The Developmental Therapeutics Program develops and evaluates novel therapeutics that overcome drug resistance of cancer cells mediated by a spectrum of genetic and epigenetic mechanisms; inhibit growth and drug-resistant pathways of cancer; and expand the proportion of cancer patients who benefit from novel immune checkpoint therapeutics. Program leaders leverage the creativity and expertise of scientists in the cancer center, fostering interaction and collaboration between researchers and clinicians involved in anticancer drug development. To that end, a drug development working group initiates preclinical assessment and early-phase trials with experts that advise on preclinical studies, biomarkers of drug effectiveness in clinical trials, studies to overcome drug resistance and use of PDX models.

INNOVATIVE DISCOVERIES: The impact of the program on advancing novel approaches to cancer therapy includes successful academic drug development through IND-enabling to phase 1, and now phase 2, of four novel agents. This includes a uracil glycosylase inhibitor that synergizes with thymidylate synthase inhibitors of a new chemical entity oral DNMT1-depleting drug to treat p53-null solid and liquid tumor malignancies. Several other first-in-class small molecules for novel targets and pathways have transitioned through preclinical in vivo proof-of-principle towards IND-enabling.

COMMUNITY IMPACT: Investigators continue to develop new targeted therapeutics, incorporate genomic and other molecular markers into clinical studies, and help move novel molecules through preclinical and clinical development. To facilitate this mission, the program not only conducts its own groundbreaking research, but also provides funding opportunities for pilot projects by members of the cancer center for performing correlative and biomarker studies on physician investigator-initiated trials, and for performing pharmacokinetics on early-phase trials.

Program members also work with other entities, including the Cancer Therapy Evaluation Program of the National Cancer Institute, to create new early-phase clinical trials, especially for cancers with particularly poor outcomes in the region, such as NSCLC, SCLC and triple-negative and advanced breast cancer. Early results indicate that some of these efforts will meaningfully change practice.

Cancer Imaging

LEADERS

James P. Babilion, PhD
Zhenghong Lee, PhD

The multidisciplinary Cancer Imaging Program integrates imaging research with the study of cancer biology to investigate carcinogenic mechanisms using imaging; design new targeted therapies; and develop innovative imaging modalities to improve patient care. Biologists, medical oncologists, radiologists and pathologists across all research programs are actively engaged to accomplish these goals.

INNOVATIVE DISCOVERIES: Program members have driven several highly impactful advances in nanomedicine, including the seminal work by Drs. Nicole Steinmetz and Agata Exner. Dr. Steinmetz used imaging to develop plant-virus nanoparticles that stimulate the host immune response to eliminate tumors in mice and dogs. Dr. Exner developed novel ultrasound contrast agents that are able to identify tumor tissues and aid in the detection and staging of prostate and other cancers.

In addition, there is the work being done with magnetic resonance fingerprinting by Drs. Vikas Gulani, Mark Griswold and Nicole Seiberlich. This novel method for magnetic resonance imaging is based on random magnetic wave generation and allows for quantitative assessment of MR data. MR fingerprinting is being tested in clinical trials, including the evaluation of approaches in patients with breast, liver, prostate and GI cancers.

COMMUNITY IMPACT: The Cancer Imaging Program has impacted the greater Cleveland community by using MR fingerprinting approaches to develop a noninvasive, highly sensitive, low-cost grading scheme for prostate cancer that will be implemented in a local prostate screening clinic. The initiative is led by Drs. Lee Ponsky, Gulani and Griswold.

Cancer Prevention, Control & Population Research

LEADERS

Gregory S. Cooper, MD
Susan A. Flocke, PhD

Dedicated to establishing interventions that reduce the incidence of cancer and improve outcomes, program members develop novel approaches in risk reduction, screening and early detection. They also conduct research to improve the delivery of recommended preventive services, therapies and survivorship care after diagnosis. To accomplish these goals, program members are comprised of investigators with expertise in cancer epidemiology, behavioral medicine, health services research and quality of care.

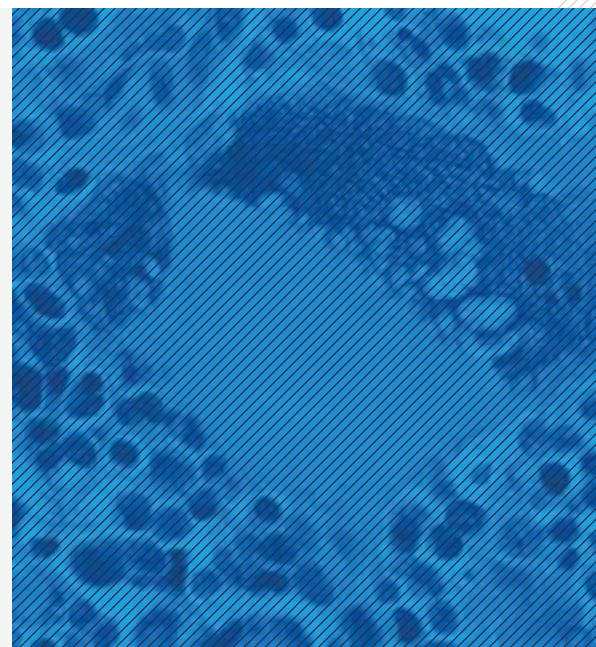
INNOVATIVE DISCOVERIES: Through collaborative efforts, investigators have substantially impacted paradigms for patient care and health policy in the region and beyond, as evidenced by new initiatives in cancer prevention in underserved urban populations, tobacco control, genetic causes of cancer, colon cancer screening and prevention, palliative care of patients with advanced cancer and cancer risk in HIV infected individuals.

Perhaps one of the program's most notable achievements is its impact on best practices in clinical trials via the Preparatory Education About Clinical Trials (PRE-ACT) program. This Web-based, interactive educational program, developed with support from the National Cancer Institute, is superior to standard text in overcoming barriers to clinical trial participation and improving patient knowledge, attitudes and decision-making about clinical trials. Based on these results, the American Society of Clinical Oncology adopted PRE-ACT for nationwide dissemination.

COMMUNITY IMPACT: The program is driving change in the community through its efforts to expand multilevel and multimethod smoking intervention and disparities research, particularly targeting underserved populations. To that end, studies identifying the high prevalence of little cigar use in Cleveland urban youth, combined with testimony given to the Cleveland City Council, led to Tobacco 21, a law banning tobacco sales to anyone under age 21 in the city of Cleveland. In recognition of these efforts, Erika Trapl, PhD, received the 2016 Ohio Public Health Association Public Health Policy Award, and Dr. Flocke's research enabled Ohio to become the 16th state to implement tobacco cessation eReferral capacity for a healthcare system. An NCI supplement award and the CVS Cancer Moonshot initiative, both led by Monica Webb Hooper, focus on smoking cessation strategies in cancer patients.

SHARED RESOURCES FUEL Collaboration

Pooled institutional resources, also known as shared resources, contribute subject-area expertise and access to leading-edge technology to investigators of the Case Comprehensive Cancer Center. This level of collaboration enhances the rigor, quality and capacity of the research conducted and elevates the Cancer Center to the forefront of basic science research, translational medicine and clinical applications in oncology. Read on to learn more about each shared resource and their important research contributions.



ATHYMIC ANIMAL & PRECLINICAL THERAPEUTICS

DIRECTOR

Analisa DiFeo, PhD

CO-DIRECTOR

Daniel Lindner, MD, PhD

This facility provides immune-deficient mice and professional consultation regarding animal-model selection for investigators, and performs human xenograft studies. Expanded patient-derived xenograft (PDX) development has generated ovarian and uterine, breast and lung PDX models, with ongoing development of liver, esophageal and pancreatic cancer models.

RESEARCH HIGHLIGHTS: Its contributions were critical in identifying a central role for CDK5 in immune-checkpoint regulation in medulloblastoma; crosstalk mechanisms between post-transcriptional gene-expression modulators that regulate tumorigenesis; and a novel strategy to activate tumor-suppressor proteins in cancer.

BIOSTATISTICS & BIOINFORMATICS

DIRECTOR

Ming Li, PhD

CO-DIRECTOR

Paul Elson, ScD

Data scientists offer expertise in statistics, bioinformatics and clinical informatics to investigators in critical elements of project-specific design, planning and the conduct of research. They are intimately involved in the analysis and interpretation of data, and protocol review and study monitoring.

RESEARCH HIGHLIGHTS: As study co-investigators, facility members have made numerous contributions to collaborative research grants across all research programs, leading to successful funding, execution and publication of basic science, clinical research and clinical trials.

CYTOMETRY & MICROSCOPY

DIRECTOR

James Jacobberger, PhD

CO-DIRECTORS

Judy Drazba, PhD

Howard Meyerson, MD

Scott Sieg, PhD

Philip Woost, PhD

This group supports cell-based assays in basic, translational and clinical cancer research, providing access to expertise, instruments and assistance in cytometry, microscopy and cell sorting. Notably, in 2016, the facility acquired an Attune NxT flow cytometer, chosen for its high-quality DNA content-measuring capabilities and cost-saving benefits.

RESEARCH HIGHLIGHTS: The facility contributes to multiple drug discovery projects, including the analysis of intracellular protein expression and activity in natural killer cells of patients with acute myeloid leukemia (AML), and in research investigating potential cell-therapy strategies.

 **Learn More** To view more information about each shared resource, including services and pricing, visit cancer.case.edu/research/sharedresources.

HEMATOPOIETIC BIOREPOSITORY & CELLULAR THERAPY

DIRECTOR

David N. Wald, MD, PhD

OPERATIONS AND QUALITY DIRECTOR

Jane Reese, MBA

This shared resource provides investigators with cells derived from human blood, bone marrow and umbilical cords; assists investigators with specialized hematopoietic assays; and supports the development and implementation of cellular therapy clinical trials. The biorepository has an extensive collection of samples from patients with hematological malignancies and those undergoing stem cell transplant.

RESEARCH HIGHLIGHTS: Dr. Wald's lab identified that in acute myeloid leukemia (AML) patients the kinase GSK3 is dysregulated in natural killer (NK) cells and that targeting GSK3 leads to improved NK cell function. The facility will perform the cell manufacturing for a phase I clinical trial to test NK cells in patients with advanced malignancies.

IMAGING RESEARCH

DIRECTOR

Chris A. Flask, PhD

Besides imaging expertise, Imaging Research offers cancer investigators a comprehensive array of preclinical and clinical imaging capabilities, as well as quantitative image analysis capabilities for essential in vivo and in situ imaging assessments of cancer.

RESEARCH HIGHLIGHTS: This shared resource has established a portfolio of human MRI services. In addition, the novel magnetic resonance fingerprinting technology continues to expand with studies in both cancer patients and molecular imaging assessments of cancer.

INTEGRATED GENOMICS

DIRECTOR

Martina L. Veigl, PhD

CO-DIRECTORS

Alexander Miron, PhD
Yu-Wei Cheng, PhD
E. Ricky Chan, PhD

Integrated Genomics provides project-level genomic consultation to investigators on experiment design, technology and sample preparation, as well as data generation, analysis and interpretation. Investigators have access to a full range of genomic technologies including multi-site next-generation sequencing for DNA and RNA analyses.

RESEARCH HIGHLIGHTS: An Analytics Component, comprised of experts in genomics, biostatistics and bioinformatics, was developed to confirm that each proposed research project has a robust experimental design and data analysis plan, and to ensure detailed attention to key success factors for genomic studies.

MULTIMETHOD CANCER OUTCOMES RESEARCH

DIRECTOR

Susan Flocke, PhD

CO-DIRECTORS

Siran Koroukian, PhD
Kurt Stange, MD, PhD

Members provide expertise and consultation for methods relevant to population and cancer outcome research, including multilevel intervention design; and analyzing, linking and geo-mapping public health and healthcare system databases.

RESEARCH HIGHLIGHTS: A recent study assessed barriers to discussions about clinical trials between oncology nurses and patients. The findings reveal that educational interventions are needed to build nurses' knowledge, leading to better support for patients' decision-making.

PROTEOMICS

DIRECTOR

Mark Chance, PhD

CO-DIRECTORS

Janna Kiselar, PhD
Belinda B. Willard, PhD

This facility provides advanced proteomic and metabolomic technologies and small-molecule analysis via state-of-the-art instruments and computational resources, to support clinical, translational and structural biology research.

RESEARCH HIGHLIGHTS: Members performed immunoprecipitation experiments that helped identify a novel genomic driver of metastatic prostate cancer. They also developed a novel structural biology approach for drug-protein mechanisms assessment, which was used to discover a novel small-molecule cancer therapy.

RADIATION RESOURCES

DIRECTOR

Mitchell Machtay, MD

CO-DIRECTOR

Junran Zhang, MD, PhD

Radiation Resources offers consultation, instrumentation and training to investigators irradiating samples, cells or animals in studies exploring radiobiology, bone marrow biology and radiation as an experimental tool.

RESEARCH HIGHLIGHTS: Collaborations have resulted in the discovery of the potentiation of tissue regeneration by inhibition of 15-PGDH, and the development of a device for small animal irradiation using the Gamma Knife to accurately irradiate targets. Members also elucidated the role of RNF126 in repairing radiotherapy-induced DNA damage through homologous recombination repair.

SMALL MOLECULE DRUG DEVELOPMENT

DIRECTOR

Drew J. Adams, PhD

This shared resource designs and optimizes high-throughput assays tailored to specific research projects, and provides screening services across chemical libraries to identify small molecules that may be candidates for innovative cancer therapeutics.

RESEARCH HIGHLIGHTS: The group's support drives scientific advancement and secures external funding for investigator-initiated discovery and development efforts. One investigator received a \$900,000 Gund-Harrington Scholar Award, supporting continued collaboration with this shared resource to identify and optimize new small molecules to inhibit retinal degeneration.

TISSUE RESOURCES

DIRECTOR

Marta Couce, MD, PhD

CO-DIRECTORS

Daniel Lindner, MD, PhD

Jennifer Ko, MD, PhD

This specialized unit acquires, preserves and distributes high-quality human tissues from UH and CC to investigators, and provides efficient standard operating procedures for tissue procurement, central-biorepository access to human tissue samples and expert experimental-design guidance, as well as customized technical histology, immunochemistry and in situ hybridization.

RESEARCH HIGHLIGHTS: This group's standardization of tissue-collection procedures and unification of existing biorepositories have facilitated the collaboration of clinical investigators and basic science researchers. Future alignment of disease-based repositories through a common database at each institution, will further enhance this collaboration.

TRANSGENIC & TARGETING

DIRECTOR

Ron Conlon, PhD

The Transgenic & Targeting shared resource develops transgenic, chimeric, knockout and knock-in mice, and provides services in rederivation, cryopreservation, reanimation, in vitro fertilization and surgery.

RESEARCH HIGHLIGHTS: Members have successfully completed numerous gene-targeted mutations in mice using the CRISPR/Cas9 approach. Leveraging this expertise, the group has secured funding to advance CRISPR/Cas9-based methodologies, focusing on replacing mouse genes with human genes modified with disease-causing mutations.

TRANSLATIONAL RESEARCH

DIRECTOR

John Pink, PhD

CO-DIRECTOR

Daniel Lindner, MD, PhD

Translational Research coordinates bioanalytical components of clinical trials and provides support for preclinical drug-discovery efforts, including biospecimen processing, laboratory analyses, preclinical drug testing and pharmacodynamic assay development and assessment.

RESEARCH HIGHLIGHTS: This group conducts preclinical testing of new agents (e.g., novel ribonucleotide reductase inhibitor) and laboratory analyses for TRC102 clinical trials. It has also conducted DNA extraction services for the brain tumor group's submission to The Cancer Genome Atlas, leading to the recognition of a new glioma subclass.

The geographic area served by the Case Comprehensive Cancer Center includes medically underserved populations that disproportionately bear the burden of cancer. Groups that are disproportionately affected by cancer incidence, prevalence, mortality and survivorship may be characterized by:

- RACE OR ETHNICITY
- AGE
- HEALTH INSURANCE STATUS
- SOCIO-ECONOMIC STATUS
- SEX OR GENDER
- GEOGRAPHIC LOCATION
- DISABILITY

Populations that experience disparities often do not have access to or receive high-quality health-care, which are major drivers of the problem.

The Office of Cancer Disparities Research at the Case CCC was created to reduce and ultimately eliminate disparities by promoting health-equity-focused research and outreach. "Our mission is to cut across all research programs to build a culture of cancer disparities science and outreach to address access to care, risk factors, disease burden and survivorship," says Monica Webb Hooper, PhD, associate director for Cancer Disparities Research.

The office focuses on education, innovative research, training, outreach and collaborations with academic and community-based organizations that are committed to health equity. In addition, it awards annual pilot grants to researchers to help generate data and encourage research, and it held its first cancer disparities symposium this year, with the second planned for March 2018.

"One Size Does Not Fit All"

Dr. Hooper is well-prepared to lead this effort. For the last 18 years, she has researched tobacco use and cessation, focusing on adapting evidence-based interventions to increase their relevance for specific individuals and groups by identifying unique concerns.

For example, African-Americans and Hispanics have greater difficulty with long-term abstinence from tobacco, compared to the general population. This difficulty may stem from targeted marketing by the tobacco industry, a preference for

menthol or factors like discrimination and racism that are associated with tobacco use. "With interventions, one size does not fit all," Hooper says. "We need to focus on the underlying reasons why people smoke, beyond the common triggers."

Putting It into Practice

As the office works to combat cancer disparities locally and nationally, one of its current outreach efforts is making an impact close to home. Its goal is to increase human papillomavirus (HPV) vaccination rates in the geographic areas served by the Case CCC. Partnering with University Hospitals Rainbow Babies & Children's Hospital, the office's staff is working to educate physicians, patients and the community about the link between HPV infection and the risks for cervical and other cancers. The effort is just one example of the office's mission in action.



The Office of Cancer Disparities Research focuses on groups where cancer hits hardest

THE QUEST FOR EQUITY



ADDRESSING CANCER DISPARITIES IN THE COMMUNITY

Five years ago, the Case Comprehensive Cancer Center established a Community Advisory Board to help advise the center and its investigators on cancer disparities and to facilitate community engagement in outreach and research. "The goal is to improve the health of the community," says Monica Webb Hooper, PhD, associate director for Cancer Disparities Research. "Membership is diverse to ensure that the community's voice is heard with regard to addressing the cancer burden."

The board includes representatives from the American Cancer Society, Asian Services in Action, Case Western Reserve University, Cleveland Clinic, Cleveland State University, the Cuyahoga County Board of Health, The Gathering Place, Medical Mutual, MetroHealth Medical Center and University Hospitals, as well as cancer survivors.

With support from the Case Cancer Council, researchers investigate some of cancer's greatest mysteries

The Case Cancer Council is a volunteer leadership group dedicated to advancing and accelerating cancer research by providing expertise, guidance and resources to support investigator initiatives at the Case Comprehensive Cancer Center. It was formed to promote and publicize the work of the 370 researchers who work tirelessly to discover new cancer treatment protocols, as well as earlier and more effective detection tools, with the ultimate goal of successfully treating cancer at its earliest possible stage. Of course,

the goal of raising much needed private funding for future research needs."

Funding the Next Generation of Cancer Research

In 2015, the council played a pivotal role in launching the Research Innovation Fund, which supports the investigation of questions with potentially transformative impacts on cancer research and patient benefit. Through a competitive application process open to members from partner institutions and a review process led by Case CCC Director Stan Gerson, MD, the

ADVANCING THE FUTURE

finding a cure for cancer is always at the forefront of the group's work, although a daunting task.

OF CANCER CARE

most promising projects receive critical early stage support, laying the groundwork needed to collect preliminary data. This in turn increases the likelihood these projects are able to secure additional government and foundation funding for continued investigation.

"We're proud to create opportunities for our community to support innovative research pilot projects through our Research Innovation Fund and to help advance conversations about cancer research and the future of cancer care throughout the region," Weinberger says.

Exciting advances in areas such as genomics, stems cells and drug development place the Case CCC at the forefront of cancer research. To ensure continued excellence in this area, five pilot grants were recently awarded in support of the following innovative research projects.

Join the Case Cancer Council

You can help move cancer research forward. Contact Kristy Short at 216.368.0768 or kristy.short@case.edu to learn more about joining the council.

"I am proud to lead this council, composed of community leaders with a demonstrated interest in supporting cancer research, which strives to support the Case CCC's research mission," says Peter H. Weinberger, chair of the Case Cancer Council and managing partner at Spangenberg Shibley & Liber. "We meet several times a year to discuss the impact of our researchers and to create a strategy that increases awareness of our cancer center, with

RESEARCH INNOVATION FUND GRANT WINNERS

Jill Barnholtz-Sloan, PhD

Associate Director for Bioinformatics, Case CCC Professor, Oncology, CWRU

Profiles of protein heterogeneity and invasiveness in glioblastoma

Ruth Keri, PhD

Associate Director for Basic Research, Case CCC Professor, Pharmacology, CWRU

Epigenetic modulation of super-enhancers to enhance platinum sensitivity in high-grade ovarian serous carcinoma

Peter Scacheri, PhD

Professor, Genetics and Genome Sciences, CWRU Targeting metastasis in osteosarcoma by inhibiting tissue factor

Bill Schiemann, PhD

Professor, Oncology, CWRU Regulation of breast cancer metastasis and dormancy by the lncRNA BORG

Bingcheng Wang, PhD

Co-Leader, Molecular Oncology Program, Case CCC Professor, Pharmacology, CWRU Targeting EphA2-HSP27 signaling axis in glioblastoma

Training the Next Generation of Cancer Experts

The Office of Cancer Trainee Education and Research equips students and faculty with the skills they need to move medicine forward

The Case Comprehensive Cancer Center provides rigorous training in cancer research and career enhancement activities through the Office of Cancer Trainee Education and Research (OCTER), led by Mark Jackson, PhD, associate director, and Damian Junk, PhD, assistant director.

Directors collaborate with scientific leadership and training program leads to coordinate existing training activities and develop new educational initiatives for high school students through junior and senior faculty. These concerted efforts equip trainees with the skills required to perform innovative research and provide outstanding clinical care.

OCTER is supported by the Cancer Education and Research Committee, comprised of training program directors from Case CCC member institutions. Leveraging expertise and best practices from each, the committee promotes coordination, integration and monitoring of training efforts; establishes effective recruiting practices; and evaluates training outcomes. OCTER's training programs include:

CLINICAL ONCOLOGY RESEARCH CAREER DEVELOPMENT PROGRAM:

Interdisciplinary training (NCI K12 grant) in clinical and translational oncology research for junior faculty physicians pursuing academic research careers as physician scientists.

CANCER BIOLOGY [NCI T32] TRAINING GRANT: Basic cancer research, enriched by educational forums that address the importance of interdisciplinary, collaborative, clinical and translational cancer research.

TRAINING IN COMPUTATIONAL GENOMIC EPIDEMIOLOGY OF CANCER:

Postdoctoral training (NCI R25 grant) in a novel, transdisciplinary area at the intersection of cancer research, genetics, epidemiology, biostatistics and computer science.

CANCER BIOLOGY PHD TRAINING PROGRAM: Training for PhD and MD/PhD scientists who will advance research on the causes, diagnosis, progression and treatment of cancer.

CANCER PHARMACOLOGY TRAINING PROGRAM: Multidisciplinary training for doctoral students and postdoctoral fellows pursuing basic or clinical science cancer research careers.

An associate membership is offered to all trainees, emphasizing their critical role in the center. Information gathered through the membership database is used to communicate educational and career enrichment opportunities, highlight accomplishments and act as a networking resource for current trainees and alumni.

AWARD-WINNING ACHIEVEMENTS

Case Comprehensive Cancer Center members mentored 1,622 trainees over the last five years. In 2017, new individual research fellowships (4 F30, 4 F31) and postdoctoral fellowships (2 F32, 1 K99/R00) were awarded. To top it off, trainees received numerous career development awards, including three American Society of Clinical Oncology (ASCO) awards (Conquer Cancer Award; and two Annual Meeting Merit Awards); an American Association for Cancer Research (AACR) Scholar-in-Training Award; and a CWRU Junior Faculty Professional Development Award. Here are three highlights.

- 1 ASCO's Conquer Cancer Foundation awarded the 2017 Advanced Clinical Research Award in Breast Cancer to **Mohamed E. Abazeed, MD, PhD**, a radiation oncologist at Cleveland Clinic and assistant professor of medicine at Case Western Reserve University, for his research, "Targeting the Achilles' shield of TNBC by androgen blockade."
- 2 A previous K12 scholar, **Jennifer Eads, MD**, assistant professor of medicine at CWRU and oncologist at UH Seidman Cancer Center, leads a team of investigators participating in the clinical trial portion of a prestigious Stand Up to Cancer Colorectal Cancer Dream Team award, testing a novel combination therapy in the genetic subset of CRC patients whose cancers express PIK3CA mutations.
- 3 **Raffaella Spina, PhD**, received a Scholar in Training Award from the AACR, which facilitated her participation at the 2017 Annual Meeting. Dr. Spina, a postdoctoral fellow in the lab of Case CCC member **Dr. Eli Bar**, is researching strategies to inhibit tumor growth in human glioblastoma.

LOOKING FORWARD: RESEARCH INITIATIVES FOR 2017 AND BEYOND



Investigators at the Case Comprehensive Cancer Center set their sights on improving the treatment of brain tumors and cancers that strike women, teens and young adults

TARGETING BRAIN TUMORS

The brain tumor initiative, led by Justin Lathia, PhD, and Jill Barnholtz-Sloan, PhD, focuses on basic, clinical and translational research that leads to improved diagnosis and prognosis, and novel drug development. The multi-institutional initiative's work integrates basic biology, imaging, use of human tissues and genomics, and new therapeutics. The research centers on:

- Basic biology of brain tumors, including brain-tumor-initiating cells. Discoveries in this area include hypoxia signaling, alterations in connexins and changes in the tumor microenvironment.
- Causes and risk factors for brain tumors. The initiative participates in international

brain tumor epidemiology consortia, bringing access to the largest brain tumor epidemiology dataset worldwide. With this dataset, researchers can study sex-, age- and race/ethnicity-specific genetic risk factors to help explain related differences in brain tumor incidence.

- Better diagnosis and prognosis using imaging and large-scale data. Magnetic resonance fingerprinting and studying DNA, RNA and proteins help build better understanding of options for adults and children with brain tumors. Investigators participated in The Cancer Genome Atlas project, which has changed the diagnosis of gliomas worldwide via the World Health Organization.

WORKING TO ELIMINATE WOMEN'S CANCERS

William Schiemann, PhD, and Ruth Keri, PhD, lead this team of 23 basic breast or ovarian cancer biologists and 20 physician scientists/clinical researchers, all focused on breast, ovarian and endometrial cancer etiology, genomics, detection and treatment. These investigators are working on topics ranging from basic molecular mechanisms to new therapeutic approaches, and are advancing women's cancer research in the following ways:

- Jame Abraham, MD, is leading a clinical trial studying multiple drugs that target an aggressive form of breast cancer. The clinical research team is also examining whether applying tamoxifen to the skin might treat early breast cancer.

- Population scientists are studying how genetic variation, exposure to risk factors and healthcare disparities impact breast cancer susceptibility.
- Analisa DiFeo, PhD, leads a group that has created a gynecological cancers biobank with more than 100 samples. The biobank allows researchers to study genetic alterations in patient tumors and to test new drugs.
- A project funded by the University of Pittsburgh's Specialized Programs of Research Excellence (SPORE) is focused on identifying a new driver of ovarian cancer aggressiveness and determining if it could be used as a biomarker for early detection.

ATTACKING ADOLESCENT AND YOUNG ADULT CANCERS

Supported by a \$6.7 million philanthropic gift and endowment, this initiative, led by John Letterio, MD, focuses on cancers in 15- to 30-year-olds. The gift has been pivotal in elevating AYA cancer research in northeast Ohio. In fact, Case CCC will be one of the featured institutions in the upcoming AYA Cancer Congress. Recent research highlights include:

- The development of unique inhibitors that have the potential to disrupt an enzyme and could target many cancers, particularly brain tumors.
- Research in mouse models examines how cells from a primary tumor spread to the lung and what they need to grow there.

- Studies of how the HER2 protein, found in medulloblastoma and osteosarcoma, might be targeted with immunotherapy.
- Investments in adolescent and young adult tissue biorepositories that increase representation and identify unique characteristics for this age group.
- Two new researchers have been added to the team: Lewis Shi, PhD, a specialist in immunotherapy for melanoma, and Mari Dallas, MD, who focuses on bone marrow transplants and immunotherapy.

PROGRESS AT OUR PARTNER INSTITUTIONS

Three new cutting-edge additions advance cancer care throughout the region



CASE WESTERN
RESERVE UNIVERSITY

Health Education Campus

Case Western Reserve University, one of the country's leading private research institutions, offers forward-thinking educational opportunities in an inspiring cultural setting. Faculty engage in teaching and research in a hands-on environment across arts and sciences, dental medicine, medicine, nursing and social work programs.

With the 485,000-square-foot Health Education Campus scheduled to open in 2019, the university continues to be at the forefront of medical education. The new facility will allow students from the schools of medicine, dental medicine and nursing to work side-by-side in a common building with a shared goal – to improve the quality of patient care. This collaborative, team-based education approach will create efficiencies, reduce cost of services and, most important, cultivate future healthcare professionals who prioritize a patient-centered approach to multidisciplinary care.

The technology available at the Health Education Campus will be just as innovative as the curriculum. Notably, the Microsoft HoloLens will bring holograms and mixed reality into the classroom to enhance medical students' understanding of anatomy and physiology through a digital anatomy curriculum.



UNIVERSITY HOSPITALS
CLEVELAND MEDICAL CENTER

Proton Therapy Center

The UH Cleveland Medical Center is a nationally ranked hospital and home to some of the most prestigious oncology clinicians and researchers in the nation. Now, the medical center lays claim to Ohio's first Proton Therapy Center, one of only 24 in the nation, and the only one located on-site at a full-service children's hospital, UH Rainbow Babies & Children's Hospital. The technology, effective for certain types of pediatric and adult solid tumors, allows radiation oncologists to precisely target tumors with a maximum amount of radiation while minimizing the radiation that reaches healthy tissues and organs.

The Proton Therapy Center utilizes a next-generation proton beam delivery system, the MEVION S250 — a compact, efficient and cost-effective model with DirectDose™ beam-modulating technology — to shape and regulate the proton therapy beams. The model's six-degree robotic couch allows the patient to be positioned at the optimal treatment angle.

Compared with traditional radiation therapy, additional benefits of this non-invasive, outpatient procedure include using the technology with chemotherapy or surgery, and with sedation during treatment sessions. It may also lower the risk for radiation-induced secondary cancers, developmental delays and growth abnormalities.



CLEVELAND
CLINIC

Taussig Cancer Center

Cleveland Clinic, a nonprofit, academic medical center that integrates hospital care with research and education, has pioneered many breakthroughs in cancer research and care over its long history. Now, the new Cleveland Clinic Taussig Cancer Center will continue this tradition of innovation.

Opened this year, the 377,000-square-foot facility features 126 exam rooms, 98 treatment rooms and comprehensive clinical and support services. In addition, all outpatient services – including teams of medical and radiation oncologists, surgeons, nurses, genetic counselors and social workers – are in one location, leading to increased collaboration, communication and research among physicians and care providers improving the experience and clinical outcomes of patients with cancer.

Designed with the patient in mind and based on feedback from cancer patients, the new Taussig Cancer Center is organized by cancer type, features sources of natural light throughout the entire facility, and includes purposefully-designed details to make the patient experience as convenient, healing and welcoming as possible.



CASE
COMPREHENSIVE
CANCER CENTER

