Our Discoveries Drive Cures

CASE COMPREHENSIVE CANCER CENTER

ANNUAL REPORT 2015

CASE COMPREHENSIVE CANCER CENTER

The Case Comprehensive Cancer Center is an NCI-designated Comprehensive Cancer Center, and a recently elected member of the prestigious National Comprehensive Cancer Network (NCCN). Our consortium brings together the best and brightest research faculty of its partner institutions, Case Western Reserve University, University Hospitals Case Medical Center and Cleveland Clinic. Located in Cleveland, Ohio, the Case Comprehensive Cancer Center serves a population with higher than average cancer rates. Our researchers dedicate themselves to improving cancer outcomes through basic studies into signaling pathways giving rise to cancer and its genetic and epigenetic causes, pursuing novel therapeutic targets, and analyzing lifestyle interventions to prevent cancer and detect it earlier.

We are proud to be one of only 41 NCI-designated Comprehensive Cancer Centers in the nation. To learn more about our Center, please visit our website at **cancer.case.edu**.

Case Western Reserve University | Case Comprehensive Cancer Center

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

University Hospitals | Case Western Reserve University Est. 1826 | Cleveland Clinic

TABLE OF CONTENTS

ON THE COVER

Nima Sharifi, MD is the Kendrick Family Endowed Chair for Prostate Cancer Research, Cleveland Clinic; Co-Leader, Genitourinary Malignancies Program, Case Comprehensive Cancer Center. The image on the cover is a nitrogen evaporator from Dr. Sharifi's laboratory, which is used to prepare steroids involved in treatment resistant prostate cancer, for subsequent analysis by high performance liquid chromatograph and mass spectrometry.

11100 Euclid Avenue | Cleveland, Ohio 44106-5065 | Phone: 216.844.8797
cancer.case.edu **facebook.com/CaseCCC** **twitter.com/caseccc**

FROM THE DIRECTOR

The 2014-2015 year exemplified the Case Comprehensive Cancer Center's mission to promote a coordinated translational research-focused culture of scientific discovery applied to human cancers, with dissemination to patients and populations. We honed our focus on developing better preventive interventions, screening methods and treatments, for individuals with cancer. This year our investigators boldly crossed boundaries and broke tradition to pool powerful, transdisciplinary brain trusts capable of addressing the most pressing scientific questions in the cancer arena today.

I'm proud to share that these efforts were recently recognized by our election to the National Comprehensive Cancer Network, an alliance of the world's leading cancer centers dedicated to quality, efficiency and effectiveness in cancer care. Through this alliance, we join 25 other elite cancer centers responsible for defining care guidelines and raising the quality of care for patients nationwide. This announcement comes on the heels of a year of accomplishments for our cancer center. In 2014-2015, our center saw:

- More high impact publications than in any single year over the past 23 years
- More national awards than in any single prior year
- 30 new members, bringing the total to 370 members
- Active recruitment efforts across departments and institutions
- 20+ member participation in an NCI Provocative Questions initiative workshop

And, the coming year holds great promise in thanks to many new initiatives launched in 2014-2015, including:

Program-led multi-investigator research projects
We launched a new funding award to foster multi-investigator team projects selected by our Program Leaders.

NCCN National Comprehensive Cancer Network®

Brain tumor SPORE initiative
We organized a multi-investigator and multi-institutional group to pursue a Specialized Program of Excellence (SPORE) application.

Adolescent and young adult cancer research
We initiated a transdisciplinary effort to promote cancer research targeting diseases in the 15 to 30-year age group. The generous support of the Angie Fowler Family Foundation provided a gift of $6.7 million over four years to recruit investigators and support pilot and transdisciplinary, multi-investigator efforts.

Genomics-based therapeutic decision-making
One year since clinical use of genomic testing of cancer samples for directing therapy decisions began in practice, we eagerly anticipate early results to guide development and refinement of guidelines for testing and link to national efforts to coordinate decision-making and develop more comprehensive approaches to genomic tumor boards.

High-risk genomics initiative
A multidisciplinary focus group of investigators is implementing a comprehensive family analysis with the hope to identify both private and applicable novel genes associated with families with a high prevalence of cancer.

Cancer immunotherapeutics
We are developing our basic and therapeutic efforts in cancer immunotherapeutics, linking to the stem cell therapeutics focus area in our Hematopoietic Disorders Program.

Inside this report you will meet many of our exceptional member investigators and learn how our researchers and clinicians are melding mind power from all facets of the field to address cancer with creative, ambitious approaches.

Stanton L. Gerson, MD
Asa and Patricia Shiverick · Jane Shiverick (Tripp) Professor of Hematological Oncology, Distinguished University Professor, Director of the Case Comprehensive Cancer Center and Director of the Seidman Cancer Center at UH Case Medical Center

LEADERS

SENIOR LEADERS

Stanton L. Gerson, MD
Director,
Case Comprehensive Cancer Center
slg5@case.edu

Brian J. Bolwell, MD
Associate Director
for the Taussig Cancer Institute
bolwelb@ccf.org

Jill S. Barnholtz-Sloan, PhD
Associate Director for Bioinformatics
jsb42@case.edu

Mark W. Jackson, PhD
Associate Director
for Training & Education
mark.w.jackson@case.edu

James W. Jacobberger, PhD
Associate Director
for Shared Resources
jwj@case.edu

Ruth A. Keri, PhD
Associate Director for Basic Research
keri@case.edu

Li Li, MD, PhD
Associate Director
for Prevention Research
lxl62@case.edu

Jaroslaw P. Maciejewski, MD, PhD
Associate Director for the Lerner
Research Institute
maciejj@ccf.org

Neal J. Meropol, MD
Associate Director
for Clinical Research
neal.meropol@case.edu

Anne Duli, MPA
Associate Director for Research
Administration & Finance
anne.duli@case.edu

EXECUTIVE COMMITTEE

Afshin Dowlati, MD
Deputy Associate Director
for Clinical Research and
Director, Center for Cancer Drug
Development
axd44@case.edu

Mikkael Sekeres, MD, MS
Deputy Associate Director
for Clinical Research
and Director, Clinical Trials
sekerem@ccf.org

Sanford D. Markowitz, MD, PhD
Principal Investigator,
Case GI SPORE
sxm10@case.edu

George R. Stark, PhD
Strategic Advisor to the Director
starkg@ccf.org

NEW PROGRAM LEADERS

Program leaders strive for a deeply collaborative environment within and across Cancer Center basic science programs, which are at the root of the Center's scientific investigations.

The Case Comprehensive Cancer Center appointed four members to program leadership roles last year:

Zhenghe John Wang, PhD – Cancer Genetics

Dr. Wang, Genetics, Case Western Reserve University, has high hopes that the lab-to-clinic translational channels of the Case Comprehensive Cancer Center and GI SPORE at Case Western Reserve University will smoothly transition a scientific phenomenon his lab discovered into development of a compound safe for patients and ultimately a clinical trial. *(continued on page 4)*

Nima Sharifi, MD – GU Malignancies

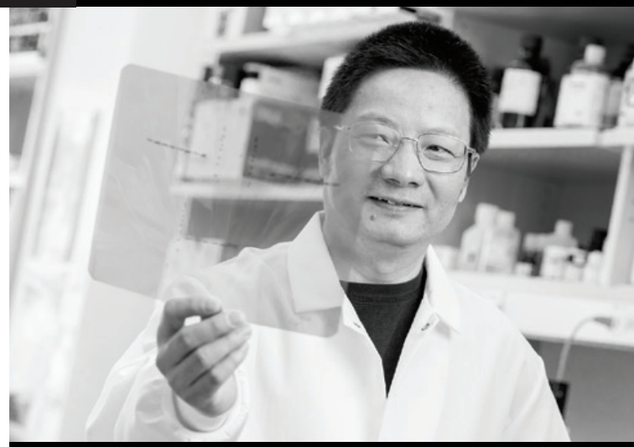
As a prostate cancer specialized medical oncologist with a lab studying how tumors become resistant to hormonal therapy in metastatic prostate cancer, Dr. Sharifi, Cancer Biology, Cleveland Clinic, walks in the realms of both clinical care and laboratory science and sees how important these arenas are to one another, both in the formulation of relevant research hypotheses and in conducting research. *(continued on page 4)*

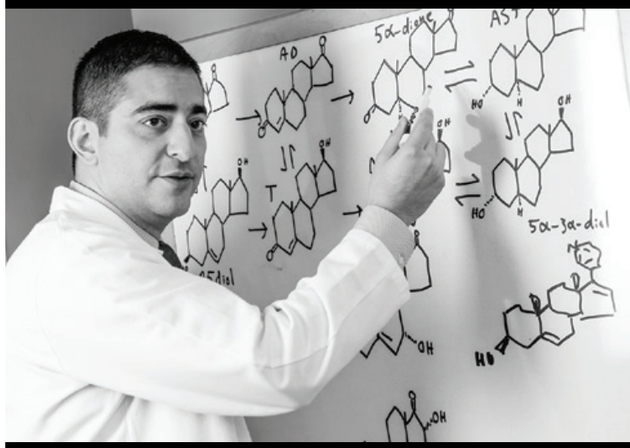
Yogen Saunthararajah, MD – Developmental Therapeutics

With the pharma industry's success rate of 1 in 20 oncology drugs that progress from phase 1 to phase 3 clinical trials, the need for more input from the science arena, and the potential for its impact, is clear. We have precision medicines to target no more than 15 genetic alterations in cancer, but these are rare alterations, says Dr. Saunthararajah, Hematology and Oncology, Cleveland Clinic. *(continued on page 4)*

Bing-Cheng Wang, PhD – Molecular Oncology

Since the last Cancer Center grant renewal, the Molecular Oncology program reorganized, forming focus groups for the biology of brain tumors, cell signaling and metabolism, DNA damage response, and tumor immunology and immunotherapy. The focus groups meet regularly, engaging in cross-specialty dialogue and formulating project concepts. *(continued on page 4)*





NEW PROGRAM LEADERS

Zhenghe John Wang, PhD – Cancer Genetics

PIK3CA, which encodes the p110α catalytic subunit of PI3K, is the most frequently mutated oncogene in human cancer, including in approximately 30 percent of colorectal cancers. Most p110α oncogenic mutations occur at two hot spots, one in the helical domain and another in the kinase domain, with approximately 50 percent of p110α mutations located in the helical domain. Dr. Wang's lab published in *Cancer Cell* the finding that the p110α helical domain mutant proteins, but not the wild-type and kinase domain mutant proteins, directly associate with IRS1 independent of the p85 regulatory subunit of PI3Kα. This compelling evidence pointed to the p110α E545K mutant-IRS1 interaction playing a critical role in tumorigenesis and demonstrated how this mutant-specific protein interaction may be exploited for cancer therapy.

"With this mutation, it's as if the cancer can turn on a light without using the switch; it shortcuts the circuit. We think that if we can cut off the short circuit and turn off the light, we can inhibit the tumor growth," says Dr. Wang. In addition to co-leading the Cancer Genetics Program, Dr. Wang is a project co-leader of the GI SPORE, which he says greatly enhances the resources and depth of specialized, multi-pronged talent focused on colorectal cancer at the Case Comprehensive Cancer Center.

"For me personally, as a basic research scientist, just by interacting with clinicians, I understand the clinic better and have learned a lot about patient-oriented research and can better translate research," says Dr. Wang. He attributes the PhD-MD team model for co-leading Cancer Center programs with regular opportunities to interact with other multidisciplinary program leaders and SPORE colleagues to foster dialogue that spurs expression of lab concepts and clinical challenges.

Nima Sharifi, MD – GU Malignancies

"We're looking at the enzymatic machinery that enables the tumor to make its own androgens, and we think if we can figure out the details of those mechanisms, then we might be able to figure out how to block that process and develop new treatments. Different machinery may be in place in different patients' tumors, so part of the idea is to identify which tumors have which drivers so we can individualize treatments for patients rather than one-size-fits-all, which is how things are done today," explains Dr. Sharifi.

His lab identified the first mutation in an enzyme, 3β-hydroxysteroid dehydrogenase type 1, that drives this process. They determined that this mutation (N367T) can be passed through germ line DNA, which may help provide personalized treatment guides for aggressive versus less intensive treatment protocols.

Having ties to the clinical realm and the infrastructure of the Cancer Center simplifies the tissue collection that's necessary for this type of work, says Dr. Sharifi, whose research benefits from an ongoing clinic-based sample collection program. Dr. Sharifi notes that one of the primary objectives of the GU Malignancies Program is to seamlessly enable the fundamental discoveries that occur in the lab to move into clinical work and then back to the lab."We're studying the same disease, but the worlds and challenges of pure lab scientists and someone who is a pure clinician are very different," he says.

The program helps bridge this cross-specialty dialogue, bringing in oncologists or physician scientists who treat patients but also have done laboratory science and understand the language of both worlds to help bridge dialogue across the continuum of research. It helps bring together a critical mass of investigators with a focus on GU, and pools the resources of institutions, such as Dr. Sharifi, who is based at Cleveland Clinic collaborating with Molecular Imaging based at Case Western Reserve University.

Yogen Saunthararajah, MD – Developmental Therapeutics

"At the Case Comprehensive Cancer Center, we have rational, science-based models for the most common genetic alterations in cancer. We have clinical proof of principle that we can address the most common alterations scientifically, using nontoxic, effective therapies," says Dr. Saunthararajah. His lab, for example, conducted the first proof of principle of noncytotoxic epigenetic differentiation therapy and published results on evaluation of noncytotoxic DNMT1-depleting therapy in patients with myelodysplastic syndromes in *The Journal of Clinical Investigation*. There are hundreds of treatments aimed at activating an emergency brake self-destruction or suicide program, but none that broadly use differentiation or specialization, the natural and main control on cell growth and division. "We simply did not know how, and now that we do, we see a new domain of drug therapy development that is truly alternative to existing therapies. We are working hard to develop drugs that do not activate self destruction, but elegantly renew the specialization program that is latent in every cancer cell," says Dr. Saunthararajah.

With this era of precision medicine, the Developmental Therapeutics Program prioritizes technology to allow efficient therapeutic model evaluations. A high-throughput screening facility with advanced robotics and molecule libraries is under construction. Additionally, the program is exploring novel technologies that can evaluate combinations of drugs preclinically and novel mouse models for liquid and solid cancers for preclinical in vivo body experiments. The program depends on broader resources to support its work, noting a clear marriage between genetics and therapeutics in precision medicine and the need for predictive biomarkers to help individualize drug dose and scheduling.

"I believe perhaps as soon as 10 years from now the kinds of treatments that we are developing will be personalized and we will have tens of agents as opposed to zero that work by using the natural, main brake of specialization, and thereby address some of the most common genetic alterations in cancer. And, treatment will be much kinder and much more effective," says Dr. Saunthararajah.

Bing-Cheng Wang, PhD – Molecular Oncology

Dr. Wang, Professor of Medicine-Nephrology and Pharmacology, Case Western Reserve University, notes that the most striking research developments of the past year in the Molecular Oncology program are the result of strong inter- and intra-programmatic interactions. Newly recruited to the program, Paul Fox, PhD, bridges the Tumor Immunology and the Signaling and Metabolism focus groups. First, he has discovered a novel anti-angiogenic isoform of VEGF, VEGF-Ax, which he has shown is generated through translational readthrough. These basic mechanistic insights are now applied to Glioblastoma Multiforme (GBM), as are those based on his second discovery of a new mechanism of GBM vascularization and progression. Finally, he made a paradigm-shifting discovery for the mechanism of iNOS-S100A8/A9 dependent site-selective S-Nitrosylation. These studies involved interactions with Justin Lathia, PhD, Dolores Hambardzumyan, PhD, Jeremy Rich, MD, and Edward Plow, PhD, and use of animal and proteomics cores. Another large intra-programmatic collaboration showed that EphA2 promotes infiltrative invasion of glioma stem cells in vivo through cross-talk with Akt and regulates stem cell properties and revealed a major role of EphA2 in the diffuse invasion and stem properties of GBM in vivo. The study was possible because of the unique collection of glioma stem cells and specialized expertise in GBM research at the Case Comprehensive Cancer Center. Finally, a collaboration revealed that cancer stem cells selectively use the scavenger receptor CD36 to promote their maintenance using patient-derived cancer stem cells, resulting in their survival and metabolic advantages.

Ongoing discussion of work underway gives Program Leaders familiarity and depth of knowledge to identify the most promising work in their areas for Cancer Center Executive Committee designated funding. A recently funded multidisciplinary Molecular Oncology Program project represents the joint effort of Cancer Center members Dr. Lathia and Mark Brown, PhD, covering tumor metabolism, immunology and signaling. Dr. Wang considers opportunities to discuss the potential for such collaborations as one of the Cancer Center's valuable member benefits.

"You are all in town, but to facilitate these collaborations, you need certain mechanisms that make it easy to initiate conversations and actually work together," says Dr. Wang, who appreciates the transdisciplinary project insight and synergistic dialogue that the intra- and inter-program meetings, annual Cancer Center retreat and seminar series provide.

PROGRAM LEADERSHIP

Cancer Genetics
Program Leaders: Sanford D. Markowitz, MD, PhD and Zhenghe John Wang, PhD

Molecular Oncology
Program Leaders: Alexandru Almasan, PhD and Bing-Cheng Wang, PhD

Breast Cancer (Developing Program)
Program Leaders: Lyndsay Harris, MD and William P. Schiemann, PhD

GU Malignancies
Program Leader: Brian I. Rini, MD and Nima Sharifi, MD

Hematopoietic Disorders
Program Leaders: Jaroslaw P. Maciejewski, MD, PhD and Marcos de Lima, MD

Developmental Therapeutics
Program Leaders: Afshin Dowlati, MD and Yogen Saunthararajah, MD

Cancer Imaging
Program Leaders: James P. Basilion, PhD and Zhenghong Lee, PhD

Cancer Prevention, Control & Population Research
Program Leaders: Gregory S. Cooper, MD and Susan A. Flocke, PhD

Notable Papers Result
from Center Collaborations

HIGH-IMPACT PUBLICATIONS

Significant 2014-2015 member publications show research strides on many fronts, from stem cells to genomics to therapeutic impact.

Gradual Implementation of the Meiotic Recombination Program via Checkpoint Pathways Controlled by Global DSB Levels

Molecular Cell – March 5, 2015

Member: G. Valentin Börner, PhD, Associate Professor, Biology

This study provided insight into the processes behind the genetic instability that leads to cancer. Findings showed that the number of chromosome breaks within the same nucleus determines break processing during meiosis. When early, low-level double-strand breaks (DSBs) are induced, repair is controlled by cell cycle checkpoint components. In contrast, with high DSB levels, Mec1^{ATR} assumes control.

"The Cancer Center's core services such as high-resolution microscopy and next generation sequencing are important for us to complete this type of work at Cleveland State, as we have a smaller program and don't have this type of infrastructure on campus," says Dr. Börner.

Novel Recurrently Mutated Genes in African American Colon Cancers

Proceedings of the National Academy of Sciences - Jan. 27, 2015

Members: Sanford D. Markowitz, MD, PhD, Professor, Medicine-Hematology/Oncology

Kishore Guda, DVM, PhD, Assistant Professor, General Medical Sciences (Oncology)

Joseph E. Willis, MD, Associate Professor, Pathology

Using DNA sequencing to compare colorectal cancer samples from African American and Caucasian individuals, investigators first uncovered 20 new gene mutations in the colorectal cancers of African Americans never before seen in patients with this disease. Investigators then confirmed that 15 of these gene mutations preferentially affected the African American patients. Just over 40 percent of cancers in African Americans carried mutations in one or more of these genes. In addition, the scientists found these mutations were 3.3-fold more common in African American cancers than in colorectal cancer tissues from Caucasians.

The investigators particularly focused on mutations in 2 of these 15 genes, EPHA6 and FLCN, detected exclusively in African American patients. EPHA6 belongs to a family of proteins linked to causing cancer; this study marks the first time this gene has been implicated in colorectal cancer. In addition, individuals born with FLCN mutations are known to be susceptible to certain cancers. This study only recently became possible because of technological advances in gene sequencing and computational analysis.

"This milestone study builds on our previous genetic research on colorectal cancer," says Dr. Markowitz. "It illustrates the extraordinary impact that dedicated, collaborative teams can make when they combine scientific experience and ingenuity with significant investment."

Aspirin and the Risk of Colorectal Cancer in Relation to the Expression of 15-Hydroxyprostaglandin Dehydrogenase (HPGD)

Science Translational Medicine - April 2014

Members: Stephen Fink, PhD, Assistant Professor, Medicine-Hematology/Oncology

Sanford D. Markowitz, MD, PhD, Professor, Medicine-Hematology/Oncology

A review of clinical samples showed that individuals whose normal levels of 15-Hydroxyprostaglandin Dehydrogenase (15-PGDH), a normal enzyme that degrades prostaglandins, were above the median level, benefited from aspirin therapy to prevent development of colon cancer, cutting their cancer risk in half, while those whose normal level of 15-PGDH fell below the median show no benefit from aspirin use.

"You want to try to determine the people aspirin would benefit, and those who aspirin wouldn't benefit, to minimize potential side effects, such as bleeding. So, this could, down the road, be a potential biomarker to guide treatment," says Dr. Fink. Collaboration with colleagues at Dana-Farber Cancer Institute allowed the necessary sample quantities for this retrospective study. The team hopes to secure funding for a prospective study as a next step.

Epigenomic Comparison Reveals Activation of "Seed" Enhancers During Transition from Naive to Primed Pluripotency

Cell Stem Cell – June 2014

Members: Peter C. Scacheri, PhD, Associate Professor, Genetics and Genome Sciences

Paul J. Tesar, PhD, Associate Professor, Genetics and Genome Sciences

By comparing closely related embryonic and epiblast pluripotent stem cells, collaborating stem cell and cancer biology researchers identified a new class of enhancers, which they refer to as seed enhancers. Unlike most enhancers, which are only active in specific times or places in the body, seed enhancers play roles from before birth to adulthood.

Dr. Scacheri commented on the potential implications of this finding, "It is clear that cancer can be driven by changes in enhancers, and we are interested in understanding the role of seed enhancers in cancer onset and progression." This work generated from interaction between two typically non-overlapping areas.

"Joint lab meetings allow us to spur new interaction or collaborative opportunities that we didn't think about before. The ability to have two groups with divergent but complementary skill sets, with

Dr. Scacheri's lab being world experts in epigenomics and really understanding that side, and then my lab having expertise in stem cell biology, provided a really unique opportunity to explore the understanding of these early developmental states in a new way," says Dr. Tesar.

Conserved Oncogenic Behavior of the FAM83 Family Regulates MAPK Signaling in Human Cancer

Molecular Cancer Research - 2014

Member: Mark W. Jackson, PhD, Associate Professor, Pathology

FAM83B, a novel oncogene involved in activating CRAF/MAPK signaling and driving epithelial cell transformation, is one of eight members of protein family FAM83 characterized by a domain of unknown function, DUF1669, which drives transformation. By analyzing multiple FAM83 members using quantitative PCR and database mining, this study showed that additional FAM83 members have significantly elevated expression levels in human tumors. Each FAM83 member was elevated in at least one of 17 tumor types examined. These findings suggest that elevated expression of FAM83 members is associated with elevated tumor grade and decreased overall survival. In addition, multiple FAM83 proteins also exhibit oncogenic properties when expressed in non-transformed cells. This novel family of oncogenes offers opportunities for development of cancer therapies aimed at suppressing MAPK signaling.

"Using Cancer Center tumor tissue working groups and genomics working groups ensured that my group, as basic researchers, is communicating with clinicians who are seeing patients and has access to the information and patient samples that we need to confirm our laboratory findings. This helps make sure our models are faithful with what's happening in the clinic," says Dr. Jackson.

Synthetic Triterpenoid Induces 15-PGDH Expression and Suppresses Inflammation-driven Colon Carcinogenesis

The Journal of Clinical Investigation - May 16, 2014

Members: John J. Letterio, MD, Professor, Pediatric Hematology/Oncology

Sanford D. Markowitz, MD, PhD, Professor, Medicine-Hematology/Oncology

Colitis-associated colon cancer (CAC) is a consequence of inflammation-induced epithelial transformation which is promoted by an inflammatory cytokine-dependent downregulation of 15-hydroxyprostaglandin dehydrogenase (15-PGDH) and subsequent suppression of prostaglandin metabolism. This study found that oral intake of a synthetic triterpenoid (CDDO-Me) by mice predisposed to develop colon cancer increased survival and suppressed intestinal epithelial neoplasia by decreasing production of inflammatory mediators and increasing expression of 15-PGDH. This opens the potential for small molecules of the triterpenoid family to serve as effective agents for the chemoprevention of CAC in humans.

"I'm a pediatric oncologist, and my specialties are signaling, basic biology and inflammation. I'm not a colon cancer expert. Fortunately, my lab is adjacent to Sandy Markowitz's lab. Together we decided to focus on one of the tumor suppressor genes that they identified in colon cancer," says Dr. Letterio.

HIGH-IMPACT PUBLICATIONS

Programmed Translational Readthrough Generates Antiangiogenic VEGF-Ax

Cell – June 19, 2014

Members: **Paul L. Fox, PhD,** Professor, Cellular and Molecular Medicine, Lerner Research Institute

Belinda B. Willard, PhD, Director, Proteomics Core, Lerner Research Institute

Daniel J. Lindner, MD, PhD, Staff and Associate Medical Director, Department of Translational Hematology and Oncology Research, Taussig Cancer Institute and Lerner Research Institute

The Fox laboratory has reported the discovery of a novel variant of the important angiogenic protein, vascular endothelial growth factor protein, or VEGF-A. The new protein, dubbed VEGF-Ax, has a short extension that provides a function entirely opposite to VEGF-A, namely, it blocks angiogenesis and tumor growth. The extension is generated by readthrough of the stop signal in the messenger RNA to a second, downstream stop codon.

"This readthrough event is almost unheard of in mammalian cells. We know a few viruses that do it, but mammalian cells do not. So, not only did we discover a new molecule, but we discovered a new mechanism of making a protein," says Dr. Fox. They produced an antibody for the unique peptide extension in VEGF-Ax and conducted high-sensitivity mass spectrometry to verify its presence.

MicroRNA-181a Has a Critical Role in Ovarian Cancer Progression through the Regulation of the Epithelial–mesenchymal Transition

Nature Communications – January 7, 2014

Members: **Analisa DiFeo, PhD,** Assistant Professor, General Medical Sciences (Oncology)

Goutham Narla, MD, PhD, Assistant Professor, Medicine and Transformative Molecular Medicine

Here we show that microRNA-181a promotes TGF-β-mediated epithelial-to-mesenchymal transition via repression of its functional target, Smad7. miR-181a and phosphorylated Smad2 are more prominent in recurrent than matched-primary ovarian tumors. A screen of humans who responded well to chemotherapy and those with tumor recurrence within six months found that with higher miR-181a, tumors returned much faster and resulted in poor outcomes.

"We looked at the biological effect of this microRNA, and why it correlates with poor outcomes. We saw that with overexpression of two to three-fold, these cells became much more aggressive and much more invasive. When implanted into mice they metastasized more than the control that does not express the microRNA, validating that it is driving phenotype, not simply correlating with patient outcomes," says Dr. DiFeo.

Dr. DiFeo says this microRNA could eventually be used as a biomarker and, if an individual has high expression, they could be monitored more closely. Potentially, this microRNA also could be a target for therapeutic development.

Low PIAS3 Expression in Malignant Mesothelioma Is Associated with Increased STAT3 Activation and Poor Patient Survival

Clinical Cancer Research – October 14, 2014

Members: **Afshin Dowlati, MD,** Professor, Medicine-Hematology/Oncology

Pingfu Fu, PhD, Associate Professor, Epidemiology & Biostatistics

This publication highlights a mesothelioma cancer cell pathway that, when activated, promotes cancer cell growth and could provide a novel therapeutic target. In the study, the use of a PIAS3 expression in STAT3-driven mesothelioma cells, either by overexpression of exogenous PIAS3, stimulation of endogenous PIAS3 expression by curcumin or incubation with a PIAS3 peptide mimetic, led to decreased cellular STAT3 activation and promoted apoptosis.

"We explored why the pathway is activated and what we can do to shut it off. We were able to do it with a natural product, curcumin. Currently, mesothelioma is a cancer that has only one chemotherapy that works temporarily," says Dr. Dowlati.

Dr. Fu collaborated on the study providing the analytical perspective. "My role was to make sense of the expression data and determine relations to outcomes. We were able to make the association between PIAS3 protein expression and survival outcome using survival data analysis techniques among others," says Dr. Fu.

Conversion of Abiraterone to D4A Drives Anti-tumour Activity in Prostate Cancer

Nature – June 1, 2015

Member: **Nima Sharifi, MD,** Associate Professor, Cancer Biology

Researchers found that abiraterone, a steroid inhibitor, is converted into the more physiologically active D4A (Δ4-abiraterone) in both patients and animal models with prostate cancer who receive the drug. Additionally, D4A is more effective than abiraterone at killing aggressive prostate cancer cells, suggesting that some patients may benefit from direct treatment with D4A.

"More studies are needed to uncover the exact mechanisms involved, but we would predict that direct treatment with D4A could prolong survival in some patients with metastatic prostate cancer," says Dr. Sharifi. "Further studies also will help us develop a potential biomarker profile to predict which patients will respond to abiraterone."

TRAINING AND MENTORING

Breast Cancer Research Program an Incubator for Mentoring, Collaboration

Ruth A. Keri, PhD, Associate Director for Basic Research, has seen a breast cancer focus grow from just two basic science researchers, herself and Monica Montano, PhD, to more than 30 in the Case Comprehensive Cancer Center's Breast Cancer Research Program-in-development, poised for a full program request in the upcoming center renewal grant. She is hands-on recruiting faculty and engaging colleagues in breast cancer research, which culminated in several collaborative successes this past year.

One 2014 publication showed that two FDA-approved drugs, which historically have not been effective when used individually for breast cancer, have been found when used together, obliterate breast tumors in four days in mice. The drug combination shuts down alternate survival pathways sought by the cancer cells. Now, the team is pursuing approval for a Phase 1 safety trial.

Dr. Keri also jumped on a research opportunity presented by a clinical colleague, Leona Cuttler, MD, Professor of Pediatrics, prior to her passing in 2013. A longstanding relationship prompted Dr. Cuttler and her colleague, Beth Kaminski, MD, to reach out to Dr. Keri regarding a genetic breast development abnormality observed in a patient's family. Because stem cell pathway messaging that regulates typical breast tissue development is similar to what directs tumor growth, Dr. Keri theorized that the family's genetic mutation, previously undocumented in any other cases, could lead to identification of a new breast cancer gene. Genetic epidemiologist Cheryl Thompson, PhD, collected family members' DNA, and the team narrowed to 150 possible genes with genome sequencing directed by Alexander Miron, PhD. The group recently secured a grant to pursue isolating the single gene responsible.

As the Cancer Center's Associate Director for Basic Research, Dr. Keri works to ensure that junior faculty have mentoring support to promote their engagement in similar collaborative, translational projects, regardless of their specialty focus. She works as a research matchmaker, keeping a pulse on projects underway throughout the center and proposing collaborations across department lines.

Training Programs Focus on Cross-disciplinary Opportunities

Mark W. Jackson, PhD, launched his role as the Case Comprehensive Cancer Center Associate Director for Training and Education with a satisfaction survey that went out to clinical and PhD trainees in member's laboratories. Approximately 70 percent of trainees classified their overall training environment as outstanding or excellent. Opportunities noted include standardized training in grant writing and presentation development and increased exposure to the clinical side for laboratory researchers.

Understanding of the clinical experience gained, for example, by shadowing physicians, provides a viewpoint that is really important to fueling how you approach research in the laboratory, explains Dr. Jackson. To create more transdisciplinary interaction, a monthly trainees seminar series pairs presentations from a laboratory student researcher and a clinical fellow to give both the lab view and patient care experience perspective, such as a case report and description of

diagnostic testing and patient interactions. In development are programs that allow trainees to also participate in topic-focused basic researcher-clinician working groups, discussing the experiments that are going on in clinic and lab and how those can be fused, and participation of trainees in genomics tumors boards.

"It is a really great way to make sure basic researchers are plugged in to the clinical end and connected to the physicians who are seeing patients, and have access to the information and patient samples that we like to study in the lab to make sure our disease models are faithful to what's happening in our patients," Dr. Jackson says.

Many trainees initially hope to one day run a laboratory, yet see the funding challenges and limitations, and aren't fully aware of other career path options. The program is evaluating opportunities to expose trainees to diverse disciplines and opportunities, such as business, advocacy, government, biotech, clinical laboratories, and diagnostics. Mentors help facilitate this currently, and the program may develop workshops and other programming to enhance this exposure. Professional development in practical areas, such as grant and manuscript writing, are other skills the center hopes to also achieve in a more open workshop format across institutions, rather than relying on one-on-one mentoring.

DRUG DISCOVERY PIPELINE

Programs foster drug development and commercialization through funding and industry expertise.

Case Western Reserve University School of Medicine Council to Advance Human Health

Cancer cells use the protein BCL-2 to stay alive, making it a therapeutic target. Previous drugs target one mechanism involved, but Clark Distelhorst, MD, Professor, Medicine-Hematology/Oncology, Pharmacology, and his lab have identified a second mechanism and are currently evaluating potential drug compounds – with help from commercialization experts.

"I'm a cancer biologist. I know how BCL-2 protein works. To take compounds and turn them into real therapeutics is a new focus. For that we need guidance and financial support," explains Dr. Distelhorst.

In addition to support from University Hospitals' Harrington Institute advisors, Dr. Distelhorst has benefited from the input of industry experts serving on the Case Western Reserve University School of Medicine's Council to Advance Human Health (CAHH) and the School of Medicine's Chief Translational Officer William Harte, PhD, who advised regarding experiments needed to validate lead compounds.

Case Western Reserve University's Technology Transfer Office provides support for intellectual property, but also practical funding to help advance discoveries. Dr. Distelhorst, for example, acknowledged Technology Transfer funding for a high-throughput screen which helped refine their focus to four lead compounds.

Sanford D. Markowitz, MD, PhD, also has benefited from the support of these programs. The CAHH advisers gave biotech perspective on experiment design and medicinal chemistry perspective to help poise a new inhibitor drug for commercialization.

Cleveland Clinic Innovations

Yogen Saunthararajah, MD, Professor, Hematologic Oncology and Blood Disorders, is laser focused on the fact that we do not yet have precision medicines in clinical practice to match the most common genetic alterations in cancer.

"One strength of the Case Comprehensive Cancer Center is that we have rational, science-based approaches to address the most common genetic alternations in all of cancer, as unfortunately, there are no solutions for these highly frequent mutations. Very excitingly, we already have generated clinical proof of principle that our solutions can work, and in a nontoxic way" says Dr. Saunthararajah.

He credits assets such as Cleveland Clinic Innovations with facilitating the institutional leap from laboratory to drug development, which is very difficult and a skill set in its own right. Institutions need to develop the capacity and expertise to connect across groups, to reach out to angel and venture capital investors, in order to move science-based treatments towards the commercialization that is needed for mass availability to patients, he says.

"I think we are complementary, very meaningfully, to big pharma development because we work from science, and this where the answers lie," says Dr. Saunthararajah.

Qing Yi, MD, PhD, Chair, Cancer Biology, notes that, in the past, if you did not have a grant or other funding, the project would simply die. He also acknowledges the risk an institution takes when supporting potential new drug therapies.

"It's risky, but always highly rewarding if successful. This kind of support is extremely important to individual research," he says of Cleveland Clinic Innovations funding for early pre-clinic studies.

University Hospitals Harrington Discovery Institute

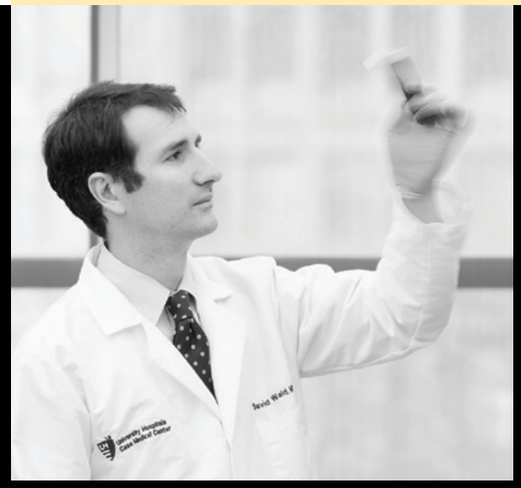
David N. Wald, MD, PhD, Assistant Professor, Pathology, received support as a Harrington Scholar through University Hospitals' Harrington Discovery Institute, as he embarked on development of a new drug. He's taken advantage of in-person meetings, teleconferences and email exchanges with industry experts who foreshadow potential issues and provide crucial guidance on necessary steps in the drug development process.

"That's been the biggest help, the expertise right at your fingertips. When you run into a hurdle, you see someone who's been there a hundred times before and can guide you," Dr. Wald says. His team was focused on a specific compound that looked very promising in terms of its anti-cancer activity, but had a few issues that limited its viability as a drug that could be safely given to patients. An adviser helped steer his lab to take a different approach that led to the development of a new drug candidate much sooner than they would have otherwise. Harrington Scholars receive funding awards as well as the invaluable expertise from a team of advisors.

Dr. Markowitz, also a Harrington Scholar, says, "Support for initial studies is indispensable. Funds are needed to bring an idea to point, and in order to compete for NIH funding there is an expectation of early stage data." In addition to funding, he also has benefited from Harrington Discovery Institute consultants' industry perspective regarding drug chemistry, toxicity and FDA regulations.

Goutham Narla, MD, PhD, Assistant Professor, Medicine, seeks out ways to drug those proteins which previously had been considered undrugable.

"You could turn off accelerators very well, that's the basis we use for a lot of drugs to treat cancer, but to turn on the brakes—that's been more challenging. When I came here, we had some early-stage ideas on how to do that, but it's really been with both the support of the Harrington Discovery Institute, its accelerator, BioMotiv, and the Case Western Reserve University School of Medicine that we have been able to leapfrog our efforts forward to develop a novel set of drugs for cancer patients," Dr. Narla says. He gained deep insight into drug development, including how to formulate a drug, determine ideal dosages and identify toxicities. These are skills that an academic medical center does not normally have access to, or physicians and scientists do not learn as part of their training, Dr. Narla says.



BRAIN TUMOR INITIATIVE

Realizing a growing stronghold of brain tumor research in Cleveland and throughout the state of Ohio, Steven S. Rosenfeld, MD, PhD, and Jill Barnholtz-Sloan, PhD, who co-direct the Case Comprehensive Cancer Center's Brain Tumor Initiative, leapt at the opportunity to formally open intra-state channels of collaboration in brain tumor research. Initially, the group is pursuing two priorities:

Critical Mass of Brain Tumor Research Spurs SPORE Application Prep, Statewide Trials Collaborative

Brain Tumor* Specialized Program of Research Excellence *(SPORE) – The initiative has pooled researchers at Case Western Reserve University, Cleveland Clinic, University Hospitals Case Medical Center, MetroHealth Medical Center, Cincinnati Children's Hospital Medical Center, Nationwide Children's Hospital and Greehey Children's Cancer Research Institute at the University of Texas Health Science Center, San Antonio, to complete an application for a Brain Tumor Specialized Program of Research Excellence (SPORE) in fall of 2015.

"The focus is on the biology of malignant brain tumors and how we might be able to better target some of those biological changes using novel drugs in clinical trials in Ohio," says Dr. Barnholtz-Sloan. The Case Comprehensive Cancer Center already leads in accrual of participants in the NCI-funded multi-institutional clinical level consortium of adult brain tumor studies.

Ohio Clinical Trials Collaborative – Established through governor's funding, the Case Western Reserve School of Medicine took the lead on establishing the Ohio Clinical Trials Collaborative with the goal of bolstering multi-site clinical trials spanning the three Clinical Translational Science Award (CTSA) sites in Ohio. The collaborative's oncology focus currently centers on neuro oncology. One multi-site study is online, and three more are slated to open soon; these trials are in both adults and children with brain tumors. This group is lead by Dr. Barnholtz-Sloan, David Peereboom, MD, from Cleveland Clinic and Jonathan Finlay, MD, from Nationwide Children's Hospital.

"Our goal is to really make Ohio and the Case Comprehensive Cancer Center the go-to place for brain tumors for people all around the country," says Dr. Rosenfeld. "I think the strength of this collaborative in Ohio and in the Case Comprehensive Cancer Center is that people work together. You have to have multiple fires blazing all the time and make sure you have the flexibility to go down the direction that looks promising for this difficult disease."

Inaugural Cancer Stem Cell Conference Draws International Following

STEM CELL RESEARCH MOMENTUM

In the relatively young field of cancer stem cell (CSC) research, enthusiasm and momentum have supplanted novelty, evidenced by robust attendance at the first International Cancer Stem Cell Conference in August 2104. The Case Comprehensive Cancer Center and National Center for Regenerative Medicine at Case Western Reserve University launched the inaugural event in Cleveland, under the direction of Case Comprehensive Cancer Center members Jeremy Rich, MD, Stanton Gerson, MD, Arnold Caplan, PhD, Justin Lathia, PhD, and Huiping Liu, MD, PhD.

"Over the last 10 years, there's been a lot of building momentum suggesting that stem cell programs are essential for cancer maintenance, progression and resistance," says Dr. Lathia. The thrust and translational opportunities in cancer stem cell efforts proved compelling at the conference's debut. More than 320 researchers attended the four-day event, which featured 55 invited international speakers, 25 short oral presenters and 100 poster presenters, exploring the role of complex roles of cancer stem cells and potential therapeutics.

"We have a critical mass of one cancer after another showing very clear, strong evidence that not only are cancer stem cells present in cancer, but incredibly important in the biology of these cancers," says Dr. Rich. "This is really just transitioned from being a possibility in cells in a dish to real therapies in people."

Session topics ranged from genetics and epigenetics to cancer origin and evolution; microenvironment and exosomes; metabolism and inflammation; metastasis and therapy resistance; single cell and heterogeneity; and plasticity and reprogramming, among others. Dr. Lathia, for instance, shared insight into how CSCs are selectively helping kick the immune system balance toward more suppressive and potential molecular mechanisms to target therapeutically.

"Cancer treatments we thought were targeting the cancer cells may actually have been targeting the environment and changing the way cells maintain themselves. It's an exciting idea that may explain a lot of observations in clinic," says Dr. Rich, speaking to the complexity of CSC interactions explored at the conference.

The conference also included a career development workshop for young investigators featuring panelists from the National Cancer Institute and Case Comprehensive Cancer Center who offered grant writing and professional pathway guidance.

COMMUNITY COMMITMENT

Through extensive outreach efforts and initiatives, the Case Comprehensive Cancer Center's impact on the Northeast community continues to grow in support of better healthcare and improved lifestyles to reduce cancer risk, incidence and death.

HPV Vaccination Focus of Environmental Scan

Across the nation, uptake of the human papilloma virus (HPV) vaccine is low in male and female adolescents and young adults. In October 2014, Case Comprehensive Cancer Center and other comprehensive cancer centers received NCI funds to perform environmental scans focusing on pediatric HPV vaccination uptake. The Cancer Center is focusing on Cuyahoga County through collaboration with the Cuyahoga County Board of Health. The center also is partnering with The Ohio State University Comprehensive Cancer Center, which is scanning the entire state.

"One of the main factors found to be important is a strong clinician recommendation. We know that initially a lot of physicians recommend the other immunizations strongly and then waffle on HPV. Given that little bit of hesitancy, many parents decide to delay or forgo vaccination," says Heidi Gullett, MD, MPH, Case Western Reserve School of Medicine's liaison to the Cuyahoga County Board of Health. "It hasn't been marketed as an anti-cancer vaccine, which is one of the main messages that we hope these scans will help communicate as an important strategy for increased vaccine uptake."

The Case Comprehensive Cancer Center team will present their scan findings in the Fall. Dr. Gullett says they hope to next pursue an intervention grant to evaluate health systems-based interventions, taking into account the complexities of large hospital networks, community health centers, school-based clinics, and vaccine supply identified in their initial scan.

$7 Million from CDC for Healthier Neighborhoods

When Centers for Disease Control and Prevention (CDC) Director Tom Frieden visited the Prevention Research Center for Healthy Neighborhoods (PRCHN) at Case Western Reserve University in 2014, he described current health inequities "where lifespan is determined more by zip code than genetic code."

To help address the issues Dr. Frieden described, the PRCHN received a five-year $4.35 million grant from CDC to renew its operation, and an additional $2.97 million to continue projects focused on smoking cessation and managing epilepsy, chronic disease and dementia in 2014. The PRCHN's renewal funding will primarily support Fresh Link, a long-term project aiming to improve access to fresh, healthy foods in low-income neighborhoods.

"For a lot of years, Cleveland has been one big food desert," says Elaine A. Borawski, PhD, Professor, Epidemiology and Biostatistics, and PI for the grant. "The core project is a test of dissemination of peer-to-peer training initiatives, including participating in the farmer's market and alternative fresh produce outlets with people in the neighborhood serving as navigators to others."

The PRCHN also provides data and statistics on the health of Cleveland residents, breaking down information on chronic diseases such as asthma, diabetes and obesity, as well as health behaviors like tobacco use, by neighborhood.

County Collaboration

The HPV environmental scan is one example of collaboration between public health and clinical research made possible through increased partnership between the Case Comprehensive Cancer Center, Case Western Reserve University and the Cuyahoga County Board of Health. Dr. Heidi Gullett, serves as the Case Western Reserve University School of Medicine population health liaison to the Board of Health, embedded at the Board of Health for the past two years, building relationships and helping to bring together initiatives on public health and clinical care.

Her relationship with Vaccine and Preventable Disease Director Cindy Modie supported baseline data sharing, which enabled funding of the HPV vaccination scan. University Hospitals Public Health/Preventive Medicine residents also spend time at the Board of Health office, engaging in activities such as cancer cluster investigations.

"I think when you start talking about equity, the conversation changes. It's truly about justice and what is best for our community, and I think the Board of Health serves as a catalyst for this work," Dr. Gullett says. Case Western Reserve University School of Medicine is also an anchor organization in the Health Improvement Partnership-Cuyahoga (HIP-Cuyahoga), initiated by the Board of Health and engaging numerous other organizations and County residents to address health priorities from both a public health and clinical perspective.

VELOSANO

Bike to cure.

VeloSano 2015: Cycling event raises money for cancer research

"VeloSano, Latin for 'swift cure,' is a community fundraising initiative for cancer research. At its core, it's a cycling event where riders commit to raise a pre-determined dollar amount by requesting support from personal contacts. 100% of the dollars raised by participants benefits cancer research. The 2014 inaugural event featured 800 riders, 700 volunteers and more than 12,000 philanthropic supporters raising nearly $2 million for cancer research, with support growing each year the event is held."

Brian Bolwell, MD, FACP Chairman, Taussig Cancer Institute, Cleveland Clinic; Associate Director, Case Comprehensive Cancer Center; Professor of Medicine, Cleveland Clinic Lerner College of Medicine of Case Western Reserve University

(continued on page 22)

COMMUNITY ADVISORY BOARD

The Case Comprehensive Cancer Center Community Advisory Board, established in 2012, has improved cancer care for Northeast Ohio residents. The Cancer Center's community outreach and partnership with community leaders has launched a dialogue that allows the Case Comprehensive Cancer Center to better engage and understand complex issues and to coordinate efforts and resources.

For a full list of Community Advisory Board members, visit: cancer.case.edu and click on patients/community.


PETRINA PATTERSON


NEAL DAWSON


TOINETTE PARRILLA


SAMIR ABRAKSIA


GERI BLAIR


KIM BELL


ANGELA BAILEY


LI LI


NANCY KURFESS JOHNSON


LENA GRAFTON


FRAN WILLIS


JAME ABRAHAM


BONNIE WEST

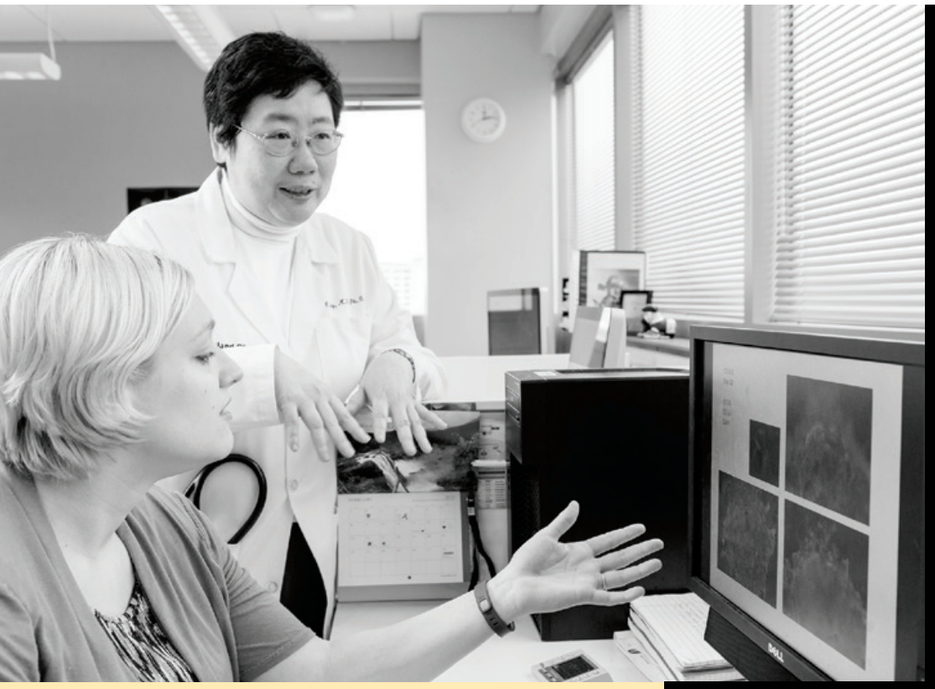

MICHAEL TO


SHARON JEFFERSON

HIGH-RISK GENOMICS

Breast Cancer Initial Focus of High-risk Germline Genomics Initiative

Given that five to 15 percent of cancers have an inherited cause, the Case Comprehensive Cancer Center's new High-Risk Germline Genomics Initiative aims to elevate the study of genetic predisposition to cancer.



The initiative takes advantage of the critical mass of breast cancer researchers and field-wide body of work to focus initially on breast cancer genetics, and will eventually branch out to study other cancers.

Initiative co-leader Lyndsay Harris, MD, says, "The intellectual input from both sides of town plus the patient volume to do projects really gives you a very powerful initiative. At the same time, the field of genomics has moved very quickly and we have to respond to that at both the clinical and research levels, so it's good to have these joint discussions to really think about the best way to do that."

Currently the group is recruiting appropriate Cancer Center members and focusing on funding to support a coordinator and sample collection. The initiative secured its first grant from the VeloSano Foundation to investigate how many children, adolescents and young adults with solid tumors have an inherited risk of cancer, whether they have a family history or not. The principal investigators are Charis Eng, MD, PhD, initiative co-leader, and Johannes Wolff, MD, initiative member.

Forming data collaborations between the Case Comprehensive Cancer Center and international consortia and ensuring that relevant biorepositories' databases can talk to each other with use of tools such as REDCap will help research teams harness power in numbers as they approach sample studies. A genetics database for breast cancer is in initial development.

"Another thing we'd like to concentrate on, because it hasn't been studied very well, is the genetic alterations in the cancer itself, which may be different in people with an inherited mutation versus people who have sporadic breast cancer," says Dr. Eng.

One project team is examining triple negative breast cancers in individuals with BRCA1 and BRCA2, to determine what other clinical or pathological attributes are consistently present in their tumors.

A 2014 philanthropic pledge of $6.7 million to University Hospitals and Case Western Reserve University from Chuck and Char Fowler injected critical support for research into cancers affecting adolescents and young adults (AYA). The funding infuses support for recruitment, pilot studies and transdisciplinary, multi-investigator research at a time when there is little NIH support for this sector.

Fowler Gift Brings Focus to Cancer in Teens and Young Adults

ADOLESCENT AND YOUNG ADULT RESEARCH

"It's hard to incentivize young scientists to pursue AYA research with the limited resources available," says John Letterio, MD, Director of the Angie Fowler Research Initiative. The support of the Fowlers and prioritization by the Case Comprehensive Cancer Center of studies focused on cancers occurring in the 15 to 30 age range marks the first creation of an AYA-dedicated center within a Comprehensive Cancer Center.

With cross-center collaboration, Dr. Letterio hopes the institute can make an impact on the prognosis for distinct cancers that affect the AYA population, such as Ewing sarcoma and osteosarcoma. These cancers, while rare in young individuals, are often highly metastatic with few or no curative treatments in advanced stages. The initiative promotes basic understanding of the biology of the metastatic process and of therapy resistance in cancers that occur in this age group, and it also leverages expertise in imaging, drug development and other cross-institutional facets of the Case Comprehensive Cancer Center in relation to AYA cancers.

An important program goal is to increase the opportunities for participation in the clinical trials process, as currently less than two percent of patients between the ages 15-30 are actively involved in clinical trials. "Raising awareness of the importance of clinical trials will have benefits that include increasing the representation of AYA cancers in our tissue biorepositories, a step necessary to make strides," Dr. Letterio says. In addition to education to help build this important foundation for research, the initiative launched a tissue biorepository for genomic testing and Patient-derived Xenograft (PDX) model development.

"Twenty percent of triple negative breast cancers are associated with BRCA1 and 2 mutations. That's a really high incidence, and it made me think that there has to be a link between what's going on in the germline and what's going on in the tumor. Maybe there is a link that is making these tumors aggressive, and causing them to form in the first place," explains Shaveta Vinayak, MD, University Hospitals Case Medical Center, who is co-leading the project with Holly Pederson, MD, Cleveland Clinic.

Drs. Eng and initiative member Mahmoud Ghannoum, PhD, also envision evaluating the microbiome or methogenome of people with inherited cancers. This could allow a simple, inexpensive monitoring of genetically predisposed individuals through a urine or oral wash test in place of a breast MRI.

"If we think that the microbiome transduces the environmental input to the genes, we can manipulate the microbiome with antibiotics or probiotics to actually prevent cancer in people who have an inherited risk. That is the blue sky this group is working toward," Dr. Eng shares.

TO OUR SUPPORTERS

The Case Cancer Council of the Case Comprehensive Cancer Center was formed to promote and publicize the work of the 400 researchers who work tirelessly to discover new cancer treatment protocols and earlier and more effective detection tools with the ultimate goal of successfully treating cancer at its earliest possible stage. And of course finding a cure for cancer is always at the forefront of our work, although a daunting task.

There have been exciting developments at our center in the areas of genomics, immunology, stem cells, and drug research that place the Case Comprehensive Cancer Center at the forefront of cancer research among the 41 NCI designated comprehensive cancer centers.

While the Center's collaborative partners – Case Western Reserve University, Cleveland Clinic, and University Hospitals Case Medical Center – are well known and nationally respected for innovation and research in the cancer field, it is less known both locally and nationally that the Case Comprehensive Cancer is the vehicle that allows the 400 researchers from these three institutions to work with a combined and singular purpose. No other designated cancer center has the synergistic powerhouse of member institutions that we have.

I am proud to lead the Case Cancer Council that is composed of members of our community all of whom have demonstrated a special interest in supporting cancer research. 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 the goal of raising much needed private funding for future research needs.

The Case Comprehensive Cancer Center has the potential of also being an economic juggernaut for the Northeastern Ohio region. The Center has stimulated a number of ventures with biomedical companies that has caused our region to become a focus for bringing our research from the lab bench to the patients' bedsides.

We hope that all with an interest in cancer research will join our Leadership Council in supporting the Case Comprehensive Cancer Center.

Peter H. Weinberger, Chairman
Managing Partner, Spangenberg, Shibley, & Liber, LLP
Chair, Case Cancer Council

Institute Launch Spawns Cross-institution, Researcher-driven Database

HARNESSING DATA POWER

Jonathan L. Haines, PhD, the Mary W. Sheldon, MD, Professor of Genomic Sciences, joined Case Western Reserve University in late 2013 with a vision for sharing study data and spawning new collaborations based on accessibility of data. In addition to chairing Epidemiology and Biostatistics, Case Western Reserve University School of Medicine, Dr. Haines took on a cross-institution charge as Director of the newly created Institute for Computational Biology, a joint endeavor of Case Western Reserve University, Cleveland Clinic and University Hospitals.

"I think we have made great progress in getting a lot of researchers very interested in collaborating and sharing their data. One of the major hurdles for doing that has been how to actually physically share the data. We've been working hard to build the infrastructure to make that easy," Dr. Haines says.

Through the institute, a new secure physical data center and software infrastructure will help standardize the way that clinical study date is stored and described, making it much easier to see on an aggregate level what data is available across all projects and with what consent without actually exposing individual data. The Case Comprehensive Cancer Center is participating as the alpha test project, with brain tumor data uploading under the direction of Jill Barnholtz-Sloan, PhD, Associate Director of Bioinformatics at the Case Comprehensive Cancer Center and Associate Director of Clinical Informatics at the Institute for Computational Biology.

If enough samples are available from prior studies to facilitate the sample size needed for a new study, then duplicate sample collection is eliminated, taking a study timeline from years down to months and saving significant collection costs, explains Dr. Haines. By offering aggregate search capability to researchers, Dr. Haines envisions new collaborations as researchers connect with those who conducted relevant initial sample collection.

The software function power comes from mating the existing OnCore system, which handles the patient piece, with Labmatrix, which handles larger scale biological data well, Dr. Haines says. A data project concierge will serve as the "front door" point of contact for research groups. The concierge will determine the appropriate level of participation and data support, and address regulations, as in the case of FDA studies.

15 SHARED RESOURCES

Pooled institutional resources create the foundation for scientific progress driven by Case Comprehensive Cancer Center members and affiliated investigators. The center's investment in emerging technologies and specialized experts fast tracks the research cycle and elevates the quality and scope of members' investigations.

Athymic Animal & Xenograft Core: Multiple Mutation Model

With physical sites at Case Western Reserve University and the Cleveland Clinic Taussig Cancer Institute, this core assists PIs performing tumor experiments, angiogenesis studies and pharmaco-kinetic studies in mice. This year, the core began offering new genetic mouse models combining two cancer-related mutations, Kras and Tp53, which cause spontaneous cancer development over time. The mutations can be activated in only the desired organs, and lay silent in the rest of the body. Several months after these mutations are turned on in pancreatic cancer, for instance, 100 percent of mice will develop pancreatic cancer, explains the core's director Daniel J. Lindner, MD, PhD.

Biostatistics & Bioinformatics Core: Shared Databases

The informatics core assembles a powerful team of data analysts from across the Case Comprehensive Cancer Center who develop and implement the means to measure thousands of genes in the human genome.

"Technology changes very rapidly which means the methods have to change rapidly," says Co-Director Jill Barnholtz-Sloan, PhD. "We try to leverage our institutional investments in computational biology to try to bolster our services in the Cancer Center so that we have the expertise for all the different types of data that cancer researchers would need help with." The newly formed Institute for Computational Biology, led by recent recruit Jonathan Haines, PhD, chair, Epidemiology and Biostatistics, Case Western Reserve University School of Medicine, formalizes the cross-institutional commitment to high-throughput data analysis and centralized databases allowing for sharing of information and biospecimens for furthering research.

Genomics: Gene Sequencing

More than two-thirds of investigators using Case Western Reserve University School of Medicine's genomics services are Case Comprehensive Cancer Center members, says recently recruited director Alexander Miron, PhD, who also serves as an Associate Professor in the Department of Genetics and Genome Sciences. Services include Next Generation Sequencing (NGS), Illumina-based high-throughput genotyping, standard Sanger sequencing, and now consultancy access to Dr. Miron for perspective determining the best, most efficient sequencing approach to meet a study's scientific objective. Last year, the program implemented plans to bring an additional HiSeq 2500 instrument online in 2015, which is now operational.

Transgenic & Targeting Core: CRISPR-CAS Ramps Efficiency Four-fold

The Case Transgenic & Targeting Core Facility generates transgenic and gene-targeted mice, in addition to offering pathogen control, cryopreservation and other services. With game-changing CRISPR-Cas technology brought on board in 2013, the core can generate mice with multiple mutations in one pass. Since last summer, the core facility completed six projects with this highly efficient technique. Previously, developing multiple mutations through gene targeting took approximately a year and $50,000 to $100,000. With CRISPR-Cas, the same mutation combination is accomplished on a $10,000 to $20,000 budget in three months. In the past, investigators struggled to secure funding for new multi-mutation models because of the high stakes – a one in a million shot at success, explains Ron Conlon, PhD, the core's director. The CRISPR-Cas technique, he says, offers a one in 10 success rate.

Athymic Animal & Xenograft

Provides facilities for breeding and housing of athymic nude mice (NCRnu/nu) and rats, and other immunodeficient mice, and performs tumor experiments, angiogenesis studies and pharmacokinetic studies.

Director: Daniel J. Lindner, MD, PhD

Behavioral Measurement

Provides expertise in the development of new measures and in the evaluation and interpretation of new, modified or established behavioral variables.

Director: Susan A. Flocke, PhD

Biostatistics & Bioinformatics

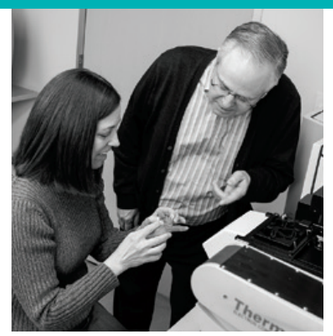
Provides and coordinates statistical, bioinformatics and clinical informatics research support in the design, planning, conduct, analysis and reporting of research studies.

Director: Mark D. Schluchter, PhD
Co-Director: Jill Barnholtz-Sloan, PhD
Co-Director: Paul J. Elson, ScD

Cytometry & Imaging Microscopy

Provides access to instrumentation to perform cell based assays and cell sorting. Trained users schedule time on instruments, then come to the facility and run their own samples. Core staff are on-site to help if difficulties arise.

Director: James W. Jacobberger, PhD
Manager: Mike Sramkoski, BS, MT(ASCP)H



Dr. James Jacoberger, PhD
Associate Director for Shared Resources
Professor, General Medical Sciences (Oncology)

Gene Expression & Genotyping

Facilitates implementation of high throughput genetic technologies for the research conducted by members of the Case community.

Director: Martina L. Veigl, PhD

Genomics

Offers genomics services, including next generation sequencing, gene expression and genotyping arrays using the Illumina platforms, and Sanger sequencing options using an ABI Prism 3730 DNA Analyzer.

Director: Alexander Miron, PhD

Hematopoietic Biorepository & Cellular Therapy

Provides for the procurement, processing, production, storage, banking, analysis and distribution of cells derived from human blood, bone marrow and umbilical cords.

Scientific Director: David N. Wald, MD, PhD
Operations Director: Jane Reese Koç, MBA, MT

Hybridoma

Provides resources for generating and producing monoclonal antibodies to novel antigens that will enable investigators to discriminate among proteins relevant to their research.

Director: Ofer Reizes, PhD

Imaging Research

Provides a wide range of preclinical and clinical imaging services associated with technologies such as X-ray, PET, MRI and SPECT imaging modalities and image analysis.

Director: Chris A. Flask, PhD

Practice Based Research Network

Supports implementation of Cancer Center investigators' research studies in practice-based research networks, and supports network practice-initiated research.

Director: James J. Werner, PhD
Co-Director: Kurt C. Stange, MD, PhD

Proteomics

Provides advanced mass spectrometric protein analysis methods.

Director: Mark R. Chance, PhD
Co-Director: Belinda B. Willard, PhD
Assistant Director: Janna Kiselar, PhD

Radiation Resources

Houses equipment for irradiating cells and small animals at a range of dose rates.

Director: Scott Welford, PhD
Co-Director: Nancy L. Oleinick, PhD

Tissue Resources

Acquires, preserves and distributes high-quality human tissues, and provides priority histology, immuno–histochemistry and tissue microarray services for both human and animal tissues.

Director: Gregory T. MacLennan, MD
Associate Director (IHC): Dawn M. Dawson, MD
Medical Advisor: Joseph E. Willis, MD

Transgenic & Targeting

Generates transgenic and gene-targeted mice, in addition to providing pathogen control, cryopreservation and other services.

Director: Ronald A. Conlon, PhD

Translational Research & Pharmacology

Provides support for implementation of scientifically rigorous correlative study components for Cancer Center clinical trails.

Director: John J. Pink, PhD
Co-Director (Pharmacology): Yan Xu, PhD
Cleveland Clinic Site Director: Daniel J. Lindner, MD, PhD
Operations Director: Paul Hartman, MS

For more information visit:
http://cancer.case.edu/research/sharedresources/

continued from page 14

COMMUNITY COMMITMENT

Cancer Prevention Across Populations
Over the past year, the Case Comprehensive Cancer Center's Cancer Prevention, Control and Population Research Program addressed cancer from a population health perspective, exploring opportunities for widespread screening enhancement and preventive lifestyle changes. Program co-leaders Susan A. Flocke, PhD, Associate Professor, Family Medicine and Community Health, and Gregory S. Cooper, MD, Professor, Medicine-Gastroenterology, noted highlights from 2014-2015:

- Colon cancer modeling – Modeling was applied to develop surveillance programs to detect recurrence after an initial colon cancer diagnosis, creating individualized testing intervals and recommended protocols.
- DNA screening for colon cancer – An evaluation found high accuracy for large polyp detection via stool DNA screening as an alternative to colonoscopy. The test base included a 40 percent African American base to also evaluate genetic-based differences compared to Caucasian participants.
- Affordable Care Act mammography impact – As out-of-pocket preventive service costs were removed as a result of the Affordable Care Act, one study noted a significant uptake in mammography screenings among Medicare recipients.
- Primary care smoking cessation intervention – An intervention study engaged 32 primary care clinicians and provided strategies and brief communication approaches for tobacco cessation. The techniques proved effective in changing clinician behavior, and as a next step, researchers will pursue a systems-based approach engaging the electronic health record to facilitate a quit line referral.
- Primary care residency obesity intervention training – A Center for Disease Control and National Cancer Institute funded study assessed the preparedness of primary care residents to address obesity, including nutrition, physical activity, counseling, and how well current curricula prepare residents. Resident surveys and program curricula audits revealed a strong need for improvements to prepare residents to effectively provide obesity, nutrition and physical activity counseling in the primary care setting.

FINANCE

CANCER RELATED FUNDING – TOTAL COSTS

Sponsor	Projects	Total Awarded
NCI	150	$ 41,394,562
Other Peer Reviewed	234	$ 80,199,963
Non Peer Reviewed	313	$ 25,705,127
Total	697	$ 147,299,652
NEW PATIENTS IN CANCER REGISTRY		**11,186**

CANCER CLINICAL TRIALS ACCRUAL

367 Investigator Initiated Clinical Trials	381 Cooperative Group Clinical Trials	1,035 Total Therapeutic Clinical Trials
5,257 Total Non Therapeutic Clinical Trials	506 Minority Clinical Trials	

Minority Accrual to Clinical Trials Committee Promotes Cultural Competency
Cultural competency demonstrates caring and leads to trust and understanding of potential participants' desires, concerns and values, according to Smitha S. Krishnamurthi, Associate Professor, Medicine-Hematology/Oncology, who heads the Minority Accrual to Clinical Trials Committee. In March 2014, the Case Comprehensive Cancer Center held a Cultural Competency Retreat attended by research staff and physicians, with keynote speaker Sonja Harris-Haywood, MD, Director, NEOMED/CSU Partnership for Urban Health. The retreat provided strategies for incorporating minority considerations in the informed consent form and addressing potential barriers to participation with minority populations. To continue cultural competency awareness, the committee launched educational articles in the Cancer Center Director's newsletter and developed informational recruitment tools for research staff to share with African American trial participants.

"We know that in Cleveland and broadly, minorities are less likely to participate in trials, yet every advance comes through trials. Cutting edge may be better than standard care, and we want to make sure all individuals have the tools appropriate to them to evaluate their options regarding trial participation. We aim to dispel myths, provide the information needed and avoid disparities in outcomes," says Dr. Krishnamurthi.

SPOTLIGHT: MEMBERS

The Case Comprehensive Cancer Center is comprised of approximately 400 collaborating scientists and physicians in the largest medical collaborative in Ohio: Case Western Reserve University, University Hospitals Case Medical Center and Cleveland Clinic. As a consortium cancer center, members come together for the benefit of research and discovery, patient treatments and community impact.

Emina Huang, MD, Staff and Vice Chair, Stem Cell Biology and Regenerative Medicine; Staff, Department of Colorectal Surgery, Cleveland Clinic

"I came to Cleveland to work with Sandy Markowitz, MD, PhD, and the GI SPORE and study colorectal cancer from every angle, from the colitis link to colon regeneration. The cross-campus relationships are fruitful and may translate therapies sooner than later. As a colorectal surgeon, I have seen the suffering of patients which motivates me to contribute in any way I can. Through the Cancer Center, I get outstanding support from experts in other areas, like biostatistics and stem cell basic science, and guidance from leadership on how to navigate the center and get things done."

Shaveta Vinayak, MD, Co-leader, Center for Breast Cancer Prevention, University Hospitals Seidman Cancer Center

"In my job search, one of the most important things for me was to have some protected time and support for research. Being a part of the K12 Clinical Oncology Research Career Development Program through the Cancer Center is allowing me to develop as a junior clinical researcher. Good mentorship was the other thing, which I've received from Dr. Lyndsay Harris and the Case Comprehensive Cancer Center leadership."

Mark Griswold, PhD, Professor of Radiology, Director of MRI Research, Case Western Reserve University

"We develop imaging methods specifically made to see cancer, including virtual biopsies for prostate cancer and treatment efficacy verification early in the chemo or radiation cycle, before a tumor changes size and shape. Without the connection to the people who are diagnosing and treating cancer, we wouldn't really know what we should be looking for. So, having that feedback and connection to people on the ground is absolutely critical. Through the Cancer Center, we have access to the clinical side. I always know who to go to for a particular cancer type and they always have an interdisciplinary team around them that makes life so much easier."

CASE COMPREHENSIVE CANCER CENTER MEMBERS

Mohamed Abazeed, MD, PhD CG
abazeem@ccf.org

Derek W. Abbott, MD, PhD MO
derek.abbott@case.edu

Fadi W. Abdul-Karim, MD BC
karimf@ccf.org

Jame Abraham, MD BC
abrahaj5@ccf.org

Louise S. Acheson, MD, MS PC
lsa@case.edu

David J. Adelstein, MD DT
adelstd@ccf.org

Anjali S. Advani, MD HD
advania@ccf.org

Manmeet S. Ahluwalia, MD DT
ahluwam@ccf.org

Jeffrey M. Albert, PhD NA
jma13@case.edu

Alexandru Almasan, PhD MO
almasaa@ccf.org

Eben Alsberg, PhD CI
eben.alsberg@case.edu

James M. Anderson, MD, PhD DT
james.anderson@case.edu

Suneel S. Apte, MD, PhD MO
aptes@ccf.org

Bruce J. Averbook, MD DT
baverbook@metrohealth.org

Norbert E. Avril, MD CI
norbert.avril@UHhospitals.org

Joseph Baar, MD, PhD BC
joseph.baar@UHhospitals.org

Shideng Bao, PhD MO
baos@ccf.org

Gene H. Barnett, MD DT
barnetg@ccf.org

Jill S. Barnholtz-Sloan, PhD CG, PC
jsb42@case.edu

Elma D. Baron, MD DT
edb4@case.edu

James P. Basilion, PhD CI
jxb206@case.edu

Rose Chu Beck, MD, PhD HD
rose.beck@case.edu

Barbara Bedogni, PhD MO
bxb278@case.edu

Jerome L. Belinson, MD DT
belinsj@ccf.org

Anthony J. Berdis, PhD DT
a.berdis@csuohio.edu

Nathan A. Berger, MD CG
nab@case.edu

Tithi Biswas, MBBS, MD DT
tithi.biswas@uhhospitals.org

G. Valentin Boerner, PhD MO
g.boerner@csuohio.edu

Joseph A. Bokar, MD, PhD DT
jab5@case.edu

Brian J. Bolwell, MD HD
bolwelb@ccf.org

Elaine A. Borawski, PhD PC
elaine.borawski@case.edu

Jeremy S. Bordeaux, MD, MPH PC
jeremy.bordeaux@UHhospitals.org

Ernest C. Borden, MD DT
bordene@ccf.org

Susann M. Brady-Kalnay, PhD CI
smb4@case.edu

Jonathan Mark Brown, PhD MO
brownm5@ccf.org

Matthias Buck, PhD MO
mxb150@case.edu

G. Thomas Budd, MD BC
buddg@ccf.org

Clemens Burda, PhD DT
cxb77@case.edu

Tatiana V. Byzova, PhD GU
byzovat@ccf.org

Paolo F. Caimi, MD MO
paolo.caimi@case.edu

Erica L. Campagnaro, MD HD
Erica.campagnaro@UHhospitals.org

Steven C. Campbell, MD, PhD GU
campbes3@ccf.org

Arnold I. Caplan, PhD HD
aic@case.edu

Jennifer S. Carew, PhD HD
carewj@ccf.org

Cathleen R. Carlin, PhD MO
cxc39@case.edu

Hetty E. Carraway, MD, MBA HD
carrawh@ccf.org

David N. Cavallo, PhD, MPH,RDN CP
david.cavallo@case.edu

Amitabh Chak, MD CG
axc22@case.edu

Mark R. Chance, PhD CG
mark.chance@case.edu

Samuel T. Chao, MD CI
chaos@ccf.org

Chee-Wai Cheng, PhD DT
chee-wai.cheng@uhhospitals.org

Edward E. Cherullo, MD GU
edward.cherullo@UHhospitals.org

Jay P. Ciezki, MD GU
ciezkij@ccf.org

Valdir C. Colussi, PhD CI
valdir.colussi@uhhospitals.org

Ronald A. Conlon, PhD NA
ronald.conlon@case.edu

Matthew M. Cooney, MD GU
matthew.cooney@UHhospitals.org

Kevin D. Cooper, MD HD
kevin.cooper@UHhospitals.org

Gregory S. Cooper, MD PC
gxc12@case.edu

Brenda W. Cooper, MD HD
brenda.cooper@UHhospitals.org

Linda S. Cummings, MD CG
linda.cummings@case.edu

Kenneth C. Cummings, MD NA
kcc31@case.edu

Barbara J. Daly, PhD, RN, FAAN PC
barbara.daly@case.edu

David Danielpour, PhD GU
dxd49@case.edu

Mellar P. Davis, MD DT
davism6@ccf.org

Dawn M. Dawson, MD CG
dmd2@case.edu

Jean-Eudes J. Dazard, PhD CG
jxd101@case.edu

Peter de Blank, MD DT
peter.deblank@UHhospitals.org

Marcos J.G. de Lima, MD HD
marcos.delima@UHhospitals.org

Chris G. Dealwis, PhD MO
cxd114@case.edu

Robert M. Dean, MD HD
deanr@ccf.org

Gary T. Deimling, PhD PC
gtd@case.edu

Catherine A. Demko, PhD PC
catherine.demko@case.edu

Laxminarayana R. Devireddy, PhD MO
laxminarayana.devireddy@case.edu

Joseph A. DiDonato, PhD GU
didonaj@ccf.org

Analisa DiFeo, PhD BC
analisa.difeo@case.edu

Clark W. Distelhorst, MD MO
cwd@case.edu

Jennifer Dorth, MD CI
jennifer.dorth@uhhospitals.org

Sara L. Douglas, PhD, RN CP
sld4@case.edu

Afshin Dowlati, MD DT
axd44@case.edu

George R. Dubyak, PhD HD
gxd3@case.edu

Jeffrey L. Duerk, PhD CI
duerk@case.edu

Hien K. Duong, MD HD
duongh@ccf.org

Jennifer R. Eads, MD DT
jennifer.eads@UHhospitals.org

Thomas T. Egelhoff, PhD BC
egelhot@ccf.org

Rachel A. Egler, MD, MS DT
rachel.egler@UHhospitals.org

Rodney J. Ellis, MD CI
rodney.ellis@UHhospitals.org

Paul J. Elson, ScD DT
elsonp@ccf.org

Robert C. Elston, PhD CG
robert.elston@case.edu

Charis Eng, MD, PhD PC
engc@ccf.org

Agata A. Exner, PhD CI
agata.exner@case.edu

Robert L. Fairchild, PhD HD
fairchr@ccf.org

Yan Feng, MD, PhD DT
yan.feng@UHhospitals.org

Stephen P Fink, PhD CG
stephen.fink@case.edu

James H. Finke, PhD GU
finkej@ccf.org

Claudio Fiocchi, MD CG
fiocchc@ccf.org

Chris A. Flask, PhD CI
caf@case.edu

Susan A. Flocke, PhD PC
susan.flocke@case.edu

Paul L. Fox, PhD MO
foxp@ccf.org

Lois C. Friedman, PhD DT
lois.friedman@UHhospitals.org

Pingfu Fu, PhD DT
pxf16@case.edu

Jorge A. Garcia, MD GU
garciaj4@ccf.org

Brian R. Gastman, MD GU
gastmab@ccf.org

Aaron T. Gerds, MD, MS HD
gerdsa@ccf.org

Thomas A. Gerken, PhD MO
thomas.gerken@case.edu

Stanton L. Gerson, MD HD, DT
slg5@case.edu

Meg R. Gerstenblith, MD CG
meg.gerstenblith@UHhospitals.org

Michael K. Gibson, MD, PhD DT
michael.gibson@UHhospitals.org

Timothy D. Gilligan, MD GU
gilligt@ccf.org

Hannah L. Gilmore, MD BC
hannah.gilmore@UHhospitals.org

Candece L. Gladson, MD MO
gladsoc@ccf.org

Anton V. Gorbachev, PhD MO
gorbaca@ccf.org

Edward M. Greenfield, PhD MO
emg3@case.edu

Mark A. Griswold, PhD CI
mag46@case.edu

Stephen R. Grobmyer, MD BC
grobmys@ccf.org

Kishore Guda, DVM, PhD CG
gkishore@yahoo.com

Vikas Gulani, MD, PhD CI
vikas@case.edu

Neetu Gupta, PhD HD
guptan@ccf.org

Sanjay Gupta, PhD GU
sanjay.gupta@case.edu

John R. Haaga, MD CI
jrh7@case.edu

Subrata Haldar, PhD MO
shaldar@metrohealth.org

Dolores Hambardzumyan, PhD MO
hambard@ccf.org

Thomas A. Hamilton, PhD MO
hamiltt@ccf.org

Betty K. Hamilton, MD HD
hamiltb2@ccf.org

Rabi Hanna, MD HD
hannar2@ccf.org

Jeffrey M. Hardacre, MD DT
jeffrey.hardacre@UHhospitals.org

Clifford V. Harding, MD, PhD HD
cvh3@case.edu

Lyndsay N. Harris, MD BC
lyndsay.harris@UHhospitals.org

Sonja Harris-Haywood, MD, MS PC
shaywood@case.edu

Peter J. Harte, PhD CG
pjh3@case.edu

Marian (Nikki) L. Harter, PhD CG
mnh5@case.edu

Warren D.W. Heston, PhD GU
hestonw@ccf.org

Brian T. Hill, MD, PhD HD
hillb2@ccf.org

Christopher J. Hoimes, DO GU
christopher.hoimes@case.edu

Kord S. Honda, MD DT
kord.honda@UHhospitals.org

Charles L. Hoppel, MD DT
clh5@case.edu

Janet A. Houghton, PhD MO
houghtj@ccf.org

Eric D. His, MD HD
hsie@ccf.org

Chao-Pin Hsiao, PhD, RN CP
cxh416@case.edu

Alex Y.C. Huang, MD, PhD HD
alex.y.huang@case.edu

Emina Huang, MD CG
huange2@ccf.org

Steve Shih-Lin Huang, MD, PhD CI
huangs2@ccf.org

Sudha K. Iyengar, PhD CG
ski@case.edu

Mark W. Jackson, PhD BC
mark.w.jackson@case.edu

James W. Jacobberger, PhD CI
jwj@case.edu

Mukesh K. Jain, MD BC
mukesh.jain2@case.edu

Damir Janigro, PhD DT
janigrd@ccf.org

Eckhard Jankowsky, PhD CG
exj13@case.edu

Ge Jin, PhD PC
ge.jin@case.edu

Hui (Grace) Jin, PhD GU
hui.jin@case.edu

Eva F. Kahana, PhD PC
exk@case.edu

Matt E. Kalaycio, MD HD
kalaycm@ccf.org

Hung-Ying Kao, PhD BC
hxk43@case.edu

David R. Kaplan, MD, PhD HD
drk5@case.edu

Efstathios Karathanasis, PhD CI
stathis@case.edu

Jonathan Karn, PhD PC
jonathan.karn@case.edu

Michael W. Kattan, PhD PC
kattanm@ccf.org

Malcolm E. Kenney, PhD DT
mek9@case.edu

Ruth A. Keri, PhD BC
keri@case.edu

Bethany A. Kerr, PhD GU
kerrb2@ccf.org

Alok A. Khorana, MD DT
khorana@ccf.org

Julian A. Kim, MD BC
julian.kim@UHhospitals.org

Simon P Kim, MD, MPH GU
simon.kim@UHhospitals.org

Eric A. Klein, MD GU
kleine@ccf.org

Eric D. Kodish, MD PC
kodishe@ccf.org

Henry B. Koon, MD CI
henry.koon@case.edu

Siran M. Koroukian, PhD PC
sxk15@case.edu

Mehmet Koyuturk, PhD CG
mxk331@case.edu

Smitha S. Krishnamurthi, MD DT
ssk7@case.edu

Charles A. Kunos, MD, PhD DT
kunosc@summahealth.org

Vinod Labhasetwar, PhD CI
labhasv@ccf.org

Thomas LaFramboise, PhD CG
txl80@case.edu

Minh Lam, PhD NA
minh.lam@case.edu

Gary E. Landreth, PhD DT
gel2@case.edu

Justin D. Lathia, PhD MO
lathiaj@ccf.org

Pierre Lavertu, MD DT
pierre.lavertu@UHhospitals.org

Hillard M. Lazarus, MD HD
hillard.lazarus@case.edu

Patrick Leahy, PhD NA
patrick.leahy@case.edu

Michael M. Lederman, MD PC
mxl6@case.edu

Zhenghong Lee, PhD CI
zxl11@case.edu

Jeongwu Lee, PhD MO
leej7@ccf.org

John J. Letterio, MD MO
john.letterio@UHhospitals.org

Nathan A. Levitan, MD DT
nathan.levitan@UHhospitals.org

Li Li, MD, PhD PC
lxl62@case.edu

Jing Li, PhD CG
jingli@case.edu

Xiaoxia Li, PhD MO
lix@ccf.org

Bibo Li, PhD MO
b.li37@csuohio.edu

Daniel J. Lindner, MD, PhD DT
lindned@ccf.org

David G. Litaker, MD, PhD PC
david.litaker@med.va.gov

Huiping Liu, MD, PhD BC
hliu@case.edu

Kenneth A. Loparo, PhD CI
kal4@case.edu

Hua Lou, PhD CG
hxl47@case.edu

Zheng-Rong Lu, PhD CI
zxl125@case.edu

Guangbin Luo, PhD CG
gxl35@case.edu

Janice A. Lyons, MD BC
janice.lyons@UHhospitals.org

Patrick C. Ma, MD, MSc DT
map@ccf.org

Paul N. MacDonald, PhD MO
pnm2@case.edu

Mitchell M. Machtay, MD CI
mitchell.machtay@UHhospitals.org

Jaroslaw P. Maciejewski, MD, PhD HD
maciejj@ccf.org

Roger M. Macklis, MD MO
macklir@ccf.org

Gregory T. MacLennan, MD GU
gregory.maclennan@UHhospitals.org

Anant Madabhushi, PhD, MS BC
anant.madabhushi@case.edu

Cristina Magi-Galluzzi, MD, PhD BC
magic@ccf.org

Navneet S. Majhail, MD, MS HD
majhain@ccf.org

Hideki Makishima, MD, PhD HD
makishh@ccf.org

Danny Manor, PhD MO
danny.manor@case.edu

David Mansur, MD CI
david.mansur@UHhospitals.org

Sanford D. Markowitz, MD, PhD CG
sxm10@case.edu

Patricia A. Marshall, PhD BC
pam20@case.edu

Yousif Matloub, MD HD
yousif.matloub@UHhospitals.org

Shigemi Matsuyama, PhD MO
sxm193@case.edu

Edward V. Maytin, MD, PhD MO
maytine@ccf.org

Susan R. Mazanec, PhD PC
susan.mazanec@case.edu

Suparna Mazumder, PhD BC
mazumds@ccf.org

Peter Mazzone, MD, MPH PC
mazzonp@ccf.org

Keith R. McCrae, MD MO
mccraek@ccf.org

Christine L. McDonald, PhD MO
mcdonac2@ccf.org

Gordon McLennan, MD CI
mclenng@ccf.org

M. Edward Medof, MD, PhD HD
mxm16@case.edu

Neal J. Meropol, MD PC
neal.meropol@case.edu

Howard J. Meyerson, MD HD
howard.meyerson@case.edu

John J. Mieyal, PhD DT
jjm5@case.edu

Booki Min, PhD, DVM HD
minb@ccf.org

Alexander Miron, PhD CG
alexander.miron@case.edu

Saurav Misra, PhD MO
misras@ccf.org

Monica M. Montano, PhD BC
mxm126@case.edu

Alberto J. Montero, MD, MBA BC
montero2@ccf.org

Halle C.F. Moore, MD BC
mooreh1@ccf.org

OVER
30
NEW MEMBERS 2014/2015

Shirley M. Moore, PhD, RN PC
smm8@case.edu

Sudipto Mukherjee, MD, PhD, MPH HD
mukhers2@ccf.org

Raymond, Jr. F. Muzic, PhD CI
raymond.muzic@case.edu

Goutham Narla, MD, PhD BC
gxn71@case.edu

Carvell T. Nguyen, MD, PhD GU
cnguyen4@metrohealth.org

Marvin T. Nieman, PhD MO
nieman@case.edu

Timothy W. Nilsen, PhD CG
twn@case.edu

Nora L. Nock, PhD PC
nln@case.edu

Charles J. Nock, MD DT
Charles.Nock@va.gov

Robin E. Norris, MD, MS, MPH DT
robin.norris@UHhospitals.org

Noa Noy, PhD BC
noyn@ccf.org

Timothy E. O'Brien, MD DT
tobrien@metrohealth.org

Nancy L. Oleinick, PhD MO
nlo@case.edu

Elizabeth E. O'Toole, MD PC
exo5@case.edu

Cynthia Owusu, MD, MSc BC
cynthia.owusu@case.edu

Z. Meral Ozsoyoglu, PhD CG
meral@case.edu

Richard A. Padgett, PhD DT
padgetr@ccf.org

Holly J. Pederson, MD BC
pedersh@ccf.org

David M. Peereboom, MD DT
peerebd@ccf.org

Nathan A. Pennell, MD, PhD DT
penneln@ccf.org

James G. Phillips, PhD DT
phillij5@ccf.org

John J. Pink, PhD BC
john.pink@case.edu

Gregory E. Plautz, MD HD
plautzg@ccf.org

Donna Plecha, MD BC
Donna.Plecha@UHhospitals.org

Edward F. Plow, PhD HD
plowe@ccf.org

Tarun Podder, PhD CI
txp172@case.edu

Brad L. Pohlman, MD HD
pohlmab@ccf.org

Lee E. Ponsky, MD GU
lee.ponsky@UHhospitals.org

Jun Qin, PhD MO
qinj@ccf.org

Tomas Radivoyevitch, PhD CI
radivot@ccf.org

Diana L. Ramirez-Bergeron, PhD HD
Diana.ramirez@case.edu

Ofer Reizes, PhD BC
reizeso@ccf.org

Kimberly E. Resnick, MD DT
kimberly.resnick@UHhospitals.org

Frederic J. Reu, MD DT
reuf@ccf.org

Jeremy N. Rich, MD, MHSc MO
richj@ccf.org

Brian I. Rini, MD GU
rinib2@ccf.org

Lisa R. Rogers, DO DT
lisa.rogers1@UHhospitals.org

Andrew M. Rollins, PhD CI
amr9@case.edu

Pablo R. Ros, MD, MPH, PhD CI
pablo.ros@UHhospitals.org

Peter G. Rose, MD DT
rosep@ccf.org

Johnie Rose, MD, PhD PC
johnie.rose@case.edu

Julia Hannum Rose, PhD PC
jhr8@case.edu

Steven S. Rosenfeld, MD, PhD MO
rosenfs@ccf.org

Brian P. Rubin, MD, PhD CG
rubinb2@ccf.org

Kurt W. Runge, PhD CG
rungek@ccf.org

Eileen Saffran, MSW PC
saffran@touchedbycancer.org

Gerald M. Saidel, PhD CI
gms3@case.edu

Robert G. Salomon, PhD CI
rgs@case.edu

Yogen Saunthararajah, MD HD, DT
saunthy@ccf.org

Peter C. Scacheri, PhD CG
pxs183@case.edu

William P. Schiemann, PhD BC
william.schiemann@case.edu

Mark D. Schluchter, PhD DT
mds11@case.edu

Alvin H. Schmaier, MD MO
alvin.schmaier@case.edu

W. David Sedwick, PhD CG
wds@case.edu

Mikkael A. Sekeres, MD, MS HD
sekerem@ccf.org

Ganes C. Sen, PhD MO
seng@ccf.org

Anirban Sen Gupta, PhD CI
anirban.sengupta@case.edu

David Serre, PhD CG
serred@ccf.org

Nima Sharifi, MD GU
sharifn@ccf.org

Robert R. Shenk, MD BC
robert.shenk@UHhospitals.org

Dale R. Shepard, MD, PhD DT
shepard@ccf.org

Girish C. Shukla, PhD DT
g.shukla@csuohio.edu

Robert H. Silverman, PhD GU
silverr@ccf.org

Paula Silverman, MD BC
paula.silverman@UHhospitals.org

Andrew E. Sloan, MD DT, CI
andrew.sloan@UHhospitals.org

Mitchell R. Smith, MD, PhD HD
smithm14@ccf.org

Ronald M. Sobecks, MD HD
sobeckr@ccf.org

Davendra P.S. Sohal, MD, MPH DT
sohald@ccf.org

Jason W. Sohn, PhD CI
jason.sohn@case.edu

Khalid Sossey-Alaoui, PhD BC
sosseyk@ccf.org

Sree N. Sreenath, PhD CI
n.sreenath@case.edu

Kurt C. Stange, MD, PhD PC
kcs@case.edu

George R. Stark, PhD MO
starkg@ccf.org

Duncan Stearns, MD MO
duncan.stearns@case.edu

Nicole F. Steinmetz, PhD BC
nicole.steinmetz@case.edu

Olga Stenina Adognravi, PhD MO
stenino@ccf.org

Mary M. Step, PhD PC
mary.step@case.edu

Andrew J. Stephenson, MD GU
stephea2@ccf.org

David W. Stepnick, MD, FACS DT
david.stepnick@UHhospitals.org

James P. Stevenson, MD DT
stevenj5@ccf.org

Jean T. Stevenson, MD DT
jstevenson@metrohealth.org

Scott A. Strong, MD CG
strongs@ccf.org

Hoonkyo Suh, PhD MO
suhh2@ccf.org

John H. Suh, MD DT
suhj@ccf.org

Matthew K. Summers, PhD MO
summerm@ccf.org

Jeffrey L. Sunshine, MD, PhD CI
Jeffrey.Sunshine@UHhospitals.org

Charles S. Tannenbaum, PhD GU
tannenc@ccf.org

Derek J. Taylor, PhD MO
derek.taylor@case.edu

Paul J. Tesar, PhD CG,MO
paul.tesar@case.edu

Lois Teston, MD BC
lois.teston@UHhospitals.org

Cheryl L. Thompson, PhD BC
cheryl.l.thompson@case.edu

Angela H. Ting, PhD GU
tinga@ccf.org

Ramon V. Tiu, MD HD
tiur@ccf.org

Pallavi Tiwari, PhD MO
pxt130@case.edu

Gregory P. Tochtrop, PhD DT
gpt6@case.edu

Erika S. Trapl, PhD PC
erika.trapl@case.edu

Joan E. Trey, MD DT
jet2@case.edu

Vincent K. Tuohy, PhD BC
tuohyv@ccf.org

Carl V. Tyler, MD, MS PC
catyle@ccf.org

Saba Valadkhan, MD, PhD CG
saba.valadkhan@case.edu

Vinay Varadan, PhD CG
vxv89@case.edu

Martina L. Veigl, PhD CG
mlv2@case.edu

Shaveta Vinayak, MD, MS BC
shaveta.vinayak@UHhospitals.org

Michael A. Vogelbaum, MD, PhD DT
vogelbm@ccf.org

Horst A. von Recum, PhD CI
horst.vonrecum@case.edu

Steven E. Waggoner, MD DT
steven.waggoner@UHhospitals.org

David N. Wald, MD, PhD DT
dnw@case.edu

Bing-Cheng Wang, PhD MO
bxw14@case.edu

Qing K. Wang, PhD, MBA NA
wangq2@ccf.org

Yanming Wang, PhD CI
yanming.wang@case.edu

Zhenghe John Wang, PhD CG
zxw22@case.edu

Aaron Weinberg, DMD, PhD PC
axw47@case.edu

Scott M. Welford, PhD MO
scott.welford@case.edu

Brian J. Wells, MD, MS PC
wellsb@ccf.org

James J. Werner, PhD PC
james.werner@case.edu

Barry W. Wessels, PhD CI
barry.wessels@UHhospitals.org

Belinda B. Willard, PhD NA
willarb@ccf.org

Basem M. William, MD HD
basem.william@UHhospitals.org

Joseph E. Willis, MD CG
joseph.willis@case.edu

David L. Wilson, PhD CI
dlw@case.edu

Anthony Wynshaw-Boris, MD, PhD CG
ajw168@case.edu

Ping Xia, PhD GU
xiap@ccf.org

Rong Xu, PhD PC
rxx@case.edu

Yan Xu, PhD DT
yan.xu@case.edu

Sichun Yang, PhD BC
sichun.yang@case.edu

Yu-Chung Yang, PhD DT
yxy36@case.edu

Min Yao, MD, PhD CI
min.yao@UHhospitals.org

Vivien C. Yee, PhD MO
vcy2@case.edu

Qing Yi, MD, PhD HD
yiq@ccf.org

Kristine M. Zanotti, MD DT
kristine.zanotti@UHhospitals.org

Maciej Zborowski, PhD DT
zborowm@ccf.org

Chad A. Zender, MD PC
chad.zender@uhhospitals.org

Amy Y. Zhang, PhD PC
amy.zhang@case.edu

Guo-Qiang Zhang, PhD CI
guo-qiang.zhang@case.edu

Junran Zhang, MD, PhD MO
junran.zhang@case.edu

Mei Zhang, PhD DT
mxz128@case.edu

Youwei Zhang, PhD MO
yxz169@case.edu

Lan Zhou, MD, PhD HD
lan.zhou@case.edu

Guang Zhou, PhD CG
guang.zhou@case.edu

Hui Zhu, MD GU
hui.zhu@UHhospitals.org

Alan Jian Zhu, PhD DT
zhua@ccf.org

Junmin Zhu, PhD CI
junmin.zhu@case.edu

Stephen J. Zyzanski, PhD PC
sjz@case.edu

CG **Cancer Genetics**
MO **Molecular Oncology**
BC **Breast Cancer**
GU **GU Malignancies**
HD **Hematopoietic Disorders**
DT **Developmental Therapeutics**
CI **Cancer Imaging**
PC **Cancer Prevention, Control and Population Research**
NA **Nonprogrammatically Aligned**

New Members

Case Comprehensive Cancer Center membership list as of Spring 2015

CASE WESTERN RESERVE UNIVERSITY

CASE
COMPREHENSIVE
CANCER CENTER

11100 Euclid Avenue
Cleveland, Ohio 44106-5065
216.844.8797 **cancer.case.edu**

University Hospitals

CASE WESTERN RESERVE UNIVERSITY EST. 1826

Cleveland Clinic