Report to the Community

OCR

Ohio Cancer Research

Funding seed money cancer research projects
and supporting cancer awareness and early detection.

50 W. Broad Street
Suite 1132
Columbus OH 43215-3388

phone 614-224-1127
toll free 800-232-6272
fax 614-224-0654

ohiocancer.org

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Funding seed money cancer research projects
and supporting cancer awareness and early detection.

Ohio Cancer Research is an independent statewide, nonprofit organization dedicated to the cure and prevention of the many forms of cancer and the reduction of its debilitating effects through aggressive basic seed money research, cancer information and awareness. Ohio Cancer Research is not affiliated with any other organization.

Individual researchers have been or are being funded at Case Western Reserve University, The Cleveland Clinic, University Hospitals of Cleveland, MetroHealth Medical Center in Cleveland, The Ohio State University, Nationwide Children's Hospital in Columbus, Cincinnati Children's Hospital Medical Center, University of Cincinnati, University of Toledo, Bowling Green State University, Ohio University, University of Dayton, Wright State University and the former Hipple Cancer Research Center in Dayton.

Over $18 million has been spent on cancer awareness and seed money research projects. Of that amount, over **$7 million** in seed money provided to researchers by Ohio Cancer Research has generated more than **$220 million** in new money from other sources to continue basic cancer research on projects initially funded as well as translational clinical trials at institutions including University Hospitals Seidman Cancer Center, The Cleveland Clinic,Cincinnati Children's Hospital Medical Center and The Ohio State University.

Programs of Ohio Cancer Research

Seed Money Cancer Research

With the support of people all over Ohio, progressive and innovative ideas are given a chance to help in the fight. Ohio Cancer Research's seed money projects often give a researcher the preliminary data needed to secure major funding from other sources.

Cancer Information

Cancer awareness and prevention information is disseminated to tens of thousands of persons throughout Ohio each year.

Radio and newspaper support reaches in excess of one million each year.

Public service announcements are being carried on cable and broadcast television reaching more than 5 million people annually.

Speakers are available to groups throughout the state such as Rotary Clubs, fraternal organizations, TV and radio talk shows, etc.

We provide information to callers regarding their experience with cancer. Staff informs callers of cancer information services such as (1-800-4CANCER) which answers questions concerning the disease.

Cancer Awareness

Staff and volunteers are committed to the public gaining knowledge of the many forms of cancer, the advancement of Ohio Cancer Research, and its seed money cancer research projects.

Fitness Awareness

A dance program for children in grades 1-12 and adults stresses dance as an exercise for a prudent healthy lifestyle.

Symposiums

A limited amount of funds are available to provide scientific meetings. Recent symposiums were held at the Case Comprehensive Cancer Center and the Cincinnati Cancer Consortium.

Special Events

Ohio Cancer Research Special Events are presented to raise funds for seed money cancer research and to increase awareness of the importance of early detection in saving lives.

A sampling of how the "seed money" concept works for Ohio researchers throughout the state.

I am happy to inform you that one of my papers is in print now in Molecular Microbiology. This paper has work that is primarily due to the opportunity provided to me by the OCRA grant. This work explains how DNA damage is recognized by the MutS protein. The human homologs of this protein, (MSH2 and in some cases MSH6) are mutated in colon cancers hence this work gives functional relevance to the mutations as we understand the protein more. Hopefully in future experiments I can utilize this in translational science.

Samir Acharya, PhD
The Ohio Sate University

"Receiving OCRA seed money at a critical time in the establishment of my laboratory ensured we could pursue our ideas, attain financial stability to continue our work, and generate results that could be translated one step closer to patients. There are many young scientists in a similar position that could greatly benefit from support at the early stages in their career. Empowering OCRA to support projects with seed money is not only an investment in the future but an assurance that cancer patients have access to more effective therapies. Thank you for your generosity. "

Justin Lathia, PhD
Cleveland Clinic Lerner Research Institute

"The RO1 grant from the National Institutes of Health and National Institute of Environmental Health Sciences is for a period of 4 years, beginning April 1,1995 and will provide me with a total of $395,859 in direct cost. This would not have been possible without the grant support I received from Ohio Cancer Research Associates, which enabled me to obtain sufficient preliminary data which served as the cornerstone for this NIH grant."

Zalfa Abdel-Malek, PhD
University of Cincinnati

"My group recently received national recognition for our publication in *Science* of the discovery of a new gene, the RII gene that is most important in causing colon cancer both in families with inherited colon cancer and also many individuals in the population at large.

"With your help my laboratory's work on colon cancer genetics has been going great guns. Our most recent NIH grant...has been recommended for funding for 5 years at $250,000 per year. Without the support of Ohio Cancer Research Associates this work would be dead in the water while we waited for a year or more for money from NIH to come through."

Sandy Markowitz, MD, PhD
Case Western Reserve University

"I am writing to let you know that after being the recipient of an award from Ohio Cancer Research Associates for two years, I have been granted funds from the Case Cancer Center ($30,000 for one year) and from the American Cancer Society ($720,000 for four years). I am extremely grateful to your organization for giving my idea a chance during these crucial transition years when I was developing my research program, and I am proud that your choice to support me now results in more funding brought in Ohio.

Marie-Odile Parat, PharmD, PhD
The Cleveland Clinic

"The seed money grant from Ohio Cancer Research Associates helped my lab receive major funding for four years ($308,000) on a different project in lung molecular biology from the American Heart Association at the National level."

Vrushank Davé, PhD
Case Western Reserve University

"I would like to let you know that I just received a Research Scholar Grant from The American Cancer Society for three years totalling $840,000. The research funded by Ohio Cancer Research Associates contributed to my getting the ACS grant. Much of the preliminary data included in the ACS application resulted from the experiments proposed in my Ohio Cancer Research Associates grant proposal. I submitted a manuscript on Gfi-1/Miz-1 interaction to Proc Natl Acad Sci USA (PNAS) last year, which was supported in part by my Ohio Cancer Research Associates grant. This manuscript has just been accepted.

Fan Dong, MD, PhD
University of Toledo

Seed Money Research Program

Ohio Cancer Research's scientific investigators are exploring innovative areas of cancer research in the genetic causes and preventions of cancer, skin cancer, stomach cancer, prostate cancer, colon cancer, liver cancer, kidney cancer, breast cancer, leukemia, vaccine studies, DNA studies, and new therapeutic strategies.

Projects are selected by a Scientific Review Committee with the help of out-of-state reviewers from across the country and the world.

The Scientific Review Committee is made up of doctors and scientists around the state. Committee Chair Amanda Simcox, PhD, The Ohio State University is joined by these distinguished researchers and cancer experts in 2015:

Zalfa Abdel-Malek, PhD, University of Cincinnati
Robert Brueggemeier, PhD,The Ohio State University
Susan E. Cole, PhD, The Ohio State University
Ivana de la Serna, PhD, University of Toledo
Chunying Du, PhD, University of Cincinnati
Sohaib Khan, PhD, University of Cincinnati
Gustavo Leone, PhD, The Ohio State University
Deborah Parris, PhD, The Ohio State University
John Pink, PhD, Case Western Reserve University
Michael A. Vogelbaum, MD, PhD, The Cleveland Clinic
Dawn Wooley, PhD, Wright State University

Following is a recap of past projects and a listing of currently funded projects with a brief description of each.

OCR
Ohio Cancer Research

These researchers have had "seed money" projects funded by Ohio Cancer Research. The area of cancer research is denoted in red. These projects have generated over $216 million in new research funds.

BOWLING GREEN STATE UNIVERSITY

Doris J. Beck, PhD Molecular Genetics
Vladimir Popik, PhD Breast Cancer
Lakshmidevi Pulakat, PhD Breast Cancer
William Scovell, PhD Molecular Genetics

CASE WESTERN RESERVE UNIVERSITY

Rajesh Agarwal, PhD Prostate Cancer
Nihal Ahmad, PhD Skin and Prostate Cancer
Barbara Bedogni, PhD Skin Cancer
Matthias Buck, PhD Molecular Genetics
David Danielpour, PhD Prostate Cancer
Clark W. Distelhorst, MD Hormone Therapy
Philip R. Garner, PhD Gene Mutation
Antonio Gualberto, MD Gene Mutation
Zhongwu Guo, PhD Molecular Genetics
Zhilin Hu, PhD Lung Cancer
Hung-Ying Kao, PhD Leukemia
Efstathios Karathanasis, PhD Chemotherapy Treatment
Santosh Katiyar, PhD Skin Cancer
Huiping Liu, MD PhD Breast Cancer
Hua Lou, PhD Thyroid Cancer
Sanford Markowitz, MD, PhD Colon Cancer
Monica Montano, PhD Breast Cancer
Narenda Narayana, PhD Leukemia
Ellen Rorke, PhD Cervical Cancer
Nicole Franziska Steinmetz, PhD Breast Cancer
Hortst von Recum, PhD Chemotherapy
David Wald, MD, PhD Leukemia
Scott Michael Welford, PhD Radiation Oncology
Yanwu Yang, PhD Tumor Research

CINCINNATI CHILDREN'S HOSPITAL

Robert Arceci, MD, PhD Leukemia
Takiko Daikoku, PhD Endometrial Cancer
Vrushank Dave, PhD Lung Cancer
Brian Andrew Gebelein, PhD Leukemia
Raphael Hirsch, MD Lymphoma
Gang Huang, PhD Leukemia
Anil G. Jegga, DVM Molecular Genetics
Tanya Kalin, PhD Gene Mutation
Xinhua Lin, PhD Kidney Cancer
Ruhikanta Meetei, PhD Genetic Research
James Mulloy, PhD Leukemia
Saulius Sumanas, PhD Tumor Studies
Susan E. Waltz, PhD Skin Cancer
Susanne Wells, PhD Cervical Cancer

CLEVELAND CLINIC FOUNDATION

Munna Agarwal, PhD Gene Mutation
Marina Antoch, PhD Cancer Therapy
Sipra Banerjee, PhD Breast Cancer
Christine Campbell, PhD Breast Cancer
Justin D. Lathia, PhD Brain Cancer
Tao Lu, PhD Colon Cancer
Patrick Ma, MD Lung Cancer
Marie-Odile Parat, PHARMD,PhD Molecular Genetics
Nywana Sizemore, PhD Breast Cancer
Matthew K. Summers, PhD Breast Cancer
Michael Vogelbaum, MD, PhD Brain Cancer
Lan Zhou, MD, PhD Leukemia

HIPPLE CANCER RESEARCH CENTER

Sten Jacobsen, MD, PhD Leukemia

METROHEALTH MEDICAL CENTER

Bruce Averbook, MD, F.A.S.C. Brain Cancer
Aruna Basu, PhD Colon Cancer
Subrata Haldar, PhD Skin Cancer

NATIONWIDE CHILDREN'S HOSPITAL

Joan Durbin, MD, PhD Rhabdomyosarcoma
Risa Kitagawa, PhD Tumor Studies
Natarajan Muthusamy, DVM, PhD Lymphoma
Sue O'Dorisio, MD, PhD Gastrointestinal

OHIO UNIVERSITY

Elisar Barbar, PhD Tumor Research
Monica Burdick, PhD Breast Cancer

THE OHIO STATE UNIVERSITY

Samir Acharya, PhD Colon Cancer
Keiko Akagi, PhD Leukemia
Rami Aqeilan, PhD Tumor Cell Research
Xue-Feng Bai, MD, PhD Gene Mutation
Robert Baiocchi, MD PhD Lymphoma
Brent C. Behrens, MD Molecular Genetics
Robert W. Brueggemeier, PhD Breast Cancer
Ing-Ming Chiu, PhD Leukemia
Susan Cole, PhD Molecular Genetics
Robert W. Curley, Jr., PhD Chemoprevention
James W. DeWille, MPH, MS, PhD Breast Cancer
Harold A. Fisk, PhD Molecular Genetics
Darrell R. Galloway, PhD Skin Cancer
Denis C. Guttridge, PhD Molecular Studies
Tsonwin Hai, PhD Molecular Genetics
Paul Kenneth Herman, PhD Molecular Genetics
David H. Ives, PhD Molecular Genetics
Sissy Jhiang, PhD Brain Cancer
Victor Jin, PhD Breast Cancer
Lee F. Johnson, PhD Thyroid Cancer
Laura A. Kresty, PhD Esophageal Cancer
Michael D. Lairmore, DVM, PhD Lymphoma
Jennifer Leight, PhD Cancer Therapy
Mary MacVicar, RN, PhD Breast Cancer

Louis Malspeis, PhD Chemotherapy Delivery
Louis Mansky, PhD Lymphoma
George Milo, PhD Gene Mutation
Stefan Niewiesk, DVM, PhD Leukemia
Gregory Otterson, MD Lung Cancer
Deborah Parris, PhD Molecular Genetics
Paivi Peltomaki, MD, PhD Colon Cancer
John Rinehart, PhD Chemotherapy
Arthur L. Sagone, Jr., MD Hematology
James Shaw, PhD Gene Mutation
Amanda Simcox, PhD Molecular Genetics
Duxin Sun, PhD Chemotherapy
Anne M. Strohecker, PhD Lung Cancer
Werner Tjarks, PhD Head and Neck Cancer
Harald Vaessin, PhD Molecular Genetics
Jian Z. Wang, PhD Prostate Cancer
Michael E. Weinstein, PhD Molecular Genetics
Karl Werbovetz, PhD Chemotherapy
Marshall Williams, PhD Colon Cancer
Jian-Qui Wu, PhD Molecular Genetics
Sung Yoon, PhD Molecular Genetics
Pan Zheng, MD Prostate Cancer
Bruce Zwilling, PhD Gene Mutation

UNIVERSITY OF CINCINNATI
Zalfa Abdel-Malek, PhD Skin Cancer
David Askew, PhD Leukemia
Michelle Craig Barton, PhD Breast Cancer
Arthur Buckley, PhD Genetic Research
Rodney DeKoter, PhD Leukemia
Joanna Groden, PhD Genetic Research
Ana Luisa Kadekaro, PhD Skin Cancer
Sohaib A. Khan, PhD Breast Cancer
Erik Knudsen, PhD Gene Mutation
Andrew Lowy, MD Stomach Cancer
Shan Lu, PhD Prostate Cancer
Shiuh Wen Luoh, MD Prostate Cancer
Mario Medvedovic, PhD Breast Cancer
R. C. Samaratunga, PhD Radiation
Yolanda Sanchez, PhD Gene Mutation
Jeffrey Sussman, MD Skin Cancer
Glenn Talaska, PhD Bladder Cancer
Neville Tam, PhD Prostate Cancer
Craig R. Tomlinson, PhD Breast Cancer
Ying Xia, PhD Chemotherapy
Jinsong Zhang, PhD Leukemia
Xiaoting Zhang, PhD Breast Cancer

UNIVERSITY OF DAYTON
Amit Singh, PhD Gene Mutation

UNIVERSITY OF TOLEDO
Gloria Borgstahl, PhD Genetic Research
Ivana de la Serna, PhD Skin Cancer
John David Dignam, PhD Molecular Research
Han-Fei Ding, MD, PhD Genetic Research
Fan Dong, MD, PhD Gene Mutation
Rafael Garcia-Mata, PhD Breast Cancer
Song-Tao Liu, PhD Gene Mutation
Steve M. Patrick, PhD Gene Mutation
Douglas L. Pittman, PhD Breast Cancer
Randall Ruch, PhD Lung Cancer
Lirim Shemshidini, PhD Gene Mutation
Cynthia Smas, DSc. Prostate Cancer
Steven J. Sucheck, PhD Tumor Cell Research
James P. Trempe, PhD Tumor Cell Research
Yian Wang, MD Liver Cancer
Kam Chi Yeung, PhD Molecular Research
Ming You, MD, PhD Lung Cancer
Jianglong Zhu, PhD Tumor Study

WRIGHT STATE UNIVERSITY
Steven Berberich, PhD Gene Mutation
John J. Turchi, PhD Gene Mutation
Yongie Xu, MD, PhD Genetic Research

Total research funded:
over $7 million

Total research generated to date:
over $220 million

Research Projects funded by Ohio Cancer Research

July 2015 - June 2017

Funded with the support of The John and Mary Alford Foundation

Jennifer Leight PhD **(Cancer Therapy)**
THE OHIO STATE UNIVERSITY
Impact of the tumor microenvironment on matrix metalloproteinase activity

Metastasis, the spread of cancer from the original tumor to other sites in the body, is the main cause of death in most cancer patients. During the first step in metastasis, invasion, cancer cells break away from the original tumor and migrate through the tissue. In order to escape the primary tumor, cancer cells need to break down barriers in the dense surrounding tissue using enzymes called matrix metalloproteinases (MMPs). High levels of MMPs are observed in almost all types of cancers, including breast, colon, and pancreatic cancer, and increased levels of MMPs are associated with poorer outcomes. The goal of this proposal is to understand the factors that lead to increased levels of MMPs during disease progression. During disease progression, one of the first signs of a tumor is a hard lump. This tissue stiffening was once thought of as just a byproduct of the cancer cells growing uncontrollably. However, more recently, it has become clear that this tissue stiffening is not just an after effect but can also control the behavior of the cancer cells. Here, we will investigate how tissue stiffening controls MMP activity during the first stages of cancer progression. First, we will use a cell culture model system in which we can carefully control tissue stiffness to investigate how the changes in tissue stiffness observed during cancer progression affect MMP activity and cell migration. Then we will extend these studies to human tissue samples in which we will spatially map MMP activity and tissue stiffness to understand how MMP activity changes with disease progression. Through this investigation, we will develop a clearer picture of the factors that lead to increased levels of MMPs during cancer progression. Understanding these factors will contribute to the identification of new therapeutic targets to reduce cancer cell invasion and metastasis.

Funded with the support of John and Gennie Roberts

Huiping Liu, MD PhD **(Breast Cancer)**
CASE WESTERN RESERVE UNIVERSITY
Targeting IL-11 in breast tumor initating cell-mediated metastasis

The lifetime risk of developing invasive breast cancer is 1 in 8 in women in the United States and 20% of the breast cancer patients die. Cancer cell spread from the breast tissue to distant organs accounts for 90% of breast cancer caused deaths. We aim to discover how cancer cells interact with each other and talk to other blood cells, such as platelets, during the traveling (circulation) and spreading (metastasis) from one place to another. We have identified a subset of breast cancer cells with stem cell properties, called breast cancer stem cells or tumor-initiating cells which tend to mediate metastasis. These cells promote metastasis by forming multi-cell clusters with platelets during circulation. A secreted molecule, interleukin-11 (IL-11), enhances the process. This project is to identify the molecular mechanisms by which IL-11 regulate breast cancer stem cell and platelets clusters. We will explore strategies to block IL-11 functions with a goal of reducing metastasis and decreasing breast cancer deaths in the clinic.

Anne M. Strohecker, PhD **(Lung Cancer)**
THE OHIO STATE UNIVERSITY
Regulation of Autophagy by the Small GTPase Rab20

Funded with the support of David and Celeste Loewendick

Lung cancer is poorly understood and current therapies are insufficient to save the lives of patients. Cancer cells require abnormal levels of energy to maintain their high growth rates. Tumors exploit autophagy, a normal cellular process, to meet their increased metabolic needs and survive periods of nutrient limitation and cellular stress. Activation of the pathway undermines the efficacy of many of our present chemotherapeutic strategies. Recent work with mouse models representing roughly 30% of Non Small Cell Lung Cancers (NSCLC) revealed that inhibition of the autophagy pathway extends survival of the mouse, suggesting that autophagy-inhibiting therapies may have clinical benefit for this and potentially other tumor types. The small GTPase Rab20 emerged as a potent regulator of autophagy in a recently conducted large-scale screen for novel autophagy regulators. This proposal determines the mechanism by which Rab20 positively regulates autophagy and examines whether it may be a new therapeutic target in lung cancer.

July 2013 - June 2015

Rafael Gaeci-Mata PhD **(Breast Cancer)**
UNIVERSITY OF TOLEDO
Molecular Mechanisms of Invadopia Formation in Breast Cancer Cells

The migration of cancer cells away from the primary tumor and their subsequent spread to distant organs is regarded as a fatal step in cancer progression and is associated with the majority of cancer mortalities. This process, called metastasis, is the leading cause of mortality from breast cancer patients. Therefore, understanding the process of tumor metastasis and preparing strategies that may be able to alter this property of cancer cells is a significant priority. In this context, we have found a protein called RhoG that can inhibit the formation of cellular structures called invadopodia that cancer cells use to digest tissue barriers to allow invasion of surrounding tissue. In this proposal, we will characterize this important biochemical pathway to understand the fundamental mechanisms of how invadopodia form and how they contribute to breast cancer invasiveness and metastasis.

Efstathios Karathanasis PhD **(Chemotherapy Treatment)**
CASE WESTERN RESERVE UNIVERSITY
Treatment of cancer metastasis using a multicomponent nanoparticle

The vast majority of cancer deaths are due to metastatic disease. While various treatment options are available, chemotherapy prevails as the principle treatment especially in the case of highly aggressive and metastatic cancers. However, even though potent chemotherapeutic drugs are available to oncologists, the dose of these agents is constrained by their toxicity to normal tissue, because they are distributed within cancer and healthy tissues in a non-specific manner. Furthermore, metastases present unique challenges due to their smaller size, higher dispersion to organs, and lower vascularization than primary tumors, making them less accessible to therapeutic agents. To effectively seek and destroy metastases, we exploit nanotechnology to fabricate a 100-nm-long multi-component nanoparticle, called the nanochain. Due to the unique material properties that appear at the nano-scale, nanoparticles provide many potential benefits and new opportunities to address the complexity of metastatic cancer. The nanochain particle is made of different nanospheres connected one to another much like a stack of Legos. Specifically, we link three magnetic nanospheres made of iron oxide and one a lipid nanosphere filled with the drug. We then decorated the surface of the nanochain with multiple sites that bind with integrins. Integrins act as glue between the metastatic cancer cell and the lining of a blood vessel in the colonized organ. To home in on the cancer marker (integrin), we need a nanoparticle that would drift out of the central flow of the blood stream and to the blood vessel walls. The most common shape of nanoparticles is a sphere, but a sphere tends to go with the flow. However, due to its size and shape, the oblong nanochain tumbles out of the main current and skirts along vessel walls. Then, once the nanochain laches on one integrin binding site, others grab hold resulting in superior attachment of the nanochains onto metastases compared to spherical nanoparticles. A few hours later, after nanochains slip from the blood stream and congregate in metastases, a wire coil is placed, called a solenoid, outside near the body. Electricity passed through the solenoid creates a “mild” radiofrequency field (similar to frequencies of FM radio). The field causes the magnetic tails to vibrate, breaking open the liposome spheres. The application of radiofrequency facilitates rapid release of high amounts of free drug into metastatic tumors capable of spreading to deep regions of metastases, which are otherwise inaccessible by current drug delivery strategies. In animal studies, we found that this can result in at least 10 times greater cell death in metastatic tumors compared to traditional treatments.

Saulius Sumanas PhD **(Tumor Studies)**
CINCINNATI CHILDREN'S HOSPITAL MEDICAL CENTER
Inhibition of Etv2 function as a novel strategy to prevent tumor-induced angiogenesis

Blood vessel growth is commonly associated with cancer. Inhibition of blood vessel growth is one of the most promising strategies to prevent tumor growth. However, current strategies often fail to prevent tumor growth due to the development of resistance to the therapies. Zebrafish has emerged as a novel powerful model system to study blood vessel development and tumor growth which can be easily observed in transparent embryos and adults. We have previously identified a novel protein, Etv2 as a key regulator of blood vessel development in zebrafish embryos. We have also established a system to study growth of human tumors in zebrafish embryos. In this proposal we suggest that inhibition of Etv2 function may prevent tumor-induced blood vessel growth and reduce tumor growth. The proposed experiments will utilize zebrafish model to test if Etv2 is important for blood vessel growth during later developmental stages and in adults, when tumors typically arise. Furthermore, it will be tested if blocking Etv2 function will prevent tumor growth. In addition, it will be analyzed if similar to zebrafish, Etv2 in humans is associated with tumor growth. This study will determine if inhibition of Etv2 function may present a novel and potentially advantageous strategy to inhibit tumor growth. In the long term, these results may lead to the design of new drugs and treatments to prevent tumor formation in humans.

July 2012 - June 2014

JUSTIN D. LATHIA, PhD **(Brain Cancer)**
CLEVELAND CLINIC FOUNDATION
Targeting CXCR7 Mediated Vascular Interactions in Glioblastoma

Despite major clinical and basic science efforts, malignant brain tumors remain highly lethal. These tumors are treated aggressively and a fraction of the tumor still remains resistant to current therapies. Recent work has suggested that these resistant cells are capable to regrowing the entire tumor and as such, are referred to as cancer stem cells (CSCs). Key to the function and malignancy of CSCs is how they interact with their surrounding microenvironment. We are interested in signals produced by the microenvironment that contribute to CSC growth as well as therapeutic resistance and have identified a class of signaling molecules that are likely to be involved in CSC-microenvironment communication, the chemokines. We hypothesize that chemokines directly regulate the interaction between the CSCs and their microenvironment in malignant brain tumors, and targeting chemokines will prevent this interaction and result in decreased CSC and overall tumor growth. The short term goal of the project is to evaluate how chemokines and CSCs interact directly during tumor formation using live imaging models of chemokines and CSCs enriched directly from human patients. An additional short term goal is to test the effect drugs that target chemokine receptors and evaluate CSC growth under these conditions. The long term goal of this project is to develop a strategy to uncouple the communication between CSCs and their microenvironment that can easily be translated into clinical practice for malignant brain tumors and other cancers in which CSCs represent a therapeutic target. The drugs we proposed to test in our brain tumor model are under development so our results will provide rationale for early phase trials. Our project directly relates to cancer in that we are testing an important cancer biology concept, how CSCs communicate with their surrounding microenvironment using both tumor models and primary human tumor tissue. Our efforts are aimed at identifying communication pathways used by CSCs and developing therapies to disrupt the communication, thereby providing a new therapeutic strategy for a variety of tumors in which CSCs are driving malignancy including brain, breast, colon, leukemia, and lung.

NICOLE FRANZISKA STEINMETZ, PhD **(Breast Cancer)**
CASE WESTERN RESERVE UNIVERSITY
TA Novel Plant Viral Nanoparticle Drug Delivery System for Treatment of Aggressive HER2+ Breast Cancer

Approximately 200,000 women will be diagnosed with breast cancer this year and more than 40,000 of those will die from the disease. 25–30% of breast cancers are classified as HER2 positive (HER2+). HER2+ means that the cancer cells in these patients upregulate the protein human epidermal growth factor receptor 2 (HER2). HER2+ cancers are aggressive, and a woman with this diagnosis has a poor prognosis, high rate of metastasis, high risk of relapse, resistance to hormone replacement therapies, and high risk of rapid progression to death. The treatment of HER2+ cancers typically involves chemotherapy combined with an antibody known as trastuzumab (the commercial name of this therapeutic is Herceptin). Herceptin treatment is successful because this antibody specifically recognizes and binds to HER2, thus blocking its ability to signal cell growth and invasion. Nevertheless, cardiotoxicity and development of resistance are critical hurdles to overcome. Consequently, improving therapies for the treatment of HER2+ breast cancer patients is not only a critical goal for medicine, but also the key to increasing survival. We propose the next-generation of HER2-targeted therapies based on nanoparticles from plants. These nanoparticles can be engineered with hundreds of HER2 targeting ligands and chemotherapy. This is expected to increase efficacy of the treatment while reducing side effects.

Matthew K. Summers, PhD **(Breast Cancer)**
CLEVELAND CLINIC FOUNDATION
The Role of p31Comet in Breast Cancer Progression and Therapy

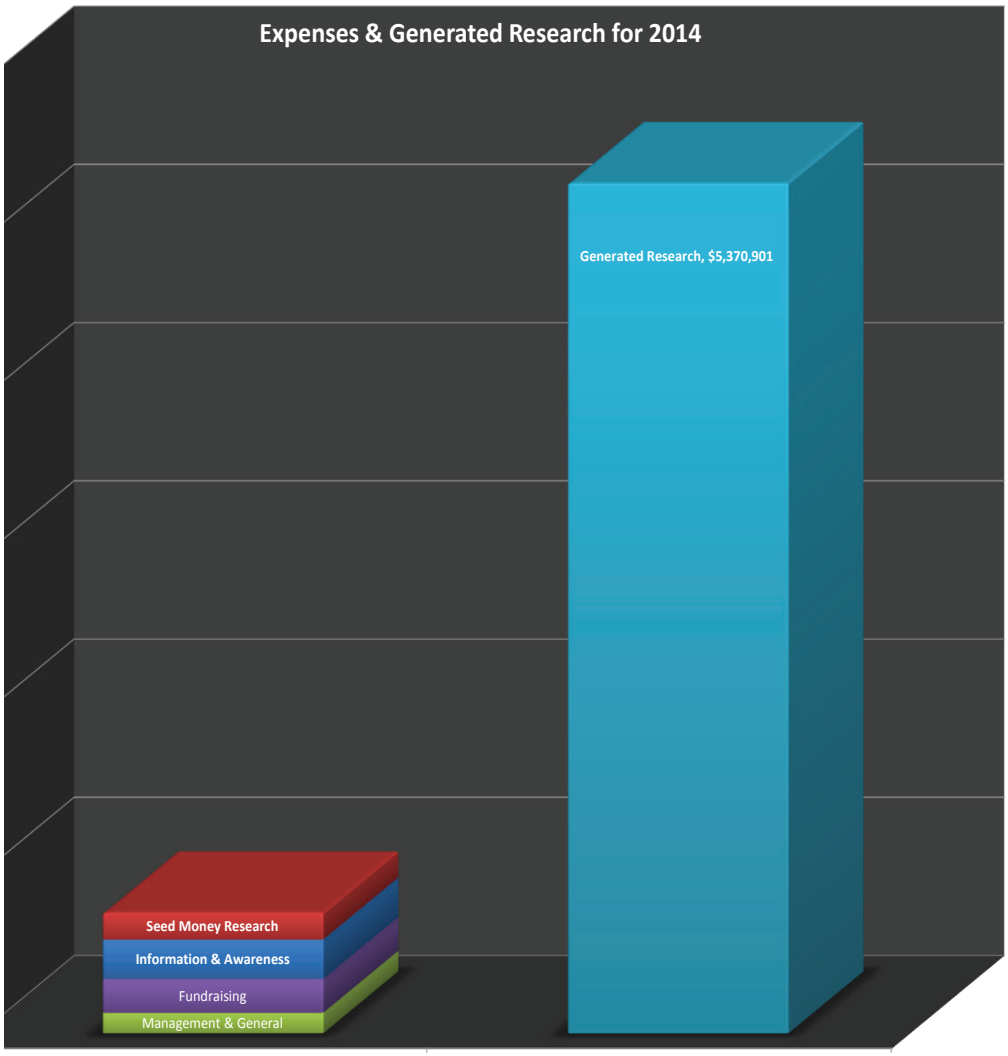
The spindle assembly checkpoint (SAC) ensures the stability of the genome (DNA) by preventing cell division until the duplicated genome is accurately segregated between the newly forming daughter cells. Errors in this process greatly contribute to the generation of cancer. SAC activity is also required for the function of a family of drugs, the taxanes, used in the treatment of breast cancer. Although the characteristic genomic instability in breast tumors and the frequency of resistance to taxanes implicate impaired SAC function in tumors, the evidence for widespread deficiencies in the SAC is lacking. However, cells possess machinery for inactivating the SAC and allowing cells to divide and proliferate. The role of this machinery in tumors is not well known. Our preliminary data indicate that the activity of p31Comet, a component of this machinery, is increased in breast tumors. The goal of this proposal is to determine the role that increased p31Comet has in the creation of tumors, whether this role can be exploited to treat cancer, and what impact increased p31Comet activity has on the successful use of taxanes in treating breast cancer. Successful testing of our hypotheses will improve our understanding of breast cancer biology and will provide the foundation for the development of an assay to predict a patient's response to taxanes and may lead to the generation of novel therapeutic agents.

Jianlong Zhu, PhD **(Tumor Study)**
UNIVERSITY OF TOLEDO
Stereoselective Synthesis of 2-Deoxy-glycosides and Thioglycosides in Antitumor Natural Products

2-Deoxy glycosides are a class of biologically important carbohydrates which often exist as critical subunits in naturally occurring potent antitumor antibiotics. Due to the fact that only limited amounts of these antibiotics can be isolated from natural sources, it is critical to develop efficient methods and strategies for the chemical synthesis for the 2-deoxy sugar subunits in order to access sufficient quantities of these natural antibiotics and their analogues for biological studies. The goal of this proposal is to develop new synthetic methodologies for stereoselective preparation of 2-deoxy glycosides and their more stable thioglycoside analogs in a highly efficient manner. These methods, once developed, will be applied to the synthesis of 2-deoxy-sugar subunits of potent natural antitumor antibiotics in order to facilitate further total synthesis for their structure and activity relationship (SAR) studies. It is the hope that our synthetic efforts will ultimately lead to development of effective therapeutic agents for the treatment of cancer diseases.

2014 FINANCIAL INFORMATION SUMMARY

The best investment!



I.	Generated research	$ 5,370,901
II.	Seed money research program	$ 169,570
III.	Cancer information and awareness program	$ 249,645
IV.	Fund raising	$ 212,598
V.	Management & General	$129,924

Over $7 million in seed money provided to researchers by Ohio Cancer Research has generated more than $220 million in new money from other sources to continue basic cancer research on projects initially funded.