Toward a Cancer-Free World

2012 ACCOMPLISHMENTS REPORT

The Ohio State University’s cancer program, embodied in both our OSUCCC and The James, is working to create a cancer-free world, one person, one discovery at a time. We strive to eradicate cancer by integrating groundbreaking research with personalized patient care and excellence in education.

This report offers a look at some of our most notable achievements and activities of 2012 in our continuing pursuit of a world without cancer.
Because cancer isn’t just one disease but has multiple causes that will require many cures, effective treatment strategies are possible only through teamwork.

That’s why excitement continues to grow within Ohio State’s cancer program as we recruit more and more of the brightest minds in oncology to conduct scientific research that translates to innovative care. In the past year, we have added some 45 multidisciplinary faculty to our team. Our Comprehensive Cancer Center now has more than 300 scientists who collectively represent 11 of the 14 colleges at Ohio State and whose groundbreaking research is often published in leading scientific journals as they probe the molecular and genomic mechanisms of cancer and seek new ways to treat or prevent it.

Among the major attractions at Ohio State for our new recruits are our outstanding facilities, including the new James Cancer Hospital and Solove Research Institute that is under construction and targeted for completion in 2014. The design of this visionary hospital will allow for much closer interaction among researchers, clinicians and educators, accelerating discovery and science-based cancer treatment.

The new James, which is the centerpiece of a $1.1 billion expansion of Ohio State’s Wexner Medical Center, will contain 276 private patient rooms that will help us meet a projected 21-percent increase in patient admissions over the next 10 years. One tremendously valuable aspect of our expanding facilities and caseload is that even more patients will be able to contribute to curing cancer by participating in clinical trials — a hallmark of our cancer program.

In the past year, more than 6,400 patients (about 25 percent) at The James participated in clinical trials, well above the national average of 3-5 percent and the National Cancer Institute (NCI) benchmark of 10 percent. When patients aren’t enrolled in clinical trials, the field stands still — both in their treatment and in the treatment of future cancer patients. For that reason, we keep setting our sights higher for clinical trials; our participation goal for fiscal 2013 is 30 percent.

No accomplishments report would be complete without acknowledging the support we enjoy from our central Ohio community and from our advocates throughout the country. In the past fiscal year, the OSUCCC – James received a record $52.2 million from more than 111,000 donors. Our Pelotonia grassroots bicycle tour has raised more than $42 million in four years for cancer research.

In February 2012, the University’s Board of Trustees renamed our academic medical center as The Ohio State University Wexner Medical Center in honor of a $100 million gift that Leslie and Abigail Wexner and their Limited Brands Foundation gave to Ohio State in February 2011. Much of that gift benefits Ohio State’s Wexner Medical Center and our cancer program.

With this combination of community support and our own resolve to cure cancer, we are never content to rest on our laurels, which include being named a “top hospital” by the Leapfrog Group for the fourth consecutive year and receiving the NCI’s highest rating, “exceptional,” during our most recent NCI redesignation as a comprehensive cancer center. The latter earned us an NCI support grant of $23 million – 16 percent more than our previous support grant. This money is vital to administering our operation and providing shared resources for our researchers.

This 2012 Accomplishments Report highlights some of our work over the past year, including: discoveries and advancements in cancer care; establishment of a drug-development institute to create a pipeline for taking new compounds through phase II clinical trials; and notable awards that reflect international acknowledgment of our quest to create a cancer-free world.

Michael A. Caligiuri, MD
Director, The Ohio State University Comprehensive Cancer Center
CEO, The James Cancer Hospital and Solove Research Institute
Lung Cancer Authority Joins OSUCCC – James

Internationally renowned lung cancer specialist David Carbone, MD, PhD, joined Ohio State’s faculty to develop and lead an OSUCCC – James Thoracic Oncology Center that will help physicians and scientists devise and optimize targeted approaches to treating this disease, the No. 1 cause of cancer death among both men and women in the United States. Carbone is an expert in the molecular biology of lung tumors, which includes understanding the genetic, proteomic and metabolic features of each patient’s cancer, and developing drugs that take advantage of this information to optimally target tumors. He came to Ohio State from Vanderbilt University, where he directed the Experimental Therapeutics Program and the Thoracic and Head and Neck Cancer programs at the Vanderbilt-Ingram Cancer Center. Carbone also led the Thoracic Oncology Center at Vanderbilt.

Renowned Oncologist Leads Breast Radiation Oncology

Julia White, MD, regarded as one of the world’s leading breast radiation experts, became the new director of breast radiation oncology at the OSUCCC – James and vice chair of Ohio State’s Department of Radiation Oncology. As a physician and radiation oncologist, her goal is to deliver radiation personalized to each patient’s cancer by using advanced technology to better treat breast tumors and improve survival. White chairs the national Radiation Therapy Oncology Group’s (RTOG) Breast Cancer Group and is on the National Cancer Institute Breast Cancer Steering Committee. She has served as principal investigator for a number of clinical studies that have helped establish standards of care for breast cancer.

Another Cancer Genetics Expert Comes Aboard

Paul Goodfellow, PhD, joined Ohio State’s faculty as a professor of Obstetrics and Gynecology and a member of the Molecular Biology and Cancer Genetics Program at the OSUCCC – James. He was recruited from Siteman Cancer Center, Barnes Jewish Hospital, at the Washington University School of Medicine in St. Louis, Mo., where he was principal investigator for a Specialized Program of Research Excellence (SPORE) in Endometrial Cancer and co-directed the Hereditary Cancer Core. Goodfellow’s research focuses on identification and characterization of genetic events important in tumor initiation and progression, and on understanding molecular events that can be used to develop approaches to preventing and treating endometrial (uterine) and breast cancers.
Cancer Program Gains Specialist in Genomics and Tumor Sequencing

Sameek Roychowdhury, MD, PhD, a specialist in genomics and tumor sequencing whose research focuses on personalized approaches to patient treatment through genomics, was recruited to Ohio State as an assistant professor in the Department of Internal Medicine’s Division of Medical Oncology. He also is an assistant professor in the School of Biomedical Science’s Department of Pharmacology. Roychowdhury previously was at the University of Michigan, where between 2006 and 2012 he consecutively completed an internal medicine residency, a clinical fellowship in medical oncology and a postdoctoral fellowship. He had been a clinical lecturer in the Division of Hematology/Oncology at Michigan since 2011. Roychowdhury earned both his MD and his PhD in immunology at Ohio State, where he also received his undergraduate degree in molecular genetics.

Study Reveals How Normal Cells Fuel Tumor Growth

A study led by researchers at the OSUCCC – James and published in the journal *Nature Cell Biology* discovered how normal cells in tumors can fuel tumor growth. The study examined what happens when normal cells known as fibroblasts in mouse mammary tumors lose the *PTEN* tumor-suppressor gene. The findings suggest new strategies for controlling tumor growth by developing drugs that disrupt communication between tumor cells and normal cells within the tumor. Co-principal investigators Michael Ostrowski, PhD, and Gustavo Leone, PhD, say the study is the first to define a pathway in tumor fibroblasts that reprograms gene activity and the behavior of multiple cell types in the tumor microenvironment, including tumor cells themselves.
Oral HPV Infection 3 Times More Common in Men Than Women

An OSUCCC – James study showed that men are three times more likely to have an oral human papillomavirus (HPV) infection than women – findings that helped explain why HPV-related oral cancers are three times more common in men than women. **Maura Gillison, MD, PhD**, a medical oncologist and head and neck cancer specialist at the OSUCCC – James, led the study, which was published in the *Journal of the American Medical Association* to coincide with her presentation of the findings at the Multidisciplinary Head and Neck Cancer Symposium in Phoenix, Ariz. Gillison and collaborators sought to determine the prevalence of oral HPV infection in the United States and understand factors associated with this infection and oropharyngeal cancer.

Beyond the Thymus: Tonsils Make T Cells Too

Research led by scientists at the OSUCCC – James provided evidence that immune cells called T lymphocytes (T cells) can develop in human tonsils. These cells had been thought to develop only in the thymus, an immune system organ. This study, published in the *Journal of Clinical Investigation*, could improve understanding of T-cell cancers, autoimmune diseases and how stem-cell transplantation is done. “We’ve long known that a functional thymus is necessary to develop a complete repertoire of T cells, but whether a T-cell factory existed outside the thymus has been controversial,” says principal investigator **Michael A. Caligiuri, MD**. “Our study is the first to describe a comprehensive, stepwise model for T-cell development outside the thymus.”

MutationSignals High Recurrence Risk in Older AML Patients

Older people with acute myeloid leukemia (AML) and normal-looking chromosomes in their cancer cells have a higher risk of recurrence if they have mutations in a gene called ASXL1, according to a study by OSUCCC – James researchers. The study, published in the journal *Blood*, was the first to investigate the influence of these mutations on prognosis in patients with cytogenetically normal AML (CN-AML) and in conjunction with other prognostic gene mutations. It also reported the first gene-expression signature for CN-AML with mutated ASXL1. “Our findings could lead to more effective targeted therapies and improved cure rates,” says principal investigator **Clara D. Bloomfield, MD**, a Distinguished University Professor who serves as cancer scholar and senior adviser to the OSUCCC – James.
Revised Glioblastoma Classification Should Improve Patient Care

Radiation oncology researchers have revised the prognostic model used by doctors since the 1990s for glioblastoma, the most devastating of malignant brain tumors. The previous system was devised for malignant glioma patients who were treated by radiation therapy only, relying on histopathology and clinical variables. The new system accommodates advances in treatment – particularly the use of radiation therapy plus the chemotherapy drug temozolomide – and it incorporates molecular biomarkers as well as clinical variables. Arnab Chakravarti, MD, the study’s national chair for translational research and co-leader of the brain tumor program at the OSUCCC – James, says the new model is more relevant and should better identify patients requiring the most aggressive therapy.

Surgeons Pioneer Removal of Skull Base Tumors Through Nose and Mouth

Surgeons at the OSUCCC – James Cranial Base Center developed a minimally invasive technique to reach and remove skull base tumors through the nose or mouth, sparing patients considerable pain from traditional open surgery and allowing for quicker recovery. The procedure combines endoscopic endonasal surgery with minimally invasive robotic surgery to treat many tumors that are difficult to reach, including some previously considered inoperable. The endoscopic endonasal approach gives surgeons access to the base of the skull, intracranial cavity and top of the spine by operating through the nose and paranasal sinuses. The surgical team includes Ricardo Carrau, MD, Daniel Prevedello, MD, and Enver Ozer, MD.
Study Reveals Mechanism of Lung Cancer Drug Resistance

Research published in the journal *Nature Medicine* indicated that targeted drugs such as gefitinib might better treat non-small-cell lung cancer if they are combined with agents that block certain microRNAs. The OSUCCC – James study, led by principal investigator Carlo Croce, MD, showed that overexpression of the *MET* and *EGFR* genes causes the deregulation of six microRNAs, leading to gefitinib resistance. Findings support the development of agents that restore the levels of these microRNAs, offering a new strategy for treating this disease. The study also suggested that measuring expression levels of certain microRNAs – those controlled by the *MET* gene – might predict which lung-cancer cases are likely to resist gefitinib.

Possible Therapy Identified for Tamoxifen-Resistant Breast Cancer

A study that discovered how tamoxifen-resistant breast-cancer cells grow and proliferate also suggested that an experimental agent called vismodegib may offer a targeted therapy for patients with this cancer. The study, published in the journal *Cancer Research*, showed that a signaling pathway called hedgehog (Hhg) can promote breast cancer cell growth after tamoxifen shuts down the pathway activated by the hormone estrogen, and that a second signaling pathway, called PI3K/AKT, is also involved. Researchers led by principal investigator Sarmila Majumder, PhD, and Bhuvaneswari Ramaswamy, MD, say activation of the Hhg pathway makes tamoxifen treatment ineffective, enabling the tumor to resume progression. They analyzed more than 300 human tumors and found that those with an activated Hhg pathway had a worse prognosis.
Scientists Discover Switch That Turns White Fat Brown

OSUCCC – James scientists discovered a biological switch that gives energy-storing white fat the characteristics of energy-burning brown fat. The findings could lead to new strategies for treating obesity, a risk factor for cancer. The animal study, published in the journal *Cell Metabolism*, showed that the change stems from activation of a nerve and biochemical pathway that begins in the hypothalamus, an area of the brain involved in energy balance, and ends in white fat cells. “One of the holy grails of obesity therapy is to understand how to switch white fat to brown fat; this study describes a way to do that,” says study leader Matthew During, MD, PhD. “Our findings suggest we can induce this transformation by modifying our lifestyle or pharmacologically activating this brain-fat pathway.”

Researchers Identify ‘Life-and-Death’ Molecule on Chronic Leukemia Cells

A study at the OSUCCC – James identified a life-and-death signaling role for a molecule on the surface of the immune cells involved in chronic lymphocytic leukemia (CLL), a finding that could lead to more effective therapy for this incurable cancer. The study, published in the journal *Cancer Cell*, examined how a drug called SMIP-016 kills CLL cells. Earlier work by these scientists showed that the drug targets a molecule called CD37 on CLL cells. The newer study found that the CD37 molecule has two regions that concurrently activate two pathways in CLL cells, one leading to cell death and another promoting cell survival. Principal investigator (PI) John C. Byrd, MD, says the findings showed SMIP-016 activates the “death” part of the molecule, which suggests that blocking the “survival” part could improve the drug’s effectiveness. Co-PIs for the study are Michael Freitas, PhD, and Natarajan Muthusamy, DVM, PhD.
OSU, Malaysia Centre Join Forces to Develop Anticancer Drug

Ohio State has signed an agreement with the Sarawak Biodiversity Centre in Malaysia to collaborate on further development and commercialization of a promising anticancer agent derived from a tropical tree that grows in the Malaysian state of Sarawak. Researchers with Ohio State’s College of Pharmacy and the OSUCCC – James have worked on the agent, called silvestrol, since 2004. Their early studies indicated silvestrol might help treat acute and chronic leukemia, mantle cell lymphoma and other incurable malignancies. “We will be working with the National Cancer Institute to isolate and purify the agent, and conduct the laboratory and animal studies needed to demonstrate its safety and effectiveness,” says Michael Grever, MD, co-leader of the Experimental Therapeutics Program at the OSUCCC. A. Douglas Kinghorn, PhD, DSc, of the College of Pharmacy, led the work that characterized the molecular structure of silvestrol.

OSU Leads International Pancreatic Cancer Treatment Development Effort

The OSUCCC – James is leading an international pancreatic cancer research effort in collaboration with scientific investigators based in Taiwan and Germany to develop new targeted therapies and biomarkers for pancreatic cancer. Tanios Bekaii-Saab, MD, section chief for gastrointestinal oncology at the OSUCCC – James, and Cheng-Shih Chen, PhD, of the Molecular Carcinogenesis and Chemoprevention Program at the OSUCCC – James, are partnering with doctors at National Cheng-Kung University in Tainan City, Taiwan, and with researchers at the German Cancer Research Center in Heidelberg, to conduct the initiative. The researchers will work to identify new targets in pancreatic tumors and develop novel agents to strike those targets and halt the progression of this disease, for which the overall five-year survival rate is only 5.8 percent.
OSUCCC – James Earns NCI Phase II Contract Renewal

The National Cancer Institute (NCI) awarded the OSUCCC – James a phase II clinical trials contract that could be worth more than $8 million over five years if fulfilled to capacity. Principal investigator Miguel Villalona, MD, says the money, a renewal of a similar $3 million contract the NCI awarded to Ohio State in 2006, will enable the OSUCCC – James to conduct phase II clinical trials on NCI-sponsored agents as the lead institution in a consortium that includes Case Western Reserve Comprehensive Cancer Center/Cleveland Clinic, Georgetown University Lombardi Comprehensive Cancer Center, and Roswell Park Cancer Institute as collaborators. These trials will help scientists evaluate biologic effects of experimental anticancer agents and determine clinically relevant outcomes/correlates of drug efficacy and toxicity. The OSUCCC – James and collaborators constitute one of only seven consortia holding NCI phase II contracts.

NCI Grant Aids Study of microRNAs in CML

Danilo Perrotti, MD, PhD, of the Molecular Biology and Cancer Genetics Program at the OSUCCC – James, is principal investigator for a five-year, $1.52 million grant from the National Cancer Institute for studying the “Role of microRNAs in the Regulation of CML Stem Cell Survival and Self-Renewal.” Perrotti says chronic myelogenous leukemia (CML) is the first clinically cured stem cell-derived hematopoietic neoplasm, but he notes that tyrosine inhibitor therapy leaves behind a pool of CML stem cells that are resistant to these drugs. Thus, only drugs that can safely target these stem cells without harming normal ones have potential for disease eradication. He suggests that CML stem cell survival and renewal may depend on altered expression of certain microRNAs. With this grant, his team will examine the mechanism of altered microRNA expression for maintaining CML stem cells in hopes of finding therapeutic targets.

NCI Funds Ohio State Breast Cancer Intervention Training

Barbara Andersen, PhD, a professor of Psychology and researcher in the Cancer Control Program at the OSUCCC – James, received a $1.6 million grant from the National Cancer Institute (NCI) to train mental healthcare professionals in a biobehavioral intervention that helps cancer patients cope with stresses of diagnosis and treatment. Andersen and collaborators developed the intervention, which culminates more than a decade of research evaluating the benefits of psychological counseling and support for cancer survivors. She published studies in 2008, ’09 and ‘10 showing benefits of this particular intervention, including a reduced risk for cancer recurrence. Andersen wants to disseminate the intervention “to increase the pool of mental healthcare providers who understand the needs of cancer patients and adopt evidence-based psychological treatments to help them.”
Croce is Recipient of International Carcinogenesis Award

**Carlo Croce, MD**, director of Human Cancer Genetics at Ohio State, where he also chairs the Department of Molecular Virology, Immunology and Medical Genetics, received the 2012 Anthony Dipple Carcinogenesis Award at the 22nd meeting of the European Association for Cancer Research in Barcelona, Spain. The award, sponsored by Oxford University Press, is given to individuals who have made major contributions to research in carcinogenesis. Croce also is a member of the Institute of Medicine of the National Academies, the National Academy of Sciences of the United States, and the Accademia Nazionale delle Scienze detta dei XL in Italy. He is principal investigator on 11 federal research grants and has published more than 900 peer-reviewed research papers.

Gillison Lands Rosenthal Memorial Award for HPV Work in Cancer

**Maura Gillison, MD, PhD**, a member of the Cancer Control and Viral Oncology programs at the OSUCCC – James, received the 36th Annual Richard and Hinda Rosenthal Memorial Award from the American Association for Cancer Research (AACR). Gillison accepted the award at the AACR’s annual meeting in Chicago. The award recognizes her contributions to understanding the role of human papillomavirus (HPV) in head and neck cancers. As recipient, Gillison presented “Clinical Implications of HPV in Head and Neck Cancers” at the annual meeting.

Caligiuri Elected Vice President of Society for Natural Immunity

**Michael A. Caligiuri, MD**, director of the OSUCCC and CEO of The James, was elected vice president of the Society for Natural Immunity (SNI) in April 2012 at its 13th meeting. Caligiuri will serve in that capacity for three years and then become president for another three years. SNI meets every 18 months at sites around the world so investigators and trainees can hear about recent findings in the field of natural immunity. The focus is on natural killer (NK) cells, but related fields are included. The sessions blend basic science with clinical studies and advances.
Three renowned researchers at the OSUCCC – James were honored with awards or lectureships at the Alliance for Clinical Trials in Oncology annual meeting in Chicago:

**Richard Goldberg, MD**, a gastrointestinal oncologist and physician-in-chief, presented “Meaningful Outcomes: Lives Saved Due To Clinical Trials in Early-Stage Colon Cancer” as the first Charles G. Moertel Lecture, which was held during the plenary session of the Alliance’s meeting. It was the first Moertel lecture given through the newly formed Alliance, a cooperative group created by merging the North Central Cancer Treatment Group (NCCTG), Cancer and Leukemia Group B (CALGB) and the American College of Surgeons Oncology Group. This clinical research entity is sponsored by the National Cancer Institute. NCCTG initiated the lectureship in 1995 and transferred it to the Alliance after the merger.

**Clara D. Bloomfield, MD**, a Distinguished University Professor who also serves as cancer scholar and senior adviser to the OSUCCC – James, received the 2012 Richard L. Schilsky Cancer and Leukemia Group B (CALGB) Achievement Award. The award, which acknowledges individual contributions to cooperative group research, is presented annually during the plenary session of the Alliance Group Meeting, where Bloomfield presented a summary of her research done in collaboration with CALGB. In the past 20 years, Bloomfield and colleagues have conducted pioneering research on molecular changes in the approximately 45 percent of acute myeloid leukemia patients with cytogenetically normal chromosomes. Most of her talk focused on this work.

**Electra Paskett, PhD, MSPH**, associate director for population sciences at the OSUCCC – James, presented the 12th annual Jimmie Holland Lecture. Paskett, who also leads the Cancer Control Program at the OSUCCC – James, presented “Interventions to Address Cancer Health Disparities: The Case of Cervical Cancer in Appalachia.” She discussed methods to eliminate cancer health disparities, including community-based participatory research with transdisciplinary teams using multilevel interventions. She also reviewed past and current research projects in Ohio State’s Center for Population Health and Health Disparities that she leads in Appalachia Ohio.
‘Topping Out’ is Symbolic Milestone For New James Cancer Hospital

The final steel beam for completing the 21-story structure of Ohio State’s new James Cancer Hospital and Solove Research Institute was set in place at a May 21 “topping out” ceremony attended by hundreds of enthusiastic observers. This new hospital – the centerpiece of a $1.1 billion Ohio State University Wexner Medical Center Expansion – is designed around a visionary construction model that integrates spaces for research, education and patient care, placing researchers and clinicians in closer working proximity so they can translate more discoveries to innovative care. Michael A. Caligiuri, MD, director of Ohio State’s Comprehensive Cancer Center and CEO of The James, says the hospital, when finished in 2014, will break down walls that historically have divided researchers and clinicians.

‘Build Out’ of Tower Floors Provides More Cancer Research Lab Space

2012 saw the “build out” of the previously unfinished fourth and fifth floors in Ohio State’s Biomedical Research Tower to provide an additional 64,000 square feet of lab space for OSUCCC – James investigators (32,000 gross square feet per floor). The fourth-floor “build out” was supported by an $8 million Extramural Research Facilities Improvement Program Construction Grant funded by the American Recovery and Reinvestment Act. The grant was awarded by the National Institutes of Health’s National Center for Research Resources based on an application submitted by Michael Grever, MD, and others. This floor houses labs for researchers in the Experimental Therapeutics Program. The fifth-floor project, supported in part by philanthropic revenue, houses labs that support the cancer program’s commitment to expanding solid tumor basic and genetic research.

Drug Development Institute Boosting Clinical Research

The new Ohio State Drug Development Institute – a collaboration among the OSUCCC – James and the colleges of Medicine, Pharmacy and Business – is creating a cancer drug development pipeline to take promising new compounds through phase II clinical trials. Timothy Wright, director of the Drug Development Institute, says the endeavor holds great potential to benefit cancer patients in Ohio and beyond. Wright says his role is to facilitate the work of the nearly 300 cancer researchers at the OSUCCC – James and to work with Ohio State’s Technology Commercialization Office “to optimize value from our research inventions.” He notes that two targeted agents invented by OSUCCC – James investigators are already in early-phase clinical trials, and more “are in the pipeline.”
Nursing Unveils New Professional Practice Model

OSUCCC – James Nursing unveiled a Nursing Professional Practice Model (PPM) that “artistically portrays how our vision, mission and values come to life.” Nursing leaders say the PPM, inspired by the ancient mandala (see image, right), affirms a sense of professionalism and commitment to excellence; guides practice and depicts how James nurses contribute to the hospital’s patient care, education and research mission; and supports the OSUCCC – James vision of creating a cancer-free world. The PPM, which evolved through a grassroots approach that involved nurses in all roles, contains five core components: Leadership and Governance; Patient Care; Innovation and Research; Professional Relationships; Development and Recognition.

Pelotonia Raises More Than $42 Million in 4 Years

Riders and donors in Pelotonia 12, the annual grassroots bicycle tour that generates money for cancer research at the OSUCCC – James, raised a record $16.8 million, a 28-percent increase over the Pelotonia 11 total of $13.1 million. That brings the four-year fundraising total for Pelotonia, which began in 2009, to more than $42 million. Pelotonia 12, which took place Aug. 10-12 on routes between Columbus and Kenyon College in Gambier, Ohio, drew a record 6,212 riders, as well as 3,141 virtual riders and more than 2,000 volunteers. Among the participants were a record 1,635 members of Team Buckeye, the official superpeloton (riding group) for The Ohio State University – a team that included 1,198 riders, 336 virtual riders and 101 volunteers. Team Buckeye comprised 84 separate pelotons, whose members collectively raised more than $2.1 million of the Pelotonia 12 total.