Ecosystem Restoration
Can a black-raspberry drink repair oral microbiomes damaged by smoking and prevent cancers of the mouth?

ALSO INSIDE:
Pancreatic Cancer
Improving Health Care in Cameroon

The James
UPFRONT
The Director's Perspective

Year Two and Looking Forward

This is our second spring in the new James Cancer Hospital and Solove Research Institute, and we can say that this transformational facility is living up to its promise of furthering our research-based patient care.

Following a five-year site review by a National Cancer Institute (NCI) survey team in May 2015, our program again earned an “exceptional” rating, the NCI’s highest descriptor, and we have retained our designation as one of only 45 NCI-designated comprehensive cancer centers. Accompanying that distinction will be a multimillion NCI grant, which supports the OSUCCC – James scientific leadership and administration, shared research technologies, development of scientific goals, and continued collaboration among our more than 300 interdisciplinary researchers.

Through these exciting times, the pulse of groundbreaking research at the OSUCCC – James has remained steady, as stories in this new Frontiers will show.

Our cover story, for example, examines work by four OSUCCC – James researchers who want to understand the composition and function of the bacterial community, or microbiome, in the mouth, and its role in cancer. The collaborating researchers have evidence that a food-based approach, using a novel black raspberry drink, might help prevent oral cancer. They want to learn whether, and how, the microbiome contributes to this possible preventive effect.

Another story notes that medical advances of the past few years have doubled the one- to two-year survival rate for patients with pancreatic cancer—one of the deadliest malignancies—and looks at key contributions of OSUCCC – James researchers in this vitally important but still underfunded area of study.

Reflecting our global reach, a third feature reveals how an OSUCCC – James physician-researcher is contributing to his father’s program to improve education and health care in a village in the West African nation of Cameroon. Their effort is a model of educational improvement, economic development and sustainability.

The OSUCCC – James is in a better position than ever to help change the landscape of cancer care and research in Ohio and beyond as we continue pursuing our vision of a cancer-free world.
FEAT U R E S

ECOSYSTEM RESTORATION
A novel black raspberry drink might help prevent oral cancer, and the microbiome may play a key role in this relationship.

PANCREATIC CANCER
New treatment approaches and drug regimens are improving outcomes in pancreatic cancer, but more research funding and more patients on clinical trials are needed.

GIVING BACK
An OSUCCC – James physician-researcher contributes to his father’s program to improve education and health care in an African village.

FRONTLINE

SLOW ON THE UPTAKE
We have a safe, effective vaccine that prevents cervical cancer – let’s use it!

BREAKTHROUGH

DO THE MATH
Genomics Tool Could Help Predict Tumor Aggressiveness, Treatment Outcomes

IMPEDIMENT PATHWAY
Study Discovers Negative Regulator of Natural Killer Cell Maturation

PROSTATE PROGNOSTICATORS
Molecules in Prostate Tumors May Predict Whether RT Can Prevent Recurrence

MISMATCH MUTATIONS
Genetic Biomarker May Predict Cancer Patients’ Response to Immunotherapy

BENEVOLENT BIOMARKERS
Study Supports IDH Gene as Prognostic Marker in Anaplastic Astrocytoma

SMALL WONDERS
Chitosan-Coated, Chemotherapy-Packed Nanoparticles May Target Cancer Stem-Like Cells

OF NOTE
Recent grants, awards and honors, new faculty and program developments

BENCH TO BEDSIDE

YVONNE A. EFEBERA, MD
A Phase I/II Trial of Cetuximab in Combination With Interleukin-12 Administered to Patients With Unresectable Primary or Recurrent Squamous Cell Carcinoma of the Head and Neck

NEED TO KNOW
BIOSPECIMEN SERVICES SHARED RESOURCE

MICHAEL A. CALIGIURI, MD, ELECTED TO TOP AACR LEADERSHIP POSITION

ON THE COVER:
Seeking help for the smoker’s oral microbiome. Page 16

Read Frontiers online or download an issue at http://cancer.osu.edu/Frontiers.
SLOW ON THE UPTAKE

We have a safe, effective vaccine that prevents cervical cancer – let’s use it!

BY ELECTRA PASKETT, PHD, MSPH

With 12,900 new cases of cervical cancer expected in the United States in 2015, and a projected 4,100 deaths from the malignancy, cervical cancer remains a serious problem in the nation.

Virtually all cervical cancers are caused by HPV infection, mainly HPV-16 and HPV-18. These viruses also can cause vaginal and vulvar cancers in women, penile cancer in men, and anal cancer and oropharyngeal cancer in women and men.

The HPV vaccine, approved in 2006, has proven safe and able to prevent cervical cancer. Approval was extended to boys in 2011. People should be lined up around the block to get the vaccine. But uptake remains low.

Girls and boys should receive three doses of the vaccine before they become sexually active, ideally at ages 11 to 12, though the vaccine can be given up to age 26 in girls and 24 in boys.

The Centers for Disease Control and Prevention (CDC) found that, while HPV vaccination rates improved in 2014, the gap in coverage between one dose of HPV vaccine and one dose of tetanus, diphtheria and pertussis (Tdap) vaccine is large. Only 40 percent of girls and 22 percent of boys had completed the three-shot series in 2014.

By comparison, HPV vaccination rates in Australia, Canada and United Kingdom are approaching 70 percent, and virtually all countries that have widely adopted the vaccine are beginning to see decreases in markers of HPV infection.

And while we won’t see changes in cancer incidence for several years, we are seeing trends that are clearly positive.

A study in the March 2016 issue of the journal Pediatrics analyzed cervical and vaginal specimens from females ages 14 to 34 gathered by the National Health and Nutrition Examination Survey (NHANES) from 2003-2006 (pre-vaccine era) and from 2009-2012 (vaccine era). The quadrivalent HPV vaccine protects against HPV-6, -11, -16 and -18.

The study found that, since vaccine approval, the prevalence of the four HPV types declined to 4.3 percent from 11.5 percent among females aged 14-19 years, and to 12.1 percent from 18.5 percent among females aged 20 to 24 years.

Among sexually active females aged 14-24 during the vaccine era, prevalence of the four HPV types was lower in vaccinated (one or more doses) compared with unvaccinated females: 2.1 percent vs. 16.9 percent.

The study found that just six years after vaccine approval, the prevalence of four cancer-related HPV types dropped 64 percent among females aged 14 to 19 years and 34 percent among females aged 20 to 24 years.

This evidence extends earlier findings showing decreases in markers such as HPV titre levels, decreasing incidence of genital warts and of pre-invasive cervical-cancer abnormalities.

What can we do to bring U.S. HPV vaccine rates on par with those of meningococcal conjugate and Tdap?

One key reason for low vaccination rates is parents who decide they don’t want the vaccine.
for their children. Common reasons include:

- Concern with safety and side effects. FACT: Seven years of safety studies and distribution of about 57 million vaccine doses in the United States have identified no serious safety concerns with the HPV vaccine;
- A belief that the vaccine is not needed. FACT: HPV infection is the most common sexually transmitted infection among adults. Vaccination of 80 percent of adolescents and young adults could eliminate this infection;
- The young person is not sexually active. FACT: Girls and boys need three doses of vaccine when young so they can build an immune response before they become sexually active;
- This vaccine gives the child permission to have sex. FACT: Multiple studies show that HPV-vaccinated preteens and teens have sex no sooner than their unvaccinated peers.

Parents need to hear these messages from the physician. Unfortunately, many doctors don’t recommend HPV vaccination. A study in the February issue of Pediatrics examined perspectives of HPV vaccine from 364 pediatricians and 218 family physicians nationally.

Nearly one-third of the pediatricians and almost half of the family physicians reported discussing HPV vaccination only occasionally or rarely during 11- to 12-year-old visits. The most common reasons were:

- The patient is not sexually active;
- The patient is too young;
- The patient is getting other vaccines during the visit;
- The parents will refuse;
- Family physicians noted that they didn’t have time to discuss the vaccine.

The CDC recommends that physicians present the topic to parents by confidently saying, “Today your child needs three vaccines. These vaccines prevent HPV cancers, meningitis, diphtheria, tetanus and whooping cough.”

Sometimes, parents may just want reassurance from the physician that the vaccine is important for the child. Physicians can do this by saying that they would want their own children, grandchildren or close family members to be protected against HPV cancers by being vaccinated.


### HPV-vaccine and tetanus, diphtheria and pertussis (Tdap) coverage among adolescents ages 13 to 17

<table>
<thead>
<tr>
<th>Coverage among 13 to 17 year olds</th>
<th>2013(%)</th>
<th>2014(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Girls receiving one dose or more</td>
<td>56.7</td>
<td>60.0</td>
</tr>
<tr>
<td>Girls receiving three doses</td>
<td>36.8</td>
<td>39.7</td>
</tr>
<tr>
<td>Boys receiving one dose or more</td>
<td>33.6</td>
<td>41.7</td>
</tr>
<tr>
<td>Boys receiving three doses</td>
<td>13.4</td>
<td>21.6</td>
</tr>
<tr>
<td>Tdap vaccination</td>
<td>84.7</td>
<td>87.6</td>
</tr>
</tbody>
</table>

Relative coverage of HPV vaccine in girls and boys receiving one dose or more relative to Tdap coverage in 2014:  

Source: CDC 2014 National Immunization Survey – Teen
A new method for measuring genetic variability within a tumor could help doctors identify patients with aggressive cancers that are more likely to resist therapy, according to a study led by researchers now at The Ohio State University Comprehensive Cancer Center – James Cancer Hospital and Solove Research Institute (OSUCCC – James).

Researchers used a scoring method they developed called MATH (mutant-allele tumor heterogeneity) to measure the genetic variability among cancer cells within tumors from 305 patients with head and neck cancer. High MATH scores corresponded to tumors with many differences among the gene mutations present in different cancer cells.

Cancers that showed high genetic variability—called “intra-tumor heterogeneity”—correlated with lower patient survival. If prospective studies verify the findings, MATH scores could help identify the most effective treatments and predict prognosis.

Researchers have long hypothesized that multiple subpopulations of mutated cells within a single cancer lead to worse clinical outcomes; however, oncologists do not use tumor heterogeneity to guide clinical care decisions or assess disease prognosis because there is no easy-to-implement method of doing so in clinical practice.

To address this need, James Rocco, MD, PhD, and colleagues developed MATH to help doctors measure genetic variability in tumors and to help guide treatment decisions. Findings from this study confirm that high genetic variability within a patient’s tumor is related to increased mortality in head and neck squamous cell carcinoma.

“Genetic variability within heterogeneity tumors, it is likely that there are several clusters of underlying mutations—in the same tumor—driving the cancer. So their tumors are likely to have some cells that are already resistant to therapy,” Rocco was corresponding author on the study. Edmund Mroz, PhD, research associate professor in the Department of Otolaryngology – Head and Neck Surgery at Ohio State, was first author.

Published in the journal PLOS Medicine

To refer a patient, please call The James Line New-Patient Referral Center toll free: 1-800-293-5066
Impediment Pathway

Study Discovers Negative Regulator of Natural Killer Cell Maturation

A study led by researchers at the OSUCCC – James has identified a regulatory pathway in natural killer (NK) cells that impedes their maturation and homing behavior. NK cells are one of the body’s first lines of defense against viruses and cancer.

The findings could lead to strategies for boosting natural killer cell activity against cancer and viral infections. Jianhua Yu, PhD, assistant professor in the Division of Hematology at Ohio State and a member of the Leukemia Research Program at the OSUCCC – James, was principal investigator.

The study, which used an animal model and human NK cells, showed that a protein called Foxo1 inhibits NK cell development and function. It also showed that Foxo1 exerts its inhibitory effects by blocking transcription of the gene that encodes Tbx21, which is a known positive regulator of NK-cell development and function.

“We discovered a pathway that cancer cells may use to block NK-cell function and evade immune responses,” Yu says. “The findings may provide us with an opportunity to enhance NK-cell antitumor activity.”

Published in the journal Immunity
Prostate Prognosticators

Molecules in Prostate Tumors May Predict Whether RT Can Prevent Recurrence

A new study has identified a group of molecules in prostate-cancer cells that doctors might one day use to distinguish which patients should be treated with radiation therapy (RT) if rising prostate-specific antigen (PSA) levels indicate their cancer has recurred after prostatectomy.

Led by researchers at Ohio State, the retrospective study suggested that a pattern of molecules called microRNA (miRNA) in tumor cells might predict patients’ response to RT. In particular, the study suggested that two miRNAs—miR-4516 and miR-601—in tumor cells, along with Gleason score and lymph node status, may help identify patients who might experience rising PSA after they’ve been treated with RT.

“This study is the first to demonstrate that miRNA expression in tumor cells correlates with outcome after salvage radiation therapy, paving the way for the potential use of miRNA biomarkers in prostate cancer treatment,” says first author Erica Hlavin Bell, PhD, assistant professor-clinical in the Department of Radiation Oncology, and a member of the Translational Therapeutics Program at The OSUCCC — James.

In addition, the researchers correlated a pattern of 88 miRNAs with tumors that first recurred early after prostatectomy—within three years or less—versus tumors that recurred after three years.

“If validated by further studies, these findings could change clinical practice and improve the care of prostate-cancer patients,” says study leader Arnab Chakravarti, MD, professor and chair of the Department of Radiation Oncology, and a member of the Translational Therapeutics Program at the OSUCCC – James.

“Men found to have aggressive disease at the time of prostatectomy could be offered additional treatment with radiation therapy to prevent recurrence, while sparing men with slow-growing tumors,” Chakravarti adds.

“These findings are important because it is currently hard to distinguish early which patients will benefit from radiation therapy following radical prostatectomy and which will receive no benefit,” says Bell. “Our novel miRNA panel might also shed light on the underlying mechanisms of treatment resistance in prostate cancer.”

Published in the journal PLOS ONE.

To refer a patient, please call The James Line New-Patient Referral Center toll free: 1-800-293-5066
Mismatch Mutations

Genetic Biomarker May Predict Cancer Patients’ Response to Immunotherapy

Biological changes that knock out genes involved in the repair of damaged DNA might predict who will respond to certain immunotherapy drugs, according to data from a proof-of-principle study co-authored by scientists at the OSUCCC – James.

The finding comes from a phase II trial examining the effectiveness of the immunotherapy drug pembrolizumab (marketed as Keytruda). Richard Goldberg, MD, physician-in-chief at the OSUCCC – James, serves as principal investigator of the local arm of this clinical trial and co-author of the study. Luis Diaz Jr., MD, of Johns Hopkins Kimmel Cancer Center, is principal investigator of the national trial.

Defects in mismatch repair genes were originally discovered in 1993 by a team that included Albert de la Chapelle, MD, PhD, who is now in the Molecular Biology and Cancer Genetics Program at the OSUCCC – James. Defects, or mutations, in mismatch repair genes occur in both sporadic and hereditary forms of colorectal, endometrial, stomach, biliary tract, pancreatic, ovarian and small intestine cancer. The mutations disable a cell’s ability to repair small errors in its DNA. Loss of this repair mechanism leads to unchecked cellular growth.

The study suggests that patients with mutations in mismatch repair genes respond better to pembrolizumab than patients with normal mismatch repair genes.

“This study is a real-life example of how gene sequencing of tumor cells and precision cancer medicine can improve our approach to treating cancers with immunotherapy agents based on a cancer’s genetic signature, rather than on the class of cells or the organ in which the tumor occurs,” Goldberg says.

Published in the New England Journal of Medicine

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RICHARD GOLDBERG, MD, physician-in-chief at the OSUCCC – James

ALBERT de la CHAPELLE, MD, PhD
Molecular Biology and Cancer Genetics Program at the OSUCCC – James
Benevolent Biomarker

Study Supports IDH Gene as Prognostic Marker in Anaplastic Astrocytoma

New findings suggest that a gene called IDH might be a prognostic marker for a rare form of brain cancer. Patients in this study who had a mutated IDH gene lived an average of 7.9 years after diagnosis vs. 2.8 years for patients with unaltered IDH.

The IDH study was part of the phase III clinical trial RTOG 9813, which involved 301 patients with anaplastic astrocytoma. The dual-arm trial evaluated the effectiveness of radiation therapy plus either of two chemotherapy drugs: temozolomide and nitrosourea.

“We found that IDH status is not only a significant prognostic biomarker for the classification of anaplastic gliomas, but there appears to be a trend in the data that suggests that it might also be an important predictive biomarker for determining which type of chemotherapy patients should receive,” says study co-author Arnab Chakravarti, MD, professor and chair of the Department of Radiation Oncology at Ohio State, and a member of the Translational Therapeutics Program at the OSUCCC – James.

“If this novel finding is verified, it could have a critical influence on future patient care...”

with patients taking nitrosourea after a follow up of 3.6 years on average. However, the study also suggested a trend toward better survival for patients with mutated IDH who received radiation therapy plus temozolomide compared with patients receiving radiation therapy and nitrosourea.

Astrocytomas arise from astrocytes, or star-shaped cells that nourish and support nerve and blood-vessel cells in the brain. Anaplastic astrocytomas are grade III brain tumors that can become grade IV tumors, which are also called glioblastoma. Headaches, seizures, memory loss and behavioral change are early signs of the disease. Other symptoms can occur, depending on where in the brain the tumor develops.

These findings were presented at the 2015 American Society of Clinical Oncology annual meeting in Chicago.
Small Wonders

Chitosan-Coated, Chemotherapy-Packed Nanoparticles May Target Cancer Stem-Like Cells

Nanoparticles packed with a clinically used chemotherapy drug and coated with an oligosaccharide derived from the carapace of crustaceans might target and kill cancer stem-like cells, according to a study led by researchers at the OSUCCC – James.

Cancer stem-like cells have characteristics of stem cells and are present in very low numbers in tumors. They are highly resistant to chemotherapy and radiation, and they are believed to play an important role in tumor recurrence. This laboratory and animal study showed that nanoparticles coated with an oligosaccharide called chitosan and encapsulating the chemotherapy drug doxorubicin can target and kill cancer stem-like cells six times more effectively than free doxorubicin.

“This nanoparticle delivery system increased the cytotoxicity of doxorubicin with no evidence of systemic toxic side effects in our animal model,” says principal investigator Xiaoming (Shawn) He, PhD, associate professor of Biomedical Engineering at Ohio State and a member of the Translational Therapeutics Program at the OSUCCC – James. “We believe that chitosan-decorated nanoparticles could also encapsulate other types of chemotherapy and be used to treat many types of cancer.”

The study showed that chitosan binds with the CD44 receptor on cancer stem-like cells, enabling the nanoparticles to target the malignant stem-like cells in a tumor.

The nanoparticles were engineered to shrink, break open and release the anticancer drug under the acidic conditions of the tumor microenvironment and in tumor-cell endosomes and lysosomes, which cells use to digest nutrients.

He and his colleagues conducted the study using models called 3D mammary tumor spheroids (i.e., mammospheres) and an animal model of human breast cancer.

The study also found that, although the drug-carrying nanoparticles could bind to the variant CD44 receptors on cancerous mammosphere cells, they did not bind well to the CD44 receptors that were overexpressed on noncancerous stem cells.

Reported in the journal ACS Nano.

XIAOMING (SHAWN) HE, PHD, associate professor of Biomedical Engineering at Ohio State and a member of the Translational Therapeutics Program at the OSUCCC – James

To refer a patient, please call The James Line New-Patient Referral Center toll free: 1-800-293-5066
JANICE KIECOLT-GLASER, PhD, Distinguished University Professor of Psychology and Psychiatry, and director of the Ohio State Institute for Behavioral Medicine Research, has received a five-year, $3.2 million NCI grant (CA186251) to study how physical fitness influences inflammation, negative mood, fatigue, increased pain sensitivity and cognitive deficits in breast-cancer survivors.

KUN HUANG, PhD, associate professor of Biomedical Informatics, has received a three-year, $1.2 NCI grant (CA188547) to develop software tools that will integrate histologic features and genetics and help clinicians and researchers identify the most effective therapy for a patient’s particular cancer.

NADUPARAMBIL JACOB, PhD, assistant professor of Radiation Oncology, has received a three-year, $1.7 million grant from the U.S. Department of Defense’s Congressionally Directed Medical Research Program titled “Minimally Invasive Radiation Biodosimetry and Evaluation of Organ Responses.”

TONYA ORCHARD, PhD, RD, assistant professor in the College of Education and Human Ecology, A. COURTNEY DEVRIES, PhD, and MARYAM LUSTBERG, MD, assistant professor of Medical Oncology, were awarded a four-year, $2.1 million NCI grant (CA189947) to study whether dietary supplementation with omega-3 fatty acids prevents neuroinflammation in an animal model and cognitive deficits in women receiving chemotherapy after breast-cancer surgery.

MICHAEL OSTROWSKI, PhD, professor and co-leader of the Molecular Biology and Cancer Genetics Program at the OSUCCC – James, was awarded a five-year, $2.2 million grant (AR044719) from the National Institute of Arthritis and Musculoskeletal and Skin Diseases to study how the differentiation and function of osteoclasts are governed.

QUINTIN PAN, PhD, associate professor in the Department of Otolaryngology – Head and Neck Surgery, has received a $2.4 million grant (DE023555) from the National Institute of Dental and Craniofacial Research to study the role of the p300 protein in HPV-positive head and neck cancer.
ZUI PAN, PhD, research associate professor in Internal Medicine, and TONG CHEN, MD, PhD, assistant professor of Internal Medicine, received a five-year, $1.6 million grant (CA185055) to examine how the calcium channel protein Orai1 contributes to esophageal tumor initiation and progression, and whether it can be used as a biomarker for detection and prognosis.

ELECTRA PASKETT, PhD, MSPH, associate director for population sciences and co-leader of the Cancer Control Program at the OSUCCC – James, has received a five-year, $3.2 million NCI grant (CA196243) to compare an interactive computer program delivered on DVD versus the DVD program plus telephone-based patient navigation versus usual care. The goal is to increase screening rates for breast cancer, cervical cancer and colorectal cancer in older women in rural counties of Ohio and Indiana.

JENNIFER WOYACH, MD, (left) assistant professor in the Division of Hematology, and AMY JOHNSON, PhD, associate professor in the Division of Hematology, have received an NCI grant (CA197870) to improve therapy that targets Bruton’s tyrosine kinase for patients with chronic lymphocytic leukemia (CLL).

AWARDS AND HONORS

ERICA BELL, PhD, research assistant professor in Radiation Oncology, was honored by the American College of Radiation Oncology (ACRO) for having the highest-rated paper overall among faculty-level researchers at ACRO’s 2015 Annual Meeting. The paper is titled “A Novel miRNA-Based Predictive Model for Biochemical Failure Following Post-Prostatectomy Salvage Radiation Therapy.”

CLARA D. BLOOMFIELD, MD, a Distinguished University Professor who also serves as a cancer scholar and senior adviser to the OSUCCC – James, was one of 12 winners in the 2015 Giants of Cancer Care awards program sponsored by OncLive, a Web resource for physicians and other health professionals who focus on treating cancer.

CHRISTIN BURD, PhD, assistant professor of Molecular and Cellular Biochemistry and of Molecular Genetics, is among seven scientists to receive the 2016 Damon Runyon-Rachleff Innovation Award. The Damon Runyon Cancer Research Foundation noted that the award recognizes early-career scientists who are “exceptionally creative thinkers” and propose high-risk, high-reward projects. It provides $300,000 over two years. Burd will use a novel method to analyze RAS mutations in different cancers, work that could lead to new drugs that target these mutations.

JOHN C. BYRD, MD, professor and director of the Division of Hematology and co-leader of the OSUCCC – James Leukemia Research Program, received the 2015 Charles G. Moertel Lecture Award from the Alliance for Clinical Trials in Oncology to recognize his contributions to community cancer practice. Byrd was also awarded the 2015 American Society of Hematology’s William Dameshek Prize for contributions to the development of treatments for CLL. In addition, he received the 21st Annual Joseph H. Burchenal Memorial Award for Outstanding Achievement in Clinical Cancer Research at the 2016 Annual Meeting of the American Association for Cancer Research (AACR). As award recipient, Byrd lectured on “Targeting BTK in CLL: A New Treatment Paradigm.”

ARNAB CHAKRAVARTI, MD, professor and chair of Radiation Oncology, was appointed to chair the National Institutes of Health Cancer Biomarkers Study Section. Also, Chakravarti received the American College of Radiation Oncology (ACRO) 2015 Distinguished Service Award for his leadership contributions to ACRO. Chakravarti also presented an invited lecture at the 2015 International Congress for Radiation Research in Kyoto, Japan, and he received the 2016 Lifetime Achievement Award from the Society of Asian-American Scientists in Cancer Research for his sentinel contributions in the realm of translational cancer research and in the brain tumor field.

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CARLO CROCE, MD, and JOHN C. BYRD, MD, have received NCI Outstanding Investigator Awards to help further their work in cancer genetics and leukemia therapy. The multimillion-dollar awards provide long-term support for experienced investigators with outstanding records of productivity.

DELIANG GUO, PhD, assistant professor of Radiation Oncology, led a study published in the journal Cancer Cell that was recognized by the American Cancer Society as one of “10 key breakthroughs and insights for 2015.” Based on this work, which identified a new potential therapeutic target for glioblastoma multiforme, Guo also received a Young Investigator Award from the Society for NeuroOncology.

EWA MROZEK, MD, assistant professor in the Division of Medical Oncology, has received an Advancing Science through Pfizer Investigator Research Exchange (ASPIRE) Breast Cancer Research Awards from Pfizer Inc. Mrozek’s $1.6 million grant will support clinical research investigating IBRANCE® (palbociclib).

MICHAEL OGLESBEE, DVM, PhD, professor and chair of Veterinary Biosciences, was elected an AAAS fellow for contributions to the understanding of virus heat-shock protein interactions.

DANIEL PREVEDELLO, MD, associate professor of Neurological Surgery and director of Ohio State’s Minimally Invasive Cranial Surgery Program, received a Gentle Giant Award from the Pituitary Network Association for exemplary accomplishments in pituitary medicine.

SAMEEK ROYCHOWDHURY, MD, PhD, assistant professor of Medical Oncology and of Pharmacology, received an Early Career Achievement Award from The Ohio State University College of Medicine for his efforts to develop innovative therapies based on genetics, to train the next generation of physician scientists and to solve problems through team science.

JEFF WALKER, MBA, senior executive director for administration at the OSUCCC – James, is serving on the National Comprehensive Cancer Network (NCCN) Executive Committee. The NCCN is an alliance of 27 cancer centers that establishes national clinical oncology practice guidelines.

JESSICA WINTER, PhD, professor of Chemical and Biomolecular Engineering, was elected an AAAS fellow for contributions to the development of magnetic quantum dots for cell imaging and separation.

EVAN WUTHRICK, MD, assistant professor of Radiation Oncology, received the NRG Oncology Best Manuscript Award in 2015 for the paper “Institutional Clinical Trial Accrual Volume and Survival of Patients with Head and Neck Cancer” published in the Journal of Clinical Oncology.

LYNNE ABRUZZO, MD, PhD, professor of Pathology, was elected a fellow of the American Association for the Advancement of Science (AAAS) for contributions to the cytogenomics of chronic lymphocytic leukemia and other hematologic malignancies.

REBECCA JACKSON, MD (left), director of the Ohio State Center for Clinical and Translational Science (CCTS) and a member of the Cancer Control Program at the OSUCCC – James, and ELECTRA PASKETT, PhD, MSPH (right), associate director for population sciences and leader of the Cancer Control Program at the OSUCCC – James, were selected to represent the Women’s Health Initiative (WHI) the 10th Annual Team Science Award from the American Association for Cancer Research (AACR) at its 2016 Annual Meeting from April 16-20 in New Orleans. The national WHI team received this award for its collective efforts that have broadened the understanding of the effects of hormone therapy and nutrition on cancer.
SHARYN BAKER, PharmD, PhD, has joined the cancer program as professor and chair of the Division of Pharmaceutics and Pharmaceutical Chemistry in the College of Pharmacy. She came to Ohio State from St. Jude Children’s Research Hospital.

RAJGOPAL GOVINDARAJAN, DVM, PhD, has joined the cancer program as an associate professor in the College of Pharmacy’s Division of Pharmaceutics and Pharmaceutical Chemistry. His research interests include the role of solute carrier transporters on chemotherapy sensitivity, miRNA drug sensitivity and investigating epigenetic changes in pancreatic cancer cells. He came to Ohio State from the University of Georgia.

DANIEL JONES, MD, PhD, has joined the OSUCCC – James as director of Molecular Pathology. He was also named professor, vice chair and director of Molecular Pathology in the Department of Pathology. He will lead a new division that identifies the genetic changes in patients’ tumors and their significance for selecting therapy and post-therapy monitoring. He came to Ohio State from Quest Diagnostics Nichols Institute.

ANIL PARWANI, MD, PhD, MBA, has joined the cancer program as a professor of Pathology. He is also vice chair and director of Anatomic Pathology in the Department of Pathology. He directs a new digital pathology imaging and pathology informatics core facility, and the OSUCCC – James digital pathology service. He joins Ohio State from the University of Pittsburgh.

ALEX SPARREBOOM, PhD, has joined the cancer program as a professor in the College of Pharmacy’s Division of Pharmaceutics and Pharmaceutical Chemistry. His research interests include transport modulators for platinum-based drugs and tyrosine kinase inhibitors. He came to Ohio State from St. Jude Children’s Research Hospital.

THE OSUCCC – JAMES was ranked among the top 25 cancer hospitals in the nation by U.S. News & World Report in the magazine’s 2015-16 list of “America’s Best Hospitals.” It was the 17th consecutive year that the hospital has made the magazine’s list of the nation’s top 50 hospitals for cancer care.

THE COMMISSION ON ACCREDITATION OF REHABILITATION FACILITIES, or CARF INTERNATIONAL, has accredited Ohio State’s Wexner Medical Center for three years in nine rehabilitation programs, including the Cancer Rehabilitation Specialty Program at the James. The medical center was the first in Ohio, second in the nation and third in the world to achieve this specialty accreditation for Cancer Rehabilitation.

THE OHIO STATE UNIVERSITY was selected as one of 10 members of a national Consortium to Study Chronic Pancreatitis, Diabetes and Pancreatic Cancer. The designation includes $2.3 million in funding over five years and led by DARWIN CONWELL, MD, director of the Division of Gastroenterology, Hepatology and Nutrition.

OHIO STATE’S MULTIDISCIPLINARY PANCREAS PROGRAM, which treats cancerous and non-cancerous conditions, was designated as a National Pancreas Foundation (NPF) Center, one of 30 hospitals nationwide and the only adult hospital in Ohio to earn this distinction.

LEADERSHIP

CLARA D. BLOOMFIELD, MD, and CARLO CROCE, MD, appeared in the Clinical Medicine category on the 2015 list of Highly Cited Researchers compiled by Thomson Reuters.

DAVID CARBONE, MD, PhD, professor of Medicine in the Division of Medical Oncology, was appointed president of the International Association for the Study of Lung Cancer at the 16th World Conference on Lung Cancer.

JEFFREY FOWLER, MD, professor and vice chair of the Department of Obstetrics and Gynecology at Ohio State, where he also holds the John G. Boutselis Chair in Gynecology, began a one-year term as the 48th president of the Society of Gynecologic Oncology (SGO) at the conclusion of the SGO’s Annual Meeting on Women’s Cancer. Fowler, has made gynecologic oncology wellness a priority for his term as president.
The oral microbiome of a smoker. Healthy bacteria (green and blue) and pathogenic bacteria (red and orange) reside on the gum epithelium. Three neutrophils (blue) on the surface work to clear the pathogens. A neutrophil within the epithelial (lower right) releases cytokines to draw more immune cells to the site. The resulting chronic inflammation facilitates cancer development in the epithelial cells. (Note: cells and bacteria not drawn to scale.)
Ecosystem Restoration

Currently, four OSUCCC – James researchers are collaborating to learn whether a food-based approach using a novel black raspberry drink might help prevent oral cancer, with a focus on how the microbiome may play a key role in this relationship.

BY DARRELL E. WARD

Eukaryotic cells and prokaryotic cells have long enjoyed positive, intimate associations—including the most intimate of relationships.

Eukaryotic cells are the fundamental building blocks of the human body, and they prominently feature a nucleus that contains most of their DNA. Prokaryote cells are typically called bacteria. They lack a nucleus, are far smaller than most human cells and are popularly regarded as disease-causing and pathogenic.

Some 1.4 billion years ago, the two cell types shared the ultimate intimate experience: An ancestral eukaryote is believed to have engulfed an ancestral prokaryote. It was the start of something great. The nucleated cell gave the bacteria a stable, cozy place to live, and the bacteria became the energy-producing organelle called mitochondria that have powered eukaryotic-cell activity ever since.

Intimate partnerships between bacteria and the human body continue today, with rapidly emerging research defining the composition and function of various bacterial communities, called microbiomes, that inhabit the mouth, colon, skin and other areas of the body. In fact, the National Institutes of Health’s recently established Human Microbiome Project (HMP) estimates that a healthy human may have nearly as many microbial cells as human cells.

These microbial populations interact with the host, including the immune system, to maintain human health, but when the microbial population is deranged or microbes pass through host mucosal barriers, it can contribute to disease risk—leading the NIH HMP to suggest that the human genome should be broadened to include the genes of its microbes. (Growing awareness of the body’s microbial communities has given rise to the emerging field of microbiomics.)

There is great interest in understanding the role of the microbiome in cancer. Researchers at The Ohio State University Comprehensive Cancer Center –
Arthur G. James Cancer Hospital and Richard J. Solove Research Institute (OSUCCC – James) are carrying out studies investigating whether smoking-related changes in the oral microbiome raise the risk of disease.

Currently, four OSUCCC – James researchers are collaborating to learn whether a food-based approach using a novel black raspberry drink might help prevent oral cancer, with a focus on how the microbiome may play a key role in this relationship.

The study, titled “Interactive Omics: Black Raspberry Metabolites and the Oral Microbiome in Smokers,” is supported by a five-year, $3.1 million grant (CA188250) from the National Cancer Institute.

Co-principal investigators on the study are Purnima Kumar, DDS, PhD, associate professor of Periodontology at Ohio State’s College of Dentistry; Steven Clinton, MD, PhD, The John B. and Jane T. McCoy Chair in Cancer Research and leader of the OSUCCC – James Molecular Carcinogenesis and Chemoprevention Program (MCCP); Steven Schwartz, PhD, professor of Food Science and Technology in Ohio State’s College of Food, Agricultural and Environmental Sciences; and Christopher Weghorst, PhD, professor of Environmental Health Sciences in the College of Public Health.

Oral cancer occurs in more than 260,000 people worldwide and kills 127,000 people yearly. Treatment for the disease is rigorous and often disfiguring and can reduce a person’s ability to chew, swallow and speak. Smoking increases the risk of oral cancer 6 to 27 times. Furthermore, smoking rates are rising in many developing nations, which lack the expertise and resources to effectively treat this cancer.

“We urgently need new approaches to prevent this disease, particularly in high-risk populations such as past and current smokers,” Clinton says.

Earlier work by the team showed that black raspberries can reduce hallmark molecular biomarkers in the oral mucosa associated with increased cancer risk. The bioactive phytochemicals from black raspberries also influence bacterial adhesion and biofilm formation, which may in turn impact the host gene expression of mucosal cells.

For the new study, the team developed and tested a novel black raspberry nectar drink that concentrates and preserves black raspberry phytochemicals, an effort that began with a collaboration with Dale Stokes and family, who manage a large black raspberry farm in Ohio. The novel project will determine whether the drink can restore the altered microbiome typical of smokers to a healthier state and provide a viable cancer preventive intervention.

“This research highlights the advantages of a land grant university,” Clinton adds. “It
involves Ohio State’s College of Food, Agricultural and Environmental Sciences, the College of Dentistry, the College of Public Health and the OSUCCC – James. “All these disciplines are located on one campus, with the investigators integrated through cancer center activities. It illustrates what a cancer center should be doing: bringing diverse talents together to focus on a preventable malignancy like oral cancer.”

**THE ORAL MICROBIOME**

Kumar describes the oral microbiome as an ecosystem composed of some 2 billion organisms and having several distinct niches. For example, tooth surfaces above the gum line, pockets between teeth and gums, the tongue and tonsils each have a specific microbiome with characteristic species. “We’ve shown in previous studies that people of different ethnicities, of different ages or who have diabetes or are obese harbor distinct types of bacterial populations,” she says.

As in terrestrial ecosystems, environmental change can affect the oral ecosystem. “Altered microbial communities underlie the etiology of several oral diseases, especially in smokers,” Kumar says.

“Bacteria that live in a tooth pocket can also be impacted by smoking and cause bone resorption and gum disease, while related bacteria found on the mucous membrane are associated with oral cancer,” she notes.

A study led by Kumar suggested that, in addition to the direct effects of carcinogens on the mucosa, smoking makes the oral cavity less suitable for healthy microbes and encourages growth of pathogenic species. These species induce an inflammatory response that favors cancer development.

A 14-year-old boy has an established, stable, endemic microbiome, she explains. If he begins smoking, it changes the oral environment from oxygen rich to oxygen poor. The pH falls, levels of iron and other metals go up, and chemicals, metals and nicotine enter the bloodstream and circulate through the body.

Oxygen-loving aerobic species die off, and pathogenic organisms that thrive in an oxygen-poor, iron-rich, reducing environment overgrow the community.

“These include bacteria usually found in lung infections such as *Pseudomonas, Haemophilus*,
Acinetobacter," Kumar says. “We think that when a smoker coughs heavily, these bacteria may colonize the oral cavity.”

Many of the bacteria found in the microbiome of smokers have potent virulence factors and promote an inflammatory response in the host tissues. These changes may be identified by a specific series of changes in gene expression within the host oral mucosa, long before the development of cancer.

Once smoking alters the microbiome and an inflammatory process begins, the continued exposure to tobacco smoke promotes a vicious, self-perpetuating cycle that ultimately changes the oral mucosa and promotes the development of a cancer.

**BLACK RASPBERRY EFFECTS**

The OSUCCC – James has a long history of research on the effects of the role of black raspberry phytochemicals in cancers of the aerodigestive tract. These fundamental studies, led by Weghorst, Clinton, Schwartz and others led to the newly funded project on black raspberry phytochemicals and oral cancer at the OSUCCC – James.

The studies included developing various black raspberry food products, an effort led by Yael Vodovotz, PhD, a member of the OSUCCC – James MCCP and professor of Food Science and Technology. These food products, which range from confections to the nectar, have been tested in several clinical trials, suggesting that black raspberry foods provide for high patient compliance and demonstrate that the pattern of phytochemicals might be effective in cancer prevention.

The MCCP, along with funding from Pelotonia—an annual bicycling fund-raiser for cancer research at Ohio State—was instrumental in this intersection of food-product development research, preclinical anticancer laboratory testing and fundamental research on the oral microbiome.

An example of a supportive berry study was led by MCCP member Thomas Knobloch, PhD, a collaborator on the new study, and on a study recently published in the journal *Cancer Prevention Research*. It provided strong evidence for a gene-expression signature that is altered by black-raspberry phytochemicals.

The study involved 38 patients with oral squamous cell carcinoma. The patients took slow-release black-raspberry lozenges, made from freeze-dried black raspberry powder, four times a day from their diagnosis through surgery to remove the cancer (mean duration 14 days).

The researchers learned that the berry treatment significantly reduced the expression of genes...
that promote inflammation and inhibit apoptosis. “Our findings also showed that critical anticancer compounds in black raspberries were present in the tumor tissue,” Weghorst says. This work was critically supported by highly sensitive analytical chemistry provided by Schwartz, director of the OSUCCC – James Nutrient and Phytochemical Shared Resource. The current study, however, focuses on smokers and nonsmokers at high risk for oral cancer. It is designed to learn whether consumption of the black raspberry nectar, which is high in bioactive compounds, can inhibit or reverse damage to the oral microbiome and mucosa caused by tobacco smoke.

Within that, the researchers want to understand the mechanisms by which black raspberries act. To investigate this, the Clinton, Kumar, Schwartz and Weghorst laboratories are teasing out the interactions between oral mucosal cells, the microbiome and the berries.

Key questions include whether the bacteria in smokers and non-smokers metabolize and further activate the berry phytochemicals or inactivate them, which would alter the preventive effect. “We’re using metabolomics to answer those questions,” Schwartz says.

On the flip side, the researchers want to learn whether the berries influence the microbiome population. Do they perhaps restore the smoker’s microbiome to a healthier state or reduce the impact of tobacco on the microbial population?

“Investigating all these interactions is really exciting and will provide fundamental findings on how foods, tobacco and the microbiome interact to impact cancer risk,” Weghorst says.

The researchers believe their findings will reveal whether oral bacteria influence the formation of black raspberry bioactive substances and will provide a

**CLINICAL TRIAL**

To explore questions related to the oral microbiome, Clinton, Kumar and the team have initiated a clinical trial involving 120 men and 120 women divided into four groups, with 30 males and 30 females in each. Two groups are smokers and two groups are nonsmokers.

One group of smokers and one group of never-smokers consume eight ounces of black-raspberry nectar daily for 12 weeks; the remaining smokers and never-smokers consume a similarly packaged placebo:

- **60** Never smokers + nectar
- **60** Smokers + nectar
- **60** Never smokers + placebo
- **60** Smokers + placebo

Yael Vodovotz, PhD, a member of the OSUCCC – James Molecular Carcinogenesis and Chemoprevention Program and professor of Food Science and Technology, developed the nectar. Initial testing demonstrated excellent compliance and feasibility, so it was chosen as the optimal agent for the large study.

Vodovotz used state-of-the-art food science technology available at Ohio State to develop the beverage. Each 8 oz. serving contains 10 grams of freeze-dried black-raspberry powder rich in bioactive black-raspberry phytochemicals. She and her lab also developed the placebo beverage using raspberry flavoring and color.

Before the berry treatment begins and at the end of week 1 and week 12, the researchers collect oral-cavity samples from each participant for the “omics” analyses, which include:

- Genomic and transcriptomic sequencing studies by Kumar’s lab of biofilm scrapings to learn how the oral microbiome responds structurally and functionally to the nectar treatment;
- Metabolomic studies of saliva samples by Schwartz’s lab for physiological and food-derived metabolites to learn the impact of smoking on berry metabolism;
- Transcriptomic studies by Weghorst’s lab before and after berry treatment to evaluate mucosal gene expression in response to nectar and tobacco exposure.
“Key questions include whether the bacteria in smokers and non-smokers metabolize and further activate the berry phytochemicals or inactivate them, which would alter the preventive effect. We’re using metabolomics to answer those questions...”

STEVEN SCHWARTZ, PHD, professor of Food Science and Technology in Ohio State’s College of Food, Agricultural and Environmental Sciences

panel of bacterial markers for black raspberry exposure and validated timelines for berry treatment during a future phase III clinical trial in patients at high risk for oral cancer.

In the end, the researchers hope to find that carefully designed food products, such as those with black raspberries, offer a practical strategy that can prevent the initiation and progression of oral cancer in conjunction with smoking-cessation strategies.

“We’re looking for biomarkers and potential mechanisms that can be tested in a long-term phase III clinical trial,” Weghorst says.

“Our study will also help accomplish our long-term goal of developing food-based strategies for disease prevention, point-of-care diagnostics and biological metrics for successful treatment outcomes in high-risk populations,” Clinton says.

“Once the mechanisms of carcinogenesis are worked out, it might lead to valuable biomarkers that can define risk for each individual and perhaps identify new prevention or therapeutic targets,” Kumar says. “That’s the ultimate goal of all this research, of course: stopping cancer before it becomes a clinical entity.

“The oral microbiome is the canary in the coal mine,” she adds. “A smoker who is healthy might have no disease, but his microbiome tells us he’s at risk for disease.

“Keeping your oral microbiome healthy and stable is another reason to avoid smoking, and for people who do smoke to quit. Otherwise you develop a hyperinflammatory state that can quickly lead to disease. So it helps to think about the oral cavity and our other microbiomes as ecosystems, because it encourages you to keep them well,” she says.

Efforts like this study by Clinton, Kumar, Schwartz and Weghorst to understand the role of the microbiome in health and disease are just the first wave of discovery.

“Next, we have to learn how we can alter these microbial ecosystems, not just in the oral cavity but in other tissues as well, in order to treat or prevent disease,” Clinton says.

“This is a whole new world of possibilities regarding how diet and nutrition impact cancer, and it opened up in just the last few years due to the exciting advances in defining the structure and function of various microbiomes.”
Medical advances of the past few years have doubled the one- to two-year overall survival rate for patients with pancreatic cancer, a specialist at The Ohio State University reports.

“This is a substantial advance for patients with a cancer that has historically had such a dismal prognosis,” says Richard M. Goldberg, MD, referring to a malignancy that ranks as the 12th most common cancer but third leading cause of cancer-related death among men and women in the United States, with an overall five-year survival rate of only 7 percent.

Goldberg, a gastrointestinal (GI) oncologist and physician-in-chief at The Ohio State University Comprehensive Cancer Center—James Cancer Hospital and Solove Research Institute (OSUCCC – James), says advances leading to the improved one- to two-year survival rate have come through steady progress in pancreatic cancer research at the OSUCCC – James and elsewhere.

In a 2015 editorial in the Journal of the National Cancer Institute, Goldberg and his collaborator, Tanios Bekaii-Saab, MD, stated that new drug combinations are “shifting the treatment landscape for this disease,” giving physicians and their patients more choices for managing pancreatic adenocarcinoma.

In addition, they noted that recently identified predictive biomarkers might help doctors stratify patients for treatment and choose those most likely to benefit from the variety of regimens showing activity in the disease.

MAKING A DIFFERENCE

At Ohio State, the expanding GI Oncology Program offers care to a growing number of patients—the program currently sees nearly 1,300 new patients per year and schedules nearly 20,000 patient visits annually.

“As the third largest cancer hospital in the country, we see a huge volume of patients with cancer who cross the entire spectrum of tumors originating in the GI tract, from the esophagus to the anus,” Goldberg says, noting that Ohio State’s Division of Medical Oncology includes a section for...
GI oncology with eight physicians and a translational researcher. “Conservatively, 20-30 percent of our GI volume is pancreatic cancer.”

Darwin Conwell, MD, director of the Division of Gastroenterology, Hepatology and Nutrition at Ohio State, has hired several gastroenterology physicians with cancer focus for the GI clinics.

“From the time we started this, we’ve experienced a significant growth in the GI field, particularly pancreatic cancer,” Conwell says. “One of the strengths of our program is we have a multidisciplinary program that incorporates surgical, radiation, medical and interventional aspects of care.”

In addition, we have 11 to 15 surgeons and four radiation oncologists who work with us on patients with GI cancers. We have seen quite an expansion among patients with these diagnoses looking to our specialists for care,” Goldberg says.

In 2015 the university was chosen as one of 10 members of a national Consortium for the Study of Chronic Pancreatitis, Diabetes and Pancreatic Cancer. The NCI and the National Institute of Digestive and Diabetes and Kidney Disorders will provide $2.3 million in funding over five years (DK108327), with Conwell as principal investigator.

Left untreated, chronic pancreatitis can cause irreversible fibrosis and destruction of pancreatic tissue, potentially leading to malnutrition, abdominal pain, Type 3c diabetes mellitus (T3cDin) and, over time, to pancreatic cancer. Consortium members will conduct studies on chronic pancreatitis and factors that increase the risk of pancreatic cancer in children and adults with chronic pancreatitis and with T3cDM.

Conwell is principal investigator (PI) for the Ohio State consortium; co-PIs are Philip Hart, MD, and Gregory Lesinski, PhD, MPH.

Also, Ohio State’s multidisciplinary pancreas program, which treats both cancerous and non-cancerous conditions, has been designated as a National Pancreas Foundation (NPF) Center. It is one of 30 hospitals nationwide and the only adult hospital in Ohio to earn this distinction. The program is a collaboration of the Ohio State Wexner Medical Center and the OSUCCC – James.

“This major achievement demonstrates that we are one of the most comprehensive pancreatic disorders clinics in the nation,” Conwell says. “Our center is more robust than the minimal NPF requirements, housing a multidisciplinary pancreatic disorders clinic that includes GI oncology, surgical oncology, radiation oncology and advanced abdominal imaging.”

CLINICAL RESEARCH
Pancreatic cancer researchers at Ohio State are studying immunotherapeutic approaches, molecularly targeted therapies, the use of genomic selection data to define cancer pathways, and strategies for combating cachexia, a muscle-wasting condition common in patients with pancreatic and other GI cancers.

“We provide multiple clinical trials for pancreatic cancer, many of which are ideas initiated by our own faculty members, who then lead national clinical trials efforts. By collaborating with our colleagues in basic science laboratories, we also have studies under way that link treatments to the basic biology of this disease,” Goldberg says.

“Clinical trials for every stage of pancreatic cancer and every line of therapy are available at The James, from radiation to immunotherapy to chemotherapy.”

Examples include trials that incorporate PD-1 (programmed cell-death protein 1) inhibitors, which stimulate the immune system to kill tumor cells. “PD-1 inhibitors allow the patient’s own immune system to recognize cancer as a foreign invader, permitting the immune system to destroy tumors,” Goldberg says. “As we learn how to use these tools most effectively, these agents are likely to be an increasingly important part of our future treatment regimens in combination with standard cytotoxic chemotherapies, even for early-stage disease.”

REDUCING TREATMENT TOXICITY
Pancreatic cancer is typically diagnosed after it has metastasized, when the five-year survival
rate is only 2 percent. New treatments are badly needed. In 2013, findings from a multicenter phase III Metastatic Pancreatic Adenocarcinoma Clinical Trial (MPACT) led to FDA approval of an agent called nab-paclitaxel combined with the standard-of-care drug gemcitabine for metastatic cancer.

But while this regimen improved survival, it also resulted in more toxicities than gemcitabine alone, reducing quality of life. Seeking a safer treatment, OSUCCC – James researchers recently reported the results of a study that showed administering the regimen every other week may reduce the toxic effects while maintaining effectiveness. These findings were presented at the 2015 American Society of Clinical Oncology (ASCO) Gastrointestinal Cancers Symposium and are under review for publication.

“The modified regimen is easier to administer and results in fewer neurological side effects and less compromise of the patient’s immune system while maintaining positive effects on the overall survival and lengthening the time to progression of tumors in our patients,” Goldberg says. “It also means fewer visits to the infusion center, leading to a reduction in each patient’s medical costs by about $5,500 per month.” He notes that these results are intriguing preliminary findings that will need to be confirmed in a larger randomized trial.

SURGERY FOR LOCALLY ADVANCED DISEASE

Surgical oncologist and OSUCCC – James researcher Carl Schmidt, MD, is leading a clinical trial (NCT02446093) to determine whether adding a modified herpes virus called GMCI to a neoadjuvant chemotherapy regimen (modified FOLFIRINOX) followed by chemoradiation is safe and benefits patients with borderline resectable and unresectable locally advanced pancreatic adenocarcinoma.

“The protocol is designed to deliver multiple courses of GMCI timed with a series of neoadjuvant debulking therapies to capitalize on the synergy produced by these different treatment modalities,” Schmidt says.

The adenovirus vector delivers a herpes simplex enzyme to the cancer cells that activates a prodrug, which then generates nucleotide analogs that kill the cancer cells. The dead cells release tumor antigens that stimulate a tumor-specific immune response that will help clear micrometastatic disease. “We hope that this regimen will make more patients treatable with surgical resection,” Schmidt says.

TRANSLATIONAL RESEARCH

In the December 2015 issue of the Journal of the National Cancer Institute, OSUCCC – James researchers reported a preclinical study showing that an experimental agent developed at Ohio State may stop the muscle-wasting process that patients often develop, which is called cancer cachexia, and that this intervention can restore muscle health.

The agent, AR-42, is a histone deacetylase (HDAC) inhibitor. It blocks the expression of genes that play a key role in skeletal muscle breakdown. The study team—which includes Samuel Kulp, DVM, PhD; Pearly Yan, PhD; Gregory Lesinski, PhD, MPH; Denis

CARL SCHMIDT, MD,
Surgical oncologist and OSUCCC – James researcher

“We hope that this regimen will make more patients treatable with surgical resection...”
in mice,” Goldberg adds. “We’re building a pancreas cancer mouse model to further test this and are in the process of designing our next clinical trial with AR-42 in pancreatic cancer. Cachexia is the cause of death in 30–40 percent of pancreatic cancer patients. If we have an agent that reverses cachexia and has anticancer activity, it’s a double win. We believe AR-42 has both properties.”

**MEK INHIBITION**

Over 90 percent of pancreatic cancers express KRAS oncogene mutations that activate the Raf-MEK-MAPK genetic pathway and confer resistance to radiation and chemotherapy. Because MEK inhibitors have shown promising antitumor responses in recent preclinical and clinical studies, OSUCCC – James researchers evaluated a MEK1/2 inhibitor called GSK212 and found that it suppressed major DNA repair pathways in KRAS-driven pancreatic cancer cells, making them more sensitive to radiation.

The team, led by Terence Williams, MD, PhD, assistant professor in the Department of Radiation Oncology, reported the findings in the journal *Cell Cycle*, concluding that a clinical trial combining MEK1/2 inhibition and radiation in the treatment of pancreatic cancer is warranted.

**JAK2 INHIBITION**

A biorepository of more than 500 tissue samples drawn from patients at different treatment stages enables OSUCCC – James researchers to conduct studies that are shedding light on the biology and immunology of pancreatic cancer. OSUCCC – James researcher Gregory Lesinski, PhD, MPH, associate professor in the Division of Medical Oncology, recently led a study published in the journal *Oncotarget* that revealed the promising anticancer effects of a Jak2 inhibitor in mice with pancreatic cancer.

“The Jak/STAT pathway is activated in human pancreatic ductal adenocarcinoma (PDAC) and cooperates with mutant KRAS genes to drive initiation and progression of PDAC in mouse models,” wrote the investigators, led by Lesinski and first author Thomas Mace, PhD, a research scientist at Ohio State. “We hypothesized that the small-molecule Jak2 inhibitor (BMS-911543) would elicit antitumor activity against PDAC and decrease immune suppressive features of the disease.”

Their results “indicate that Jak2 deserves further study in preclinical models of PDAC and has distinct inhibitory effects on STAT5-mediated signaling that could alter immune aspects of this disease.”

**MORE FUNDING NEEDED**

“Federal funding for pancreatic cancer research has increased dramatically from where it was just a few years ago, but the disease still remains a lethal one,” Goldberg says.

The NCI estimated that about $102 million would be spent on pancreatic cancer research in fiscal 2013, but Goldberg would like to see more resources go into research in this area.
“We need to increase awareness that pancreatic cancer is not necessarily lethal for all patients, and that many of those who get the diagnosis will benefit from being assessed and treated...”

“While it sounds like a lot, it’s not close to the resources devoted to research in breast or lung cancer, for example,” he says, especially since the incidence of this disease is expected to rise to about 100,000 cases per year by 2030 due to the aging population (median age at diagnosis is 71) and to a lack of preventive measures and methods for routine screening. A study published in the June 2014 issue of the Journal Cancer Research states that PDAC is projected to become the second leading cause of cancer-related deaths in the United States by 2030.

“The low survival rate means we have few long-term survivors who can step forward and advocate for resource investment,” Goldberg says. “Plus, some people think, ‘Why spend money on a disease where efforts to date have led to only incremental improvements in outcomes?’ However, if we don’t incentivize researchers by spending money on this problem, outcomes will remain where they are today.”

Fortunately, he adds, successes with new drug regimens have prompted pharmaceutical companies to start testing more of their products in pancreatic cancer, which should lead to more clinical trials that may advance the field if enough patients are accrued.

“We need to increase awareness that pancreatic cancer is not necessarily lethal for all patients, and that many of those who get the diagnosis will benefit from being assessed and treated,” he explains. “An estimated 20-30 percent of patients who are diagnosed with this disease never see an oncologist and are never treated.

“So we’re not capturing all of the patients that we should,” he adds. “The more we see, the more can be helped, and survival numbers may improve. More patients need to be on clinical trials. We have those trials available at Ohio State, and we’re willing to share them with the community.”

Pointing out that results from an international study called NAPOLI-1 recently led the FDA to approve yet another regimen for patients with metastatic pancreatic cancer (MM-398 in combination with 5-fluorouracil and leucovorin following prior treatment with a gemcitabine-based regimen), Goldberg says clinical progress against this disease should be encouraging to all.

“Several years ago, we essentially had one option, gemcitabine,” he says. “But studies such as ACCORD11, MPACT and NAPOLI-1 have given us stronger regimens with newer drug combinations. The treatment landscape is shifting from nihilism and futility to optimism, and we are finally moving the needle against pancreatic cancer.

“Today, we have stronger chemo therapeutic backbones to work with, and I think we are more likely to induce meaningful responses with new combinations of biologic and immunologic agents. This is an exciting time for treatment of pancreatic cancer, a time for optimism.”
An OSUCCC – James physician-researcher contributes to his father’s program to improve education and health care in an African village, an effort that is a model of educational improvement, economic development and sustainability.

BY ERIC BUTTERMAN

Like many African countries, the West African nation of Cameroon struggles to provide health care in general and cancer care in particular.

The nation’s 22.2 million people had a life expectancy for both sexes combined of 56 years in 2012, according to the World Health Organization. The leading causes of death were HIV/AIDS, lower-respiratory tract infections, diarrheal diseases, malaria, stroke and ischemic heart disease. Leading causes of cancer death were breast, cervical, prostate, non-Hodgkin lymphoma, ovarian and liver.

In terms of the healthcare providers, Cameroon has eight physicians per 100,000 people (versus 245 in the United States), and 44 nurses and midwives per 100,000 people. In terms of technology, the nation has 0.6 CT scanners and 0.1 radiation therapy units per million Cameroonians, and 17.4 mammography units per 1 million women.

The nation has virtually no cancer screening and prevention programs and few treatment options for those who develop cancer.

Patrick Nana-Sinkam, MD, a lung-cancer specialist at The Ohio State University Comprehensive Cancer Center – Arthur G. James Cancer Hospital and Richard J. Solove Research Institute
“...The people will know they have more places to turn for help to stop some problems before it becomes much larger for preventive services and to address acute issues. It will hopefully give those in the village a better sense of security for them and their families.”

(OSUCCC – James) has roots in the Cameroonian village of Bangou, and he is working with his father to improve the healthcare situation.

His father, Professor Samuel Nana-Sinkam, began a foundation in 2010 dedicated to providing educational opportunity for Bangou’s children, improve health care and provide jobs while sustaining the foundation. The approach he is using could provide a model for sustainable improvements in health care and education in other under-resourced areas as well.

Prof. Nana-Sinkam was born in Bangou, which is located in Cameroon’s western highlands about 170 miles northwest of the capital Yaoundé. His family has lived there for generations. The village’s 10,000 to 15,000 inhabitants are mainly subsistence farmers who live in homes of mud brick and thatch roofs and survive on less than $2 per day.

Dr. Patrick Nana-Sinkam, who is associate director of the Thoracic Oncology Center at the OSUCCC – James, is helping plan and design the village’s first ambulatory care clinic.

“Historically, health care in the village has been provided by a few small, state-owned centers staffed by a nurse and supplied with a few basic drugs,” Nana-Sinkam says. “They meet only the simplest medical needs.” The nearest hospital is 20 miles away.

“The new ambulatory health center will open in July and provide year-round health care,” he says. The first floor will have clinic space that includes several rooms for patient consultations, a pharmacy and a chemistry lab equipped for basic clinical tests such as glucose, complete blood counts, serum profiles and urinalysis. “We plan to have a general internist available daily,” Nana-Sinkam says. “We may add needed subspecialists and dental services at some frequency in the future.”

A second floor will have apartments for doctors.

“[The care provided by the clinic will be unbelievably important for the village,” says Nana-Sinkam, “but it also stands for something. The people will know they have more places to turn for preventive services and to address acute issues. It will hopefully give those in the village a better sense of security for them and their families.”

AN AFRICA STORY RARELY HEARD

The ambulatory health center is underwritten by the Charles Sinkam Foundation, the foundation that was started by Prof. Nana-Sinkam. The foundation is

PATRICK NANA-SINKAM, MD, associate professor of Medicine and member of the OSUCCC – James Translational Therapeutics Program at The Ohio State University Comprehensive Cancer Center – Arthur G. James Cancer Hospital and Richard J. Solove Research Institute.

PROFESSOR SAMUEL NANA-SINKAM
directed by Dr. Djomo Armel, a well-respected local cardiologist.

Prof. Nana-Sinkam's story is one of a promising young man, helped by his extended family, who leaves his village, accomplishes much and returns to help others.

Prof. Nana-Sinkam's father, Charles Sinkam, stressed the importance of education. Samuel showed promise in primary school, and family—aunts, uncles, cousins, along with his parents—rallied their resources to help him attend secondary school at College of St. John the Baptist in Bangou, then complete pre-university studies in Yaoundé.

He attended college in France, earning a PhD in Economics, Development Theory and Practice, from the University of Poitiers, along with a master's degree in Statistics and Econometrics from the National Institute of Statistics and Economic Studies (INSEE) in Paris.

For a time, he served as Minister of Economics and Finance in Cameroon, then worked with the United Nations Food and Agricultural Organization (FAO). Next, he worked for the International Monetary Fund (IMF). The family lived outside of Washington, DC. There, he attended George Washington University, earning a second PhD in Economics, Monetary and Finance.

“As a child, I remember waking at 3 a.m. and seeing him studying at the dining room table,” Nana-Sinkam says. “By 6 a.m., he'd be dressed and go to work. On Saturday and Sunday, he slept.”

At the IMF, he was promoted to executive director, representing more than 27 African countries. He was also a professor at the University of Dauphine in Paris, and a senior risk analyst and adviser with Chase Manhattan Bank New York.

His career included being appointed by United Nations Secretary General Koffi-Annan as special representative in Guinea-Bissau in a peace-keeping mission during that country's civil war. And he served as director of the Joint FAO/ECA Department in the United Nations Economic Commission for Africa; as a member of the executive committee of the Club of Rome; and as FAO country director in Democratic Republic of Congo and other African countries. This work often took him into conflict areas where he worked to ensure fair democratic elections.

**IMPROVING EDUCATION**

Yet, he returned to Bangou yearly when possible, and he helped family members with education and health needs. He founded the Charles Sinkam Foundation to do more, focusing first on providing educational opportunity to village children.

"Many leave school very early because families just can't afford it," Prof. Nana-Sinkam says. "I wanted to help students in a meaningful way. We provide scholarships to top students to try to keep them in school, and we even provide some with college scholarships.”
The foundation’s attention then turned to improving health care.

**MEDICAL DAYS**

It began in July 2011 when the foundation held its first Medical Days. During the two-day event, the foundation opens its doors to the sick and injured, to all who need medical care.

Since 2011 it’s been held twice a year, in July and December. Care and prescriptions are provided at no charge. People come from all parts of Cameroon, some as far as 250 miles away.

Nana-Sinkam notes that physicians who participate come from all over Cameroon and range from general practitioners to specialists such as a cardiologist, pediatrician, rheumatologist, hematologist and ophthalmologist.

“We first triage patients—we check vitals and test glucose and other basic parameters, then direct the person to the appropriate subspecialist,” Patrick Nana-Sinkam says. Basic surgeries such as hernia repair are performed, and the local dental school sends its mobile dental unit, staffed by dentists and dental students for onsite care.

The foundation has hosted eight Medical Days in all, and some 19,000 people have sought care. Common illnesses treated have included hypertension, degenerative joint disease and pediatric diarrheal illness. Treatments included 250 surgeries and 400 dental extractions. In December 2015, prostate and cervical screenings were offered for the first time. In July 2016, breast self-exam will be taught.

Nana-Sinkam has been impressed with the local internists who assist during Medical Days. “In the absence of the tests and diagnostic equipment we take for granted...

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**It Begins With Education**

Professor Samuel Nana-Sinkam regards the educational focus of the Charles Sinkam Foundation as among the most important. One school was a particular triumph.

“We chose one high school in the village that was scheduled to close because it had only 70 students in the sixth to ninth grades,” explains Samuel Nana-Sinkam. “We set up a test for students entering sixth grade, and the 30 best students passing the test received a scholarship and books.”

The next year they repeated the system. The best of the sixth graders who were entering seventh grade received a scholarship and books. In the meantime, the tenth-grade class was opened through the process.

After three years, the high school presented twelfth-grade students for the national test to enter the university. In the end, the students from the village achieved an 85-percent success rate and ranked No. 2 in the nation. The foundation offers scholarships to the top three to go to the university. The next year, the school ranked first.

The educational focus is also tied into Medical Days—the day before the event, students ranging from sixth grade to those graduating from high school are given scholarships. “This isn’t just top students overall, but those who excel in particular areas, such as mathematics and science,” says Prof. Nana-Sinkam.

The younger Nana-Sinkam sees these educational hopefuls as the core of what the Foundation is about—and what his father is about.

“You see a man who built a life through perseverance, and who has succeeded by many measures,” Patrick Nana-Sinkam says. “This is where his life started and education partly propelled him. Then you can’t help but be proud of these young people and what they have been able to achieve. It’s exciting to think about where they could be going.”
in high-resource counties, they rely heavily on clinical acumen, on sound and touch and on a familiarity with local illnesses. And they are very good at it.”

In addition, three or four children have been referred for open heart surgery, which is available at just one hospital in central Cameroon, Nana-Sinkam says. The foundation paid the children’s transportation to the hospital and for the surgery.

“The children have done wonderfully. They’re in school and enjoying friends,” Nana-Sinkam says.

“It has been an incredible experience—the level of excitement and commitment offers tremendous hope for the community, and they start looking forward to it weeks and months in advance,” Nana-Sinkam says.

A NUCLEUS OF HOPE

That excitement is well-founded. In fact, Medical Days is a multi-day demonstration of hope and caring. Four days are planned for July 2016.

Day 1 Academic scholarships are awarded
Day 2 Cancer screening and education
Day 3 and Day 4 Both are medical days that provide onsite general medical care and subspecialty care.

“I never thought it would become what it has,” Prof. Nana-Sinkam says. “It works because people are tremendously dedicated to it. They put other things aside and focus on what we’re trying to do. I’m grateful that they care as much as they do.”

ECONOMICS

The foundation covers the cost of Medical Days activities. The doctors who take part come mainly from across Cameroon and work under a locum tenens agreement, a legal mechanism for temporary physician help. They are paid $150 for the two days (internists in Cameroon typically receive $400 per month). The foundation also pays for the doctors’ meals and housing.

To make the foundation sustainable and provide economic benefit to the village, the foundation started several initiatives:

- A bank that offers microfinancing—small, low-interest loans—to help small businesses;
- A brick factory, which takes advantage of local resources and provides work for people in the community;
- A syringe factory, because the need is great and there are no such factories in central Africa;
- Planned: A grain mill to make animal feed.

These initiatives should mean a bright future for the Charles Sinkam Foundation, the people of Bangou and perhaps the entire country.

“The Medical Days event has received attention from local government and national government as well,” Patrick Nana-Sinkam says. “We believe strongly that every human is on Earth with a purpose and no one should go through that journey without leaving a positive contribution to be remembered.”
OSU-15004: A Phase 1b Trial of AR-42 with Pomalidomide in Relapsed Multiple Myeloma

HYPOTHESIS: AR-42, a histone deacetylase inhibitor (HDACi), in combination with an immunomodulator will increase response to therapy in patients with refractory multiple myeloma. Research has shown that AR-42, a drug designed at The Ohio State University, improves uptake of immune modulatory agents by downregulating CD44. Immune modulators then exert an antimyeloma effect by downregulating the IKZF1-IRF4-c-Myc pathway. OSU-15004 tests this hypothesis through the combination of AR-42 and the immunomodulator pomalidomide in relapsed multiple myeloma patients. The trial will identify the maximum tolerated dose and the dose-limiting toxicities of this regimen. Because most myeloma patients are already exposed to immune modulator lenalidomide, a frontline therapy, this trial focuses on pomalidomide and uses therapeutic concentrations of both pomalidomide and AR-42, even at the starting dose level.

RATIONALE: Multiple myeloma (MM) is the second most common hematologic malignancy, with approximately 22,000 new cases diagnosed annually in the United States. There is no cure for the disease, and many patients will relapse and become refractory to the first-line therapies, lenalidomide and bortezomib. Prior to the availability of carfilzomib and pomalidomide, MM patients refractory to both lenalidomide and bortezomib had an event-free survival of approximately 5 months and an estimated median overall survival of 9 months. The median overall survival has been extended with the use of pomalidomide and carfilzomib to over 15 months. Unfortunately, patients eventually become resistant to these drugs, so new agents with novel mechanisms of action are needed.

More recently, the HDACi vorinostat (SAHA) has been tested in phase II and III trials and has been shown to improve progression-free survival and overall survival in multiple myeloma, but patients have experienced serious side effects. AR-42 demonstrated a 20,000-fold improvement in deacetylase inhibitory potency relative to its parent molecule, and it has shown greater antiproliferative effects than vorinostat in vitro and in vivo. It promotes both histone H3 and H4 lysine acetylation and tubulin acetylation. Our preliminary data also show that AR-42 has a specific, dose-dependent, antimyeloma activity compared to vorinostat and other pan-HDACi.

Use of ASCO's mailing list should not be construed as ASCO's endorsement of this trial or approval of the advertising materials that are distributed. Materials advertising clinical trials may require approval by a local or central Institutional Review Board (IRB). For more information, please consult the policies of the individual institutions involved in the trial. Permitted use is limited to the correspondence and parties submitted.
The OSUCCC Biospecimen Services Shared Resource (BSSR) supports OSUCCC – James researchers by storing, organizing and dispensing biospecimens such as tumor and normal tissue, blood and serum samples, and associated clinical data.

One of the BSSR’s two arms focuses on the Total Cancer Care® (TCC) protocol; the other focuses on prospectively procured biospecimen samples. Prospectively procured biospecimen samples are obtained by the Ohio State Wexner Medical Center’s Tissue Procurement Service following a surgery at the OSUCCC – James.

THE TCC PROTOCOL
TCC is a universal consent and biorepository protocol that allows the collection of blood in conjunction with clinically indicated draws and remnant tissue from surgical procedures from patients 18 years of age and older, with and without cancer, who are seen at The James.

The protocol provides broad informed consent and allows access to pathologic and clinical data for the life of the patient. Patients can also be contacted later for clinical follow-up or to offer participation in clinical trials. Plasma, serum, DNA and snap-frozen tissue are stored at the BSSR biobank at Nationwide Children’s Hospital Biopathology Center, which is funded by the National Cancer Institute and approved by the College of American Pathologists.

TCC is the protocol used by the Oncology Research Information Exchange Network (ORIEN), a partnership among 11 North American cancer centers that was founded and is anchored by the OSUCCC – James and Moffitt Cancer Center in Tampa, Fla. ORIEN was organized to speed development of targeted treatments and to more quickly match patients to clinical trials by sharing de-identified patient data.

For more information about the Biospecimen Services Shared Resource, visit http://cancer.osu.edu/research-and-education/shared-resources/biospecimen-services, or contact BSSR Director Heather Hampel, MS, LGC, at Heather.Hampel@osumc.edu or at 614-293-7240.
OSUCCC – James’ Michael A. Caligiuri, MD, Elected to Top AACR Leadership Position

Michael A. Caligiuri, MD, director of The Ohio State University Comprehensive Cancer Center and CEO of the Arthur G. James Cancer Hospital and Richard J. Solove Research Institute, has been elected president-elect of the American Association for Cancer Research (AACR) for 2016-17.

Founded in 1907, the AACR is the world’s first and largest professional organization dedicated to advancing cancer research and to preventing and curing cancer. This is the first time in the 109-year history of the AACR that a person from Ohio State has been elected as president.

Caligiuri assumed his post as president-elect at the 2016 AACR Annual Meeting, April 16-20. He will assume the presidency in April 2017.

In these roles, he will work with the association’s board of directors and its more than 35,000 individuals from 104 countries to further its mission to prevent and cure cancer through research, education, communication and collaboration.

Caligiuri’s election to this position is a reflection of his international reputation as a cancer researcher, administrator and educator who has led the OSUCCC – James to global prominence.

Along with serving as director of the OSUCCC since 2003 and as CEO of the James Cancer Hospital and Solove Research Institute since 2008, he is a physician-scientist who is well known for his work on the biology of human natural-killer cells and their use for the treatment of hematologic malignancies and other cancers. To date, more than 1,500 cancer patients have been treated on clinical protocols that have emanated from the Caligiuri laboratory.

Caligiuri has been involved with the AACR since 1990. He has served as chairperson of the Publications Committee since 1993 and as a member of the Clinical and Translational Cancer Research Committee, among other roles. He was elected by the membership to the AACR board of directors, serving from 2013 to 2016, and he was a member of the faculty for the Scientist Survivor Program at the AACR Annual Meeting from 2003 to 2009. He was also a member of the faculty for the educational workshop, Methods in Clinical Cancer Research, from 2003 to 2007.

For more information, visit www.aacr.org.
BLOOMFIELD GAINS MAJOR HONORS

Clara D. Bloomfield, MD, a Distinguished University Professor at Ohio State who also serves as cancer scholar and senior adviser to the OSUCCC – James, received the 2016 Margaret L. Kripke Legends Award from the Office of Women Faculty Programs at MD Anderson Cancer Center in Houston, Texas. The annual national award recognizes individuals, male or female, dedicated to enhancing the careers of women in cancer medicine and cancer science. Also, Bloomfield was elected as a fellow in the American Association for Cancer Research (AACR) Academy for her research devoted to defining the chromosomal abnormalities that contribute to hematologic malignancies. The AACR Academy was created to recognize scientists whose major scholarly contributions have led to innovation and progress against cancer.

PELOTONIA 15 BOOSTS 7-YEAR TOTAL OVER $106 MILLION FOR OHIO STATE CANCER RESEARCH

Riders, virtual riders and donors in Pelotonia 15, the seventh installment of an annual bicycle tour that generates money for cancer research at the OSUCCC – James, raised a record $23,659,675 during the 2015 tour, boosting the total amount raised since the event’s inception in 2009 to $106,055,015. Thanks to the event’s major sponsors, every dollar raised by riders, virtual riders and donors goes directly to cancer research at the OSUCCC – James.

Other Pelotonia 15 numbers of interest:

- 277 Registered pelotons (riding groups)
- 7,981 Riders from 40 states, 10 countries
- 3,899 Virtual riders
- 2,770 Volunteers

Pelotonia 16 will be held Aug. 5-7. To register, or for training tips, routes, discounts at local businesses and other information, visit Pelotonia.org.

CALENDAR SPRING 2016

18TH ANNUAL MIDWEST DNA REPAIR SYMPOSIUM
MAY 28-29, OSUCCC – JAMES

FOCUS: Enable DNA Repair researchers at Midwest institutions to interact and showcase their latest scientific discoveries. Emphasizes the interaction of junior researchers with senior investigators and presentations by young researchers and faculty.

For information or to register, visit http://cancer.osu.edu/midwestdnarepair

FOURTH ANNUAL RB CONFERENCE
SEPTEMBER 25-28, OSUCCC – JAMES

FOCUS: to exchange ideas in the international retinoblastoma (RB) research community; to attract new investigators, students and postdocs; and to build interactive tools and increase interactions within the RB community.

For information or to register, visit http://cancer.osu.edu/rbsymposium