As part of the academic medicine mission, research is a vital part of what we do at The Ohio State University College of Medicine. Ohio State is home to many important research discoveries and the faculty and staff who support the research mission help make this a great place. Research in Review showcases just some of the many discoveries that occur here each day. Visit the College of Medicine’s website at medicine.osu.edu to learn more.
In a study led by Philip Payne, PhD, chair of the Department of Biomedical Informatics at The Ohio State University College of Medicine, and published in the online journal *BMC Medical Informatics and Decision Making*, a group of investigators from several academic medical centers identified and examined critical issues surrounding organizational dynamics and leadership structures that influence the effective use of information technology (IT) and informatics expertise to advance clinical and translational research.

Researchers involved in the study identified a number of important human, organizational and leadership issues that may impede access to IT and informatics tools and expertise in support of clinical and translational research. These issues included the engagement and coordination of appropriately trained leaders; a frequent fragmentation of IT and informatics personnel and infrastructure across organizational units; and the provision of institutional resources and financial support sufficient to sustain clinical and translational science-focused IT and informatics personnel and infrastructure.

Along with Payne, researchers from the University of Vermont and the University of Chicago participated in the study, which was funded by an award from Ohio State’s Center for Clinical and Translational Science, the University of Chicago and institutional funds from the University of Vermont.

A total of 31 academic medical center domain experts from across many disciplines completed structured surveys, and further thematic analysis of public-domain documentation was conducted. The researchers then identified critical factors that served to influence and/or affect access to IT and informatics expertise and tools.

Creating a Culture of Excellence
A team at The Ohio State University Wexner Medical Center is applying two well-tested applications in new ways in an attempt to improve mobility in people who have suffered a stroke. They are measuring how well people walk before and after intervention with a new system of wireless sensors that use the same technology found in cell phones and tablets.

The study led by Stephen Page, PhD, an associate professor of Occupational Therapy at Ohio State’s School of Health and Rehabilitation Sciences, uses wireless sensors that contain tiny accelerometers that measure the force of acceleration. These sensors are used in smart phones and tablets to sense movement and help adjust the image on the screen. Six sensors are placed on the study participant’s arms, legs and chest. As the person walks or performs other functional activities, the sensors relay information to each other and back to a computer that charts how and where the person is moving.

Page is using this technology to evaluate progress in a study that is testing a new type of rehabilitation intervention for stroke survivors. For the first time, Page’s team is combining electrical muscle stimulation, which has been used to improve muscle function for decades, with active stepping motion on a recumbent bicycle. The goal of the study is to determine whether the combination of active motion and electrical stimulation provides added benefit for patients through neuroplasticity.

The first phases of the study will examine 10 people who experienced a stroke within a year to 18 months prior to study enrollment and have limited ability to walk. Over the course of 10 weeks, half of the study participants will receive electrical stimulation on their legs while biking, while the other half receives placebo treatment while biking.

Page says this study challenges the notion among many physicians and rehabilitation experts that stroke survivors reach a recovery plateau within a year after their stroke.
ADHD is a neurodevelopmental disorder characterized by developmentally inappropriate degrees of inattentiveness, impulsivity and hyperactivity. Although ADHD is the most common neuropsychiatric/behavioral disorder of childhood and has been extensively studied in young children, it occurs in all age groups.

“An estimated 13 million men, women and children in the United States fit the diagnosis for ADHD or one of its subcategories,” says Arnold, who is professor emeritus of Psychiatry at The Ohio State University College of Medicine, where he was formerly director of the Division of Child and Adolescent Psychiatry and vice chair of Ohio State’s Department of Psychiatry.

Arnold collaborated with Dr. Martijn Arns of the Netherlands on a recent study published in *Biological Psychiatry* that sheds new light on the increasing rates of prevalence of ADHD. This study found that “sunny” regions with high solar intensity, such as the U.S. states of California, Arizona and Colorado, and countries like Spain and Mexico, have a lower prevalence of ADHD. An apparent protective effect of sunlight accounted for 34-57 percent of the variation in ADHD prevalence. The authors speculate that this may be related to sunlight’s effects on preventing disturbance in circadian rhythm or “biological clock.”

Researchers from Utrecht University, Research Institute Brainclinics, Leiden University and The Ohio State University published their work suggesting a possible preventive effect of sunlight on ADHD. Examining ADHD prevalence rates per U.S. state and solar intensity maps, the authors observed a striking geographical coincidence between low ADHD prevalence and high solar intensity. Solar intensity is a measure of how much sunlight a specific area receives, which is often used for calculating how much energy solar panels will generate.

States with less sunlight had as much as 10 to 12 percent higher rates of patients diagnosed with ADHD, while in states where there is more sunshine, there are fewer ADHD cases. However, there may also be a link to sleep, since those with ADHD have the same traits as those who are sleep-deprived.

The authors hypothesize that this delayed circadian rhythm and difficulty falling asleep may be caused by increased evening use of modern media, such as tablet computers and smartphones, especially with social media increasing the exposure to such blue-light sources during the evening.

Arnold is currently involved in two treatment studies of ADHD and three treatment studies of autism. He has more than 40 years of experience in child psychiatric research, including the multi-site National Institute for Mental Health Multimodal Treatment Study of Children with ADHD.
A team of researchers led by John Bolte, PhD, associate professor of Anatomy and director of the Injury Biomechanics Research Center at The Ohio State University College of Medicine, is assessing the feasibility of car seat installation, and the compatibility of the seats with various vehicles, and is providing evidence to support the proper type of seat based on a child’s age and size. Bolte is also associate professor of Mechanical and Aerospace Engineering at Ohio State.

According to previous research, 73 to 90 percent of all car seats are installed improperly, some due to installation errors and others due to incompatibilities between the car seat and the vehicle. In an effort to create a set of guidelines for caregivers to reference when shopping for a car seat, researchers at Ohio State’s School of Health and Rehabilitation Sciences in the College of Medicine collected a sample of dimensions from 54 vehicles and 59 car seats currently on the market and identified the most common sources of incompatibility among them.

Data from 3,186 car seat-vehicle combinations were collected and analyzed. The results showed that for seat pan angle, especially for rear-facing car seats, 43.6 percent of all combinations were unacceptable; for the width of the car seat compared to the width of the vehicle seat, 34.3 percent of all combinations were less than ideal; for the height of seat back, especially for forward-facing car seats, 22.2 percent of all combinations were unacceptable; for clearance space behind front-row seats, especially for rear-facing car seats, 20.5 percent of all combinations did not fit with the front seat at mid-track; and for the length of the top tether, 7.7 percent of all combinations were too loose.

Another Ohio State study is seeking to identify the comfort level of larger, older children while riding in rear-facing car seats, according to the guidelines of the American Academy of Pediatrics (AAP) and the National Highway Traffic Safety Administration (NHTSA). The AAP and NHTSA recommend that children ride in rear-facing car seats until they are two years old, or until the maximum weight limit for their car seat is reached. While research has shown rear-facing car seats to perform better than forward-facing car seats, and to protect children’s heads and necks during car crashes, studies also show that only 13 percent of children 12 – 23 months of age ride in rear-facing car seats.

For Phase I of this comfort study, 20 children 22 – 26 months of age were recruited to sit rear-facing and forward-facing for 20 minutes each in a lab setting. Video footage was analyzed and parent surveys were collected to help gauge the children’s comfort levels. Researchers concluded that parental perception scores reflecting comfort levels for rear-facing and forward-facing car seats were similar, and video footage revealed the same. Based on the preliminary data of this study, comfort scores are similar for rear and forward-facing car seats, and the data also supports the extended use of rear-facing car seats. Phase II of the comfort study will examine video from a family’s vehicle while the child rides in each car seat configuration.
In a new study led by Phillip Popovich, PhD, professor of Neuroscience in Ohio State’s College of Medicine and director of Ohio State’s Center for Brain and Spinal Cord Repair, data show that it is possible to restore immune function in mice with injured spinal cords.

People with spinal cord injury often are immune-compromised, which makes them more susceptible to infections. Why these individuals become immune-suppressed is not known, but the Ohio State study found that a disorder called autonomic dysreflexia (AD) can cause immune suppression.

Autonomic dysreflexia is a potentially dangerous complication of nerves C1 – C4. Spinal cord injury characterized by exaggerated activation of spinal autonomic (sympathetic) reflexes. This can cause an abrupt onset of excessively high blood pressure that can cause pulmonary embolism, stroke and, in severe cases, death.

Research also explains why people with spinal cord injuries develop a condition referred to as “central immune depression syndrome” when their immune systems, which are required to fight off infection, are suppressed due to damage or malfunction in regions of the spinal cord that help control immune function.

Researchers found that AD develops spontaneously in spinal cord-injured mice, and becomes more frequent as time passes from the initial spinal cord injury.

They also found that simple, everyday occurrences that activate normal spinal autonomic reflexes, such as having bowel movements or emptying the bladder, become hyperactive and suppress immune function in people with spinal cord injury.

In the study, Popovich and colleagues were able to restore immune function in mice with spinal cord injuries using drugs that inhibit norepinephrine and glucocorticoids, immune modulatory hormones that are produced during the onset and progression of AD. They also observed, in a patient with a high-level spinal cord injury, that briefly inducing AD-impaired immune function, confirmed that their findings in mice have relevance to humans.

The study found that AD causes immune suppression in part by releasing into blood and immune organs high levels of immune modulatory hormones that non-selectively kill mature and immature white blood cells in the spleen, says first author Yi Zhang, a post-doctoral neuroscience researcher at Ohio State.

The study is published in The Journal of Neuroscience.

Ohio State Researchers Restore Immune Function in Spinal Injured Mice

Discoveries With Impact
Tsonwin Hai, PhD, professor of Molecular and Cellular Biochemistry at The Ohio State University College of Medicine, and her team may have linked the activation of a stress gene in immune-system cells to the spread of breast cancer to other parts of the body.

The study suggests this gene, called *ATF3*, may be the crucial link between stress and cancer, including the major cause of cancer death—its spread, or metastasis. Previous public health studies have shown that stress is a risk factor for cancer.

They already know that *ATF3* is activated, or expressed, in response to stressful conditions in all types of cells. Under typical circumstances, turning on *ATF3* can actually cause normal and benign cells to commit suicide if the cells decide that the stressors, such as irradiation and a lack of oxygen, have irrevocably damaged the cells.

This research suggests, however, that cancer cells somehow coax immune-system cells that have been recruited to the site of a tumor to express *ATF3*. Though it’s still unclear how, *ATF3* promotes the immune cells to act erratically and give cancer an escape route from a tumor to other areas of the body.

This stress gene could function as a drug target to combat cancer metastasis if additional studies bear out these results. In the meantime, the results provide important insights into how cells in a tumor use their signaling power to coopt the rest of the body into aiding cancer’s survival and movement to distant organs.

Hai has studied *ATF3* in cancer cells for years. When she had a chance to examine human samples from about 300 breast-cancer patients, she was stunned to find that the expression of the *ATF3* gene in certain immune-system cells was associated with worse cancer outcomes in this group of patients. *ATF3* in cancer cells showed no such association.

To test that clinical data, she and colleagues conducted two rounds of studies in mice. The researchers first injected breast cancer cells into two groups: normal mice and mice that cannot express *ATF3* in any cells. The cancer in normal mice metastasized to the lungs far more rapidly and extensively than did cancer in the mice lacking *ATF3*. In the second round of experiments, they used genetically altered mice that could not express *ATF3* in a group of immune system cells called myeloid cells, and the results were similar.

In general, when cancer cells first appear, the immune system recognizes them as foreign, and various immune cells travel to the site to attack them. Early on in cancer’s development, this process typically works.

But as cancer cells grow and thrive in a tumor, they send out certain molecular messengers to promote a chronic wound-healing response. Cancer cells, by acting like a wound that never heals, hijack this process to help themselves survive and spread.

*ATF3* is a master-switch type of gene: Its gene product, the protein, turns on many genes. Knowing this, the researchers analyzed the genes that are controlled by *ATF3* using a genome-wide global approach. Combining this set of data with another set of data from human samples, Hai and colleagues were able to identify an *ATF3* gene signature that can predict whether cancer patients have a low or high risk of dying.

Though the work suggests a drug to dampen *ATF3*’s effect could lower the risk for metastasis, Hai noted that scientists don’t fully understand what the overall effects of that dampening would be.

There are lots of ways to turn on *ATF3* in cells, and stress signals sent out by cancer cells represent just one method to express this gene in immune-system cells and produce a chronic wound-healing response. Other ways include radiation, some chemotherapeutic agents, a high-fat diet, UV damage and even chronic behavioral stress.

Hai plans to test whether these other kinds of stressors also affect the immune cells through *ATF3* induction, changing them from attacking the cancer cells to helping the cancer grow and spread.

The research is published in a recent issue of the *Journal of Clinical Investigation*.
Discovery led by Chad Rappleye, PhD, a microbiologist in Ohio State’s Center for Microbial Interface Biology and assistant professor in the Department of Microbial Infection and Immunity, both in The Ohio State University College of Medicine, has uncovered a new compound that could be developed as an antifungal drug to treat histoplasmosis and cryptococcosis, two types of fungal infections that are naturally drug-resistant.

Humans and fungi share similar proteins, a biological bond that makes curing fungal infections difficult and expensive. Current costs to treat these stubborn infections can top $50,000 per patient, and no new classes of antifungal drugs that treat systemic infections have been introduced for at least 20 years.

People with weakened immune systems are more likely to develop life-threatening fungal infections. However, the airborne fungus Histoplasma capsulatum, which causes histoplasmosis, can infect healthy people as well.

Histoplasmosis is an unusual fungal disease because anyone can be infected. “Like tuberculosis, Histoplasma infects healthy hosts, attacks their lungs and can lie dormant in immune cells for years, later causing reactivation disease,” says Rappleye.

There are an estimated 100,000 Histoplasma infections each year in the United States. Most are contained by the body’s immune system, but each year a few thousand people will develop chronic or life-threatening histoplasmosis disease, requiring hospitalization and antifungal treatment. The antifungals currently used to treat the infection have undesirable toxic side effects requiring monitoring by a physician and may need to be taken for weeks or months.
Respiratory histoplasmosis manifests with flu-like symptoms, often making diagnosis difficult. People with histoplasmosis have been mistakenly diagnosed with colds, the flu and even lung cancer. In 2012, Rappleye received pilot funding from Ohio State’s Center for Clinical and Translational Science (CCTS) and the Public Health Preparedness for Infectious Disease (PHPID) program.

Searching a library of commercially available small molecules used by other investigators to find new antivirals or anticancer drugs, researchers performed a high-throughput phenotypic screen of 3,600 compounds looking for agents that inhibit fungal, but not human, cells.

To speed the selection process, the team engineered Histoplasma cells with a fluorescent protein that makes the cells glow red while inside a living macrophage—the type of mammalian immune cell that Histoplasma attacks and in which it reproduces.

As the number of fungal cells increased inside the macrophage, so did the fluorescence and consequently, the cells would glow brighter. However, when a macrophage was exposed to an active compound that prevents Histoplasma reproduction, it maintained the original level of brightness. This allowed the scientists to quickly determine the efficacy and toxicity of the drug candidate in a natural environment. It allowed them to visually screen thousands of compounds in just a few weeks, and to measure the compound’s impact in a real, live host cell.

The team narrowed the field down to a primary candidate called 41F5, which is 60 times more toxic to fungal cells than human cells. The work was published in the September 2013 issue of Antimicrobial Agents and Chemotherapy.

The team is currently working with Werner Tjarks, PhD, professor of Medicinal Chemistry and Pharmacognosy in Ohio State’s College of Pharmacy, to see if the selectivity and toxicity profile can be enhanced further for additional testing. Rappleye is also working with the Ohio State’s Technology Commercialization Office to potentially commercialize the derivatives from 41F5.

Histoplasma capsulatum spores are found across a broad stretch of the Midwestern and southern United States. Experts estimate that 80 percent of people who live in the region have been exposed, and that nearly 10 to 25 percent of all AIDS patients living in these areas will develop a histoplasmosis infection. Once inhaled, the fungal cells can cause symptoms similar to an upper respiratory infection, and disease severity is dependent on how many spores are inhaled. In rare cases, histoplasmosis can cause blindness, joint pain or life-threatening complications, including meningitis and heart problems.
New Device Allows Brain to Bypass Spinal Cord, Move Paralyzed Limbs

For the first time ever, a paralyzed man can move his fingers and hand with his own thoughts, thanks to an innovative partnership between The Ohio State University Wexner Medical Center and Battelle Memorial Institute.

A 23-year-old quadriplegic is the first patient to use Neurobridge, an electronic neural bypass for spinal cord injuries that reconnects the brain directly to muscles, allowing voluntary and functional control of a paralyzed limb. Ian Burkhart is the first of a potential five participants in a new clinical study.

The Neurobridge technology combines algorithms that learn and decode the user’s brain activity and a high-definition muscle stimulation sleeve that translates neural impulses from the brain and transmits new signals to the paralyzed limb. In this case, Ian’s brain signals bypass his injured spinal cord and move his hand, hence the name Neurobridge.

This technology has been a long time in the making. Working on the internally funded project for nearly a decade to develop the algorithms, software and stimulation sleeve, Battelle scientists first recorded neural impulses from an electrode array implanted in a paralyzed person’s brain. They used that data to illustrate the device’s effect on the patient and prove the concept.

Since then, a team from Battelle has been collaborating with Ohio State neuroscience researchers and clinicians Ali Rezai, MD, and Jerry Mysiw, MD, to design the clinical trials and validate the feasibility of using the Neurobridge technology in patients. Rezai is director of Ohio State’s Neurosciences Program and professor of Neuroscience and Neurological Surgery, and Mysiw is chair of the Department of Physical Medicine and Rehabilitation, both at Ohio State’s College of Medicine.

During a three-hour surgery, Rezai implanted a chip smaller than a pea onto the motor cortex of the patient’s brain. The tiny chip interprets brain signals and sends them to a computer, which recodes and sends them to the high-definition electrode stimulation sleeve that stimulates the proper muscles to execute the desired movements. Within a tenth of a second, Burkhart’s thoughts are translated into action.

The surgery required the precise implantation of the microchip sensor in the area of patient’s brain that controls the arm and hand movements. This technology may one day help patients affected by various brain and spinal cord injuries such as strokes and traumatic brain injury.

Battelle also developed a non-invasive neurostimulation technology in the form of a wearable sleeve that allows for precise activation of small muscle segments in the arm to enable individual finger movements, along with software that forms a “virtual spinal cord” to allow for coordination of dynamic hand and wrist movements.

The Ohio State and Battelle teams worked together to figure out the correct sequence of electrodes to stimulate to allow the patient to move his fingers and hand functionally. Different brain signals coordinate with muscles to rotate the hand, make a fist or pinch the fingers together to grasp an object. As part of the study, Burkhart worked for months using the electrode sleeve to stimulate his forearm to rebuild atrophied muscles so they would be more responsive to the electric stimulation.
Finding the Right Partners

Ohio State Named to New NIH Network Focused on Revolutionizing Stroke Research

The Ohio State University Wexner Medical Center joins an elite network of 25 regional stroke centers announced by the National Institutes of Health (NIH) that will focus on stroke prevention, treatment and recovery. As part of the NIH Stroke Trials Network (NIH StrokeNet), Ohio State will receive a five-year, $2-million grant to develop a regional coordinating stroke center.

The network will work to maximize efficiencies in order to develop, promote and conduct high-quality, multi-site clinical trials focused on key interventions in stroke prevention, treatment and recovery. Michel Torbey, MD, MPH, medical director of Ohio State’s Neurovascular Stroke Center and professor of Neurological Surgery and Neuroscience, indicates that Ohio State was selected based on its clinical science excellence and specialized multidisciplinary expertise in stroke management, a strong background in stroke research and a proven ability to recruit stroke patients.

The regional stroke centers will work with nearby satellite facilities across the country that have teams of researchers representing every medical specialty needed for stroke care.

The National Institute of Neurological Disorders and Stroke (NINDS), which will fund and manage the NIH StrokeNet, has a strong history of successful stroke clinical trials over the past 40 years, leading to advances in treatment and prevention of the disease, including the first treatment for acute stroke, announced in 1995. Stroke remains the number one cause of disability and fourth-leading cause of death in the United States.

Ohio State’s Wexner Medical Center will coordinate stroke clinical trials at its 24 Telestroke hospitals, and at Mount Carmel Health System, University of Toledo and Wright State University in Ohio.

The 25 centers selected by the NIH are strategically placed in every region of the country. Successful applicants demonstrated experience in stroke research and recruitment, including the ability to enroll underrepresented populations. Applicants were also required to offer access to the full cadre of specialties that are involved in stroke care, including emergency medicine, neurological surgery, interventional neuroradiology, vascular neurology, neurointensive care, neuroimaging, stroke rehabilitation and pediatric neurology.

Each center will receive five-year funding, with $200,000 per year in research costs and $50,000 for training stroke clinical researchers over the first three years, and additional funds driven by the completion of milestones. The University of Cincinnati will manage the national clinical coordinating center, which will oversee and coordinate the institutional review board and master trial agreements for all of the regional centers.

NIH StrokeNet investigators, working with the broader stroke community, will propose, develop and conduct stroke protocols to be administered within the network and will train the future generation of clinical researchers in stroke. The network concept evolved from an NINDS planning effort in which stroke experts were asked what is most needed to reduce death and disability due to stroke in the United States. They called for a nationwide stroke network that would allow for a more seamless transition between early safety and efficacy trials and phase II and III clinical trials.

Ohio State Named to New NIH Network Focused on Revolutionizing Stroke Research

The Ohio State University Wexner Medical Center joins an elite network of 25 regional stroke centers announced by the National Institutes of Health (NIH) that will focus on stroke prevention, treatment and recovery. As part of the NIH Stroke Trials Network (NIH StrokeNet), Ohio State will receive a five-year, $2-million grant to develop a regional coordinating stroke center.

The network will work to maximize efficiencies in order to develop, promote and conduct high-quality, multi-site clinical trials focused on key interventions in stroke prevention, treatment and recovery. Michel Torbey, MD, MPH, medical director of Ohio State’s Neurovascular Stroke Center and professor of Neurological Surgery and Neuroscience, indicates that Ohio State was selected based on its clinical science excellence and specialized multidisciplinary expertise in stroke management, a strong background in stroke research and a proven ability to recruit stroke patients.

The regional stroke centers will work with nearby satellite facilities across the country that have teams of researchers representing every medical specialty needed for stroke care.

The National Institute of Neurological Disorders and Stroke (NINDS), which will fund and manage the NIH StrokeNet, has a strong history of successful stroke clinical trials over the past 40 years, leading to advances in treatment and prevention of the disease, including the first treatment for acute stroke, announced in 1995. Stroke remains the number one cause of disability and fourth-leading cause of death in the United States.

Ohio State’s Wexner Medical Center will coordinate stroke clinical trials at its 24 Telestroke hospitals, and at Mount Carmel Health System, University of Toledo and Wright State University in Ohio.

The 25 centers selected by the NIH are strategically placed in every region of the country. Successful applicants demonstrated experience in stroke research and recruitment, including the ability to enroll underrepresented populations. Applicants were also required to offer access to the full cadre of specialties that are involved in stroke care, including emergency medicine, neurological surgery, interventional neuroradiology, vascular neurology, neurointensive care, neuroimaging, stroke rehabilitation and pediatric neurology.

Each center will receive five-year funding, with $200,000 per year in research costs and $50,000 for training stroke clinical researchers over the first three years, and additional funds driven by the completion of milestones. The University of Cincinnati will manage the national clinical coordinating center, which will oversee and coordinate the institutional review board and master trial agreements for all of the regional centers.

NIH StrokeNet investigators, working with the broader stroke community, will propose, develop and conduct stroke protocols to be administered within the network and will train the future generation of clinical researchers in stroke. The network concept evolved from an NINDS planning effort in which stroke experts were asked what is most needed to reduce death and disability due to stroke in the United States. They called for a nationwide stroke network that would allow for a more seamless transition between early safety and efficacy trials and phase II and III clinical trials.
Finding the Right Partners

The National Cancer Institute (NCI) has awarded a five-year, $11.3-million grant to a team of researchers at The Ohio State University Comprehensive Cancer Center – Arthur G. James Cancer Hospital and Richard J. Solove Research Institute (OSUCCC – James) to further their studies on thyroid cancer. Principal investigator Matthew Ringel, MD, professor of Internal Medicine and a member of the OSUCCC – James Molecular Biology and Cancer Genetics (MBCG) Program, leads the NCI Program Project Grant (CA124570). The new grant is a continuation of a study that ran from 2008 through 2013 titled, “Genetic and Signaling Pathways in Epithelial Thyroid Cancer.”

The study has four integrated projects:

1. “Genes in the Predisposition to Papillary Thyroid Carcinoma,” led by Albert de la Chapelle, MD, PhD, co-leader of the OSUCCC – James MBCG Program and professor of Molecular Virology, Immunology and Medical Genetics and of Internal Medicine. He is also a Distinguished University Professor, the highest honor the university can give to a faculty member;

2. “Genetic Alterations that Initiate Follicular Thyroid Carcinogenesis,” led by Charis Eng, MD, PhD, at the Cleveland Clinic, and co-led by Lawrence Kirschner, MD, PhD, professor of Internal Medicine at Ohio State and a member of the OSUCCC – James MBCG Program;

3. “Selective Modulation of Thyroidal Radioiodine Accumulation,” led by Sissy Jhiang, PhD, professor of Physiology and Cell Biology at Ohio State and a member of the OSUCCC – James MBCG Program;

4. “P21-Activated Kinase in Thyroid Cancer” led by Ringel, also director of the Division of Endocrinology, Diabetes and Metabolism at Ohio State.

In addition, the Program Project Grant funds three shared-resource cores:

1. “Integrated Clinical Information and Pathology Sample Repository,” led by John Phay, MD, clinical associate professor of Surgical Oncology, and Rebecca Nagy, CGC, of the Division of Human Genetics, both at Ohio State’s College of Medicine;

2. “Mouse Imaging and Pathology,” led by Kirschner;

3. “Biostatistics and Data Integration,” led by Soledad Fernandez, PhD, research associate professor in Department of Biomedical Informatics in Ohio State’s College of Medicine.
Ohio State Receives $18.7-Million Federal Grant to Establish Tobacco Center of Regulatory Science

The Ohio State University has received an $18.7-million federal grant to establish a research center devoted to the study of tobacco use patterns, industry marketing practices and public perceptions that will help the Food and Drug Administration (FDA) put science behind its new role in regulating tobacco.

Ohio State’s center is one of 14 established nationally under this new federal initiative, called the Tobacco Centers of Regulatory Science program. The National Institutes of Health (NIH) and FDA announced that they have teamed to ensure that the FDA’s regulation of tobacco is based on sound and relevant scientific evidence. The National Cancer Institute will administer the Ohio State funding.

The university has proposed a broad research program that takes into account the biological, psychological, economic and public health implications of tobacco use and the industry’s marketing of products to consumers. A total of 18 scientists from six colleges and The Ohio State University Comprehensive Cancer Center – Arthur G. James Cancer Hospital and Richard J. Solove Research Institute (OSUCCC – James) will populate The Ohio State University Center of Excellence in Regulato Tobacco Science (CERTS).

Specifically, Ohio State’s aims are to reduce addiction and shed light on health problems arising from tobacco use among youths and adults in rural and urban settings, and to decrease tobacco-related harm by studying individual disease risk and the prevalence of product use—with a focus on dual use and especially on new and emerging tobacco products.

Individual studies will assess the prevalence of smoking, smokeless tobacco and simultaneous use of these products; document carcinogen exposure and the genetics behind developing a taste for tobacco and nicotine dependence; analyze purchasing behavior and marketing practices in various environments; and explore the decision-making factors that lead people to choose to use tobacco in the first place.

Tobacco continues to be the leading cause of preventable death and disease in the United States, according to the NIH. With the FDA gaining regulatory authority over tobacco after the 2009 passage of the Family Smoking Prevention and Tobacco Control Act, the agencies are partnering to protect public health through science-based regulation.

Mary Ellen Wewers, PhD, MPH, professor of Health Behavior and Health Promotion and a tobacco cessation researcher in Ohio State’s College of Public Health, is co-leading the center with oncologist Peter Shields, MD, professor of Medical Oncology, deputy director of the OSUCCC – James and a specialist in identifying biomarkers to assess lifestyle-related cancer risk factors. The increasing dual use of cigarettes and smokeless tobacco, in particular, has ramped up the need for scientific investigation of the effects of these products.

The Ohio State colleges populating the center are Public Health, Medicine, Arts and Sciences, Nursing, the Moritz College of Law and the Fisher College of Business. Investigators from four other institutions will also participate: the universities of Kentucky and Pennsylvania, RTI International in North Carolina and the Columbus-based Strategic Research Group.

Federal funding for the 14 new centers totals $53 million in the first year and a potential total of more than $273 million over the next five years. Ohio State’s grant covers five years, with the first year of funding totaling almost $3.7 million.
Finding the Right Partners

The Ohio State University created an exclusive worldwide agreement with a new company formed by Signet Enterprises: Signet Accel LLC. The new company will license a portfolio of cutting-edge Ohio State-developed software technologies for healthcare data sharing and advanced analytics through the university’s Ohio State Innovation Foundation.

Signet Accel will provide technology solutions in a variety of healthcare and life sciences areas. The company’s applications will enable data sharing and analytics ranging from improving the design and conduct of clinical trials to supporting quality improvement in healthcare delivery in the United States and throughout the world.

The agreement between Ohio State and Signet Enterprises is projected to generate several million dollars in licensing fees, as well as equity for the university, during the life of the agreement. It includes the largest up-front licensing payment to Ohio State—$275,000, which has already been received from Signet Enterprises. These fees will result in direct benefit to the university and the College of Medicine.

While the focus of the new company is global, the company plans to locate in central Ohio near the Ohio State campus, allowing it to take advantage of a highly skilled biomedical and computational workforce being trained at the university.

Signet Accel’s technology will enable the rapid and efficient analysis of all types of healthcare data, allowing providers, patients and healthcare companies to enhance wellness and make treatment decisions based on the most current, accurate evidence.

The technologies involved in the venture were developed during the past decade by the Department of Biomedical Informatics at The Ohio State University College of Medicine, led by Philip Payne, PhD, professor and department chair. Payne and Peter Embi, MD, department vice chair and professor of Rheumatology and Immunology, are the Ohio State faculty members who serve as co-founders of the new company.
The National Institutes of Health has awarded a $25.4-million grant to The Ohio State University Center for Clinical and Translational Science (CCTS), led by Rebecca Jackson, MD, also associate dean for clinical research in the College of Medicine. CCTS is a collaboration between The Ohio State University and Nationwide Children’s Hospital (NCH) created to accelerate basic science discoveries into life-saving medical advances.

The NIH endowment is funding a multi-million dollar Clinical and Translational Science Award originally given to the CCTS in 2008. Since then, the center has helped connect hundreds of researchers across the state of Ohio with the resources needed to discover new techniques and treatments for today’s deadliest and costliest diseases, including obesity, diabetes, heart disease, cancer and Alzheimer’s, as well as a variety of disabling childhood illnesses like muscular dystrophy.

The CCTS has been also been successful in creating partnerships, infrastructure and programs that drive innovation, training the next generation of scientists and making the research process more efficient—three of NIH’s key goals.

The CCTS facilitated the development of a similar network of institutional partners in Appalachia—the Appalachian Translational Research Network—which is focused on addressing the significant health challenges and disparities specific to Appalachia.

The CCTS has also helped create shared research resources with sustainability in mind. Two of these are the Clinical Research Center, a full-service clinical research laboratory, and the Laser Capture Microdissection Core, a lab that collects precise, nano-sized tissue samples. The services were originally fully funded by the CCTS, but because they were built around a sustainable business model, both are close to being self-sufficient operations and are used by researchers across The Ohio State University campus.
Ohio State Researchers Awarded NIH Grant to Advance Pacemaker Technology

The National Institutes of Health recently awarded a more than $1.5-million grant to a team from The Ohio State University Dorothy M. Davis Heart and Lung Research Institute. Three Ohio State faculty members—Vadim Fedorov, PhD, assistant professor of Physiology and Cell Biology in Ohio State’s College of Medicine; Cynthia Carnes, PharmD, PhD, professor of Cellular and Integrative Biophysics and associate dean in Ohio State’s College of Pharmacy; and Peter Mohler, PhD, professor and chair, Department of Physiology and Cell Biology and director of the Heart and Lung Research Institute—serve as the team of co-principal investigators. Equipped with groundbreaking technological capabilities developed by Fedorov, pre-clinical techniques enabled by Carnes and molecular approaches facilitated with Mohler, the work will address human sinus node disease, a problem found in the natural pacemaker of the heart known as the sinoatrial node (SAN). Sinus node disease causes arrhythmias, is a precursor for atrial fibrillation (AF), a condition that currently afflicts over 2.2 million Americans, and is an area of clinical strength for The Ohio State University Heart and Vascular Center, which is a national leader in terms of procedural volume in cardiac electrophysiology.

The goal of the new study is to find improved therapeutic remedies beyond the electronic pacemaker, a device that has long been implanted in the heart to mitigate sinus node disease and is the current accepted standard of care.

The trio begins with a hypothesis that SAN dysfunction may result from an increased sensitivity to adenosine, a metabolite of the heart that lowers heart rate and thus conductivity in the heart, having the opposite effect of caffeine. The first priority of the researchers’ work focuses on blocking the adenosine receptor to test the hypothesis that heart failure results from adenosine-dependent signaling in the SAN.

With Fedorov’s 3-D high-resolution, near-infrared, optical mapping capabilities, he can examine the SAN internally and from all angles. In fact, it is his customized system of cameras and computers that led to these enhanced imaging capabilities.

Before they can begin healing the SAN, all three researchers reiterate that they first need to know how, why and where the SAN is failing. They agree that the heart experiencing a failure of conduction is the general problem, and that adenosine receptors are the hypothesized root cause of that problem.

However, the consensus among the team members is that at least another two years of research are needed before they can begin to work on healing the SAN. At that point, Carnes believes that drug treatments may be effective in repairing the SAN. Fedorov agrees, and adds that localized stem cell repairs may also be a viable treatment for a damaged SAN. Either way, the goal of healing the damage, rather than mitigating it with an electronic pacemaker, would be realized. Fedorov sees the work accomplished over the next three and a half years as a cornerstone of innovation.
To find out more about discoveries at The Ohio State University College of Medicine, visit us online at medicine.osu.edu, follow us on Twitter at @OhioStateMed and Instagram or find us on Facebook.