Research Progress Report

Synergizing Strengths and Leveraging Resources to Catalyze Scientific Information

CTSA Clinical & Translationa Science Awards
CCTS Center for Cli Translational
Nationwide Children's Hospital™
Ohio State Medical Center
It is our pleasure to share this inaugural issue of the CCTS Research Progress Report with you as we—a team of more than 826 investigators and support professionals—highlight key initiatives and demonstrate examples of our success in translating scientific research into clinical care. This issue can provide only a snapshot in time of the work we do, as it is in constant flux, expanding to embrace continuously evolving and multiplying opportunities for discovery. Please visit our website often (www.ccts.osu.edu) to keep apprised of our continuing progress.

In these pages, we seek to share our culture of collaboration and innovation as we build an accessible clinical and translational infrastructure to support scientific discovery across the lifespan. In partnership with The Ohio State University Medical Center, Nationwide Children’s Hospital, seven Health Sciences colleges (Dentistry, Medicine, Nursing, Optometry, Pharmacy, Public Health, Veterinary Medicine), as well as partnerships with non-Health Sciences colleges on the campus of The Ohio State University (Engineering, Social Work, Fisher College of Business), we are excited to stand at the crossroads where lifestyle, behaviors, pharmacology, genetics, biochemistry and a host of other factors come together with numerous investigators—from promising early scientists to highly distinguished faculty scholars—to inform groundbreaking clinical and translational research.

We feel proud that we are part of The Ohio State University, which (including the Health Sciences) is ranked 10th in total research expenditures among public and private universities, seventh among public universities and second in industry-sponsored research by the National Science Foundation.

We are honored to be a member of the CTSA Consortium. We are fully aware that without the funding and support of National Institutes of Health (NIH) many of the advances and successes reported here might not have been possible. We are committed to strengthening our relationship with the NIH as it rededicates itself to its mission of advancing translational sciences.

Sincerely,

Rebecca Jackson, MD
Director, Center for Clinical and Translational Science
Associate Dean for Clinical Research, College of Medicine
The Ohio State University
Ohio State’s CCTS

“Synergizing strengths and leveraging resources to catalyze scientific innovation” is more than our strategic vision. It is also what we do to translate advances in novel methodologies such as genomics, proteomics, informatics and imaging into new clinical treatments, medications and surgical procedures to improve the quality of care for all patients in our community—and around the world.

We support clinical and translational researchers by forming new teams and research partnerships; developing new tools, technologies and best practices; increasing expertise and skills; providing opportunities for pilot projects and career development; and serving as a collective voice on policy, cultural and institutional processes in support of our research mission.

As a member of the CTSA Consortium, we are charged to attract basic, translational, and clinical investigators and clinicians in our community, professional societies, and industry partners to encourage professional relationships, expansive programs and joint research projects. These efforts, along with the creation of new advanced degree programs, have the goal of speeding scientific discovery and translating it into better patient care.

Since our founding, we have awarded $3 million to 84 investigators making significant research strides the CCTS program areas such as Novel Clinical and Translational Methodologies; Pilot and Collaborative Translational and Clinical Studies; Education Training and Career Development; Comparative Effectiveness Research; and Community Engagement. These efforts are supported by one of the premier biomedical informatics programs in the country, a progressive and innovative tracking and evaluation program, a mature research subject recruitment and retention program, a strategic business consultation program, and a robust communications infrastructure all at Ohio State. In addition we have bolstered our opportunities for collaboration by adding additional Ohio State colleges to our membership; we work in collaboration with a number of universities across the country and numerous entities within our community.

Genesis of OSU CCTS

Ohio State’s Board of Trustees voted to create a new entity, The Ohio State University Center for Clinical and Translational Science (CCTS), to speed the translation of scientific discoveries into clinical therapies to improve human health. Rebecca Jackson, MD, was named to head the new enterprise based on her international recognition and outstanding leadership of numerous multicenter research collaborations. Her first task was to develop the application for an NIH (National Institutes of Health) Center for Translational Science Award (CTSA) grant to fund the new “endeavor.

In 2008, the NIH awarded a $34-million, five-year CTSA grant to The Ohio State University—along with Nationwide Children’s Hospital and Ohio State’s seven Health Sciences colleges—to fund the CCTS. Among the largest research grants in the University’s history, the CTSA award was the result of a team effort that received one of the best scores ever given by the NIH to a CTSA applicant (based on clinical and translational research enterprise, training programs, informatics capabilities, interdisciplinary collaboration and partnerships with private and public organizations).

About the CTSA

The Clinical and Translational Science Awards (CTSA) Consortium was created by the National Institutes of Health (NIH) in 2006 with the goal of developing an association of institutions across the country where investigators from various fields of research can transform scientific discoveries made in the laboratory into treatments and strategies for patients in physicians’ offices, clinics and hospitals.

Today, as Ohio State enters its fourth year in the consortium, the CTSA supports 55 medical research institutions with the aim of transforming how biomedical research is conducted. Its goals include speeding the translation of laboratory discoveries into treatments for patients, engaging local communities in clinical research efforts and training a new generation of clinical and translational researchers.

The stated goals of the CTSA are to: 1) build national clinical and translational research capability; 2) provide training and improve career development for clinical and translational scientists; 3) enhance consortium-wide collaborations; 4) improve the health of our communities and the nation; and 5) advance T1 translational research to move basic laboratory discoveries and knowledge into clinical testing.
Research Progress Profile

Translating research into world class patient care is the cornerstone of Ohio State’s CCTS. These are just a few examples of our commitment to improving people’s lives.

Moving Toward Novel Solutions to MRSA and Other Superbugs

Ching-Shih Chen, PhD, a medicinal chemist in Ohio State’s College of Pharmacy, has discovered a novel class of compounds that have the ability to kill MRSA. Methicillin-resistant Staphylococcus aureus (MRSA), colloquially known as a “superbug,” poses a serious threat to public health because of its resistance to multiple antibiotics that are most commonly used to treat infection. Since the mid-1960s, Staphylococcus aureus, known to be a source of “hospital-acquired” infections, has become increasingly resistant to numerous antibiotics, and over the last two decades it alarmingly has moved into the community, now affecting young and healthy individuals with no link to the healthcare system. Working with a team of investigators from Ohio State and National Taiwan University College of Medicine, Chen discovered that celecoxib, a cyclooxygenase-2 (COX-2) inhibitor, has modest anti-Staphylococcus activity independent of its ability to inhibit COX-2. Using the structure of celecoxib as a starting point, his research team developed a new class of agents that exhibit high potency in killing different strains of MRSA without affecting COX-2. In addition to MRSA, these agents are also effective against other “superbugs” such as vancomycin-resistant Enterococcus (VRE). His research team is working to identify the molecular target by which these agents kill MRSA and VRE to help design more potent agents for preclinical development. A patent application on these promising agents has been filed through The Ohio State University Research Foundation.

LCM – Innovative Technology Transforms Healthcare Research

One of Ohio State’s newest core laboratories was funded in 2010 through the CTSA grant. Under the direction of Sashwati Roy, PhD, the Laser Capture Microdissection (LCM) core research laboratory is transforming the way health research is done. LCM technology, which was developed by the NIH, allows researchers to be more selective than ever before in dissecting out a very small sample of diseased cells from a larger mass of surrounding tissue that is healthy. LCM helps to eliminate normal cells from being mixed in with non-responsive cells when taking a sample, and therefore the cells’ biological make-up can be more accurately ascertained.

Since its inception, the LCM core lab has helped a number of investigators with their NIH and other research proposals. Two are profiled here:

- Two new procedures i.e., using LCM to perform miR expression and proteomic analysis, developed through CCTS-funded testbeds of the CCTS Novel Clinical and Translational Methodologies Program, will allow scientists to accurately map protein and miRNA in different nonresponsive cells and compare them with proteins and microRNA in normal, responsive tissues. By being able to perform protein and microRNA analyses on very limited samples, LCM has enabled scientists to overcome one of the biggest challenges of applying systems biology to the characterization of limited samples—lack of sufficient material for detailed molecular analysis. Using LCM, Sen’s research with ischemic wounds has already shown that a specific miRNA, known as miRNA-210, silences key proteins in the wound-healing process. Sen and his research team used an experimental drug called an antagomir, designed to specifically lower the levels of miRNA-210, to increase the levels of these important proteins and skin-cell growth significantly. These findings were published [Biswas Sen et al., Proc Natl Acad Sci U S A. 2010 Apr 13; 107(15):6976-81].

- Michael Freitas, PhD, and John Shapiro, PhD, successfully used LCM to diagnose genetic kidney diseases and study chronic diabetic wounds. This technology – by allowing them to analyze the proteins present in a pure population of one cell type – enabled them to understand the physiology of chronic diabetic wounds and make a conclusive diagnosis of a genetic kidney disease among members of one family seen at Ohio State.
The LCM core laboratory will continue to disseminate this technology to other research teams as CCTS continues to award competitive funding for pilot projects using LCM to help these projects generate preliminary data for extramural funding.

Informatics Supports and Accelerates Research
Among the hallmarks of the translational researcher is that he or she is inclusive—open to sharing information, findings and data that extend and create new knowledge across disciplines, without regard to geographical barriers. In the age of cyberspace—with superfast computers and powerful bandwidth—the ability to quickly share data continues to grow exponentially, as does the need to manage it in a service-oriented way.

Out of that need grew the Translational Informatics and Data Management grid (TRIAD), which allows the collection, storage, integration, analysis, and reporting of heterogeneous and distributed data sets that span organizational boundaries. TRIAD, developed by the Biomedical Informatics Program at Ohio State led by Phillip Payne, PhD, associate professor and chair of the department of Biomedical Informatics, meets the informatics needs found in multidisciplinary and team-based clinical and translational research programs.

Currently, nearly 20 sites, including several CTSA members and other NIH-funded programs, have adopted TRIAD. Critical to the success of TRIAD are its open-source and collaborative design, development, technical documentation, best practices, and software components. Members of the TRIAD community actively participate in the adoption, adaptation and core development of the TRIAD informatics platform.

TRIAD is built upon the robust and highly scalable caGrid middleware platform originally developed by the National Cancer Institute's caBIG initiative to enable data and knowledge sharing between and among cancer researchers.

One example of successful use of TRIAD is the longitudinal tracking of phenotypic data for maternal-fetal dyads in support of perinatal outcomes research as part of an Ohio State-Nationwide Children’s Hospital collaborative (Ohio Perinatal Research Network). Similarly, TRIAD is the backbone of The Ohio State University Comprehensive Cancer Center’s Biorepository and Biospecimen Resource (BBR) that enables researchers to anonymously match stored tumor samples with de-identified clinical data from medical records sources in a seamless fashion. TRIAD protects patients’ privacy rights while making their tissue available for new studies.

TRIAD is an open metadata repository with a portal-based end-user interface, running on common platforms, including Oracle BI-based data warehouse, Microsoft SQL server, i2b2, REDCap and caTissue. The CTSA Service Oriented Architecture Affinity Group is an integral member of the TRIAD community.

Finding Participants to Change the Future of Medicine
Although not every translational research study requires living subjects, many do and a major barrier to the timely completion of such investigations is the lack of study participants. Therefore, the CCTS expends considerable effort in recruiting and retaining people who are interested in helping to advance knowledge—and helping scientists change the future of medicine—by participating in a research study.

The CCTS website informs potential volunteers about the importance of their role in collaborating with researchers to improve individuals’ health. Through an informative recruitment video and other detailed information, they learn that many diagnostic tools, surgical procedures, therapies and medications that today represent the standard of care in medicine were once part of basic research now translated into clinical care. They are educated about HIPAA compliance and how their personal health information is protected, as well as the importance of remaining in a study through completion. They also find information about how to participate in research that is specific to their personal area of interest, or in need of individuals with their unique physical and/or genetic characteristics, through the use of these tools:

- **ResearchMatch.org** - Our website provides information about this NIH-funded, web-based registry developed by Vanderbilt University where investigators and prospective study volunteers are matched. The site reduces the time needed for volunteers to find a study, improves their chances of finding a study of interest and helps inform them about research opportunities in local communities. Ohio State CCTS investigators have benefited by being matched quickly with appropriate volunteers.

- **StudySearch** - In addition, we provide access to our CCTS-developed, web-based tool to help individuals find research studies at Ohio State or Nationwide Children's Hospital. We make this informatics-supported tool available to other CTSA members upon request.

- **Research Concierge** - Our office provides an executive to assist researchers with their projects by helping them navigate the research infrastructure, matching requests for specialized expertise with appropriate faculty, assessing research needs, making recommendations for services and facilitating access to CCTS resources.
Advancing Awareness

As we focus our attention on translating rapidly evolving knowledge created through biomedical research into treatments to improve people’s lives, we must also tell the story of our efforts, successes and plans. By doing so, we may more readily engage study participants, encourage the next generation of scientists, support emerging researchers, promote early career success and sustain established clinical and translational investigators.

Central to this effort is the work of communications and marketing professionals who create and maintain our extensive website, develop interesting brochures, reports and articles, and leverage social media sites as well as traditional media opportunities, to tell our story. In addition, more than a dozen undergraduate students in journalism, photojournalism and public relations have honed their skills on our behalf, creating a recruitment video to attract participants, Web content and electronic and paper-based communications vehicles—all designed to interest the public in what we do.

We also further awareness through our commitment to establishing and supporting a culture of collaboration. Cooperation and teamwork extends our mission. We see ourselves as part of a “network of networks,” aligning scientific themes and platforms across the Health Sciences. For example, we are leveraging our relationships internally with Ohio State’s Comprehensive Cancer Center, Center for Personalized Health Care and other University and Medical Center entities. We work closely with local entities including the Fisher College of Business, Center of Science and Industry, Battelle Memorial Institute and Nationwide Children’s Hospital and also are involved in a statewide genomics initiative.

We collaborate in industry partnerships and partner with Coriell Institute in New Jersey, the Institute for Systems Biology in Washington and, of course, fellow members of the CTSA national consortium.

Specific awareness-raising and collaboration-supporting initiatives include:

Annual Scientific Meeting – The purpose of this forum is discussion and presentation of our year-long integrated focus on a defined topic or discipline to link education, pilot funding and translational infrastructure, all designed to stimulate engagement in topic-related clinical and translational activities. Our topic for 2010 was Comparative Effectiveness Research; in 2011 we will discuss Translational Therapeutics and Diagnostics.

Discovery, Innovation and Commercialization Workshop - In conjunction with the Ohio State’s Fisher College of Business Center for Entrepreneurship, we developed a two-quarter-long series integrated with the creation of a new consulting core focused on enhancing innovation and bringing new discoveries to market.

Shared Resources Symposium – This weeklong series focuses on sharing opportunities to utilize the more than 20 core laboratories across the University, including the new, CCTS-funded LCM core lab, to facilitate basic, clinical and translational science.

The Science of Team Science (SciTS) – This newly developed discipline focuses on promoting team-based research through empirical evaluation of the processes critical to successful team research. SciTS was developed through the CCTS Team Science Pilot Projects to examine the trans-disciplinary and social networking processes taking place in successful collaborations. The aim of this IRB-approved protocol is to provide insights into best practices of science teams on the Ohio State campus.

Collaborative Research Portal – OSU:Pro is a web-based program designed to help investigators get information from other researchers. By completing search fields indicating specific research interests and related parameters, investigators can quickly query a vast database to find basic and clinical scientists across campus who are working in similar related fields and who may be interested in interdisciplinary collaboration on new and innovative projects.

Comparative Effectiveness Research (CER) – Since the enactment of the 2009 American Recovery and Reinvestment Act, Comparative Effectiveness Research (CER) funding opportunities have increased dramatically. The National Heart, Lung and Blood Institute defines CER studies as “…comparing the impact of different options on comprehensive health outcomes, including patient mortality, morbidity, quality of life, and performance of the health system. The overarching goal is to provide better evidence so that individual patients will receive effective, efficient, patient-centered care.”
Last year, CCTS focused its annual Scientific Meeting on informing clinicians about CER-generated evidence, which shows the relative merits of various drugs, medical devices, surgeries and tests. With the aim of making sure patients are receiving the most effective, reliable treatment option available, we then instituted CER training program, funded by an NIH Workforce Development grant, in collaboration with OSUMC, Ohio State’s College of Public Health and Nationwide Children’s Hospital. The program consists of ten hours of didactic instruction, a two-week summer session, capstone projects and a conference in sponsorship with other regional CTSAs.

Among the scientific impacts of our CER program are enhancing collaboration among researchers and promoting dissemination and application of CER results. Led by Tom Wickizer, PhD, professor, College of Public Health, one aim of our program will be helping investigators understand that CER is different from most research because, rather than being focused on randomized, highly selective groups that assess efficacy under narrowly controlled conditions, it instead looks at “real world conditions,” and as such is a type of research we encourage them to embrace. Our CER focus in the coming year will be on inflammation, tissue injury and repair, with a special interest in prevention of ACL tears in young women.

Community Engagement - We are committed to facilitating and supporting viable and trusting relationships within communities, with the goal of educating and training community partners, the public and researchers about the importance of engaging the community in the translational research process. Over the past two years, innovative pilot work on diverse communities in Ohio has been the focus of the Community Engagement Core. Now, under the direction of Kelly Kelleher, MD, MPH, Vice President for Community Health & Services Research at Nationwide Children’s Hospital, the Core is aiming more squarely at the unique needs of the Appalachian community. Specifically, through the formation of the Appalachian Translational Research Network (ATRN*), three universities, (The Ohio State University, University of West Virginia and University of Kentucky) and others, all governed by an Appalachian Community Advisory Committee Assembly, aim to improve the health of Appalachian communities through translational research.

These partnerships build on existing research from experienced CCTS investigators. For example, Mary Ellen Wewers, PhD, MPH compared the health behavior differences among rural and urban Appalachian communities related to obesity and diabetes, food insecurity and access to fresh fruits and vegetables. Her efforts resulted in establishment of a community leadership team to improve the health of this unique population while furthering community acceptance of and participation in translational research.

A new pilot research award, jointly sponsored by Ohio State’s CCTS Community Engagement Program and the West Virginia Clinical Translational Science Institute Community Engagement and Research CER Program, is designed to stimulate collaboration between the respective campuses and to increase community-engaged research, including community-based participatory research in the Appalachian region. A second new pilot research award is jointly sponsored by the Ohio State CCTS and the University of Kentucky CCTS. These joint awards aim to catalyze the development, or enhance the maturation of, multi-institutional research teams capable of performing highly innovative, extramurally fundable, community-engaged research that will contribute to the health and wellbeing of Appalachian communities.

*ATRN is a collaborative effort among community partners (Poverty Center and Food Innovation Center). Other partners include Nationwide Children’s Hospital Partners for Kids, Appalachian Cancer Control Network, Ohio State’s Extension Service, CCTS Appalachian Supplement-University of Cincinnati and selected counties.
Developing the Researcher

Our commitment to providing a robust and unique learning experience is evidenced by the overall goal of our Research Education, Training and Career Development Program—to establish and cultivate an institution-wide teaching environment inherently linked to all aspects of the CCTS. Under the direction of Philip F. Binkley, MD, MPH, dean for Faculty Affairs in Ohio State’s College of Medicine, we have developed a program that encompasses researchers along the continuum—from high school students to postdoctoral candidates—to create and sustain a clinical and translational workforce for the future.

In addition, we promote a culture of scientific collaboration among basic, clinical and translational scientists through mentoring, modeling, and creating a common learning environment through progressively expanding our “virtual college” of science education and training programs.

OSU Graduate Interdisciplinary Specialization in Biomedical, Clinical and Translational Science (GISBCT) is our newest program, which exposes students to a broad range of topics through core courses focusing on the basic components of clinical and translational science. Students also complete electives that allow them to pursue topics related to core competencies across Ohio State’s seven Health Sciences colleges (Nursing, Medicine, Veterinary Medicine, Optometry, Public Health, Pharmacy and Dentistry), Psychology and Biophysics for a truly interdisciplinary experience. Other disciplines may be added. For example, a doctoral engineering student with an interest in applying that discipline to biomedical research is eligible, as would be an astrophysicist with ideas about novel delivery of radiation oncology treatment.

**Other degree offerings** supported by the CCTS include the MPH in Clinical Investigation, the PhD in Translational Science and the MS in Medical Science. These unique programs combine comprehensive training in the population health sciences with the principles and practices of clinical and translational research. An additional new degree program is in development: The MS in Medical and Translational Science in Biomedical Informatics develops a strong foundation in biomedical science for biomedical informaticians.

Pre-doctoral training and early stage career support are provided through our TL1 award program for students pursuing graduate education and training in clinical and translational science and through our KL2 award program for junior faculty conducting patient-oriented and/or translational research. Mentorship is an integral part of these programs. We recently participated in a CTSA-funded multisite trial led by the University of Wisconsin and have based our mentorship program components—such as access to the mentor, good rapport, honesty about progress, career advancement and expertise—on our learning there.

**Tools of the Trade** is a day-long event for early investigators representing all disciplines who need these tools and resources to initiate research. Nascent investigators learn about participant recruitment, working with mentors, publishing, and organizing and collecting data. They also have the opportunity to participate in a mock IRB review.

**CCTS Summer Research Experience Program,** funded by the American Recovery and Reinvestment Act, targets high school students from schools that emphasize preparing students for Science, Technology, Engineering, and Medicine (STEM) careers. Each student is placed with a principal investigator who encourages the student’s interest in a STEM career by allowing him or her to function as an active and contributing member of the team.

In addition, CCTS offer seminars, workshops, and practicums focused on developing translational research skills and fostering new collaborations among basic scientists and clinicians from a wide range of disciplines.

**Our Mentored Research Training Program (TL1)** provides trainees with skills required to develop a career in trans-disciplinary clinical and translational research. We build on strong programs that already exist in Ohio State’s Colleges of Medicine, Nursing, Pharmacy, Optometry, Public Health, Veterinary Medicine, and Dentistry by selecting awardees from among PhD students focused on clinical or translational science pre-professional degree students enrolled in resident or fellow education programs, and those pursuing training in health professions. Awardees are selected through a rigorous NIH-review style application process.
Spees Seeks Link Between Nutrition and Prostate Cancer Progress

Colleen Spees, MEd, RD, LD, a registered dietitian and doctoral fellow of Internal Medicine, is making an entry into the emerging field of nutrigenomics by studying TP53 mutations and gene expression patterns, which are believed to be correlated with a poorer prognosis in prostate cancer. It is well established that p53, known as the “guardian of the genome,” is a key regulator for the cell cycle, functioning as a tumor suppressor protein. p53 mutations are noted in approximately 50 percent of all human cancers. Spees is seeking to show how p53 immunostaining in human prostate cancer is related to higher grade cancer, larger cancer volume, and angiogenesis.

In addition, Spees is seeking to show that dysregulation of p53 and other markers of aggressive prostate cancer may be correlated with dietary intake. Mentored by Steven Clinton, MD, PhD and Kay Wolf, PhD, RD, LD, she is also collaborating with the Harvard School of Public Health to study tissue samples and records from a prospective cohort of men in the Health Professionals Follow-Up Study (HPFS). Although over 25 years of dietary records have been analyzed in the HPFS cohort, Spees’ project will be the first of its kind to assess the relationship of dietary patterns to p53 dysregulation in any human cancer. Her efforts are expected to provide data to support future studies of nutrition and gene interactions that may be critical to the understanding and prevention of human carcinogenesis, as well as to eventually impact treatment options and novel therapies to reduce the cancer burden on society.”

In addition she has co-authored Ohio State’s first Nutritional Genomics graduate course which was launched spring 2011.

Lustberg Studies Effect of Chemotherapy on Heart

Maryam Lustberg, MD, MPH, assistant professor of Internal Medicine, Division of Medical Oncology, is studying the possible deleterious effects of the chemotherapy drug, anthracycline, on the cardiovascular systems of cancer survivors. Anthracycline is believed to cause subtle changes in cardiac tissue over time, leading to cardiovascular problems for cancer survivors later in life. Mentored by Charles Shapiro, MD, in a National Cancer Institute (NCI)-funded study, “Novel Markers of Anthracycline Damage,” Lustberg’s goal is to find a way to detect and prevent cardiac injury in patients who are treated with this drug. Because there is currently no reliable test to determine cardiac tissue damage in cancer patients treated with anthracyclines, Lustberg will work in collaboration with Subha Raman, MD, associate professor at Ohio State’s College of Optometry, to use Cardiac Magnetic Resonance (CMR) imaging. Studies in other populations have shown that CMR has the capability to see subtle changes in cardiac tissue. In addition, Lustberg will use blood markers of research participants to study endothelial progenitor cells, primitive cells made in the bone marrow that can migrate to areas of blood vessel injury and help repair damage. The volume of these cells will be measured over time to see if they have a correlation with heart damage. Adult breast cancer patients and children with malignancies being treated with anthracyclines will be the primary participants in the study, which is being continued through funding from the NIH.

Our Career Development Program (KL2) provides salary support and protected time for highly qualified junior faculty to conduct multidisciplinary clinical or translational research. The purpose of the KL2 program is to help ensure that a diverse pool of highly trained scientists is available in adequate numbers and in appropriate research areas to address the nation’s biomedical, behavioral, and clinical research needs. The program lead by Karla Zadnik, OD, PhD, associate dean and professor at Ohio State’s College of Optometry, seeks to reward a track record of academic success and clear potential for the future by providing funding, as well as support services to faculty. Some support services: access to CCTS professional services and staff, including biostatistics, subject recruitment and human subjects approval; a training curriculum; individualized career development and mentorship from the trainee’s own appointed scientific committee; and participation in the National Association for Clinical Research Training/Society for Clinical and Translational Science Joint Annual Meeting in Washington, DC.

At this time we are able to support as many as seven KL2 scholars annually; since our inception we have sponsored 13. Of these, two are profiled here:

Heathcock Collects Novel Data Toward Helping Preterm Infants

Jill Heathcock, PhD, an assistant professor in the Department of Physical Therapy, Ohio State’s School of Allied Medical Professions, is embarking on initial studies that will allow her to identify which part of preterm infants’ brains might be most responsive to rehabilitation. Infants born before 32 weeks gestation are known to have a higher risk of developmental delay, leading to problems such as coordination disorders, cerebral palsy and learning disorders. Using motion analysis and neuroimaging, Heathcock seeks to establish a link between the behavior and brain of a preterm infant. Each infant in her study is between eight and 12 weeks old. Through motion analysis, each baby’s level of coordination, and other developmental categories, is scored over a 10-visit period and compared to that of typical, healthy infants.

Neuroimaging is accomplished through non-sedation MRI, for which Heathcock is learning techniques from her mentor, Robert Almli, PhD at Washington University in St. Louis. In addition to collecting important data for her study, she hopes to bring non-sedation MRI techniques to Nationwide Children’s Hospital in Columbus. By better understanding brain relationships and identifying which infants are at risk for problems, she hopes eventually to create and evaluate the effectiveness of rehabilitation treatments to ameliorate preterm infants’ developmental delay problems.
critical care and sleep medicine, received a KL2 grant to examine how supplemental oxygen therapy can protect neurons during brain trauma, such as stroke, to prevent brain cell death. Duringstroke, blood vessels in the brain are blocked, preventing oxygen and glucose from reaching the brain. As a result, the brain releases excessive levels of the neurotransmitter, glutamate, causing damage to brain tissues. Khanna’s research addresses whether the glutamate released during stroke can be used as a source of energy when supplemental oxygen is applied. Her past research has shown that oxygen therapy provided during stroke can correct stroke-induced oxygen deficiency and protect brain tissue. She theorized that if the brain has sufficient oxygen during trauma, it might use glutamate instead of glucose for energy. In the Journal of Cerebral Blood Flow and Metabolism, Khanna reported a reduction in brain damage when oxygen therapy was given during stroke-induced hypoxia (oxygen starvation). However, when oxygen therapy was applied after removing the blockade and blood flow was restored, damage was more severe, pointing to a limited therapeutic window of opportunity for oxygen therapy. Since current treatment for stroke includes the administration of medication that dissolves clots, this finding will be important in clinical translation. Khanna is working to strengthen her preliminary findings for a NIH proposal in hope of developing therapeutic oxygen strategies targeted to address metabolic damage in stroke.

Making Oral Cancer Treatment Stick
Susan Mallory, DDS, PhD, a professor of Oral Pathology, College of Dentistry, and her research team were awarded a pilot grant to find a way to control delivery and dose of medications for precancerous lesions in the mouth. They successfully developed a novel mucoadhesive patch for intraoral delivery of the chemopreventive, fenretinide. Earlier studies clearly showed that in cell cultures fenretinide exhibited optimum therapeutic effects. However, in human clinical trials, results were discouraging, because when given systemically, the chemopreventive resulted in toxicity and when applied directly to the oral lesions, drug concentrations were below therapeutic levels, due to saliva “washing away” the medication. Mallory and her team devised an adhesive patch that can adhere to oral mucosa, thereby delivering a therapeutic dose directly to the pre-cancerous lesions. The mucoadhesive patch consists of three layers: an impermeable backing layer (blocking delivery of fenretinide away from the precancerous lesions), a mucoadhesive “donut-shaped” layer and a drug-releasing “donut-hole” layer. Together, these layers act in harmony to provide adhesion and drug delivery to the oral precancerous lesion. This CCTS pilot grant has led to a $100,000 research award from the Fanconi Anemia Research Fund to evaluate patch-mediated fenretinide distribution in an animal model. The

Exline Determines Risk of Nosocomial Infection
Matthew Exline, MD, assistant professor, Pulmonary, Critical Care and Sleep Medicine, received a KL2 grant to determine if patients’ immune system function might predict their risk of developing a nosocomial or “hospital-acquired” infections. He is investigating immune suppression that occurs in septic patients and the subsequent risk of developing nosocomial infections during their intensive care unit (ICU) stay. Sepsis, a severe inflammatory response secondary to an infection, is the 10th leading cause of death in the United States and its incidence is on the increase. During sepsis, the body initially suffers an inflammatory surge, followed by a second phase in which the patient’s immune system is weakened. With a weakened immune system, the patient’s body can no longer respond to the primary infection. At this point, some patients develop a secondary infection—nosocomial or “hospital acquired”—that often is the ultimate cause of death in these patients.

Exline’s study is looking at the function of monocytes—a specific type of immune cell—during sepsis. His study collects blood from both septic patients and other critically ill patients who do not have infections. He then compares the monocyte function and protein expression between the two groups. His goal is to see if functional changes in a patient’s immune system might determine if hospital-acquired infections can be predicted based on the function of the immune system at time of admission to the ICU. Exline’s work has resulted in several abstracts to the American Thoracic Society’s International Conference, a publication in American Journal of Respiratory and Critical Care Medicine and a K23 grant from the National Heart, Lung and Blood Institute for further study.

Pilot and Collaborative Studies Program
Nowhere is the difference CCTS makes in advancing translational research more apparent than through our successful Pilot and Collaborative Studies Program. Directed by Chandan Sen, PhD, associate dean and professor at Ohio State’s College of Medicine, the program’s primary aims are to enhance the development of new multidisciplinary scientific teams through pilot funding, to support the generation of preliminary data, to respond to new scientific opportunities and priorities through targeted pilot Requests for Applications, to support early-stage investigator development, to enable clinical and translational science and to form strategic partnerships.

Five representative pilot programs are profiled here:

Protecting the Brain during Stroke
Savita Khanna, PhD, assistant professor of Surgery, was awarded a pilot grant to examine how supplemental oxygen therapy can protect neurons during brain trauma, such as stroke, to prevent brain cell death. During stroke, blood vessels in the brain are blocked, preventing oxygen and glucose from reaching the brain. As a result, the brain releases excessive levels of the neurotransmitter, glutamate, causing damage to brain tissues. Khanna’s research addresses whether the glutamate released during stroke can be used as a source of energy when supplemental oxygen is applied. Her past research has shown that oxygen therapy provided during stroke can correct stroke-induced oxygen deficiency and protect brain tissue. She theorized that if the brain has sufficient oxygen during trauma, it might use glutamate instead of glucose for energy. In the Journal of Cerebral Blood Flow and Metabolism, Khanna reported a reduction in brain damage when oxygen therapy was given during stroke-induced hypoxia (oxygen starvation). However, when oxygen therapy was applied after removing the blockade and blood flow was restored, damage was more severe, pointing to a limited therapeutic window of opportunity for oxygen therapy. Since current treatment for stroke includes the administration of medication that dissolves clots, this finding will be important in clinical translation. Khanna is working to strengthen her preliminary findings for a NIH proposal in hope of developing therapeutic oxygen strategies targeted to address metabolic damage in stroke.
team, which also includes Drs. Peter Larsen, Gary Stoner and Zhongfa Liu, has received a patent on the mucoadhesive ferretindole patch and anticipates that preliminary data ultimately will allow them to obtain grant support for human clinical trials.

**Imaging to Find Cause of MS Symptoms**

David Pitt, MD, assistant professor of Neurology, received a pilot grant for preliminary research for possible future studies that may result in new treatments and better treatment decisions for persons with multiple sclerosis (MS). As the initial step in that direction he and colleague Petra Schmalbrock, PhD of the OSU Wright Center of Innovation are taking a new scientific approach to observing cortical demyelinating lesions. In MS, the patient’s own immune system destroys myelin, a fatty sheath around neurons. Without myelin, nerves cannot function well, leading to intermittent neurological problems that become chronic and irreversible. The critical goal for Pitt’s research is to find a new method to image cortical lesions in each phase of the disease using ultra-high field MRI. Pitt and his team hope this will shed some light on the causes of cortical lesion formation (inflammation) or a different process entirely. Their hope is that once cortical lesions can be detected in a clinical setting, the efficacy of anti-inflammatory drugs can be tested to see if the demyelination process can be arrested or ameliorated.

**Finding New Treatments for the Most Deadly Skin Cancer**

Gregory Lesinski, PhD, assistant professor of Internal Medicine, is collaborating with Ohio State’s College of Pharmacy to discover a new class of compounds that could result in novel therapy for the treatment of melanoma, the most deadly form of skin cancer, which has very few effective therapies available. Lesinski and his team were awarded a Pilot and Collaborative Transitional and Clinical Science grant to study a novel class of anti-cancer, small molecule inhibitors derived from a natural product, curcumin. The inhibitors will target the STAT3 pathway, which is highly activated in numerous types of cancer cells, particularly melanoma. The College of Medicine designed the new drug, called FLLL-32, using computer modeling. Lesinski and his colleagues tested the compound to validate its ability to kill melanoma cells and now have data showing that it kills melanoma cells in test tubes at relatively low doses with higher specificity than any other inhibitors with which the team has worked. Further research is necessary to refine the potency and structure of the inhibitors. After completing larger studies and testing derivative compounds, Lesinski is hopeful this series of compounds might result in a suitable new drug for evaluation in future pre-clinical and possibly even human clinical studies. An article directly related to this project has been published in Molecular Cancer and other manuscripts have been submitted.

**Advancing Care for Children with Mood Disorders**

Mary A. Fristad, PhD, ABPP, professor of Psychiatry, Psychology and Human Nutrition, is evaluating a program to teach children with mood disorders and their family members about living with depression or bipolar disorder. She and her team were awarded a pilot project grant for Community Engagement in Research to examine the effectiveness of multifamily psychoeducational psychotherapy (MF-PEP) in a community setting. Partnered with Nationwide Children’s Hospital (NCH) Behavioral Health, the study is evaluating a pilot implementation of MF-PEP at two NCH community-based centers. The eight-session, educational manual-based treatment is designed as an adjunct to current medications and psychotherapy. Consisting of separate parent and child groups, participants are taught about symptoms, medication management, problem solving and communication skills and coping strategies. The current project extends a prior efficacy trial to determine whether beneficial effects observed during research will translate to a community setting. The goal of this study is to determine whether therapists, using “flexibility within fidelity,” are able to learn and implement MF-PEP, discern which aspects of MF-PEP work well in community settings and which aspects are more difficult and may require adaptation. A manuscript is in production, and data collected will be used to apply for a larger grant to study implementation of MF-PEP with more diverse populations, including urban, rural and Appalachian regions.

**Learning from Every Patient**

William E. Smoyer, MD, Vice President of Clinical and Translational Research at The Research Institute at Nationwide Children’s Hospital (NCH), and Amy Newmeyer, MD, Director of the Comprehensive Cerebral Palsy Program at NCH, are leading a team in a pilot program to fully integrate clinical care and research. This novel program utilizes a standardized patient care plan and systematic comprehensive research data collection at the point of care for all children seen for cerebral palsy. In collaboration with the Ohio State’s Motion Analysis Lab, researchers will also examine motor outcomes and swallowing function, among other factors. The overall mission of the Comprehensive Cerebral Palsy Program is to provide outstanding clinical care, while fully integrating innovative translational research that will rigorously evaluate both current and novel therapeutic interventions in order to improve the care of all children with cerebral palsy. This program’s vision is to ensure that every child with cerebral palsy will reach his/her maximum potential in physical, cognitive, and social-emotional development, and also contribute to new knowledge that will improve future care for all children with cerebral palsy. This effort is part of a “Research Best Practices” initiative of the National CTSA Consortium Child Health Oversight Committee (CC-CHOIC).
We hope you have been informed—perhaps even inspired—by learning about our translational research efforts and the incredible outcomes we have experienced thus far.

As we look to the future, we will continue to search for new opportunities to fund and participate in trans-disciplinary and multidisciplinary investigations that will lead to solutions for our most pressing healthcare problems. As our successful findings continue to mount and build upon other discoveries, we are humbled by the trust our patients and their families put in our endeavors, and we are reinvigorated as we rededicate ourselves to our mission.

We will work hard to align the major cross-cutting themes that will help direct scientific efforts to the most urgent areas; to make new drug discoveries and translational therapeutics; uncover markers for disease; and understand how immunology impacts multiple diseases. In addition to focusing on specific diseases, we will broaden our vision to look at common mechanisms that cut across multiple conditions.

We will redouble our efforts to develop and encourage a robust pipeline of future investigators, providing them with not only monetary support, but mentoring, resources, feedback and opportunities for collaboration at all levels.

In addition, we recommit ourselves to seeking new ways to activate the scientific community. We promise to continue working in collaboration with the venerable institutions that are our fellow CTSA members, other colleges and universities at home and abroad, commercial partners, members of our local community—and most importantly, the individuals who volunteer to participate in research dedicated to translating discoveries into practical healthcare solutions.

We thank you for your interest and welcome your questions or comments. We look forward to opportunities to partner with you as we move forward together.