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We Are Inventive

Inventions submitted in FY2016
Drexel total: 103  
CoM: 25

Patents issued since 2001
Drexel total: 296  
Number with CoM inventors: 73

Patents issued in 2015
Drexel total: 48  
Number with CoM inventors: 10

DID YOU KNOW?

Inventions submitted in FY2016
Drexel total: 103  
CoM: 25

Total inventions submitted
Drexel all time total: 1,884  
CoM since 2001: 648

LETTERS

I just read the article “Careers Outside the Clinic” in the Spring/Summer 2016 edition of the Alumni Magazine. I especially enjoyed Dr. Tressler’s and Dr. Khurmi’s comments about their careers in the pharmaceutical industry. I have spent the last 25+ years in drug development and pharmaceutical medical affairs, and I am developing a website for physicians in the biopharmaceutical industry or physicians or students looking for information about industry careers. The website is called BioPharm-Medicine.com. It’s still in an early phase, but the current version is posted online so my collaborators can review and send me their comments and additions.

Bernadette DeArmond, MD, WMC ’66

After reading the Vol. 2 No. 1 Alumni Magazine [Spring 2015], the idea of giving back began a thought process. Why not try to name a scholarship “Class of ’56”? Kickoff contributions from John Wright and Dorothea Johnson got it started. A blockbuster gift from Bill “Poppsie” Forrest took it to the next level. Richard Hartmann Jr. spurred it on with another needle mover. Myron Resnick and Elliott Sauertieg chipped in to take the fund to the $48,000 mark. The total keeps climbing and it appears that we will be approaching the $100,000 level to name the scholarship.

Thanks to all,
Herb Kean, MD, HU ’56

Editor’s Note: The fund has reached $96,000, thanks to a $48,000 match from the Schleyer Family Matching Gift Challenge for Scholarships in Medicine.

WE WELCOME YOUR LETTERS

Correspondence may be mailed to Editor, Drexel University College of Medicine Alumni Magazine, 1601 Cherry Street, Suite 11484, Philadelphia, PA 19102, or emailed to jracz@drexelmed.edu. Please include your contact information. The magazine staff reserves the right to edit for space and style.
Dear Fellow Alumni,

It gives me great pleasure to serve you as the new Alumni Association Board president. In my five years as a board member, I have witnessed a renewed energy and excitement about our medical school. Your continued engagement with the students, faculty and each other will keep this momentum going!

A new initiative from the board is the creation of the Cultivation and Engagement Committee, with subcommittees for the College of Medicine and Graduate School of Biomedical Sciences and Professional Studies. These groups function as alumni ambassadors, reach out to classmates to encourage them to get involved, and generate new ideas for you to participate in the life of your medical alma mater. Here are a few good ideas to consider:

• Are you a medical school graduate from a class year ending in 2 or 7? Last year we had a 19 percent increase in graduates attending Alumni Weekend! Get involved in helping to gather your classmates at reunion events May 19 and 20, 2017.

• Are you in the Philadelphia area and want to connect with students? Become a Discovery Day judge, preceptor, HOP Clinic physician or speaker at a student event.

• Are you in a different part of the country or world but want to give back to our students? Join one of our LinkedIn groups, where you can connect with MD or PhD students and offer career advice.

• Keep us updated, and please share your new contact information with us by calling 215.762.2371 or emailing medical.alumni@drexel.edu. This will ensure that you receive alumni publications, invitations to events near you and other important news. See the inside back cover for more details, and stay connected.

I encourage you to consider the ways that you can reconnect with the College of Medicine. Staying in touch has never been so easy – and I guarantee you it will be very rewarding!

Timothy A. Manzone, MD, MCP ’89, JD
President, Alumni Association Board of Directors
Cell metabolism and alterations in the microtubule cytoskeleton, a network of structural proteins with diverse cellular functions, offer important clues to understanding cancer behaviors and how cancer cells differ from their healthy counterparts. New research being conducted by biochemist Mauricio Reginato, PhD, and physician/clinical researcher Christos D. Katsetos, MD, PhD, is elucidating exactly how brain tumors grow and invade the surrounding brain and what can be done to curtail cancer growth and spread.

The cross-disciplinary partnership began two years ago with a serendipitous turn of events. Since arriving at Drexel, Reginato had been studying breast cancer, and he had focused his research on an enzyme called OGT (O-GlcNAc transferase), which was shown to be sensitive to changes in glucose. “We found that OGT is highly elevated in breast cancer, but when we turned off this enzyme, the breast cancer cells stopped growing and eventually died,” says Reginato, director of Drexel’s Graduate Program in Cancer Biology.

More recently, Reginato read an intriguing paper that suggested that OGT might also play an important role in brain cancer. Days later, he received an email from Katsetos, requesting his participation in a research project. He’d never met Katsetos and was unaware until then that their research interests aligned.

Katsetos, who holds joint appointments in pediatrics and pathology at the College of Medicine and St. Christopher’s Hospital for Children, has spent more than 25 years studying the cellular and molecular mechanisms associated with the development and progression of brain tumors in children and adults. During the past decade, his work has focused on high-grade gliomas/glioblastoma. High-grade gliomas are of particular concern to Katsetos because they are difficult to contain and refractory to current treatment modalities. “Despite major advances in the genomics and epigenomics of brain tumors, these tumors have a dismal prognosis, and no major progress has been made in their treatment in the past 10 years or so,” Katsetos says.

The project Katsetos was proposing involved looking at a different protein in brain cancer, called spastin. Spastin, an enzyme that severs microtubules, was previously found to be overexpressed in high-grade gliomas/glioblastoma by Katsetos and collaborators, including Reginato and neurobiologist Peter W. Baas, PhD, professor and director of Drexel’s Graduate Program in Neuroscience.

Earlier work by Baas, who has studied microtubule-severing proteins extensively, suggested that spastin could be a powerful target to curtail the motility and invasion of cancer cells.

The goal of the new study would be to identify novel molecular targets for the development of adjuvant therapies for cancer, particularly brain tumors. “As soon as we met and discussed our ideas, we realized we could complement each other very well,” Reginato says. In addition, Baas would lend his expertise in spastin.

“Our research approach is somewhat unique in that we are investigating both basic cellular mechanisms and translational aspects together”

The first step, with funding from the Commonwealth Universal Research Enhancement (CURE) program, was creating a preclinical animal model of glioblastoma. The first-ever orthotopic xenograft model launched at Drexel, which implants human glioblastoma cell lines into the brains of immunocompromised mice, allowed the team to study in vivo and ex vivo the effects of OGT or spastin suppression on cancer growth and spread.

Before long, their hypothesis was confirmed. “We could see that when we reduced the expression of OGT, we blocked the growth of glioblastoma,” Reginato says. “We could confirm that OGT was regulating the metabolism, both glucose and lipids, in the brain.” And, according to Katsetos, “a similar trend, leading to abrogation of glioblastoma growth, was observed, both in vitro and in vivo, after suppressing the expression of spastin.”

The CURE support has underwritten the initial proof-of-concept
work, but the team is now looking for more funding from outside sources to take the research to its next stage. “Having been able to show that suppressing the expression of OGT and spastin had remarkable inhibitory effects on tumor growth, we feel we have some very exciting and promising preliminary data with potential therapeutic implications,” Katsetos says. “Our research approach is somewhat unique in that we are investigating both basic cellular mechanisms and translational aspects together, but it has served us well.”

Along with additional collaborators, they have already developed a drug for OGT, which is currently being tested in animal models. “We know there’s no single drug that can kill cancer, but we would like to see this drug used as a first line of treatment to sensitize tumors to radiation therapy,” Reginato says. “The best case scenario, of course, would be to move this into clinical trials.”

Katsetos believes that with the use of computer modeling and translational bioinformatics, a spastin-selective drug may well be on the immediate horizon. “Certainly, it’s a matter of years rather than months, but the initial effects are forthcoming, and our data lend credence to our conceptual approach and overall hypotheses.”

Reginato credits their momentum to the help of graduate students Christina Ferrer (now a postdoctoral fellow at Harvard Medical School) and Zachary Bacigalupa. In fact, Reginato says that it was the high quality of graduate students that drew him to Drexel in the first place. “The truth is, professors and medical doctors can come up with great ideas, but you need people to help you actually carry them out in the laboratory,” he says. “Drexel’s top-notch graduate students have been crucial to the success of this research.”

The collaboration across research disciplines has also been uniquely rewarding, Reginato says. “With Christos’ help, we were able to look at a tissue microarray and compare normal brain cells to those of a glioblastoma patient. When we saw that the OGT was highly elevated in brain cancers, that gave us the rationale to then try to target it in the glioblastoma cells. In our collaboration, we can confirm things we typically only see in tissue cultures in real patients.”

The excitement around the project comes not just from achieving great initial results but also from the satisfaction of auspicious teamwork. “We know that collaborations within institutions tend to be the most effective, and to the institution’s credit, Drexel has given well-rounded basic scientists like Mauricio and physician-scientists like myself the opportunity to take on formidable problems intramurally,” Katsetos says. “No doubt we are stronger working together.”

**“Emerging Microtubule Targets in Glioma Therapy,” an article in Seminars in Pediatric Neurology, April 2015. Additional authors included Agustin Legido, MD, PhD, professor of pediatrics and neurology at Drexel and chief of the Section of Pediatric Neurology at St. Christopher’s Hospital for Children.**
Anup Katheria, MD ’04, can picture that life-changing moment, as a Drexel medical student, when an attending obstetrician let him help deliver a set of twins. “I remember thinking how these babies’ lives began right then and there,” he says. “That was a real spark — it’s when I knew I wanted to spend my career taking care of children from birth and help them achieve their true potential.”

As the founding director of the Neonatal Research Institute at Sharp Mary Birch Hospital for Women & Newborns in San Diego, Katheria is doing exactly what he envisioned.

A native of Chicago, Katheria received his undergraduate degree from UCLA before coming to Drexel University College of Medicine. After graduating, he returned to the West Coast for his pediatric training at Children’s Hospital of Orange County and a neonatology fellowship at the University of California, San Diego.
In 2013, Katheria joined Sharp Mary Birch Hospital for Women & Newborns in his current role, which allows him to help children both as a researcher and as a physician. He spends roughly half of his week in the intensive care unit, attending to premature infants and babies who have been born with other health challenges. The other half of his time is devoted to developing new ways to improve care for his patients. “I love taking care of babies on my rounds — that is something I have enjoyed since my days doing a pediatric rotation at St. Christopher’s Hospital for Children while I was in medical school,” he says. “But I’ve always had a passion for research and learning more about how we can improve what we do at bedside.”

Simple but novel concepts
With no previous research program of any kind in place at Sharp Mary Birch, Katheria has built his organization from the ground up with a mission to develop leading-edge treatments and evidence-based best practices for newborn care. He also brought with him, by means of a National Institutes of Health grant, groundbreaking “LifeStart” resuscitation beds — making Sharp Mary Birch the first hospital in the United States to have them. These beds, conceived by an obstetrician in the U.K., allow newborns who need resuscitation to stay with their mothers, leaving the umbilical cord still connected. A compact structure supports a stable, heated platform for the baby that rests over the mother’s body. Studies have shown that babies benefit from delayed or deferred cord clamping, but in cases where babies have difficulty breathing, resuscitation has taken priority. The beds’ design permits both at the same time.

Katheria’s current work involves studying how allowing babies to stay with their mothers in this way can help achieve better outcomes. “This protocol helps with bonding between mother and baby, and we know that the physiological benefits of delayed cord clamping include allowing more blood from the placenta to the baby’s lungs and brain until spontaneous breathing is established. We think the longer we can keep babies attached to their mothers, the less likely it is that they will need the ICU or develop complications like cerebral palsy,” he says.

Katheria and his multidisciplinary team have already studied this approach in premature babies to great outcomes. A new proof-of-concept study, completed in September, looked at 60 full-term babies who had a high risk of brain injury. Katheria hopes to expand to a larger multicenter trial across the United States that can follow the children to monitor their longer-term outcomes. “If we can prove that it works, there are great implications for global health care,” Katheria says. “This is a practice that can be adopted everywhere, especially with babies born in the developing world with these problems and without access to ICUs. Keeping them with their mothers longer could help save them.”

A member of the Society for Pediatric Research, Katheria has shared his findings, including some studies that involve the use of functional echocardiography and delivery room resuscitation, at national meetings. At the heart of Katheria’s research is the drive to improve care through new technologies and simple but novel concepts. “There are always ways to do things better,” he says. “In health care, you want to make something that’s uncomplicated, inexpensive and easy to replicate.”

Katheria conducted an NIH-funded pilot study to compare the effects of giving babies additional stem cell–rich blood through milking the umbilical cord versus through delaying clamping. “We focused on babies born via cesarean section, which is about 80 percent of babies born prematurely. We were able to show that these babies benefited from cord milking, with higher hemoglobin, better heart function and higher blood pressure. We hope to do a larger study and follow the babies for two years.”

He’s also studying how providing caffeine to premature babies at birth could help improve breathing and cardiovascular function, and reduce the need for a breathing tube. Caffeine has already been proven to help babies with apnea, but it is typically given 12 hours after birth or later. “In our pilot study we looked at what would happen if we didn’t wait to see if there was a breathing problem but instead administered the caffeine immediately. The results were very positive. We are now planning a large multicenter study to see what this looks like with 300 or more babies.”

There are always ways to do things better. In health care, you want to make something that’s uncomplicated, inexpensive and easy to replicate.

Katheria credits Drexel for helping him think holistically about the body and its systems from the earliest days of his medical education. “One of the things I loved most about Drexel was the multidisciplinary approach to teaching medicine. We never looked at any topic in isolation — problems were always examined in an integrated way. It’s never just the heart or the lungs, but how all the systems are being affected. That is something I took from the classroom to the clinic and continue in my practice and research to this day.”

Forward thinking
Having started at MCP Hahnemann University in 2000, Katheria was there when the school became Drexel University College of Medicine, and he was delighted to be affiliated with a technology-focused university. “It was a very neat thing to have cutting-edge access to tools that weren’t available elsewhere. For example, we were using videoconferencing ahead of everyone else.”

Katheria believes that that emphasis on forward thinking has prepared him to think outside the box, to streamline and improve long-term care for patients through innovative solutions. At the Neonatal Research Institute, he carries those goals with him every day. “What I’d really like to do as a physician-scientist is change the way birth happens. The majority of babies, of course, are fine, but for the ones that aren’t, we can keep improving care. This is where we can give babies the very best start in life, so it’s about finding ways of keeping the more vulnerable babies with their parents while they get the oxygen or medicines or blood they need, helping them get life-changing treatments and finding the interventions that make a real difference.”
By Elisa Ludwig

For as long as he can remember, Alexander Mazin has been driven by his need to understand exactly how things work. “I’ve always been interested in basic, mechanistic issues, and that goes all the way back to my training,” says Mazin, a professor in the Department of Biochemistry & Molecular Biology. At Drexel, that curiosity about basic processes may very well lead to a new approach to anticancer therapy.

Mazin’s primary research area is the mechanisms of DNA double-stranded break repair in humans and yeast. By design, DNA provides the means for its own repair, a process that is necessary for human survival, for protecting our genes and normal cells while inhibiting the growth of cancer cells. “One strand of DNA serves as a template to repair the other when it’s damaged by radiation, chemicals in our food supply or even the normal process of breathing oxygen,” Mazin says. “But what happens when both strands are damaged? The only way to repair the DNA in that scenario is to use another piece of DNA that complements it. The trick, of course, is to find that other piece of DNA.”

KEY PROTEIN PROMOTES REPAIR
This work originated during Mazin’s PhD inquiries at the Institute of Cytology and Genetics at the Russian Academy of Sciences, where he studied site-directed mutagenesis using complementary DNA that carried reactive groups to the genome targets. “That work really opened my eyes. Once I was able to specifically damage a target, I became especially interested in how modified DNA gets repaired by cell enzymes,” Mazin says.

Mazin continued his studies in France and later at the University of California, Davis, as a postdoctoral research fellow under Stephen Kowalczykowski, who was instrumental in preparing Mazin to run his own lab. “He has a profound understanding of experimental work and I took many lessons from him,” Mazin says. “Even today, I continue to discuss these issues with him regularly.”

At UC Davis, Mazin homed in on a key protein in bacteria called RecA. “This protein promotes repair of DNA that is broken by radiation. To accurately repair double-stranded DNA we can use the template of homologous dsDNA. The problem remains, how to find the template in a huge genome environment — it is truly the search for a needle in a haystack.”

A DOUBLE-EDGED SWORD
The process of homologous recombination is a double-edged sword; biochemically speaking. It contributes to the quickly proliferating cells associated with cancer, and yet it may also protect against the cell damage associated with anticancer therapies such as radiation and chemotherapy.

As such, Mazin believes that proteins like RAD51, RAD52, RAD54 and others might be the key to developing small molecule inhibitors of these processes. In hereditary breast cancer, for instance, researchers have established that there is a deficiency of the homologous recombination proteins. “If we can understand the mechanisms that help repair cells and determine how we can control their proliferation, this work can have enormous practical value.” The goal, Mazin says, is to develop a less toxic anticancer drug, one that could make existing cancer therapies more efficient.

DISCOVERING THE ANSWERS
So far, Mazin’s lab is working to purify the key proteins and then use them to reconstitute the process of human DNA repair in a test tube. “We can use this biochemical approach to generate mechanistic data,” he says. “Eventually, we will use a cellular approach, developing a specific molecule to observe the recombination process through an assay system and later in an in vivo environment.” Using their basic science findings as a guideline, Mazin’s group, in collaboration with the Broad Institute of MIT and Harvard, and the Penn Center for Molecular Discovery, is developing specific small molecule inhibitors of the proteins of homologous recombination. From there, Mazin and his collaborators can track the cancerous cells and determine whether the proteins are inhibiting their growth.

Over the past 15 years, Mazin has found that his work at Drexel has been well supported by both colleagues and the school’s administration. “There’s a true level of commitment, not just financially but also in terms of the stimulating, friendly environment,” he says.

His ongoing study and its potential implications in the fight against cancer demonstrate to Mazin the beauty of science and what drew him to become a researcher in the first place — the fact that the answers are already there, waiting to be discovered. “Science is inherently useful,” he says. “It’s up to us to make our findings applicable and use them to help solve some of the biggest problems we humans face.”
By Nancy West

By creating their own smart fabric, a multidisciplinary team of Drexel faculty has developed a fetal monitor that is wireless, accurate and comfortable to wear. Known as the bellyband, the device will be able to monitor uterine contractions and fetal heart rate in real time without tethering the expectant mother to a bed. The project has received IRB approval, and a clinical trial involving 20 pregnant patients is expected to start in fall 2016. In addition to assessment during labor, the bellyband could be used to monitor high-risk pregnancies or as a quick, noninvasive procedure during a routine check-up, according to Owen Montgomery, MD, chair of obstetrics and gynecology at the College of Medicine, who provided the vision for this device.

“My role is to think of the needs we have in health care that could be solved with the use of smart fabrics,” Montgomery says. “My colleagues in the College of Engineering and the Shima Seiki Haute Technology Laboratory have spent thousands of hours to develop the invention.” Montgomery also recruits other clinicians to the team and conducts clinical research.

The bellyband was designed by Genevieve Dion, an associate professor of design and the director of the Shima Seiki Haute Technology Laboratory, a state-of-the-art knitting facility dedicated to smart textiles. The device was developed, through some 20 iterations, by College of Engineering researchers Kapil Dandekar, PhD, a wireless communications expert; Adam Fontecchio, PhD; and Timothy Kurzweg, PhD. The collaboration is supported by the Coulter-Drexel Translational Research Partnership, based in the School of Biomedical Engineering, Science and Health Systems. The team also received a National Science Foundation grant of nearly $814,000 to support their work.

Owen Montgomery, MD, HU ’81
Devices You Can Wash and Wear

The bellyband is knitted using coated silver conductive thread. The knitting machines are programmed to seamlessly knit a pattern across the center of the band that serves as a wireless, passive radio frequency identification (RFID) tag. Signal processing algorithms developed in Drexel's Electrical and Computer Engineering laboratories process the changes in received signal characteristics from the RFID to measure the intensity of the uterine contractions and other medical information from mother and fetus.

The bellyband is designed to stretch to fit around a pregnant woman's abdomen at any point in her pregnancy. Unlike existing fetal heart monitors, the bellyband allows the woman to get up and walk around within 10 to 14 feet of the receiver, giving her much more freedom of movement and comfort.

"Because this is wireless technology, doctors should eventually be able to monitor their patients inside or outside of a hospital," Dandekar says. Eventually, he suggests, "it may be developed into a monitoring service that could immediately signal medical professionals if there is a problem."

Other Health Care Applications
Moving forward, Montgomery says, "a piece of our NSF grant is to take the concept of smart technology and envision what else we could do with it."

The team is working on applications such as monitoring for and preventing sudden infant death syndrome (SIDS). Using a new grant1 from the National Institutes of Health, the group has also been investigating a wearable wireless robotic legging device to prevent blood clots from forming in patients' legs. "Reducing blood clot risk in the mother reduces the risk of fetal pulmonary embolism," says Montgomery. The device is designed to be comfortable and washable, and potentially self-powered using body heat or electrolytes. So instead of the patient being tied to the pump and stuck in a chair or bed, she could get up and walk around; the device would sense when she is not moving and would massage the legs.

Montgomery notes that, in addition to being a physician, he is a patient who has experience with Holter monitors. "Right now, you have a device with 12 wires that you have to carry with you, and the device records the information. Wouldn't it be easier just to put on a T-shirt that has the 12 leads knitted into it and have the information sent to your cell phone? Between that idea and making it happen are thousands of hours of engineering laboratory work. These are just some of the things I can envision for smart fabric."

"As a patient — and a surgeon — I think of the needs," he continues. "Then I ask my engineering colleagues to see if they can solve them. The strength is all of us working together. This work is the embodiment of the College of Medicine linking technology to a tradition of caring."

Working with the Coulter-Drexel Partnership and the Drexel University Office of Technology Transfer, the multidisciplinary team has applied for a patent not only on the concept of smart fabric uterine monitoring for pregnancy but also on the platform technology that will allow them to develop additional applications such as SIDS and cardiac monitors and the thrombophlebitis-preventing leggins.

1 NSF Partnership for Innovation program grant no. 1430212 (PI Dandekar)
2 NIH/NSF Cyberphysical Systems grant no. 1-U01-EB023035-01 (PI Dandekar)

Scanning electron microscope image of yarn: Kristy Jost, PhD

Smart Fabric Research Leads to Role in $317 Million Institute

The U.S. Department of Defense has named Drexel University as a key leader in the creation of a national research institute that will support American textile manufacturers in bringing sophisticated new materials and textiles to the marketplace. Known as Advanced Functional Fabrics of America (AFFOA), it is one of several institutes in the White House’s National Network for Manufacturing Innovation. The AFFOA initiative is a $317 million public-private effort. The Department of Defense has provided $75 million in funding; the remainder will be provided by key business partners and local governments.

AFFOA will be a national manufacturing resource center for industry and government to draw on academic expertise in new fibers and textiles engineered to see, hear, sense and communicate. A wide array of industries will benefit, including health care, aerospace, apparel and architecture.

Drexel is one of the cornerstones of the institute along with MIT, the University of Central Florida and Cornell University, because of their complementary research endeavors in novel fibers for textiles, rapid textile prototyping and computer simulation.

Drexel competed with some of the top universities in the country to be part of AFFOA, according to Senior Vice Provost for Research Aleister Saunders. “There aren’t any places that have research on functional fabrics. We believe we are at the beginning of a brand-new industry that is going to shape all of our lives,” he said.

The University will receive funding from AFFOA to address barriers to innovation in functional fabrics and to facilitate new textile product development. Drexel has multidisciplinary teams that will continue their innovative product development efforts, such as the bellyband, touch-sensitive skin for robots, a haptic glove for hand therapy and textiles that can store energy.

Nationally, AFFOA includes more than 30 universities and an impressive list of industry partners, as well as venture capital groups and a couple of dozen startups. Drexel will serve as the anchor for partners in the Mid-Atlantic region, leading investigations into modeling, designing and predicting the utility of new fibers, yarns and materials, and using those materials to build prototypes of functional fabrics for health care, apparel, transportation, consumer electronics, architecture and the defense industry.

— Adapted from Drexel Now (4/1/2016)
A Mutual Appreciation Society
The kind and generous donors who lighten the financial burden of our medical students were honored at the annual Benefactors Jazz Brunch on April 10 at the College of Physicians of Philadelphia. A number of students attended the event to meet and thank the special people who have given them support.
Secrets of PAIN

By Elisa Ludwig

Neurologist Ricardo Cruciani, MD, PhD, sees patients dealing with excruciating pain every day, and he believes that there’s much more that can — and should — be done to help them. “Pain is part of our survival — you see it across every species. And yet within the body it’s a complex and sophisticated problem to solve,” he says.

In joining Drexel, Cruciani came to the right place. Here, he is part of a multidisciplinary group of researchers hunting for the intricate and often obscure causes for pain and uncovering novel solutions for treatment.

Persistent pain is more than a symptom — it’s a Pandora’s box of systemic issues and associated side effects impacting more than 100 million Americans, according to the Institute of Medicine. Yet, despite an aging population that makes this growing problem even more concerning, therapies and treatments for pain are quite limited.

Part of that has to do with the changing and multidimensional nature of pain itself. “You reach a point in certain pain stages where you don’t even have a painful stimulus but you are constantly in pain. There are many syndromes like that,” Cruciani says. “When that happens, you don’t have only one pathway that is involved, or one channel, or one neurotransmitter — you have many. So you target one, but then the other one is active. That’s why it gets difficult to find the right treatment.”

While pain has always been an exceedingly complicated problem for physicians to treat, very little progress in the discovery of treatments has been made since the early 20th century. “If you look at the history of pain therapeutics, you know morphine was isolated back in the mid-1800s, and aspirin was identified in the early 1900s,” says James Barrett, PhD, director of the Clinical & Translational Research Institute and a driving force behind Drexel’s pain research initiative. “By and large, we haven’t had too much since then in the way of new therapeutics that are truly effective.”

They’re on the case: Working collectively on a range of individual projects, College of Medicine scientists and physicians gain valuable information from each other, enhancing their experience as well as their progress. At left (l-r) Drs. Seena Ajit, assistant professor, and Huijuan Hu, associate professor, Pharmacology & Physiology; Ricardo Cruciani, chair of Neurology; and James Barrett, professor, Pharmacology & Physiology.
When Barrett accepted the position of chair of Drexel’s Department of Pharmacology & Physiology in 2009, he did so with the intention of focusing on that “tremendous unmet need,” hiring other researchers who specialized in this area, including Drs. Huijuan Hu and Seena Ajit, both of whom came from the pharmaceutical industry. He recognized that it would take a broad scope of approaches and perspectives to tackle the issue, so he put together what he says is “in a sense, a small biotech company within an academic setting.”

A veteran of the pharmaceutical industry himself, Barrett has brought his drug development expertise to bear in creating a molecular physiology and pharmacology research corps that spans from the bench to the bedside. “We have embedded within the department a core group of individuals focusing on animal models of pain, molecular mechanisms of pain, biomarkers of pain, and medicinal chemistry,” he says. The result, he hopes, will be a set of novel targets that can then be turned into treatment modalities.

**A Promising Candidate for Cancer Pain**

Barrett’s own work has centered on chemotherapy-induced and cancer-related pain. Somewhere between 30 and 50 percent of all cancer patients experience pain, and it’s often the first sign of the disease in patients. “Ninety percent of patients have pain at the late stage, and they are often given opioids, but we know that opioids have other debilitating effects and side effects that are not pleasant.”

Barrett and his colleagues soon closed in on sigma-1 antagonists. “These drugs were discovered in the 1980s and ’90s and classified first as an opioid-like compound, but they didn’t show any of the features of any of the opioids, and so they fell into what I call the ‘valley of death’ for a long time. Recently, they’ve been resurrected and people are now looking at a wide variety of indications,” he says.

Barrett is interested in how these compounds compare to morphine in the treatment of advanced cancer pain. Using mechanical stimulation in animals, he can measure their degree of discomfort with regard to cancer pain and then compare the effects of the drug compounds to morphine in alleviating it. “What we found is that their effects were quantitatively identical. We did full dose-response curves with the sigma-1 antagonist and compared them with morphine and got the same degree of efficacy. Then we did some chronic administration to see whether or not these drugs lose their ability to attenuate pain, and they don’t.”

Barrett found that, unlike morphine, sigma-1 compounds did not produce tolerance or related side effects at higher doses, making them less likely to be candidates for abuse. In an era when opioids are widely abused, resulting in addiction and overdose, developing a compound that is non-addictive could be a true game-changer in pain relief medication.

Barrett is currently working with medicinal chemist Joseph Salvino, PhD, in the Department of Pharmacology & Physiology, to synthesize the sigma-1 compounds. In the coming months, he plans to profile the novel chemical entities to understand their efficacy. Equally exciting is the research conducted by Felix Kim, PhD, director of the Pharmacology & Physiology Graduate Program, which suggests that sigma-1 might also be capable of shrinking tumors. “If we can identify a compound that attenuates pain and also inhibits tumor growth — well, what more could you want? We’re looking at it, and we will know that answer clearly and unequivocally within the year,” Barrett says.

Barrett is currently in the process of pursuing funding for the next phase of his research — determining the ideal compound, conducting follow-up studies and preparing for more drug development work over the coming months.

Exactly how these compounds work is what Barrett calls the “million dollar question. What’s known is that this class of drugs are what are called chaperone proteins. In pharmacology, chaperones escort different material to the surface of the receptor, where those proteins interact with other substances, and the trafficking by a chaperone seems to be the mechanism for looking at a pathophysiological state. Under normal conditions, these drugs don’t do anything, but when the system is perturbed, the chaperone proteins are activated by the compound, and in some way they appear to interact with ion channels and other receptors that are somehow mediating these effects. What we don’t know is exactly how they’re doing it.”

**Finding the Pathways for Inflammatory Pain**

Understanding the underpinnings of pain is critical to the drug development process. As Barrett uncovers a potential treatment for cancer pain, Huijuan Hu is starting with the potential cause or progression of inflammatory pain. Hu brought to Drexel an industry-honed expertise in electrophysiology and in vivo ways of assessing pain. At Drexel, her laboratory is zeroing in on the groundbreaking area of calcium channels as a pathway. “Evidence shows that intracellular calcium plays a role in persistent pain,” she says.

In particular, she is looking at store-operated calcium (SOC) entry in the central and peripheral nervous system. She has observed that a compound known as a SOC inhibitor can reduce the painful inflammation and swelling that follows the injection of an irritating substance into the hind paw of mice. With the SOC inhibitor, the animals exhibited significantly less spontaneous pain.

These results demonstrate that inhibiting SOC channels...
One component of the research looks at the use of repetitive transcranial magnetic stimulation

In addition to electrical stimulation, he’s also looking at scrambler therapy, a form of peripheral nerve stimulation in which electrical signals simulate non-pain information. “If randomized sham-controlled trials better identify those patients who may benefit from this approach, that would be terrific. We could start using these types of strategies more widely.”

Seeing pain patients on the front lines of his medical practice has impassioned Cruciani to continue to push for more answers in the pursuit of what he regards as patients’ human right to relief. “It is difficult for any of us to fully understand what it’s like for these patients, but we have to do everything that we can to reduce their suffering.” His pharmacologist colleagues would agree.

Middle: Michael Brooks, MD, MCP ’91, and Robyn Frankel-Tiger, MD, MCP ’91
Bottom: Alan Chaitin, MD, HU ’66, with his wife, Ann Chaitin

Middle: At the Simulation Station (r-l): Timothy Manzone, MD, MCP ’89, now Alumni Association president, and David Rilling, MD, HU ’66, with his wife, Karina Rilling

Bottom: Drs. Diane Hochlerin, Eugenia Marcus, Sucha Asbell, Leonard Marcus (Dr. Marcus’s husband), Sharon Kasdin, Grace Reynolds and Ruth Schiller; the women are all alumnae of WMC ’66.
Classes of 1986 at Reunion Reception (alphabetical): Drs. Richard Bowers, HU; Barbara Browne, MCP; Jay Burstein, HU; Ramona Chube, MCP; Spencer Galt, HU; Lori Garjian, MCP; Irene Kirkland-Mintz, MCP; Roman Kownacki, HU; Martin Maurer, HU; Robin Miller, MCP; Ana Núñez, MCP; Gary Perlmuter, HU; David Russo, HU; Alan Twer, MCP; and Eileen Watson, MCP


Members of the Grand Classes: Drs. Mary Eberhardt, Antoinette Eaton and Shirley Joe, all WMC ’56
Woman’s Medical College Class of 1966 at 50 Year Reunion Dinner (alphabetical): Drs. Sandra Ammon, Sucha Asbell, Constance Calogeris, Mary Ann Cohen, Marie Grabowski, Diane Hochlerin, Myrtle Keller, Grace Maher Reynolds, Mary Michalis, Eugenia Pann Marcus, Ruth Phyllis Schiller, Pauline Rock, Natalie Sarkanich-Watson, Roslyn Souer, Gail Valentine, Mariah Vassall, Maria Verso Burt and Barbara Young

Middle: Class of 2006 at Reunion Reception (alphabetical): Sonia Desikan, MD, with guest Elliott Maruffi; Christopher Drumm, MD, with guest Tawnya Drumm; Eve Khlyavich Freidl, MD, with guest Benjamin Freidl; Adam Olsson, MD, and Tina Olsson, MD

Bottom: MCPHU Class of 2001 at Reunion Reception (alphabetical): Kelly Loftus, MD, with guest Robert Richards; Till Conermann, MD; David Engle, MD, with guest Shannon Engle; Karen Ephil, MD, with guest Frank Spencer; and Megan Wynne, MD
Archives Tour: Roslyn Souser, MD, WMC ’66; Gail Valentine, MD, WMC ’66; and Diane Hochlerin, MD, WMC ’66

Middle: Richard Bower, MD, HU ’86, and his daughter Eve Bowers

Myrtle Keller, MD, WMC ’66

Hahnemann University Class of 1996 at Reunion Reception (alphabetical): Drs. Radhika Gogoi, Jeffrey Harris, Costas Kaiafas, Kiran Rajasenan, Cindy Rossi, Paresh Shah, Kamaljit Sran, Andrew N. Sun and Scott Vargo

Archives Tour (alphabetical): Mona Abaza, MD, MCP ’91; Mickey Fain; Sandra Ammon, MD, WMC ’66; Helmut Ammon, MD; William Berhard, MD, HU ’57; Richard Brooks, MD, HU ’66; Myrna Brooks; Constance Calogeris, MD, WMC ’66; Jerome Foell; Ann Catts, MD, WMC ’56; Joseph Chacko, MD, MCP ’91; David Estroff, MD, HU ’76; Judy Estroff; Francis Gamza, MD, HU ’71; Diane Hochlerin, MD, WMC ’66; Grace Maher Reynolds, MD, WMC ’66; Miriam Vitolo; Eugenia Pann Marcus, MD, WMC ’66; Leonard Marcus, VMD, MD; William Peloquin, MD, HU ’66; Wilma Peloquin; Alfred Sadler, MD, HU ’66; Edi Matsumoto; Roslyn Souser, MD, WMC ’66; Glenn Stambo, MD, HU ’91; Lori Stambo; Richard Stoltzfus, MD, HU ’66; Elaine Stoltzfus; Paul Turner, MD, HU ’66; Gail Valentine, MD, WMC ’66; and Maria Verso Burt, MD, WMC ’66
ALUMNI AWARDS

Three outstanding alumni were honored at the Dean’s Award Luncheon on May 21, the Saturday of Alumni Weekend. The Outstanding Alumnus/a Award may be presented for significant accomplishment in clinical practice, research, teaching, mentorship or professional contributions. The WMC/MCP Alumnus/a Award recognizes a highly acclaimed graduate of one of those legacy schools. The Lifetime Achievement Award is the highest honor given by the Alumni Association.


Middle: 2016 Outstanding Alumna Award Clinical Practice recipient Kelly S. Eschbach, MD, HU ‘91, with her husband, William Lundstrom, is the section chief of Physical Medicine and Rehabilitation at Christiana Care Health System, where she previously served as medical director of Rehabilitation Services. Under her leadership, the inpatient rehabilitation unit she oversees has received national recognition for quality.

2016 Lifetime Achievement Award recipient Alfred M. Sadler Jr., MD, FACP, HU ’66, pictured with his wife, Edie Matsumoto: While at NIH, he established guidelines and a model law for organ transplantation and research, and he and his lawyer brother wrote the Uniform Anatomical Gift Act. He founded one of the first physician assistant programs in the nation, and developed EMS, primary care and urgent care programs on both coasts.

2016 MCP Distinguished Alumnus Award recipient the Honorable David J. Shulkin, MD, MCP ’86, and his wife, Merle Bari, MD, MCP ’86: Shulkin is the undersecretary of health for the U.S. Department of Veterans Affairs, overseeing the country’s largest integrated health system. He has held numerous senior executive positions in health system management.

2016 Outstanding Alumna Award Clinical Practice recipient Kelly S. Eschbach, MD, HU ‘91, with her husband, William Lundstrom, is the section chief of Physical Medicine and Rehabilitation at Christiana Care Health System, where she previously served as medical director of Rehabilitation Services. Under her leadership, the inpatient rehabilitation unit she oversees has received national recognition for quality.
For decades, the hepatitis B virus has been considered the leading cause of liver cancer. In coming years, however, the growing obesity epidemic will overtake hepatitis B and contribute to millions of cases of liver cancer worldwide. Virologist Michael Bouchard, PhD, is studying the changing face of this deadly disease in groundbreaking detail.

The World Health Organization estimates that one-third of the world’s population has been infected with hepatitis B, and approximately 240 million people remain chronically infected. About 25 percent of those individuals will eventually develop liver cancer. The number of new hepatitis B infections has declined since the advent of the hepatitis B vaccine, which is universally required in many countries.

Seeing both a scientific challenge and a human need, Bouchard began researching liver cancer as a postdoctoral fellow. “I was drawn to study liver cancer and hepatitis B because even though the connection between the two has been recognized for around 50 years, the effects of the virus can be very subtle and the exact relationship with liver cancer has been difficult to define.”

Yet even as global rates of hepatitis B have declined, the rates of liver cancer have grown, and Bouchard, an associate professor of biochemistry and molecular biology at the College of Medicine, has shifted his research to focus on the rising problem of obesity.

“Research has shown that someone who is obese develops metabolic syndrome and, in particular, insulin resistance, which can lead to type 2 diabetes and nonalcoholic fatty liver disease. It’s the nonalcoholic fatty liver disease which leads to problems.”

Untreated, nonalcoholic fatty liver disease can become nonalcoholic steatohepatitis, or NASH, which is a condition of inflammation and damage in the liver that in turn leads to fibrosis and cirrhosis — both of which are considered common risk factors for liver cancer. Currently, 66 to 70 percent of the population in the United States can be categorized as overweight or obese. “We’re seeing the same types of numbers emerging on a global scale now,” Bouchard says.

“While the percentage of people who go on to the nonalcoholic fatty liver stage and then on to the NASH and cancer stages seems low, it’s actually a very large number of people.”

Bouchard’s current work in partnership with Drexel engineering professor Gail Rosen, PhD, is centered on defining the process of how obesity can lead to liver cancer. In the laboratory, mice are fed either a standard low-fat diet or a Western diet that is high in carbohydrates and fats. The mice are observed over time — not just their livers, but all of their organs, and especially their guts.

Recent interest in the biome, Bouchard says, presents new opportunities for understanding liver biology. “We are very interested in the crosstalk between the liver and the gut, given that the majority of blood dumped into the liver comes from the hepatic portal vein, so the liver is exposed to many metabolites and bacterial products. We can assume it is directly influenced by the biome,” he says.

The research, funded by a joint grant from the College of Medicine and the College of Engineering, was designed as a long-term study, to be conducted over a year, so that Bouchard and Rosen can find out how the liver and gut influence one another in the development of pathology, how factors like age and sex can influence disease progression, and how the progression to liver cancer can be stalled.

“We’ll be taking samples at multiple time points,” Bouchard says. “We will change diets midway for some mice to see if that reverses liver damage.” Fat accumulation, for example, has already been noted in mice taking the Western diet for three weeks, but it is not clear if there’s a point of no return in terms of the extent of damage or age of the mice.

That broader scope and longer duration distinguishes this research from previous studies that have only looked at disease at onset or afterward, not the holistic picture of how it occurs. Bouchard and Rosen’s objective is to figure out ways that physicians can reverse the liver damage associated with obesity. “We want to know if there are lifestyle changes we can recommend, like eating better or getting more exercise in order to prevent the onset of liver cancer in obese individuals,” he says.

Bouchard believes he’s doing this work at the right time and the right place. “We’re lucky here at Drexel to have a concentration of individuals working in the area of liver disease, from basic scientists and physicians to engineers and bioinformatics specialists,” he says. “It’s really the perfect storm — bringing a vast amount of expertise to bear on an increasingly critical problem.”
HOW WOULD YOU CHARACTERIZE our competitive impact in biomedical discovery and translation?
Faculty of the College received $18.4 million in awards from the National Institutes of Health during the 2015-2016 fiscal year and $37.0 million from all sponsors. The NIH awards included diverse multidisciplinary projects that are furthering understanding of neurological and psychiatric disorders; infectious diseases, such as HIV/AIDS and malaria; and cancer. Early-stage and proof-of-concept research; disruptive ideas; and studies that are intentionally narrow in their focus are appropriately directed to other funders. Such projects are critical to challenge scientific dogma and to lay the groundwork for major funding in the future. Our faculty succeed in these arenas too.

WHAT ARE SOME OF THE strongest areas of research here?
We are recognized nationally and internationally in many areas of basic biomedical, translational and clinical science. Research in neurosciences and in infectious diseases has had the broadest impact, with several programs funded continuously for more than 30 years. Cancer research is emerging as a notable strength. Our work in neuroscience includes spinal injury, repair and recovery; pain; neurodevelopment; and the neural mechanisms of psychiatric disorders. Infectious disease includes neuroAIDS; use of CRISPR technology to formulate a cure for HIV; immune defense mechanisms; genomics and bioinformatics of bacterial diseases; and malaria.

In cancer, faculty are making their mark in basic cellular biology, oncogenic actions of viruses, and novel drugs to inhibit primary tumors and prevent metastatic disease. Drexel is one of two highly active consortium members of the National Cancer Institute-designated Sidney Kimmel Cancer Center at Thomas Jefferson University, and four College of Medicine faculty members have leadership roles within the consortium. This partnership has worked seamlessly to expand scientific and grant opportunities for our faculty.

WHAT'S THE MOST EXCITING thing going on now?
I am excited by the increasing number of initiatives in which basic and clinical scientists are collaborating, with the clinicians setting the problem and direction. In addition to the examples highlighted in this issue, I include neurovascular and cardiovascular disease; infectious diseases and immunology; neonatology, perinatal medicine and population science; transplant medicine and surgery; and musculoskeletal disorders.

CAN YOU COMMENT ON the role of internal grant programs?
The CURE program is supported by annual funds from the commonwealth of Pennsylvania for innovative pilot studies that are selected after a rigorous NIH-style review by faculty across Drexel. It has led to significant extramural awards, scholarship, and training. The Clinical & Translational Research Institute has funded $2.2 million in studies that specifically require participation by clinicians. These proposals have also led to external support and taking discoveries towards commercialization. This investment came entirely from College funds, but was extended to all faculty across Drexel.

WHAT ARE YOUR goals for the future?
Foremost is to grow research in the clinical sphere. Broadly defined, I include translating discoveries at the scientists’ and engineers’ benches into proof-of-concept determinations in humans; full-scale studies evaluating disease mechanisms and treatments in patients; optimizing methods for delivering clinical service; and incorporating health informatics for outcomes research throughout our enterprise.

Kenny Simansky, PhD
Vice Dean for Research, Professor, Department of Pharmacology & Physiology

The Office of the Vice Dean for Research guides and supports all basic and clinical research activities involving the College of Medicine, working with departments and interdisciplinary groups to develop research programs; facilitating translational research; and promoting mentorship to advance the training of young physicians and scientists. As vice dean, Kenny Simansky has been an advocate for interdisciplinary, cross-campus and extramural collaboration, including international initiatives; secured funding for state-of-the-art technology and facilities; and raised the profile of the College — among peer institutions, federal and other grant-makers, and industry — as a source of world-class research and researchers.
GET IN TOUCH

Online resources make it easy!

- Facebook: Drexel University College of Medicine Alumni Association
- LinkedIn: Drexel University College of Medicine Alumni Association
- Website: drexel.edu/medicine/Alumni
- Email: medical.alumni@drexel.edu
- Phone: 215.762.2371

GET INVOLVED

Opportunities abound for medical and graduate alumni to interact with current students.

Medical Alumni

HEALTH OUTREACH PROJECT
Student-run clinics are eager for alumni physicians to volunteer.

PRIMARY CARE PRECEPTORS
Alumni are invited to serve as preceptors.

SPEAKING OPPORTUNITIES
Interact with students by participating in programs like career panels and the Women’s Health Seminar Series.

DRAGONS TO DOCTORS LINKEDIN GROUP
Provide insight and support to MD students from school into residency.

Graduate Alumni

SPEAKING OPPORTUNITIES
Interact with students by participating in various events, such as the Forward Seminar Series.

DRAGONCONNECTS LINKEDIN GROUP
Provide insight and support to PhD students in school and starting careers.

UPDATE YOUR INFORMATION

New address? New phone? Send your updated information to medical.alumni@drexel.edu or call 215.762.2371.
Alumni Calendar

2016-2017

**OCT 20**
*Discovery Day: New Venue*
Annual research day for medical students, graduate students, residents, fellows and postdoctoral trainees
Pennsylvania Convention Center

**OCT 30**
*AALAS Reception*
Graduate School Alumni and Friends
The Westin Charlotte

**NOV 13**
*Drexel Neuroscience Alumni Reception*
Morton’s The Steakhouse, San Diego, 5:30–7:30 p.m.

**DEC 1**
*DUCOM Classical Recital*
Showcasing the musical talents of students and faculty
Settlement Music School, Germantown Branch, 7 p.m.

**MAY**
*Save the Date for Alumni Weekend*
Calling all classes ending in 2 or 7, and our Grand Classes who graduated more than 50 years ago!
Visit drexel.edu/medicine/Alumni/Reunions/.

**MAY 18**
*Classes of 1967 Dinner*

**MAY 19**
*Commencement*

**MAY 19-20**
*Alumni Weekend for All Reunion Classes*

Details: Email medical.alumni@drexel.edu, call 215.762.2371 or visit drexel.edu/medicine/alumni/events/.