Curators Versus Cancer
A special team of medical literature experts are on the hunt for cancer’s kryptonite, one mutation at a time.

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UConn, JAX Confront Pain With First-In-State Consortium

An estimated 100 million Americans suffer from chronic pain — more than those affected by heart disease, cancer, and diabetes combined, according to the National Academies of Science, Engineering, and Medicine. How best to manage that pain in the face of a nationwide opioid crisis is the question on many practitioners’ minds.

The Connecticut Pain Consortium — a translational pain research and education collaboration between UConn Health, the UConn schools of Medicine and Nursing, and The Jackson Laboratory — aims to help answer it. Given the broad range of research interests and funding opportunities related to pain, the founders envision that centers across the University and nearly every UConn school and college — particularly the schools of Dental Medicine and Pharmacy — will join the consortium to build mutually beneficial collaborations.

Experts from Yale University and hospitals including Connecticut Children’s Medical Center will also be involved. “There is a clear need for more basic and translational research on human pain and pain management,” says the Consortium’s director, mathematician and computational biologist Reinhard Laubenbacher, a joint faculty member at UConn Health and The Jackson Laboratory for Genomic Medicine. “And there is a critical unmet need for education and training of providers and patients. This is a great opportunity to deploy our capabilities in pain research and addiction together with our Connecticut partners in an exciting and much-needed statewide initiative.”

The Consortium, the first of its kind in the Connecticut medical community, will establish a portal for pain-related health care data and facilitate research collaborations that leverage state and national resources. It will aim to translate that research into cutting-edge pain management solutions and raise awareness of the many facets of pain, pain management, and potential related ramifications including opioid addiction. The Consortium will contribute to a curriculum on pain research and management for health care providers.

The launch is being funded by a $55,000 planning grant from the Mayday Fund, whose mission is to support projects that close the gap between knowledge and practice in the treatment of pain, to the UConn Foundation. The Consortium has also received support from the UConn Office of the Vice President for Research, the schools of Nursing and Medicine, and the Jackson Laboratory for Genomic Medicine.

“This new consortium builds upon strengths already existing in the School of Medicine, with an existing core of faculty focused on pain research,” says Dr. Bruce T. Liang, dean of the School. “Thanks to this grant, we believe there will be numerous opportunities for advancement in the study and treatment of pain.”

Curators Versus Cancer

As oncology moves toward precision medicine — where we know exactly which genetic mutations make a particular cancer tick, we could pick the perfect treatment — oncologists have to keep up with an ever-expanding library of mutations and the drugs that might foil them. A new program at UConn Health and The Jackson Laboratory for Genomic Medicine has experts keeping up for them.

Together for the Kids

A decades-long partnership between the UConn School of Medicine’s Department of Pediatrics and Connecticut Children’s Medical Center has yielded life-changing translational research that improves the health of the state’s tiniest residents.
THE PULSE

HONOR ROLL

Research doesn’t stop when we report it. Here is an update on a past UConn Health Journal story:

Heart Health

Dr. Annabelle Rodríguez-Oquendo, professor of cell biology at the UConn School of Medicine, was recently issued a diagnostic patent to test for a genetic predisposition for an abnormal inflammatory response that causes several life-threatening disorders, like coronary artery disease and chronic inflammatory disease. Lipid Genomics, the start-up Rodriguez-Oquendo founded in 2010, has exclusively licensed the technology from UConn Health. The company is currently in discussion with potential investors to continue commercialization of this product, as well as other therapeutic innovations for HDL-cholesterol dysfunction.

Visit healthjournal.uconn.edu/archive to read the original story.

UConn Health First Hospital in U.S. With Augmented Reality Surgical Microscope

UConn Health is the first hospital in the nation to acquire a high-tech surgical microscope with augmented reality capabilities to visually assist surgeons during complex neurological and spinal surgeries. This technology – the latest added to UConn Health’s state-of-the-art hybrid operating room – provides surgeons with an enhanced 3D visualization of the surgical field at the highest magnification possible. It can also illuminate the blood flow through various brain tissues, making more precise surgical interventions possible.

“The advanced augmented reality, image-guided microscope allows us to go beyond what we can normally see with our naked eye and traditional microscopes. It allows practitioners from multiple surgical specialties to treat even more complex lesions more safely,” says Dr. Ketan Bulsara, chief of the Division of Neurosurgery at UConn Health. The microscope’s unique FusionOptics technology allows a surgeon to see greater anatomical detail with increased sharpness, such as the tiny distances between the smallest blood vessels and nerve structures, without needing to refocus the microscope. It also has the ability to brightly light up tiny blood vessels in the brain to distinguish them from other surrounding brain tissue, helping surgeons navigate the complex and delicate surgical field.

The microscope also includes a video camera that allows surgeons to choose one of three enhanced overlays to amplify the view of the surgical field. The three views are a real-time, highly magnified naked anatomy; a black-and-white, fluorescence-enhanced view to see greater tissue dimensions and blood flow; and a brightly colored, fluorescence-enhanced view of naturally colored anatomy to see the intricate blood flow and tissue outlines during a microsurgical procedure.

The ARveo Augmented Reality microscope is made by Leica Microsystems, a developer and manufacturer of microscopes and scientific instruments for the analysis of microstructures and nanostructures.

UConn Dental Alumna Give Back

UConn School of Dental Medicine alumna Dr. Carolina Giraldo ’95 has always persevered.

Born in Bogotá, Colombia, and raised in Bridgeport, Connecticut, Giraldo and her older sister took care of themselves and their younger brother from an early age while their parents worked three jobs. Giraldo knew she’d have to work hard to be successful, juggling work and study to put herself through college and dental school.

Now she’s paying it forward. Giraldo, who opened her own dental practice soon after earning her doctorate, recently made a $1 million planned gift to help students like herself. Giraldo established the Dr. Carolina Giraldo Scholarship in 2017 so dental students from underrepresented groups might have an easier time becoming dentists than she did.

“I want the minority population to grow in the field,” Giraldo says. “I want a bigger presence of women, of minorities, to get into the field and make a difference.”

Dr. Sarita Arteaga, the dental school’s associate dean for students, says scholarships like Giraldo’s help students with “the little things,” not just tuition.

“It also helps them to know that someone is investing in them,” she says. “They say, ‘Wow, I can’t believe somebody was in this position and not only wants to give back to the school, but wants to do the same thing for me.’”

Visit uconn.edu/giraldo to donate to the Dr. Carolina Giraldo Scholarship.

Visit healthjournal.uconn.edu/archive for more stories.
**Got Breast Milk?**

UConn John Dempsey Hospital is the first hospital in Connecticut, and only location in the Greater Hartford area, to serve as a milk depot for breast milk donations for newborns in need.

“Our new milk depot is going to benefit our tiniest patients in Neonatal Intensive Care Units (NICUs) across Connecticut and the Northeast, including our very own, the Connecticut Children’s Medical Center NICU here at UConn Health,” says Marisa Merlo, lactation consultant for UConn Health’s Department of Obstetrics and Gynecology. “UConn Health’s milk depot, which opened in August, is the fifth in Connecticut to join Mothers’ Milk Bank Northeast. The nonprofit community milk bank, accredited by the Human Milk Banking Association of North America, distributes donated, pasteurized human milk to babies in fragile health throughout the Northeast. Women interested in donating their breast milk can contact Mothers’ Milk Bank Northeast (milkbankne.org) directly to apply for eligibility and screening. Once women become eligible to donate, their breast milk donations are accepted by Merlo at UConn Health and safeguarded in the freezer of its new milk depot room. Merlo and her staff safely ship the frozen milk to Mothers’ Milk Bank Northeast for pasteurization and distribution to their network of NICUs. Not all mothers of newborns can produce a sufficient milk supply. Mothers with premature newborns especially can experience difficulty producing or pumping enough breast milk while their baby is in the NICU. Donor milk is a more beneficial substitute for fragile newborns than formula.

“This new milk depot at UConn Health will make it more accessible, easier, and stress-free for women to donate their breast milk to help other women and their babies,” says Natalie Martin, associate director of development for UConn Health. She chose to donate her breast milk for three months after her daughter turned one to help boost the health of NICU babies.

“I know just how critically important donated breast milk is,” says Martin, who used to work for the March of Dimes. “The fact that the donated milk is staying in the Northeast and Connecticut to help other moms is amazing.”

The new milk depot at UConn Health was founded and made possible with initial donations by Merlo, Martin, obstetrician/gynecologist Dr. Christopher Morosky, and Carrie Ferrindino, nurse manager of Maternal Child Health, for the purchase of a milk freezer.

“The milk depot at UConn John Dempsey Hospital is a wonderful opportunity to provide to our community,” says Ferrindino. “Our goal at UConn Health is to do everything in our power to promote and support healthy moms and healthy babies.”

**GENE EDITING CURES BLOOD DISEASE IN MICE**

A team of researchers from UConn, Yale University, and Carnegie Mellon University has successfully corrected a genetic mutation in a mammalian fetus using a targeted gene-editing technique for the first time. The scientists injected nanoparticles loaded with a combination of donor DNA and peptide nucleic acids into the amniotic fluid of pregnant mice whose fetuses carried a genetic mutation that causes the blood disorder beta thalassemia. Four months after birth, the treated mice showed enough improvement to be considered cured. Most important, the process resulted in no off-target effects from treatment, a major concern for other gene editing tools like CRISPR/Cas9, which can erroneously damage untargeted DNA. The findings, published in Nature Communications, are very encouraging, but more research is needed before the treatment can be considered for human trials.

**SYphilis Vaccine Breakthrough**

The number of reported syphilis cases is on the rise despite worldwide efforts to eradicate the infection. But now, as reported in mBio, researchers at UConn Health may be closing in on a vaccine. Microbiologists Dr. Justin Radolf and Melissa Camano began analyzing the genetics of syphilis bacteria from patients in Colombia, San Francisco, and the Czech Republic. The researchers then found proteins that were the same in all syphilis bacteria they examined; these proteins could be used as a vaccine. The researchers will test the proteins in rabbits to see if they can work as a vaccine, then enroll patients in China and Malawi to make sure the syphilis they’ve been studying is representative of syphilis worldwide so the vaccine helps as many people as possible.

**Iron: Cancer Cells’ Weakness?**

Cancer cells tend to hoard iron — ovarian cancer cells in particular. They take in more iron than normal cells, and they release less of it. UConn Health computational biologist Anna Konstorum and Center for Quantitative Medicine Director Reinhard Laubenbacher wondered if perhaps cancer cells’ iron habit was a weakness doctors could use against the disease. They analyzed data from four different publicly available datasets. And one unusual pattern appeared in all four: altered iron uptake seemed to be connected to increased fatty acid production. Fatty acid production is increased in cancer cells generally, and may be part of why they grow so fast. OMICS: Journal of Integrative Biology published the findings on July 1. UConn’s Torii lab is now testing several of the iron connections for potential as drug targets.

**Early Heart Disease Treatment Could Prevent Frailty**

A new study has found that older patients with low heart disease risk have little frailty when compared to those with higher heart disease risk. Led by the University of Exeter with researchers including UConn’s Dr. George Kuchel, the study also found that even a small reduction in cardiovascular risk factors can lead to lower incidences of dementia, chronic pain, and other conditions associated with advanced age. The study, the largest of its kind, found that severe frailty was 85 percent less likely in those with little to no cardiovascular risk factors. These findings, published in the *Journal of Gerontology: Medical Sciences*, challenge the belief that frailty is inevitable as people age.
The pulse
UConn Health News

Advanced Aneurysm Stent Means Safer Treatment

A new minimally invasive procedure has emerged as a safe way to treat certain brain aneurysms, and UConn Health’s Division of Neurosurgery is among its earliest adapters. The advancement, based on a stent that’s been in use for a decade, is known as the Neuroform Atlas.

“It’s a microstent,” says Dr. Ketan Bulsara, chief of UConn Health’s Division of Neurosurgery. “Sometimes the anatomy may prevent the navigation of a larger stent into the appropriate target area. The advantage of the microstent is, given its small size and smaller equipment requirements, we may be able to get into areas that we couldn’t normally navigate.”

That ability further broadens the range of lesion types that can be treated through minimally invasive means. Most patients who undergo this procedure can go home the following day.

Aneurysms occur when part of an artery’s wall weakens, causing the artery to bulge. Aneurysms are usually asymptomatic but in some cases can rupture and cause life-threatening internal bleeding. When this occurs in blood vessels leading to the brain, it causes a hemorrhagic stroke, which requires emergency care.

Once an aneurysm is detected, it is important to get an assessment for its risk of rupture as soon as possible. Bulsara says about a third of patients who suffer a ruptured brain aneurysm die, and another third who make it to the hospital don’t fully recover. “We’re in a time right now where the technological advancements in devices and microsurgical techniques are being made so rapidly that it’s imperative, to maintain the best possible outcome for all of our patients, that we offer the latest, newest technologies that have been deemed safe,” Bulsara says.

“Our use of this stent is another testament to that. It continues to add to our treatment armamentarium and increases the number of diseases we can treat safely.”

The first Neuroform Atlas stent placement at UConn Health was among the 20 cases neurosurgeons completed in UConn Health’s new hybrid operating room within the first month of its opening.

Tracking Opioid Overdoses in Real Time to Save Lives

A pilot program led by the Connecticut Poison Control Center and UConn Health’s Emergency Medicine department has been tracking opioid overdoses in Hartford in real time to improve surveillance of the opioid epidemic. More than 1,000 people died from opioid overdoses in Connecticut in 2017, including 80 in Hartford.

The project, launched May 1, has emergency medical service (EMS) personnel in Hartford report overdose cases to the state’s Poison Control Center, part of UConn’s Emergency Medicine department, immediately after the incident. The Center’s poison information specialists ask the emergency responders a series of brief questions and record the data.

The test program is a collaboration with American Medical Response (AMR) ambulances, which provide coverage to two-thirds of Hartford’s communities, and nearby Saint Francis Hospital and Medical Center’s emergency department.

“The new program is increasing our awareness of what is happening on the ground,” says Peter Canning, UConn John Dempsey Hospital’s EMS coordinator.

UConn Health hopes the program establishes an effective early warning system to alert public health and safety officials and community stakeholders of any sudden spike in overdoses or the potential threat of a potent batch of opioid drugs released in certain neighborhoods.

Since the program began in May, the AMR ambulance crews in Hartford reported 211 overdose cases to the Connecticut Poison Control Center. In 147 of the reported cases, emergency crews had to administer the opioid antidote naloxone to revive the overdose victims.

Early data attributes 98 percent of the overdoses where the substance was known to heroin and fentanyl, and 2 percent to other opioids such as oxycodone and methadone. The majority of victims — 77 percent — were male, 51 percent of whom were between the ages of 35 and 49. In addition, 67 percent of the overdoses occurred in public areas such as city parks, roadways, sidewalks, and restrooms. EMS also reported cases of victims who thought they bought cocaine, but instead overdosed on powdered heroin.

This fall the pilot program may expand to include Aetna Ambulance Service in the south end of Hartford.

“This new program is an important step forward and a great example of multi-agency collaboration,” says Dr. Suzanne Doyon, Connecticut Poison Control Center medical director. “Rapid real-time identification of potentially troubled areas of the state is important to public health. Using the connectivity and round-the-clock expertise of the Poison Control Center is both novel and forward-thinking.

“We hope this becomes the model for reporting statewide. The ultimate goal here is to reduce overdoses and save lives.”

Connecticut Student Researchers Shine

Afnih Ahmed of Bloomfield, a UConn second-year international graduate student majoring in applied genomics, is seen working on her Partnership for Innovation and Education (PIE) summer research project.

Ahmed was among the local college students who presented their innovative projects to distinguished guests including state legislators at UConn Health Aug. 1 during Innovation Fellows Research Day, an event that showcased PIE, a newly launched statewide consortium.

The inaugural class of PIE summer program fellows comprises 79 students from UConn, Trinity College, University of St. Joseph, Central Connecticut State University, Southern Connecticut State University, University of Hartford, and Tunxis Community College.

The ultimate goal here is to reduce overdoses and save lives.

— Dr. Suzanne Doyon, Connecticut Poison Control Center medical director

UConn Health

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If the genetic code is like a book, then a mutation is like a typo. Some typos are meaningless. Others have such dramatic consequences for a book, or a life, that the error alone could have an entire novel written about it. Cancer mutations are like that. As oncology moves toward precision medicine — the idea that if we knew exactly which genetic mutations make a particular cancer tick, we could pick exactly the right treatments — oncologists have to keep up with an ever-expanding library of mutations and the drugs that might foil them. The number of cancer research papers published increases every year; there were about 35,000 published in 2015 just in the U.S. It’s far more than any one person can keep up with.

In the same way that a university has research librarians who keep up with the literature in specific fields, JAX has experts who keep up with cancer gene and drug research, even studies that are ongoing and not yet published. JAX already successfully connects these experts with doctors in the Maine Cancer Genomics Initiative, a philanthropy-funded statewide precision medicine program. UConn Health and JAX hope to expand the concept and demonstrate its feasibility more widely.

**Bull’s-Eye Treatments**
Imagine that a patient has surgery or a needle biopsy to diagnose a tumor. It’s a particularly ugly tumor, the surgeon, oncologist, and pathologist all agree. Invasive, spreading, and perhaps this isn’t the first time this patient has had to come in for cancer surgery. The tumor is sampled and sent for genetic testing. In about two weeks, the results come back: there are three genetic variants...
in the tumor that might be drug targets.

At UConn Health, oncologists can send portions of particularly malignant tumors to a team at the JAX Clinical Laboratory. JAX sends back a report with information the oncologist can use to pick a drug regimen with the best chance to shrink that ugly tumor.

“Why is this malignant tumor very resistant to chemotherapy?” Dr. Ketan B. Bulsara, chief of neurosurgery at UConn Health and one of the principal investigators on the project, asks. “What’s the molecular mechanism involved?”

The report is intended to be a standalone reference an oncologist can use to inform a treatment plan. But if the oncologist is unfamiliar with one of the mutations identified in the report or just wants more information, they can request that a genomic tumor board be convened. The board is composed of surgeons, pathologists, and molecular oncologists who act as external advisors, sharing their opinions with the oncologist. In just 15 minutes, the oncologist can get a wealth of expert opinion to combine with their own expertise and judgment. In the end, the oncologist and patient decide on the best treatment, based on all the available information.

“In a multidisciplinary fashion, doctors and scientists work hand in hand in this with one common goal: identify the best treatment regimen for that particular patient’s pathology,” Bulsara says. “The focus is always on the patient. But behind the scenes, there’s an entire team of researchers whose work goes into the genetic tumor report. Scientists at JAX Clinical Laboratory sequence the tumor’s genetic code and report information on more than 200 cancer-related genes. The genes were picked because they are associated with both malignancy and potential drug treatments. Any mutations or variants in these genes might be a clue to the cancer’s weakness. Or a red herring.

“A typical tumor might have 2,000 mutations. Not all of them really matter,” says Andrey Antov, the program director for the Maine Cancer Genome Initiative at JAX.

Finding the key mutations that matter, the two or ten or twenty that could possibly inform treatment and a better outcome for the patient, is the job of the clinical genomic curators. Personal Librarians

The clinical genomic curators are specialists in fields such as molecular oncology and oncological pharmacology. They’re dedicated to keeping up with the literature on cancer genes and the drugs that target them. More and more of these drug-gene connections are being discovered every day. It’s exciting, but the sheer volume of papers can be overwhelming. Navigating that ocean of scientific papers is the medical curators’ full-time job. They’re like librarians curating a Boston Public Library–size collection of genes and drugs with no cross references in the card catalog and only an imperfect search function. The hope is that just as a good librarian’s knowledge of the subject matter can unearth texts a researcher would never otherwise find, a medical curator’s grasp of oncological genetics and pharmacology can identify potential treatments that would otherwise remain obscure.

Sifting the information down to something relevant and digestible is the ultimate goal.

“There is a lot of information that is disorganized and may not all be in the oncologist’s head. We’re trying to bring it together,” says Jens Rueter, medical director for the Maine Cancer Genome Initiative.

The ideal outcome of a tumor genomic analysis would be to identify a mutation such as the HER2 gene that is turned on in the most aggressive breast cancers. HER2 is responsible for the cancer’s malignancy. But it’s also the cancer’s Achilles’ heel. Once drugs were developed to block the HER2 protein, survival rates climbed sharply.

The goal of the Maine Cancer Genomics Initiative is to enable oncologists to identify other drug-gene connections as potent as the ones found for HER2. Although more and more of these drug-gene connections are being discovered, it remains difficult to provide a patient with access to these drugs. Many of them are only available if a patient participates in a clinical trial. And often, there are barriers to accessing clinical trials, and getting drugs off-label is the only way to get patients to treatments. That’s another benefit that Antov, Bulsara, and Rueter hope UConn Health’s collaboration with JAX will bring.

Positive Outcomes

Ultimately, the researchers hope to demonstrate that this approach leads to better outcomes for patients. During the past year more than 350 patients and 70 oncology practitioners (more than 80 percent of the Maine oncology community) enrolled in the Maine Cancer Genomics Initiative study protocol. A few patients have already been offered a targeted treatment through a trial or a compassionate drug access program as a result of enrollment in the program. And Maine health care professionals have logged more than 1,200 certified education hours through 35 genomic tumor boards, online modules, and annual forums held by JAX.

So far, five patients have done this at UConn Health within the last two months. Generous donors have given enough to fund 20 more.

“We hope to get funding for at least 100 patients to show the feasibility of this approach,” Bulsara says. “We want to show we can do this reliably, and that it reliably improves patient care.”

UConn Health already has the infrastructure to do this, in particular a biorepository for tumors set up by Neag Cancer Center Director Dr. Pramod Srivastava and pathologist Dr. Melinda Sanders. With that foundation and support from UConn medical school Dean Dr. Bruce Liang and UConn Health CEO Dr. Andrew Agwunobi, the program was piloted in the Department of Surgery by its chief of neurosurgery, with support from Department of Surgery Chairman Dr. David McFadden, hematologist and oncology chief Dr. Susan Tannenbaum.

The hope is that just as a good librarian’s knowledge of the subject matter can unearth texts a researcher would never otherwise find, a medical curator’s grasp of oncological genetics and pharmacology can identify potential treatments that would otherwise remain obscure.
Connecticut Children’s Medical Center is the teaching hospital where medical students, pediatric residents, and fellows are trained, as well as the home of the faculty’s clinical care work.

“UConn’s Department of Pediatrics’ strong relationship with Connecticut Children’s is excellent and seamless. There is no us and them. We are truly one, and we couldn’t exist without each other,” says Dr. Bruce T. Liang, the dean of the UConn School of Medicine since 2015. Liang has helped expand the two institutions’ joint recruitment of world-renowned physician-scientists and has led much of their growth in pediatric research.

FOR THE GREATER GOOD

The seeds of excellence in pediatric care in the Hartford area were planted in 1967 with the founding of UConn’s Department of Pediatrics, shortly before the medical school admitted its first class in 1968. UConn John Dempsey Hospital offered pediatric hospital care when it opened in 1975. Hartford-area hospitals had an informal agreement not to duplicate pediatric specialty services – patients were transferred among the hospitals based on their specialty care needs.

Connecticut Children’s was born in April 1996 after Newington Children’s Hospital, Hartford Hospital, and John Dempsey voluntarily closed their pediatric services so a comprehensive children’s hospital could open. It was established by state legislation and a 99-year lease of land on Hartford Hospital’s campus for $1 per year. St. Francis Hospital and Medical Center’s pediatric programs were also incorporated. Uniquely, the leadership structure of the new pediatric hospital required that the same individual serve as both UConn’s Department of Pediatrics chair and Connecticut Children’s physician-in-chief.

I am honored to have seen firsthand the strong evolution in pediatrics since my 1980s UConn pediatric residency training,” says Dr. Juan C. Salazar, who has served in that joint leadership role at UConn and Connecticut Children’s since 2013. “It is amazing that the strengths of four different Hartford hospitals came together for the greater good of our children and continue to offer the best pediatric care. It’s been an incredible success, allowing us to grow pediatrics clinically and educationally, along with our research mission.” Salazar cites pediatric endocrinologists Dr. David Weinstein and Dr. Emily Germain-Lee as “two of several perfect examples of how the partnership of Connecticut Children’s and UConn really works seamlessly, with clinical services provided at Connecticut Children’s while robust laboratory research and clinical trials are under way at UConn.”

For 2018–19, U.S. News & World Report ranks Connecticut Children’s among the best hospitals in four pediatric specialties: cardiology and heart surgery, diabetes and endocrinology, neonatology, and urology. As one of the state’s largest care providers with 300 faculty members, UConn’s Department of Pediatrics has 31 medical and 13 surgical specialties.

FOR A BRIGHTER FUTURE

In addition to translational research and top clinical care, UConn Health’s mission includes a third focus on teaching the practitioners of tomorrow. UConn is the largest educator for the state’s pediatric medicine workforce, as up to 60 percent of pediatricians in Connecticut have graduated from UConn’s medical school or its pediatric training programs.

Historically, UConn has also provided the largest pipeline of medical students into the state’s pediatric residency programs – each year up to 20 percent of UConn’s graduating medical school class chooses to specialize in pediatrics, entering residency training programs here or around the country.

“Along with research advancements, our significant focus is the education and training of our next generation of pediatricians and pediatric specialists, many of whom stay right here in Connecticut to serve the state,” says Liang.

UConn and Connecticut Children’s continue to strengthen their partnership in all three areas by building relationships with other organizations.

By Lauren Woods

National recognition by external sources such as U.S. News & World Report comes as no surprise to the thousands who pass through Connecticut Children’s Medical Center each year.

What may be unexpected to those patients is that such success is the fruit of a more than 50-year legacy of the pediatric department at UConn School of Medicine advancing pediatric medicine, research, and education in Connecticut – and putting the health of the state’s tiniest residents first.

The life-changing work done by UConn’s Department of Pediatrics is made possible by a special partnership.
World-renowned physician-scientists across specialties bring to life the vision of Connecticut Children’s Medical Center and UConn School of Medicine’s Department of Pediatrics. Read on to learn about three of the groundbreaking physician-scientists who are currently dedicated to improving the lives of children in Connecticut and around the world.

A VISION FOR THE FUTURE OF PEDIATRIC CANCER

In 2016, Connecticut Children’s and UConn joined with another collaborator, The Jackson Laboratory (JAX) for Genomic Medicine located on UConn Health’s campus, to recruit Dr. Ching C. Lau, an internationally recognized pediatric brain and bone tumor clinician and researcher, from Texas Children’s Hospital in Houston. As a medical director of hematology-oncology at Connecticut Children’s and head of the Division of Pediatric Hematology-Oncology in the Department of Pediatrics at UConn, Lau’s JAX-based laboratory aims to leverage new, sophisticated genomic medicine techniques, mouse models, and therapeutic treatments to choose the best therapy for patients and discover new treatments.

When he was awarded the inaugural Martin J. Gavis Endowed Chair in Hematology/Oncology at Connecticut Children’s, Lau said he was attracted to the vision and dedication of Connecticut Children’s Medical Center.

“I dream that one day when I look at a child diagnosed with cancer, I can look him or her in the eye and say, ‘You will be cured without having to come to the hospital for therapy. You just have to go home and take this medicine,’” he said.

Lau is focused on accelerating the pace and success rate of clinical trials in pediatric cancer patients. “Although the incidence of cancer among children is much lower than that in adults,” he says, “it can be just as deadly. And because of the smaller number of patients available, clinical trials of new treatments for pediatric cancers are conducted at a much slower pace. Typically patients are enrolled in clinical trials after their cancers progress or are found not to be responsive to standard therapy.”

As a result, he says, pediatric cancer patients are exposed to side effects of standard therapy without therapeutic benefit. “This is a particularly serious problem for children because they are still undergoing normal growth and are particularly vulnerable to the side effects of anticancer drugs.”

By using the combined approach of genomic medicine and accurate mouse models to choose the best therapy for each patient, Lau hopes to improve the speed and outcome of clinical trials as well as to reduce unnecessary side effects for children with cancer.

One way he’s speeding up the process is through Smash Childhood Cancer, an initiative he’s spearheading for the U.S. alongside international researchers and IBM to find prospective treatments for childhood cancers by conducting millions of virtual experiments to help pinpoint promising drug candidates for further study using IBM’s World Community Grid.

“This kind of research expedites finding new treatments for childhood cancers,” Lau says. “Crowdsourcing computer processing power enables us to perform millions of virtual experiments virtually and will save us years of experiments. It is bringing us that much closer to finding the right drug for each type of cancer.”

ADMINISTERING NEW THERAPY AND hope

In late July, a patient named Jerrod received a drug infusion that he’s been waiting for his entire life. Jerrod was the first patient to receive a promising investigational gene therapy to treat glycogen storage disease type Ia, the rare, potentially deadly genetic disorder he was born with. Dr. David Weinstein, a world-renowned pediatric endocrinologist and director of the Glycogen Storage Disease Program at Connecticut Children’s Medical Center and UConn Health, has been working to develop the treatment for two decades and calls the trial “a big leap forward for GSD.”

Healthy livers store excess sugar from food and release it into our bloodstream when we need it as processed sugar enzymes called glycogen. However, in the seven forms of GSD, the liver fails to break down glycogen into glucose, causing the body’s blood sugar levels to drop dangerously low, which can lead to seizure or death. Patients stay alive by consuming a cornstarch munch every few hours to keep their blood sugar up.

The gene therapy undergoing the Phase 1/2 clinical trial, approved by the FDA in April, delivers a new copy of the gene to the patient’s liver to replace deficient sugar enzymes and jumpstart the body’s glucose control. Studies in animal models have already shown the promising gene therapy to be safe, effective, and long-lasting.

The clinical trial is in conjunction with the biopharmaceutical company Ultragenyx and will soon expand from UConn Health in the U.S. to other sites including Canada, Spain, and the Netherlands.

“This gene therapy is hope for all GSD patients,” says Jerrod, who asked that his last name be withheld. “We are all extremely excited. Dr. Weinstein is a savior and so is the entire GSD program.”

Weinstein moved his GSD program — the largest in the world — to Connecticut Children’s and UConn Health in early 2017. His multidisciplinary team cares for 600 patients from 48 countries.

“The strong synergies and collaborative team science happening at UConn and Connecticut Children’s are world class and the most fertile ground to make a GSD cure reality,” says Weinstein.

WRITING THE RULEBOOK

Dr. Emily Germain-Lee, a professor of pediatrics and chief of pediatric endocrinology and diabetes, moved her first-of-its-kind Albright Center from Johns Hopkins School of Medicine and Kennedy Krieger Institute to UConn and Connecticut Children’s in October 2016. She has cared for more patients with a specific rare set of endocrine diseases than any other doctor in the world.

“She has redefined the field of pediatric endocrinology,” Salazar said when the hire was announced. “Patients and families travel from all over the world seeking Dr. Germain-Lee’s care.”

Germain-Lee’s patients suffer from pseudohypoparathyroidism and its related disorders, including Albright hereditary osteodystrophy (AHO), a rare inherited bone disorder caused by a genetic mutation that often leads to short bones and short stature. It is also frequently accompanied by severe multihormonal dysfunction in the body.

“This summer, Germain-Lee co-authored the first international guidelines to help doctors around the globe diagnose and manage patients with the diseases. The new guidelines call for human growth hormone treatment for the vast majority of the patients who are at risk for short stature due to growth hormone deficiency. Germain-Lee was the first to discover that part of the reason why AHO patients are short is that two-thirds of them have a growth hormone deficiency.”

Her long-term global clinical trial studies have shown the promising benefits of growth hormone treatment, including its ability to dramatically increase a patient’s short stature to their original destined height potential while also improving their lipid levels and reducing obesity. With her research in the final stages, Germain-Lee is working toward gaining FDA approval of the therapy, which would be the first new therapy for the disorder in 70 years.

“I am thrilled to be a part of the combined power of UConn School of Medicine and Connecticut Children’s Medical Center for advancing children’s health and discovering new treatments of disease through research,” says Germain-Lee.
Q&A with Dr. Leo J. Wolansky, professor and chair of UConn Radiology

Dr. Leo J. Wolansky Chair and Professor, UConn Radiology

Sharing Knowledge for Better Patient Care

**What other projects are you focused on?**

We have a number of other initiatives, such as the Linda Clemens Foundation Free Mammogram Program, which provides funds for screening and diagnostic mammograms, breast ultrasounds, and breast biopsies for uninsured and underinsured UConn Health patients. We have added a new CT scanner in the Musculoskeletal Institute building that will increase our capacity significantly and will create a more patient-friendly outpatient setting. We will also offer weekend MRI appointments at the Musculoskeletal Institute. Additionally, we have a new attending, Dr. Abner Gershon, who strengthens our stroke service and is opening a minimally invasive neck and back pain clinic. In the area of nuclear medicine, we are now offering DaTscan brain scans for differentiation of Parkinsonian syndromes from essential tremor.

**What can you tell us about the new imaging center in Storrs? How will it benefit patients in the area?**

When I started here, I immediately saw how important to the state the UConn athletics program is. It seemed strange that it was so difficult for us to image our own athletes, or any UConn students, in Storrs. From my previous research, I was aware of the Brain Imaging Research Center (BIRC) in Storrs, which has a fabulous scanner. It occurred to me that their MRI scanner could provide patient care without interfering with the research mission of the BIRC.

Once we converted it, we’d be able to read the images here at UConn Health. This would allow us to care for our own student-athletes, other students, faculty, staff, as well as the general public in the Storrs area, sparing them the 45-minute trip to Farmington. I explored a partnership with the BIRC leadership, working closely with Inge-Marie Eigsti, Jay Rueckl, and now the new director, Fumiko Hoeft, who has been extremely helpful.

**I thought it would be a waste not to share this valuable equipment.**

Technology has changed the way we get information, and we find that most people answer questions by looking online. Radiology, which relies so heavily on technology, is a specialty that is much more visual than most other fields of medicine. Every day we encounter an abundance of complex digital images created by sophisticated equipment. The digital images can be captured, uploaded, and sent throughout the world with relatively little effort. I thought it would be a waste not to share this valuable material with everyone.

Medical students and radiology residents will likely use it the most. Furthermore, resident doctors in many different fields are tested on the imaging that relates to their specialty. Even after their training, patients expect doctors and other providers to be knowledgeable about everything related to their care, including imaging. Radiology Online can further educate providers and even educate patients about their health. It also provides the opportunity for resident doctors in many areas to use it the most. Furthermore, resident doctors in many areas could provide patient care without interfering with the research mission at the BIRC.

**What can you tell us about the new imaging center in Storrs? How will it benefit patients in the area?**

Dr. Ryan Millea hasn’t lost focus on what drives him, whether responding at a moment’s notice to the surgical needs of a car accident victim or an intensive care patient with a life-threatening gastrointestinal burst.

“My philosophy is to always deliver patient-centered care,” says Millea, who is also a general and critical care surgeon. “I’m very hands-on to improve a patient’s overall experience. No one likes being sick, so I try to make things as seamless and smooth as possible from preoperative care to recovery.”

Millea applies this attitude not only on a patient-by-patient level but also through large-scale initiatives to improve the experience of all surgical and critical care patients.

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TRAUMA DIRECTOR PUTS PATIENTS FIRST

As he marks his first year as Medical Director of Trauma at UConn Health, Dr. Ryan Millea hasn’t lost focus on what drives him, whether responding at a moment’s notice to the surgical needs of a car accident victim or an intensive care patient with a life-threatening gastrointestinal burst.

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— Dr. Ryan Millea, Medical Director of Trauma

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