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UNIVERSITY OF COLORADO SCHOOL OF MEDICINE

# CUMEDICINE

*Today*

## Going Viral

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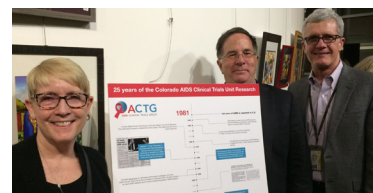
Cover photo: Jeffrey Kieft, PhD, studies how viruses “hijack the cell.”

Photo by Trevr Merchant.

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## Leading the Way

Mental health wellness is a top priority for our care providers and the communities we serve, and there is an increased recognition that we must actively address this issue to maintain and improve health – our own and those who depend on us.

Earlier this year, our School's Department of Family Medicine was featured in an article in the *New England Journal of Medicine* as an example of improving the quality of care for patients while also reducing the level of stress on providers.

The department established a team-based model called ambulatory process excellence, or APEX. Under this system, medical assistants gather data, reconcile medications, set the agenda for patient visits, and identify opportunities to increase preventive care.

The medical assistants report to the physician or nurse practitioner and then remain in the room to document the visit with the patient. After the clinician leaves, the medical assistant remains to provide follow-up education.

Corey Lyon, DO, associate professor of family medicine and medical director of the A.F. Williams Family Medicine clinic, described the result: "The chaos in exam rooms before APEX was akin to texting while driving. The greatest advantage now is that the computer no longer stands between me and my patients. This allows for deeper thinking and connection."

The provider-patient experience is personal, face-to-face. Eyes are not staring at a computer screen. Ears are used to truly listen.

A dilemma of our hyper-connected era is that technology can make us better at what we do—more information is available to us faster than ever—but it can also interfere with the personal connection that any caring profession must forge.

As a society, we must come to grips with this concern.

This spring, the Helen and Arthur E. Johnson Depression Center of the School of Medicine hosted a lecture by Jean M. Twenge, PhD, professor of psychology at San Diego State University, on the impact of smartphones and social media on mental health and suicide risk.

Twenge's research focuses on how the ubiquity of smartphones is reflected in the lives of young people. Her book, "iGen," documents a shift in behavior among the current generation of teens compared with previous ones that she attributes in part to an overreliance on socializing through screens rather than in personal contact.

"But the twin rise of the smartphone and social media has caused an earthquake of a magnitude we've not seen in a very long time, if ever," Twenge wrote in an excerpt of her book that was published in *The Atlantic* last fall. "There is compelling evidence that the devices we've placed in young people's hands are having profound effects on their lives—and making them seriously unhappy."

She sees a generation with many connections but few deep bonds. Technology itself isn't bad, but it shouldn't be used to isolate ourselves from one another, she said.

Our work requires care and attention and we must not let the tools we use get in the way of a better understanding of our students, peers, and patients. We also need to recognize that sharing some tasks can equal improvements for all.

As Lyon explained, "Providers have to be willing to give up a little control to get the support they need so that they can build better connections with patients without technology interfering."



While it required hiring and training medical assistants, it showed that working together improves the quality of care. Referral rates for mammography and colonoscopy screening improved. Providers reported a sharp decrease in burnout. Appointments for an additional three patients per provider per day could be scheduled.

Our School of Medicine team is showing us a potential way forward.

With warm regards,

A handwritten signature in black ink that reads "John J. Reilly, Jr." The signature is fluid and cursive.

John J. Reilly, Jr., MD  
 Richard D. Krugman Endowed Chair  
 Dean, School of Medicine  
 Vice Chancellor for Health Affairs  
 University of Colorado

## Reporters locally and nationally turn to the School of Medicine for expertise and research news. Here are examples from near and far.

**Christopher Hoyte, MD**, associate medical director for the Rocky Mountain Poison and Drug Center and assistant professor of emergency medicine told CBS News in November that it is unlikely that a person can overdose from being exposed to fentanyl on a shopping cart. “I never say never, but it is highly, highly, highly, unlikely someone could become that systemically ill just from having fentanyl touch their skin,” he said. “It’s not absorbed just touching it.”

**Robert Eckel, MD**, professor of medicine and interim vice chancellor for research, explained that average cholesterol levels could be declining for several reasons. “It can’t be because we’re losing weight, because that’s still going up,” he said in the Washington Post in October, “but it could be statin use. It could be a result of the decline in smoking. Or a combination of factors.”

**Greg Allen, MD**, associate professor of otolaryngology, discussed a patient who was born with Treacher Collins syndrome. “Michael has continued to surprise me,” he said in the Denver Post in November. “When he came in and told me he was playing hockey, or when I listen to a recording of him play his cello, those are two examples of when I was very surprised. His tenacious attitude, his skill and level of accomplishment are exemplary for any kid.”

**Christopher Stille, MD, MPH**, associate professor of pediatrics, in December outlined to Colorado Public Radio who was at risk if federal officials failed to provide funding for the Children’s Health Insurance Program. “These are kids whose parents work and make a little too much money to qualify for Medicaid,” he said. “It’s a lifeline for them.”

**Kennon Heard, MD**, professor of emergency medicine, described to National Public Radio in November an increase in a rare vomiting illness linked to heavy marijuana use. “Five years ago, this wasn’t something that [doctors] had on their radar,” he said. “We’re at least making the diagnosis more now.”

**Meredith Mealer, PhD, RN**, assistant professor of medicine, explained the importance of a study on burnout among nurses. “Burnout syndrome in nurses is associated with decreased patient satisfaction, reduced quality of care, medication errors, higher rates of healthcare related infections and higher mortality rates,” she said in a December article by the news service Reuters. “What this study adds to the literature is that there is a direct association between shift work and burnout syndrome.”

**Stephen Daniels, MD, PhD**, chair of pediatrics, commented on a new study that found American children are continuing to gain too much weight and that the greatest increase in obesity is occurring among children between two and five years old. “What’s concerning ... is that we know that once obesity is established, it’s really hard to reverse,” he told Consumer Reports in February.

**Muhammad Aftab, MD**, assistant professor of surgery, discussed heart surgery outcomes at UHealth University of Colorado Hospital in a February report on the ABC affiliate in Denver. “Currently our patients have really extraordinary life expectancy and quality of life after heart transplantation,” he said. “And we are talking in terms of decades.”

**Michelle Barron, MD**, professor of medicine, described the risks for getting sick while traveling in a December article in Men’s Health: “Planes, trains, and automobiles are the mainstay for travel during the holidays and are also the perfect breeding ground for illness.”



**Margaret Schenkman, PT, PhD**, director of the Physical Therapy Program, explained the results of her study of high-intensity exercise for people with early-stage Parkinson disease (PD). “There is a growing body of evidence demonstrating the benefits of a variety of types of exercise for people who have PD, including strength training, flexibility training, balance training and combination training approaches,” she told MD Magazine in January.

**Lilia Cervantes, MD**, associate professor of medicine and a hospitalist at Denver Health, described her study of undocumented immigrants with kidney failure and the impact of policies that require providing dialysis only in cases of emergency rather than on a regular schedule. “To receive emergency-only hemodialysis, undocumented patients with kidney failure must be near death,” she told Reuters in December.

**Joaquin Espinosa, PhD**, professor of pharmacology and executive director of the Linda Crnic Institute for Down Syndrome, explained in the January-February issue of American Scientist the results of his recent research. “The public at large thinks of Down syndrome as a condition of the brain,” he said, “but our studies are recasting Down syndrome as a condition of the immune system, which then goes on to have impacts on the brain and many other organs.”



**Dan Theodorescu, MD, PhD**, director of the CU Cancer Center and Distinguished Professor of the University, discussed with the journal *Nature* the challenge of focusing a career on research rather than surgery. “It’s a different kind of satisfaction,” he said. “There’s the satisfaction of helping the human in front of you, seeing the sparkle in their eyes when you tell them you may be able to cure them, versus seeing an experiment that cures cancer in mice.”

**Nanette Santoro, MD**, chair of obstetrics and gynecology, was quoted in *Glamour* in December about the pressure on women when they are directed to fertility treatment options. “Bullying might not be the right word, but it is close to what it feels like sometimes,” she said. “Women are being told what to do, and we need to be making sure that what they are being told is based on careful science.”

**Benjamin Honigman, MD**, professor of emergency medicine, explained altitude acclimation to the *Austin American-Statesman* in January. “Where people get into trouble is if they come up to altitude—especially to some of our resorts that are higher elevation—and don’t allow their bodies to adjust,” he said. “They’ll fly into Denver and drive up to one of the resorts or they’ll fly into Aspen or Vail and they’ll immediately want to get some skis and go downhill skiing.”



**Larry Allen, MD**, associate professor of medicine, discussed with *The New York Times* in November an article he wrote for the *Journal of the American College of Cardiology* that reviewed the number of ways in which heart patients are let down at the end of life. “Getting shocks at the end of life is not really helping patients live longer or better,” he said.

**Corey Lyon, DO**, associate professor of family medicine, described for the *New England Journal of Medicine* the team-based model the department uses to improve patient care. “The chaos in exam rooms before APEX (ambulatory process excellence) was akin to texting while driving,” he said in January. “The greatest advantage now is that the computer no longer stands between me and my patients. This allows for deeper thinking and connection.”

**Judith Regensteiner, PhD**, professor of medicine and director of the Center for Women’s Health Research, was quoted by *Consumer Reports* in January in an article about the health benefits of two-and-a-half hours of moderate-intensity aerobic exercise and at least two hours of full-body strength workouts per week for adults age 65 and older. “This amount has been shown to help reduce your risk of heart disease, high blood pressure, depression, stroke, type 2 diabetes, colon and breast cancer, and decreased cognitive function,” she said.



**Jean Kutner, MD, MPH**, professor of medicine and chief medical officer for University of Colorado Hospital, was quoted by the *Loveland Reporter-Herald* in December: “The absolute best way to protect yourself and others from the flu is to get vaccinated.”

An article published in the journal *Injury Prevention* by **Daniel Goldberg, JD, PhD**, associate professor of family medicine and faculty for the Center for Bioethics and Humanities, was quoted in February by the *MinnPost*. “The league has a record of promoting unsound research, both to downplay the risks of brain trauma as well as to oversell the potential for making tackling safe,” he wrote with co-author Kathleen Bachynski, a postdoctoral fellow in medical humanities at New York University’s School of Medicine.

**Jennifer Wiler, MD, MBA**, associate professor and vice chair of emergency medicine, in February discussed with *The Wall Street Journal* what hospitals of the future will look like. “Hospitals aren’t going away anytime soon, nor should they,” she said. “But the traditional model of a hospital as the hub of care with a single facility providing every facet of treatment is changing.”

## Exercise is Good for the Mind and the Body

Patricia Heyn studies how activity affects the brain

By Cynthia Pasquale



Patricia Heyn, PhD, studies how activity affects cognitive function, especially for people with Alzheimer's disease.

In 2004, while doing a post-doctoral fellowship at the University of Texas Medical Branch, Heyn was invited to join the CU School of Medicine to develop and establish her area of research with the Division of Geriatric Medicine's IMAGE (Investigations in Metabolism, Aging, Gender and Exercise) Research Group, which conducts investigations in metabolism, aging, gender and exercise.

She joined the Department of Physical Medicine and Rehabilitation in 2008 to work on projects with the Assistive Technology Partners. Heyn also works with the Center for Gait and Movement Analysis on a longitudinal research health outcome study evaluating the effects of aging on disability for people with cerebral palsy.

She also works with Rocky Mountain Alzheimer's Disease Center investigators. Currently, she is working with a CU colleague on evaluating neurotrophic brain markers and cognitive function in individuals with cerebral palsy.

"My work is multidisciplinary, and to be successful in this line of research, you need to work collaboratively and effectively with the

disciplines involved in advancing the science of Alzheimer's disease for individuals with complex disabilities."

### How did you choose this profession? Was there a person or event that influenced your decisions?

Growing up in Brazil exposed me to a broad range of social issues, diversity and inequality. In Brazil in the 1980s, individuals with disabilities were significantly underserved and neglected. Their health needs were so glaring that when I was a college student, I volunteered with nonprofit organizations to assist with the needs of the underserved population.

In 1988, when I was an exercise physiology research intern at the Hypertension Lab from the Heart Institute of Sao Paulo, I was asked by one of the volunteering organizations, Project Agape, to develop physical therapies for neglected adults with intellectual and developmental disabilities. I understood well the importance and significance of what I was asked to do and I immediately accepted the challenge. This experience gave me the strength and creativity to investigate exercise-based approaches that could increase the well-being of these individuals, and, at the same time, decrease the burden of social neglect.

While all my lab peers, who were also interning at the Hypertension Lab, were investigating the cardiovascular responses to exercise training, I was developing a new passion and career path by investigating novel exercise approaches as a potential therapy for mental and cognitive enhancement. It was the birth of my research on physical and sensory-based cognitive therapies for adults with cognitive impairments. I integrated music, musical instruments, physical movements, storytelling and sensory objects to stimulate physical and mental engagement in individuals with severe cognitive impairments.

I moved to the United States in 1991 for my graduate studies and expanded my initial work to focus on aging and dementia. In 2001, I completed my doctoral studies investigating the effects of exercise training on Alzheimer's disease. I developed an exercise-based, multi-sensory cognitive therapy for individuals with severe Alzheimer's disease and I presented my study results at professional meetings and published the findings.

### You mentioned using everything from music to movement to protect or enhance functions of an aging or diseased brain. What activities have been used to fend off brain issues and who should engage in these types of activities?

The past 20 years has been filled with abundant information about

different approaches aimed to impact positively the brain health span. Although the evidence is still uncertain, exercise—especially endurance-type exercise like swimming, biking, walking—has been shown to be one of the most effective treatments for cognitive enhancement. Abundant evidence supports the benefit of exercise to ameliorate cognitive decline as well as to be protective against dementia development.

The Mediterranean Diet, which is rich in fresh vegetables, whole grains, seafood, nuts, olive oil, etc., also shows promise for protective and enhancing benefits on cognition. Lately, and probably because of the explosion of mobile technologies and apps, the brain gaming training approach, which is a new science, also is showing potential to aid in the health span of cognitive function.

My suggestion is to do them all. Combine endurance exercise, including complex physical activities like dance with the goal to increase sensory activity, with the Mediterranean Diet, cognitive training (gaming, or learning a new language or how to play a musical instrument) and have

believe the next 10 years will provide us with ample scientific information about the effects of brain-gaming technologies on health, including whether too much of a good thing is a bad thing.

#### **What other research topics are you focusing on now?**

My current research includes investigating the early timing of chronic disease development in individuals at risk for health decline due to the process of growing older with a disability. The question is, if someone has a disability, like a brain or spinal cord injury or Down syndrome, how early can we identify health risk factors associated with cardiovascular disease or Alzheimer's disease? Cardiovascular disease is associated with Alzheimer's disease; therefore, are individuals with a lifetime disability at higher risk for developing such conditions, and if so, why and when does the disease process start in these individuals?

This research has important health care implications as well as great potential for positive quality of life impact for patients with disabilities.

**“Try to learn something new every day with the goal of stimulating new memories and brain proteins to enhance brain activity.”**

an engaging full and rich social life. All these approaches together will most likely increase your chances for good health, wellness and vital cognitive function for lifetime.

Also, try to learn something new every day with the goal of stimulating new memories and brain proteins to enhance brain activity. Exposing the brain to new information is similar to what exercise does for muscle tissue.

#### **Does it matter at what age you begin these activities? Do young people, who constantly use gaming technology, have an advantage later in life?**

I always say that ‘one’ is better than ‘zero,’ and that means any stimulation, be it physical or mental, is better than none. You must use it or you will lose it, and the earlier you start with physical and mental training, the better are your chances to benefit from them.

Regarding the use of the brain-gaming approach and its longitudinal effects, this knowledge most likely will emerge in the coming years. I

We don't know much about the development of Alzheimer's disease in individuals with disabilities. We need to understand and learn more about how Alzheimer's manifests in persons with disabilities to properly treat, manage and improve the person's quality of life.

Living a life with a disability can be quite challenging for the person and for their family. Developing chronic health conditions while the person with a disability is growing older can have detrimental effects on the person's lifespan, function and quality of life.

#### **Do you follow your own advice and continue to be physically and mentally active every day?**

Yes. I swim, walk, run, bike and love to dance. I also love to learn about world cultures, behaviors and languages. If a day was composed of 48 hours, I would be learning Latin, Italian and French—and how to play a Spanish guitar.

## AIDS Clinical Trials Unit Saving Lives

CU offers experimental treatments and hope to patient volunteers

By Debra Melani

When he tested positive for HIV in 1991, David Dillon was certain he received a death sentence.

He'd watched friends die, struggling with intense side effects caused by the only drugs available at the time, medications that were barely effective on the AIDS virus, which could adapt, often within months, to build resistance to them.

Dillon found hope in the words of a social worker, who told him that experts were on the verge of turning the deadly affliction into a chronic but manageable disease.

"That's what I grabbed on to right away," Dillon said. "And that's what I've hung on to ever since."

Dillon was one of the first HIV-positive patients to volunteer for studies with the Colorado AIDS Clinical Trials Unit (ACTU), now part of the University of Colorado Anschutz Medical Campus. Today, as the ACTU celebrates 25 years of major contributions in revolutionizing HIV/AIDS treatment, Dillon is alive, grateful to the CU team that helped him, and he's confident that he helped make a difference.

### Recruiting a leader

CU established itself as a center for HIV/AIDS research in 1990 by recruiting Robert Schooley, MD, a Harvard Medical School professor and prominent HIV investigator.

At Harvard, Schooley's research group was among the first to delineate the humoral and cellular immune responses to HIV infection. He also was involved in the discovery and development of antiretroviral chemotherapeutic agents including reverse transcriptase inhibitors, protease inhibitors and entry inhibitors.

"It was a big deal," Thomas Campbell, MD, who was an infectious disease fellow at CU at the time and is now principal investigator of the Colorado ACTU. "I remember sitting on my back porch and reading about his recruitment on the front page of The Denver Post. Bringing him to Colorado was like recruiting John Elway to the Denver Broncos. It's bringing a superstar to Colorado, which helps elevate the whole team."

At CU, Schooley established the AIDS Clinical Trials Center, bringing



David Dillon, one of the first HIV-positive patients to volunteer for studies with the AIDS Clinical Trials Unit. Photo by Debra Melani.

experimental drugs to the region. While at CU, Schooley was elected to serve as Chair of the National Institute of Allergy and Infectious Diseases AIDS Clinical Trials Group (ACTG), which he headed from 1995 until 2002 and CU's unit joined the growing number of sites in the ACTG. With Schooley's national role, research funding followed, including \$4.8 million for adult AIDS research and \$3 million for pediatric AIDS research.

CU's unit joined a growing number of national sites within the AIDS Clinical Trials Group, initially formed in 1987, as the urgency for new drugs intensified.

"Schooley was the key person that made that happen, and so all of the great HIV/AIDS research capacity that we have today is largely possible because of the groundwork that he laid and the foundation that he built in the early '90s," said Campbell, who is now medical director of the University of Colorado Hospital Clinical and Translational Research Center of the

Colorado Clinical and Translational Sciences Institute.

### Dillon's many trials

Schooley's arrival at CU may have saved Dillon's life.

In 1991, Dillon was an employee in the CU Boulder housing department and just learning of his infection. He wore a beeper that every four hours reminded him to take his pills. While he didn't suffer side effects as severely as others, he recognized that the benefits were waning.

Dillon found Graham Ray, RN, who is still a study coordinator with the Colorado ACTU, and signed up for one of its first clinical trials. The study involved spending some nights in the hospital, and Dillon recalled a trial patient in a nearby bed.

"He had pretty much run the gamut of drugs available. He'd run out of options, so this trial was one of his last hopes," Dillon said. "I lost several friends that were in the same boat. There just wasn't new treatment coming fast enough to help them."

"Few drugs and rapid resistance were major problems for patients in those days," Campbell said. "We could only give one or two drugs at the most together, and drug resistance developed very rapidly. The medicines lost their effectiveness."

For Dillon, who estimates he has tried as many as 20 single experimental drugs, the trials always came right in time, with Ray and his CU doctor, Steven Johnson, MD, professor of medicine in the Division of Infectious Diseases, regularly alerting him to new studies.

In its 25 year history, the Colorado ACTU has conducted more than 177 clinical trials, with more than 2,500 participants coming forward to help scientists and providers in their search for a more effective treatment.

“It just seemed like I was already right at the cusp, so when a drug came into testing, I was ready for it,” said Dillon, now 65, who still travels to the Anschutz Medical Campus from his Loveland home. “Dr. Johnson saved my life more than once.”

HIV attacks patients’ immune systems by binding to and killing CD4 cells, which are white blood cells that fight infection. Doctors monitor CD4-cell counts to assess the progression of the disease. A normal CD4 count is between 500 and 1,400 cells per cubic millimeter of blood. At levels below 200, patients are at high risk of developing serious illnesses. Dillon’s counts were once as low as five.

### Trial participants are part of a mission

Patrick Terry, a Denver-area native, has done “probably a dozen” trials since 2000. Because of his dedication to the trial process, he calls himself a go-to volunteer for ACTU research nurse Cathi Basler, RN. Taking part in trials is about staving off AIDS (his CD4 count has never fallen below 500), and putting an end to the epidemic.

“To me, it’s so important that we find out more about it,” Terry said, “and if there’s any chance that there could be a cure, then I’d like to be a part of it.”

Both Dillon and Terry acknowledge that helping science isn’t always easy. But their perseverance has paid off, for them, and for many of the more than 30 million people worldwide living with HIV.

While Dillon said he feels “lucky” because he’s apparently always received the active drug in the double-blind studies, he recalled a nearly five-year trial that required injecting a drug in his abdominal muscles



*Patrick Terry, a Denver-area native, says he has participated in about a dozen clinical trials since 2000. Photo courtesy of Patrick Terry.*

twice a day. “It just hurt, and you had to just keep doing it.”

“You know when you are on the real drug,” said Terry, 60, who began volunteering for clinical trials after being diagnosed with HIV in 1995. “I’ve had some very difficult studies,” he said, noting one in which the drug was so strong, it caused hallucinations, and another in which he had to have lymph nodes removed.

### Sticking with the treatment

In 1996, a Colorado ACTU-led research study played a key role in the development and widespread use of what was commonly termed “drug cocktails.” That was a major turning point in HIV/AIDS treatment, Campbell said.

“When we first really had the ability to put three drugs together to make an effective combination, it greatly reduced the risk of drug resistance. It did so by having much more effective suppression of viral replication,” he said. “We suddenly had a way to effectively treat HIV and prevent all the damage it does to the body.”

Currently part of a two-drug combination trial, Terry’s CD4 counts hover around 1,000, and his viral load is undetectable. For Dillon, although his CD4 counts aren’t quite as high, and his “cocktail” includes five drugs, his viral load is also undetectable.

Terry emphasizes that the effective drugs are still not a cure and he advocates for medication adherence. “I’ve never missed a dose, and that’s probably one of the most important things,” said Terry.

“Take it seriously,” Terry said. “Don’t skip your medicine. That’s a problem with so many people. The medicine doesn’t work if you don’t take it. And take care of yourself,” he said.

### Researchers still have work to do

While noting significant progress in treatment, which would not have been possible without dedicated volunteers, Campbell, also emphasized that HIV remains a serious virus with no cure.

“Yes, a person diagnosed today who seeks treatment early and adheres to it should live a near-normal lifespan,” Campbell said. “But near normal is not normal. There’s still a lot of work that needs to be done.”

Dillon said he’s grateful for that first social worker’s hopeful words and for finding the Colorado ACTU. “It saved my life, and it saved a lot of other lives.”

## Untangling the Secrets of RNA Form and Function

Biochemist Jeffrey Kieft on understanding how viruses hijack the cell

By Mark Couch



Biochemist and structural biologist Jeffrey Kieft sees promise and beauty in the tangles of an RNA molecule and an almost limitless potential for exploration.

“The primary focus of my lab’s research has been RNA molecules of viral origin and there are a few reasons for that,” said Kieft, PhD, professor and vice chair in the Department of Biochemistry and Molecular Genetics and part of the RNA BioScience Initiative in the CU School of Medicine. “Of course, viruses make people sick and we want to make a difference

in treating deadly viral infections. In fact, there are projects in my lab that are moving towards translating our basic science discoveries into new therapies.

“But also, studying viral RNAs teaches us so much about basic biological processes. The sheer number and diversity of viruses is lost on most people. It’s estimated that there are 10 to the 37<sup>th</sup> individual viral particles on Earth at this moment. That’s more stars than are in the universe, and we know almost nothing about most of them.”

That’s right. He said there are 10,000,000,000,000,000,000,000,000,000,000,000,000,000,000 viral particles on the planet, making the viral world the largest repository of unexplored genetic material.

As if such an expansive universe of material to study isn’t daunting enough, consider an RNA molecule itself. It twists and turns and flexes and folds and moves and stacks up on itself and does a dance that dictates what it does and how it fulfills its function.

“The overarching questions that have driven my research are ‘How is RNA able to assume so many complex three-dimensional folds? What are those folds? How do they drive function? And then, of course, how does that relate to health and disease? Can we exploit that knowledge to make a difference in the world?’”

But wait, it gets more complicated in ways that raise even more questions. The RNA molecule, complex in structure and surprisingly diverse in function, is based on a simpler set of building blocks.

“What got me fascinated by this molecule is the idea that RNA is chemically less diverse than proteins,” Kieft said. “It only has four bases as opposed to the 20 amino acids in proteins, but it’s arguably more diverse in terms of its function in the cell. It can store genetic information,

it can do catalysis, it is part of many dynamic and large macromolecular machines, it regulates gene expression using many different mechanisms, etc. So that’s a paradox: How is something that is less chemically diverse more functionally diverse?”

Kieft’s lab on the Anschutz Medical Campus is studying these questions and more in an attempt to understand how viruses take over a cell’s machinery.

In Kieft’s parlance, viruses “hijack the cell.”

“Viruses are obligate intracellular parasites in that they can’t reproduce on their own. They have to invade a cell and many of them use structured RNA in very elegant ways as part of their strategy to hijack the cell’s machinery; they take what is normally machinery the cell is using to stay alive and turn it into virus-making machinery.”

Kieft graduated from the U.S. Military Academy at West Point in 1990 and served as an army officer in Germany. Throughout his time in the military, he said, he spent time reading science books.

“I’ll admit that as an undergraduate, I never took a biochemistry course. I was drawn to physical chemistry. I liked numbers and quantitative measurements of thermodynamics and kinetics, but then I realized I could use physical chemistry to study the complexity of biology. In the end, biology is a big physical chemistry process and I think it can be broken down and understood at that level.”

Even today, he still describes the effort to understand the RNA in terms of a battle. “There was a great review that was written by Bryan Cullen a little under 10 years ago, called ‘Viral RNAs: Lessons from the Enemy,’” he said. “I’ve always liked that title, because it illustrates how viruses cause diseases that we want to stop, but also how they can teach us things about basic

cellular processes and also how we might use viral RNAs as the basis for new treatments to diverse ailments. I wish I had thought of that title.”

After leaving active duty, Kieft went to graduate school at the University of California Berkeley, where his PhD adviser described the potential in studying RNA. “He said these molecules fold up just like proteins, but we know almost nothing about how that works. We just haven’t seen enough structures. At that minute I was hooked.”

Kieft did postdoctoral work at Yale University. In 2001 he was awarded the Roger Revelle/AAAS Fellowship in Global Stewardship, working as a member of the White House Office of Science and Technology Policy for a year before joining the CU faculty, where he was also an Early Career Scientist of the Howard Hughes Medical Institute.

He joined the CU School of Medicine just prior to its move to Aurora and the Anschutz Medical Campus and part of the pitch to bring him here was to put a hard hat on his head and give him a tour of the construction zone.

Still, more than a decade later, the building work goes on because there are always new tools that make it possible to learn more. Kieft spearheaded the effort to build the campus’ new cryo-electron microscopy facility and he now directs the CU School of Medicine’s Structural Biology and Biophysics Core Facilities (cryo-EM, X-ray crystallography, NMR, metabolomics, proteomics, biophysics and peptide cores). These core facilities require a significant expense to keep them functioning, but it’s essential to have the ability “to look directly at the molecules of life and their interactions at this level and to understand the structures of macromolecular machines and their changes.”

“Sometimes when people who are not involved in this type of research see the cost of the

facilities and equipment, their eyebrows go up and they say, ‘Why are we spending so much on this?’” he said. “My answer is: that’s what it takes if you are going to be on the cutting edge of these molecular studies, if you want to understand the basic molecular underpinnings of disease and really get at the mechanisms involved. There really is no other way to get this information.”

CU researchers could try to conduct this work at other universities where charges would be higher and the work would be a lower priority than the home-grown research at those schools. However, Kieft believes the CU School of Medicine should be a national leader in this research and that there are opportunities for collaborations combining molecular studies with more clinically-focused research on campus.

“You look at those up-front costs and say, ‘Wow that’s expensive,’ but these shared resources make us competitive for research dollars that require this sort of equipment. Awarded grants then help pay for these resources, and they lead to new research projects and collaborations. Sustained investments can create an upward cycle.” Kieft said. “I want researchers here to be able to do the same science that is being done at the top research institutions in the world. I want to see new collaborations forged on our campus and want to make these technologies available to the greater campus community.”

The science conducted by Kieft and his colleagues focuses on critical issues for human health and has been featured in high-profile journals, such as *Cell*, *Science*, *Nature*, *Nature Structural and Molecular Biology*, *Proceedings of the National Academy of Sciences*, *Nature Communications*, and *eLife*.

“We’re studying RNAs from the flaviviruses, which include Zika and dengue and many, many others, like Hepatitis C virus. We’ve just started a project as part of a multi-University

team to do some work on Ebola. We’ve got a polio virus project. We also study viral RNAs that come from more unusual viruses like some that infect plants. I realize some might think ‘Why are you studying plant viruses at a medical school?’ The truth is there are interesting RNAs that these viruses produce and we can learn a lot of fundamental, basic biology by studying them. Even though right now a particular RNA and a particular phenomenon may have only been found in a virus infecting plants, it probably exists somewhere else...we just haven’t found it yet.”

There is abundant common ground for research projects on campus.

“When we got to the point of working on Zika, I talked several times with David Beckham, who is an infectious disease expert here on campus. He’s working on Zika as well, but he is an MD who spends time in the clinic. His perspective and experience with these viruses is very different from mine.

“In my lab, we are more reductionist; we are biochemists looking at individual RNA molecules and he’s doing infections in mice, so we realized we can start asking and attacking important questions in different, but complementary ways. Opportunities just sprang up immediately.”

Kieft and Beckham have several trainees who can take advantage of the experiences of both labs and share ideas and data. This extends beyond research on Zika. “Zoe O’Donoghue is a graduate student in my lab whose dengue virus research benefits from this sort of cooperation: she can move easily between our labs. Ben Akiyama is a post-doc who is accessing the expertise of the Beckham Lab as well. It’s great because we all learn from one another, we can share ideas, we can contribute to the training of each other’s lab members, and we can support each other’s grant applications.”

## Crnic Institute Makes “A Game-Changing Discovery”

CU researchers find links between Down syndrome and immune system

By Mark Couch

Researchers from the University of Colorado School of Medicine are conducting breakthrough research indicating that Down syndrome could be considered a disorder of the immune system.

The findings announced in the journals *eLife* and *Scientific Reports* are a significant development in understanding Down syndrome.

“Down syndrome has been classified as a mental disorder, as an intellectual disability, as a brain condition,” said Joaquín Espinosa, PhD, director of the Linda Crnic Institute for Down Syndrome at the CU Anschutz Medical Campus. “And that’s fine, those are all fair labels. But you can also understand Down syndrome under a different light.”

In between meetings with his laboratory’s researchers on a busy day last January, Espinosa rattled through a list:

- “You can say that Down syndrome is a genetic condition where people are protected from solid cancers.
- “You can say that people with Down syndrome are the largest human population with a predisposition to autoimmune disorders—30 percent—celiac disease, autoimmune hypothyroidism, type 1 diabetes, autoimmune skin conditions, rheumatoid arthritis.
- “People with Down syndrome are the largest human population with a genetic predisposition to early-onset Alzheimer’s disease—100 percent.”

Then, he ties together the conditions on the list: “So Down syndrome is many things,” Espinosa said, “and then when you put every one of those through the prism of an immune disorder, it makes sense every time.”

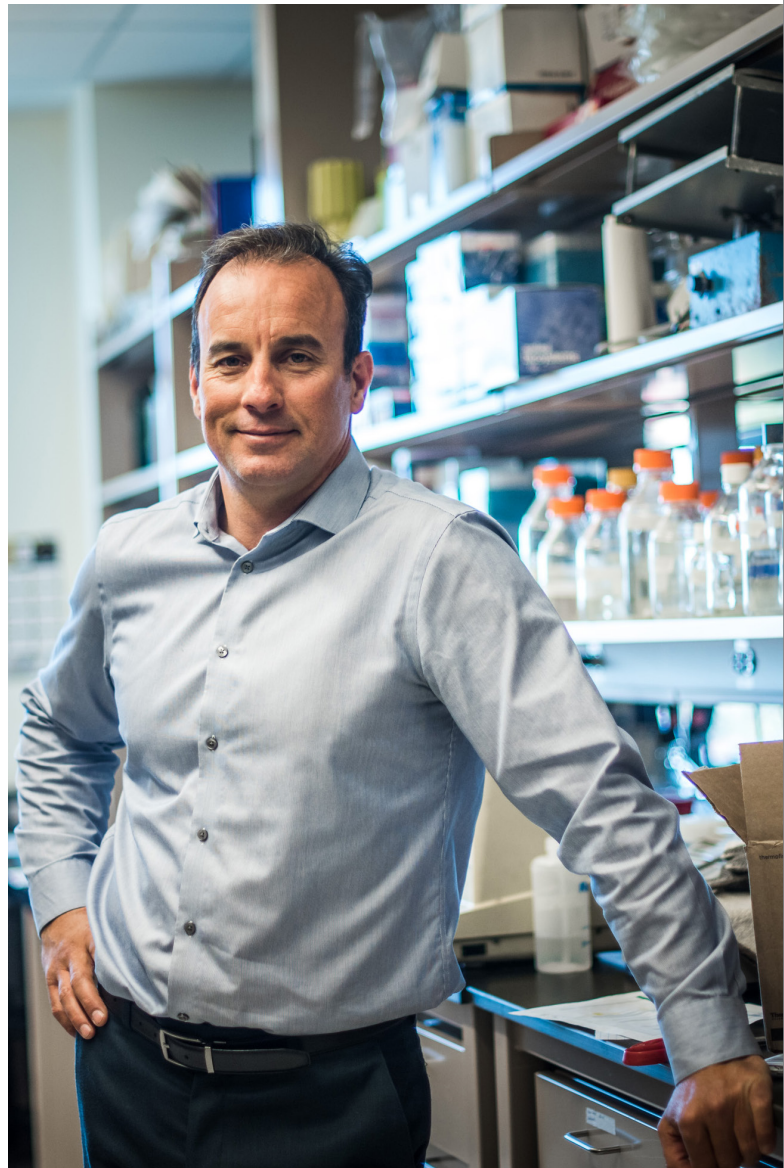
Michelle Sie Whitten, president and CEO of the Global Down Syndrome Foundation, which has funded Espinosa’s research, called the work a “game-changing discovery.”

That discovery is now the foundation for a scientific program that could have health benefits for all.

“It’s one of those beautiful scientific journeys, where we just followed the data, followed the science and it may take you places you didn’t want to go or to places you didn’t anticipate you were going to go,” Espinosa said.

For Espinosa, that is certainly true. A cancer biologist, he was recruited CU Boulder in 2004 and he continues to serve as co-leader of the CU Cancer Center’s molecular oncology program. But along the way, he applied for a grant offered by the Crnic Institute.

“The Crnic Institute had recruited Dr. Tom Blumenthal as executive director, who was my chair in Boulder,” Espinosa said. “What he did was



Joaquín Espinosa, PhD, director of the Linda Crnic Institute for Down Syndrome. Photo courtesy of the Global Down Syndrome Foundation.

create a grant program for scientists who were within the University of Colorado. I applied. I knew Tom very well and I wanted him to do well. I was super busy at the time with my cancer research. I didn’t necessarily have an interest in Down syndrome, but I thought OK, this seems like a good opportunity to start a new line of research.”

That project opened a new path in Espinosa's career, first as associate director for science at the Crnic Institute since 2015 and now as its executive director since July 2017.

"I'm not an immunologist. In fact, to some degree I was trying to stay away from immunology. I think it's so complex and sophisticated and I had my plate full with the complexity of cancer biology. But the data from that first grant and from experiments we did afterwards, and from other experiments that other people in the Crnic Institute were doing, started converging—dysregulation of the immune system in people with Down syndrome.

"And now this has become the centerpiece of a research program, trying to understand how this immune dysregulation contributes to the many facets of Down syndrome."

Triggering the immune system to fight cancer has been intensified focus of researchers for decades, but they also know that an out-of-control autoimmune system has detrimental effects.

"It makes sense that a person who has a hyper-activated antiviral response will have a tendency to autoimmune conditions," Espinosa said. "The interferon pathway, the same set of molecules that we use to fight viruses, when deregulated, will give you an autoimmune condition because basically they attack healthy cells."

Espinosa cites health conditions, such as leukemia and congenital heart defects, that can result from overactive autoimmune systems and that are more common among people with Down syndrome. Also, hyper-activation of the immune system in the brain is toxic, killing neurons.

Connecting the dots, though, is much harder than it sounds and more work needs to be done before safety and efficiency of any therapies can be determined.

"It is simple in concept, although technologically quite an amazing feat," Espinosa said. "We did a functional genomics approach, meaning you measure thousands and thousands of genes or thousands and thousands of proteins and hundreds of metabolites. You're taking a lot of measurements. It's difficult in practice, but simple in concept."

The Human Trisome Project at the Linda Crnic Institute is designed to be the largest and most comprehensive study of why individuals with Down syndrome, also called trisomy 21, are protected from some health condi-

tions, such as cancer, while highly predisposed to others, such as Alzheimer's disease. For the project, the research team is recruiting persons between 6 months and 89 years old, with or without Down syndrome. "You're looking at as much as you can, casting a big net and then asking, 'What are the things that are different in people with Down syndrome

relative to our control group of individuals that don't have Down syndrome but as far as we can tell they don't have any other differential variable in the control group?' When we do that, in every case, at the top of the chart is the immune system and specific aspects of the immune system."

By identifying the potential source of concern, options for therapies can be considered. One way is to consider how the human body naturally blocks interferon, proteins that activate usually to respond to a virus or other pathogen. The Crnic Institute is looking at proteins that neu-

tralize interferon and developing experiments to study them.

Getting a good map and charting the multiple paths is a daunting task that will require help from many supporters. Supporters include the Global Down Syndrome Foundation, the Anna and John J. Sie Foundation, the School of Medicine and Biogen.

Historically, the primary federal agency providing funding research on Down syndrome has been the National Institute of Child Health and Human Development because the syndrome was originally cast as a pediatric condition. But today, people with Down syndrome commonly live into adulthood, with some living into their 60s.

Espinosa hopes to build on the understanding that there are health benefits for all that can result from the Crnic Institute's work and that deserve support from other federal agencies. Earlier this year, U.S. Rep. Mike Coffman, who represents the congressional district that includes the Anschutz Medical Campus, introduced legislation directing the U.S. Department of Veterans' Affairs to establish Alzheimer's disease research, education, and clinical centers that include a scientific focus on the connection between Down syndrome and Alzheimer's disease.

"It's what we call therapeutic leverage," Espinosa said. "As you're trying to help people with Down syndrome, you end up learning about other conditions and most likely helping typical people with related conditions. The immune system is everywhere in your body, so it has this power either making trouble or fixing things for a large number of things."



Joaquin Espinosa, PhD and advocates representing the Global Down Syndrome Foundation. Photos courtesy the Global Down Syndrome Foundation.

## Tracking Diseases Around the World and in Colorado

Neurologist Daniel Pastula looks after the public's health

By Tonia Twichell

Straight out of residency and searching for a way to pursue his combined interests in epidemiology and neurology, Daniel Pastula, MD, MHS, joined the Centers for Disease Control and Prevention's office in Fort Collins in 2013 where he tracked diseases spread by ticks, mosquitoes and sand flies.

What he expected to be mostly a desk job—his supervisor told him he would not travel often—changed with sudden outbreaks of several arboviruses. No longer tied to his desk, Pastula trekked to Missouri, Micronesia, Fiji, the U.S. Virgin Islands, Georgia, Ohio and finally Puerto Rico.

"I've been pretty busy," said Pastula, who assisted in tracking and fighting the spread of Zika, dengue, chikungunya, Heartland, Bourbon, Jamestown Canyon and La Cross viruses, as well as Guillain-Barré syndrome and acute flaccid myelitis among other diseases.

During his travels Pastula met with physicians, patients and public health officials in remote locales, and he spent more than a few sunless



Daniel Pastula, MD, in long pants and mosquito repellent during a chikungunya virus outbreak in 2013 in Yap State, Federated States of Micronesia. Photo courtesy of Daniel Pastula.

days in hospital basements.

"That's where they usually keep medical records," said Pastula, now a CU assistant professor of neurology, infectious disease and epidemiology who was recently appointed to the Colorado Board of Health.

While digging deep into dusty contents of those buried records, Pastula nurtured his disparate interests of neurology and epidemiology, an unlikely combination given that few neurologists are also epidemiologists.

"I always thought I'd have to pick one or the other—either neurology or public health – because very few people I know of do both."

### "I Liked Talking to People"

In high school and college Pastula became captivated by the book "And the Band Played On" about the HIV/AIDS epidemic during the 1980s.

"I thought it was fascinating how all these public health experts were able to piece together the cause of the outbreak just by meeting with clinicians and patients, sometimes in their homes, and systematically asking all kinds of questions. That's really what got me interested in public health and epidemiology.

"I already knew I was interested in science and that I liked talking to people. I just didn't know all the ways one could put them together."

One clue came during a neurology lecture in his first year of medical school at Duke University when the instructor discussed the epidemiology of amyotrophic lateral sclerosis (ALS) including clusters of the disease discovered in Guam, the Kii Peninsula of Japan, and among Italian soccer players.

Pastula stayed after class to talk to Richard Bedlack, MD, PhD, who in turn invited him to spend time in his ALS clinic.

"My first clinical experience ended up being in the ALS clinic learning about ALS and neurology but also about its epidemiology. I did my other core rotations, but I kept coming back to neurology and working with Dr. Bedlack."

He stayed an extra year in medical school to earn his master's degree in clinical research by studying ALS epidemiology. During that time he asked mentors and friends about choosing between neurology and public health.

"Several people said, 'Why don't you just ,do both?'"

After a residency at University of California, San Francisco, Pastula decided that the CDC seemed like the ideal place to do that.

### On the Road

Much of Pastula's time as a CDC Epidemic Intelligence Service officer was spent among teams of researchers focused on measuring and curbing the spread of disease around the United States and the world.

He loved the teamwork and the opportunity to immerse in local culture while traveling in remote areas.

"We'd go to the local restaurants and try to learn local language. You'd get laughed at a bit, but then everyone appreciates you trying. I made friends in various places."

Pastula was often at a site during the height of an outbreak, and the disease cycle could be hard to watch. He especially remembers the chikungunya virus outbreak in Micronesia.

“A large portion of the population was just really sick. They couldn’t walk and had horrible fevers and were bedridden for days to weeks. That was really hard to watch. So was the Guillain-Barré syndrome cluster in Fiji, where a handful of people were paralyzed and on ventilators. It’s hard to watch what people with Guillain-Barré go through here in our hospital, let alone in some rural areas of Fiji.”

In 2016, one year after joining the University of Colorado, the Puerto Rican Department of Health and CDC asked Pastula to assist in developing a surveillance system in Puerto Rico to determine whether the Zika virus, which was just hitting the island, was related to clusters of Guillain-Barré. So Pastula and his public health colleagues from the Puerto Rican Department of Health and CDC designed a system that allowed clinics and hospitals to report cases of the syndrome. He spent weeks collecting medical records for baseline numbers.

As a result, several papers were published showing that the Zika virus is probably a risk factor for Guillain-Barré.

“Not that Zika causes the syndrome in everyone, but it seems to contribute to an increased risk in Guillain-Barré. Exactly how that is, we don’t fully understand. We suspect it might be an autoimmune mechanism, where Zika virus may trick the body into attacking nerves.”

## Fighting Disease in Colorado

Despite the outbreak of so many viruses in the past few years, Pastula says many of them have likely been around for a while but have become better recognized.

“I think a lot of the diseases have been there for centuries and I think we’re just now defining them. Maybe what everyone historically called malaria wasn’t always malaria at all and we’re just finally identifying it correctly now. That being said, as populations move closer to animals and areas that humans haven’t typically lived, are we going to see new diseases? I think that’s possible. It definitely shows the importance of public health, epidemiology and surveillance. The only way we’re going to know about new outbreaks is through good public health surveillance.”

For vector-borne diseases, he advocates prevention techniques—long pants, long sleeves, socks, insect repellent, air-conditioning or window screens indoors, removal of standing water—to foil many arboviruses, and he faithfully adhered to them while on the road because the

chance of contagion was high.

“The first rule of an outbreak investigation is don’t get the disease that you’re studying,” he said. “I was walking around in 95 degree, humid weather in long pants and insect repellent.”

Does that mean no tropical vacations?

“Not at all. But I think my family rolls their eyes at me a little because I’m constantly saying ‘Wear insect repellent.’”

In his position on the state board of health, he’ll be called on to use his expertise to help limit infectious outbreaks, but he’s also become familiar with a broad range of issues facing the board, such as community paramedic programs assisting rural patients with chronic disease care and updating the food safety code to match evidence-based federal guidelines.

“I thought it would be a good way to use my skill set to give back to my state.”

After traveling the globe fighting disease, Pastula largely concentrates on Colorado, where West Nile is the most common arbovirus. He’s also been involved in treating and researching a cluster of acute flaccid myelitis possibly associated with enterovirus D-68 that affected children in Colorado.

As a consultant, Pastula could be recruited to travel again to help with a crisis.

“At the end of the day, if I can be of help anywhere, I’m happy to go and do whatever is needed.”



*Right, Daniel Pastula, MD, interviewing household residents in 2014 during a concurrent dengue virus outbreak and Guillain-Barre syndrome cluster in Suva, Republic of Fiji. Photo courtesy of Daniel Pastula.*

## Coffee's Link to Heart Health

CU researchers grind through the data

By Mark Couch

A cup of coffee a day might not keep the doctor away, but an extra cup or two could keep the cardiologist at bay.

Investigators from the University of Colorado Anschutz Medical Campus recently presented research that shows drinking coffee is linked with reduced risks for heart failure, stroke and coronary disease.

Just don't ask if coffee is a magic elixir that will let you live longer.

"This was the main question we received: 'Should I drink more coffee to live longer?'" said David Kao, MD, assistant professor of medicine in the Division of Cardiology. "I don't think you can take it quite that far because we don't know whether it's the coffee itself or something else."

Kao and Laura Stevens, a doctoral candidate in the University's computational biosciences program, were invited to present their findings at the annual scientific meetings of the American Heart Association (AHA) last December.

While they can't say conclusively that drinking coffee extends your life, they were able to show that drinking coffee is associated with a lower risk of some serious life-limiting conditions.

According to their review of data collected in the Framingham Heart Study, which has tracked the eating patterns and cardiovascular health of more than 15,000 people since the 1940s, they found that every extra cup of coffee consumed per day reduced heart failure by 8 percent, and stroke by 7 percent.

The news perked interest around the globe, with reports in the International Business Times in London, Time magazine, and in the online pages of the "the voice of Clarksville, Tennessee."

"Everybody drinks coffee," Kao said. "It's a high impact idea that a lot

of people can relate to. Plus, it validates what a lot of people had hoped would be true – that more coffee is better. It justifies their behavior. I figured that that would resonate."

Stevens and Kao explained that grinding through the data is a massive project that required "machine learning" to identify associations that would be buried under the multiple possible connections between numerous variables.

Machine learning is a way of getting computers to recognize patterns and make predictions, rather than simply executing pre-programmed tasks. It's teaching the computers to discover or 'learn' new patterns within large amounts of data, and it works the same way that online shopping sites aim to predict a shopper's preferences based on previous purchases

or an email provider tries to separate spam from other messages.

"What machine learning allows us to do is to identify factors that may be important when we don't know what we're looking for in large pools of information," Kao said.

"In this case we were interested in stroke, heart failure, and cardiovascular disease and then we used machine-learning to determine what lifestyle, dietary factors, and medical conditions are most important for predicting each disease," Stevens said. "Basically, what you do with machine learning is you put in the hundreds of factors into a model, and results will tell you which factors are the most important for predicting a given outcome, such as heart failure or stroke."



Their study of the Framingham data confirmed that certain well-known factors—such as smoking and high cholesterol—had strong association with stroke, heart failure, and cardiovascular disease. Sifting through the results they found the tantalizing potential benefit of coffee drinking.

While the machine learning process found that coffee may be important

for predicting heart disease, it didn't establish a connection to increased or decreased risk of getting the disease. It simply showed that coffee was in the top 15 percent of important factors among the hundreds of factors poured into the mix.

"Once you have an idea that coffee is important at predicting risk, what you don't know from machine learning is whether it is associated with increased risk or decreased risk, so from there we used more traditional methods to evaluate if coffee drinking was harmful or protective," Stevens said.

"In this case we used survival analyses to evaluate whether people who drink coffee survived longer, and determined increased coffee consumption was associated with decreased risk of heart failure and stroke."

While coffee consumption was associated with the decreased risk, the study doesn't show a cause and effect relationship.

"This specific data analysis doesn't give you that," Stevens said. "And that's what we're looking into now. We are curious if it is some other habit that people who drink coffee have that is related, or if it is the caffeine or the antioxidants in the coffee itself?"

To check their results, Stevens, Kao and their colleagues used traditional analysis in two other studies with similar sets of data – the Cardiovascular Heart Study and the Atherosclerosis Risk In Communities Study. The association between drinking coffee and a decreased risk of heart failure and stroke was found in all three studies.

Now that the AHA presentation has been completed, Stevens and Kao are working on drafts of papers on the work.

"I think the tricky part is where to stop with this first paper because people want to go all the way down the rabbit hole and you just can't take on everything at once," Kao said. "So that's where we are right now is trying to decide where to stop with this presentation with an eye toward what happens next."

The importance of the study wasn't just the finding about coffee, but also a recognition that the process of discovery could be useful in the design of future studies.

"Our findings suggest that machine learning could help us identify additional factors to improve existing risk assessment models," said Stevens, who is a data scientist for the Precision Medicine Institute at the AHA. "The risk assessment tools we currently use for predicting whether someone might develop heart disease, particularly heart failure or stroke, are very good but they are not 100 percent accurate."

Stevens conducts research seeking to connect genetic information to lifestyle, environmental, and clinical factors.

"I think the kind of work that Laura did is the next wave in personalized



*Laura Stevens and David Kao, MD, were invited to present their findings at the annual scientific meetings of the American Heart Association. Photo by Mark Couch.*

medicine," said Kao, who is a member of the Colorado Center for Personalized Medicine. "There are so many things that could be important, that you could modify, that you can't study in the way we've studied medicine in the past.

"This was an interesting result in and of itself, but as just interesting is that the method can work and find novel information in other datasets that are important to people, and that may represent a potential intervention, positive or negative. I think without that, personalized medicine is going to be very hard to pull off."

## CU Faculty Train Guatemalan Nurses to Improve Care

Project aims to boost health of mothers and newborns

By Tonia Twichell

After the birth center at Trifinio Center for Human Development opened in rural Guatemala in December 2016, Gretchen Heinrichs, MD, and the clinic staff realized that effort to lower the death rates for women and newborns needed to extend into the homes of poor farmworkers and their families.

Situated in southwest Guatemala along the border with Mexico, the clinic provides health services in one of the country's most impoverished regions, where the neonatal mortality rate is among the highest in Central America at 31 per 1,000 live births, and the maternal death rates is one of the highest at 80 per 100,000 live births.

Half of the women in the area lack prenatal care and one-third give birth at home assisted by traditional birth attendants, who have little formal training.

Most local women are in good health, said Heinrichs, CU associate professor of Obstetrics and Gynecology and director of maternal health programs at the Colorado School of Public Health Center for Global Health, so "we realized that the best way to make a difference was to create a safety net around a birth at home."

CU physicians, nurses and midwives have helped train birth clinic and birthcenter health professionals who in turn act as preceptors to CU students from medicine, dentistry, pharmacy, nursing and public health schools and colleges. The center is a partnership of the University of Colorado, Children's Hospital Colorado and the Jose Fernando Bolaños Foundation.

The effort to improve the health of Guatemalan women and their babies faces significant obstacles:

- Families lack funds to pay for hospital births. "A lot of women delivering at home would love to deliver in a clinic, but they can't afford it," Heinrichs said. She recalled a couple so poor the husband chose to deliver the couple's child alone. Nurses from the center rushed to the family's home when neighbors reported the baby had breathing problems. "The nurses' relationship with the community provided a kind of safety net that day," she said.
- Few physicians practice in remote areas. Before the clinic opened, the closest doctor was at least an hour away. Those who were nearest were often not trained in obstetrics so complications often went unnoticed or unaddressed. Most developing countries rely on

trained midwives, but Guatemala only began its midwife training program in 2015.

- Traditions can stand in the way of basic services. Many women refuse to leave home once labor begins based on a local belief that fresh air can be dangerous to women for several weeks around childbirth. Plus "this idea that birth needs to be monitored by someone who doesn't know you is a hard concept to accept," Heinrichs said.

To better understand the health of the community, CU physicians and public health practitioners have been working with residents to learn about social, economic, health, cultural, geographic and genetic factors. Heinrichs and her colleagues at the Center for Global Health joined with the community to create Creciendo Sanos: Madres Sanas y Ninos Sanos, a program for pregnant women and their young children living in the community with a population of about 25,000. Birth center nurses offer



Gretchen Heinrichs, MD, teaching two traditional birth attendants.

group and individual prenatal care, newborn and child home visits and classes on nutrition and hygiene.

Outcomes are tracked via a mobile phone clinical data collection system to warn staff about problem pregnancies or child health conditions.

Expecting many women to continue home births, CU faculty and center staff offer training and friendship to traditional birth attendants in hopes that these women will become the first line of defense when facing problem deliveries.

## Training Outreach

Traditional birth attendants fulfill a role similar to doulas in the United States, but have less education and limited knowledge of hygiene and sanitation though they recognize that complicated births can be disastrous for newborns and mothers.

“Attendants are women of respect in the community and we really need to draw them in and not try to

exclude them. We want to be partnered with them and learn what their practice is like,” Heinrichs said.

CU staff hold classes twice a year for about 20 traditional birth attendants to teach basic emergency obstetrics skills for the most common killers of women, such as hemorrhage, long labor and hypertension and of infants including shoulder dystocia, sepsis and respiratory infection.

Center nurses supply attendants with birth supplies and train them to recognize complications before labor begins so attendants can encourage patients to get medical attention. Unlike hospitals in the region, the center welcomes traditional birth attendants and the mother’s family to support the patient.

“Traditional birth attendants are key players who we want to enlist and act as informants in the community to ensure women have safe pregnancies and births,” said Amy Nacht, DNP, CNM, MPH, assistant professor and director of the University Nurse Midwives Faculty Practice at the College of Nursing.

Some of the training has helped, Heinrichs said.

“A few have told us, ‘I used the shoulder (dystocia) maneuver and it worked! It felt so great!’” Heinrichs said. “But our biggest success is getting these women to bring in their patients. We do have a trusting relationship and we’ve had a couple of big successes. And the families know the birth center is clean and they will get a high level of care. They don’t have to drive to the city and wait in long lines.”

But training traditional birth attendants has its limits.

“We found that some things are very difficult for them to learn,” Heinrichs said. “That’s why we began focusing our efforts pretty quickly on skilled birth attendants.”



Amy Nacht, DNP, CNM, MPH, left, in a health class with two traditional birth attendants, center, and a clinic nurse. Photos by Michelle Shiver.

## Building Skills

CU faculty have begun training center nurses to become skilled birth attendants, Nacht said.

“We developed what might be considered site-specific curriculum to help increase the knowledge, skills and attitudes of the nurses.”

CU faculty teach emergency obstetric care to center nurses using simulation models and e-learning,

and rely on the World Health Organization’s safe childbirth checklist to help nurses recognize warning signs from admission to discharge. The center provides obstetric ultrasounds performed by a local nurse who was trained at CU Anschutz Medical Campus.

“WHO recommends eight prenatal visits (for each pregnancy),” said Heinrichs, who travels to the center twice a year. “We’re having trouble getting to four. Sixty percent have had three prenatal visits and our goal has always been to get to four visits with 75 percent. It’s hard to get out to rural communities and there are a lot of transportation issues.”

CU faculty, students and residents rotate through the clinic, but Nacht says the goal is to support the local health care staff to become clinical leaders and sustain the programs.

“We want the clinical staff to move forward with as much independence as possible,” Nacht said. “This is truly an interdisciplinary project, and I think it’s possible as long as all the teams stay involved with ongoing educational support.”

Nurses have stepped up to take the lead in labor and delivery.

“There are physicians (at the Center for Human Development) but most have almost no training in birth,” Heinrichs said. “Our nurses started to have more modern training in obstetrics than their physician supervisors and that has created an interesting dynamic. In Guatemalan culture, medicine is very paternalistic.

“Our job as trainers and partners is to promote their growth and self-sufficiency. We have seen such growth in our staff there. It has been an inspiring project to work with.”

## Physician Assistant Students Train in Guatemala

### Learning skills abroad to use at home

By Tonia Twichell

Alix Armstrong arrived at the Trifinio Clinic in rural Guatemala last summer with good credentials.

A second-year physician assistant student at the CU School of Medicine, Armstrong had strong Spanish language skills—she had previously taught English in Spain—and she'd witnessed extreme poverty at refugee camps while serving as part of a public health brigade in Thailand.

Still, some of what she found defied her expectations. The Trifinio clinic offered an on-site lab that returns patient results within an hour. A trained technician performed ultrasounds for expectant mothers. A team of researchers was studying the Zika virus and other diseases. And the clinic itself had a well-stocked pharmacy, several patient rooms and a clean, organized central work station.

"I went in with a little apprehension. It's a developing country, and safety is always a concern. There were surprises in Guatemala, but they were all good surprises," said Armstrong, one of 15 physician assistant students from CU who traveled to the clinic last year to do a supervised clinical rotation.

In the living quarters for visiting students and professionals, rooms were clean and new, and there was even a trained chef.

"Honestly, I was so impressed. She was an actual chef. And then there was always peanut butter, popcorn and fruit. They knew Americans were coming and they made sure we always felt at home."

Despite Armstrong's solid ability to speak Spanish, she spent her first week in Guatemala at Celas Maya, a Spanish-language immersion program in nearby Quetzaltenango. Those lessons included five hours of one-on-one instruction each day and improved her knowledge of medical terminology and colloquialisms.

Some students decide to spend as long as a month in the language school before progressing to the clinic, said Claudia-Luna Asturias, LGSW, a faculty instructor in the CHA/PA program. They live with local families and can tour the area.

Armstrong says she rode a zip line over a coffee plantation and took salsa lessons. But she said her host family was the highlight.

"I loved them," Armstrong said. "The grandma was so sweet. She loved to tell stories about Guatemala history."



Alix Armstrong, right, at the Trifinio Center with classmate Rachel Shaffer.

CU students who rotate through the clinic see people with ailments associated with poverty such as malnutrition, diarrhea from poor quality drinking water and pulmonary problems caused by fires for heating and cooking in unventilated homes. Armstrong also recalled seeing several cases of uncontrolled diabetes.

Even with the medical needs, the region's poor farm workers often equate western medicine with impersonal hospitals and expensive treatment. As a result, clinic staff has had to work hard to build trust.

Armstrong remembers a case of an infant diagnosed by clinic doctors with meningitis. The family resisted going to a hospital even after the doctors offered to pay for the ambulance.

"To them, when they go to the hospital, someone dies," she said. "I don't think they ended up going."

Guatemalan nurses are an important link to the community. Students often travel with them to patient homes to check on the health of newborns and mothers. The home visits are essential to understanding the medical needs of the community.

"They realize that the community nurses don't harm the babies. They help them get better."

In addition, nurses are familiar with local beliefs in magic and traditional remedies which helps build rapport and a trusting relationship.

"People believe that if you look at a baby with jealousy it will cause illness," Armstrong said. "The way you cure it is to put an egg under the bed. There are other rituals too, and they sounds silly to us. To them it's a reality. When families brought in babies and said that this is why they think the baby is sick, we would say 'Absolutely it could be that. We can't dismiss it. But how about we try this too?'"

Luna Asturias says students come back to Colorado with improved cultural awareness for poor immigrants who often lived in huts with dirt floors and had little access to clean water in their home countries.

"When they return to the U.S. to where they will practice and provide care to the Hispanic population they have a better understanding of why families migrate and their background at home," Luna Asturias said.

Armstrong agrees her time in Guatemala improved her ability to work with the Spanish-speaking community in Colorado.

"Seeing the beliefs and cultural differences in Guatemala versus here was very helpful in bringing empathy to my patient care now that I understand where they're coming from."

## From the Olympics to Medical School

Loree Thornton's new dream: Becoming a surgeon

By Amanda Blackman

From throwing a hammer in the Bird's Nest stadium in Beijing during the 2008 Summer Olympics to studying to become a surgeon at CU Anschutz, Loree Thornton is no stranger to pushing herself to the limits in pursuit of her dreams.

Watching the 1996 Summer Olympics, Thornton knew she wanted to be an Olympian. She just didn't know what her sport would be. She imagined competing in the games and meeting a Russian gymnast. She went so far as to take four years of Russian in high school.

"I was like, 'I need to speak Russian so I can meet him,'" Thornton said with a laugh, "because, you know, I'd meet him and get married."

But she didn't even discover her event until she was in college when her coach suggested she the hammer throw.

"I was like, 'Cool what's that?'" Before that day, Thornton admitted, she'd never heard of hammer throwing. In track and field, the hammer is a metal ball that weighs about nine pounds and is attached to a steel wire. The athlete twirls the ball and releases it to fly across the field.

"I think it picked me," she said.

### Breaking records

From that moment, Thornton worked toward the Olympics. At Colorado State University, she trained about four hours a day, ultimately setting a hammer-throw record.

"I broke the collegiate record—the farthest-throwing female to throw a hammer of all time," said Thornton. "That's why I think it chose me; I loved it."

In 2008, she earned one of three spots on the U.S. hammer throwing team for the Summer Olympics in Beijing. She described walking into the Bird's Nest stadium as a surreal experience. After devoting 10 years to her training, she was fulfilling a dream.

"You question yourself, you question the process, and then to walk into a stadium that's vibrating with energy, wearing USA across your chest, is one of the best feelings," she said. "I cried when I walked out. I thought, 'All that work for this moment.' It was pretty exciting."

### Connection to Winter Olympics

Even though Thornton participated in the summer games, she feels a connection to the Winter Olympics because some former track teammates participate in bobsledding.

She most enjoys watching figure skating during the Winter Olympics.



Loree Thornton is on track to graduate in the CU School of Medicine's class of 2020. Lower left, Loree Thornton competing for the U.S. in the hammer throw. Photo by Matt Kaskavitch.

"I love figure skating. It's really cool to see all those years of hard work come out so beautiful," she said. "It's where sport meets art."

After the 2008 Olympics and four more years of throwing hammers, Thornton retired from competition in 2012 to pursue another dream: to become a surgeon. Being a doctor had always been on her mind, but she had doubted her abilities – even after going to the Olympics.

"I came from a pretty underprivileged background. Saying you want to be a doctor is on par with saying you want to be an astronaut. People don't do that, not people like you," she said. Going to the Olympics taught Thornton that any dream, even those that seem unattainable, can come true with enough hard work and dedication.

### A new goal: surgeon

When she heard she had been accepted into CU School of Medicine class of 2020, she cancelled all other school appointments.

"I thought, 'I got my number one choice—I'm done!'" she said.

Training to become a surgeon doesn't require long hours in the gym, but there are plenty of new challenges. Thornton said people suggest she should become an orthopedic surgeon; she is considering other specialties just to prove them wrong. Regardless of the surgical route she chooses, Thornton continues to work tirelessly.

"There are some weeks where I get five hours of sleep a night. I'm getting my butt kicked, and I'm tired, but then I go into clinicals and I'll learn about a disease in class and I'll see it and feel like I'm helping a patient. That's my favorite part: It reminds me of why we do what we do," she says. "One day someone's going to need the best of us."



## Physician Teamwork Keeps Train Engineer on Track

### Hearing threatened by brain tumor

By Katie Kerwin McCrimmon

Rumbling along the rails, a train lugging 18,000 tons of freight hisses and chugs, and then the engineer blows the whistle.

It's the sound of American progress. For Stephen Mullen, it's the especially sweet echo of his life's work.

For 20 years, Mullen has worked as a train engineer. These days, he guides freight runs from Denver to Trinidad in southern Colorado.

A scary experience last year threatened his future on the railroad and his ability to hear the trains.

In January 2017, Mullen, 46, felt some tingling in his jaw. At first, he thought he was having some sort of allergic reaction. But the dull feeling persisted.

Mullen called his primary care providers at UHealth's Family Medicine Clinic in Westminster. A nurse said the strange sensation could be a sign

of something serious, like a stroke. It was nearly 4 p.m., too late to get in that day, so she urged him to go to an ER.

At about 5 p.m., another nurse followed up with Mullen, arranging an appointment for the following day with Mullen's primary care provider, Anju Visweswaraiyah, MD. She also told Mullen that he should get checked out that night. He took her advice.

The next day, Mullen came in to the Westminster clinic and shared some shocking news with Visweswaraiyah.

"I have a brain tumor," he said.

Scans from the ER the night before showed he had a large growth on the left side of his brain called an acoustic neuroma or a vestibular schwannoma. To his relief, Mullen learned that his tumor was almost certainly non-cancerous.

But brain tumors can threaten hearing, and Mullen faced losing his hearing on his left side.



*Left, Stephen Mullen. Above, train engineer Stephen Mullen can hear the whistles he sounds for work after surgeons removed a brain tumor that threatened his hearing. Photos by Cyrus McCrimmon.*

Without his hearing, Mullen feared he would not be able to do his job. On the trains, Mullen communicates constantly with dispatchers through a radio system and he must respond regularly to sonic alerts.

Visweswaraiah, who is also a senior instructor with the University of Colorado School of Medicine's Department of Family Medicine, immediately connected Mullen with a neurosurgeon and an ear, nose and throat specialist at UCHealth University of Colorado Hospital.

Samy Youssef, MD, PhD, professor of neurosurgery, and Samuel Gubbels, MD, associate professor of otolaryngology, met with Mullen within days.

They confirmed that the tumor was not cancerous. But if left alone, the tumor would continue to grow. It had to come out, but the surgery could leave Mullen unable to hear on one side.

"That was probably the scariest moment," Mullen said. "They told me that I had a 95 percent chance of losing all my hearing on my left side because the tumor was intermingled with the hearing and balance control (centers) in my brain."

Even so, Mullen felt lucky he'd learned about the tumor relatively early.

"Many people wake up one day and have no hearing and never get it back. I was lucky I was paying attention to my body."

### Sweet sounds: Train whistles, birds, dog collars

Mullen's wife, parents and siblings, two of whom also work for the railroad, rallied around him and he went in for the surgery on February 23. The surgeons carefully removed nearly all the tumor. They deliberately left a small piece – while cutting off blood supply to the tumor – in hopes that Mullen could still hear the whistles and other sounds at work.

When he woke up, he got great news.

"They told me it was a very successful surgery," Mullen said.

The one side effect has been a persistent ringing in his ear, but the surgery preserved Mullen's hearing. At first, he felt like his ear was plugged up. Then, little by little, his hearing improved.

"By the third month, I was up to 95 percent. It's incredible. I'm so grateful to Dr. Youssef and his team. They did such a wonderful job," Mullen said.

Mullen has found himself appreciating even mundane sounds.

"We take things for granted: horns honking, the dogs barking," he said.

He and his wife have two Morkies, a mix of Yorkshire terriers and Maltese.

"Being able to hear the jingling of their collars as they were climbing up into bed was great," Mullen said. "And you notice the small things, listening to birds, even the traffic."

Along with the brain tumor, Mullen had also been dealing with high blood pressure. So, all year, he has continued to see Visweswaraiah and her team frequently.

"We have been fine-tuning my blood pressure medications," he said.

"I've been lucky to have her as my primary care physician. I have the best of the best."

### 'Love my job'

Visweswaraiah credits Mullen for being caring about his health and paying attention to the subtle tingling in his face.

"He's an amazing patient," she said.

Mullen's good instincts allowed her team to provide seamless care.

Any time Visweswaraiah needs to consult with a specialist, she can call UCHealth's DocLine and immediately speak with an expert.

"I can have a neurosurgeon on the line in two minutes," she said.

And Mullen had to have his blood pressure under control.

"When someone has very high blood pressure, it's less safe to have brain surgery," Visweswaraiah said.

When Mullen was first recovering, he had to be careful about his balance and the left ear felt like it was underwater. He felt like his brain compensated and he was able to tune in to sounds more intently with the right side.

Once he's a full year out from his surgery, Mullen's doctors can try to address the ringing. For now, he's learned to live with it.

Along with hanging out with his wife and her two children, Mullen enjoys riding his motorcycle and building and flying drones.

Getting to go back to work has been a real blessing.

"I missed it. I love my job. It was a wonderful feeling to get back out there," he said. "I'm so happy and grateful to do the simplest things that I used to take for granted, like blowing the horn for a crossing. The first time I was able to do that and I didn't have any problem was unbelievable. The confidence comes back and you think, 'Hey, I can do this.'"

*This article first appeared in UCHealth Today in January 2018.*

## Tell Me More

### Gold Humanism program encourages compassionate care

By Debra Melani

In the end, his patient died.

But as Ajay Major, MD, MBA, then an intern, flipped through the old veteran's medical record, he found comfort in the memories the notes inspired.

Major, now a second-year internal-medicine resident on the University of Colorado Anschutz Medical Campus, calls up those memories of the witty old man with terminal cancer who always asked for bourbon (and his devoted wife who always rolled her eyes in response), as a reminder

ing the society's annual Solidarity Week in February by encouraging his colleagues to take part in the week's centerpiece program, Tell Me More.

### Changing the conversation

Armed with a questionnaire and a smile, second-year internal-medicine resident Megan Griff, MD, entered her patient's room, finding Betty Redwine, 77, wrapped in a light blanket and relaxing in a chair. "Is it OK to talk and find out about your life?" Griff asked, after explaining the

program and introducing Major and attending physician, Jeannette Guerrasio, MD.

"OK," Betty Redwine said, returning her doctor's smile. "But it's nothing exciting," she said, grinning up from beneath a black-suede, shower-like cap that she informed her guests was taming her unruly hair.

Prompted by four Tell Me More questions, Redwine soon was sharing pieces of her past. Discussions of capillaries and high blood pressure gave way to remembrances of children's feats and life's treasures, sounding more like tea-time chatter than bedside diagnoses. When Redwine let a little secret slip, the room filled with utterances of disbelief.

"What?" Guerrasio said, after Redwine revealed she worked as a

registered nurse for 35 years. "Why didn't you tell us?" asked Griff. "My mom is a nurse, too," Griff said, when the commotion subsided. "You guys are hard-workers," she said, patting Redwine's hand.

### Staying centered on the cause

While it might seem small, a dose of compassion can result in an array of benefits, Major said.



Megan Griff, MD, chats with University of Colorado Hospital patient Frances Cory as part of a program aimed at teaching the value of compassion in medicine.

of the importance of compassion in health care.

"Medicine is hard," Major said. "We see a lot of patients with a lot of difficult medical issues, and I think burnout stems not just from feeling overworked, but also from feeling that we're not truly caring for our patients on a human level."

Major, co-president of the CU Anschutz School of Medicine Resident Chapter of the Gold Humanism Honor Society, spread his message dur-

**"The more passionate individuals are about their profession, and the more they enjoy what they are doing, the more engaged they become. These things feed on each other in very positive ways." David Schwartz, MD, chair of medicine**

“It allows the patient to feel that the care team really cares about them, but it also brings some catharsis for providers,” Major said. “Just finding out a little bit more about our patients’ lives outside of the hospital can help re-center us in the work that we are doing as physicians and, I believe, help prevent burnout.”

On the patient side, studies show compassionate healthcare results in higher patient satisfaction, a higher pain threshold, reduced anxiety and better outcomes, according to the Arnold P. Gold Foundation, which is named after a renowned pediatric neurologist who became an international leader and advocate for humanism in health care.

“People develop diseases for lots of reasons, and everyone’s lives really affect the way they respond to health problems,” said David Schwartz, MD, chair of the Department of Medicine. It makes sense that patient-provider relationships based on trust result in better care, he said. “We need to know how their lives might be contributing to the development of disease, and how their lives might contribute to our ability to effectively treat their disease,” he said.

### “I’m a person”

Looking up from her bed as the Tell Me More trio walked into her room, Frances Cory, 79, had them laughing before even agreeing to chat.

“You want to talk *beyond* my medical condition? You mean you don’t *care* about my medical condition anymore?” said the mother and grandmother, who later responded to a question about her biggest strength: “My sense of humor.”

Cory, who shared with her visitors that she had served more than 5,000 volunteer hospital hours during her lifetime, said she thought the program was important. “It’s nice to know that you take the time to talk to your patients. I’m a person.”

The Tell Me More program offers a valuable reminder for medical providers that their patients are people, and not just medical mysteries to solve, Guerrasio said. “I actually, as a doctor, find these conversations really helpful. And it’s what makes me come to work every day.”

Notes about the patient-doctor chat are jotted down on the Tell Me More questionnaire, which is then displayed on the wall so that everyone involved in that patient’s stay, from therapists and nurses to doctors and janitors, can use it as conversation fodder, Major said.

### Nothing is too small

By getting to know his end-stage cancer patient and his wife, Major learned not just about his patient’s bourbon routine, but that he was a



*Ajay Major, MD, MBA, left, and Jeannette Guerrasio, MD, right, talk with Anne Marie Fleming, RN, about the Tell Me More program.*

strong war veteran who had “always been a fighter.” That helped Major, when the man opted for a late chemo-treatment that was questionable at his stage and age. While the old veteran fared well through therapy, he developed an infection afterward that ended his fight.

When his patient was transferred to hospice, Major told the palliative caregivers about his patient’s taste for bourbon. Looking through his patient’s medical record after learning of his death, Major was jolted by one caretaker directive: Bourbon, one ounce at bed time, as needed.

“It seems like such a small detail,” said Major, who published an article in JAMA Oncology about the patient experience. “But when his fighting wasn’t working anymore, he started thinking about things he really enjoyed in life. And having his little bit of bourbon was kind of important to him. So we made sure he could have that to the end.”

## ALUMNI CORNER

## Medical Alumni Association's Night at the Opera

Last November, the Medical Alumni Association continued an annual tradition, A Night at the Opera, bringing together alumni, students, residents, faculty and staff for an evening for a reception and performance of "La Bohème," presented by Opera Colorado. More than 300 attendees enjoyed a reception where William Maniatis, MD, a member of the Medical Alumni Association board of directors, greeted guests. First-year medical student Jahmel Jordon, speaking on behalf of students at the CU School of Medicine, thanked generous alumni supporters. The evening was filled with connecting, great conversation, and a brilliant performance.

The Medical Alumni Association offers its appreciation to all who attended A Night at the Opera and will continue to offer opportunities for cultural events. The Medical Alumni Association's past programs to strengthen the relationship between the arts and medicine have included performances with Colorado Ballet, the Colorado Symphony Orchestra and Opera Colorado.

## 2018 Alumni Celebration & Reunion

You are invited to the 2018 CU School of Medicine Alumni Celebration and Reunion May 24-25. The reunion is a chance for you to reconnect with classmates, share memories and more. The reunion features events on and off campus for all CU School of Medicine alumni, residents, interns, fellows, and faculty. Class years ending in 3 or 8 will celebrate Class Reunion dinners.

To register for the reunion, visit [www.medschool.ucdenver.edu/reunion](http://www.medschool.ucdenver.edu/reunion).

## Letter from the President

Dear Alumni,

At the University of Colorado's Medical Alumni Association, we are excited about all the activities happening on and off campus. In the spring, we join fourth-year medical students for Residency Match Day and celebrate their recent academic achievements. We also will welcome many of you to campus for different festivities celebrating your reunion.

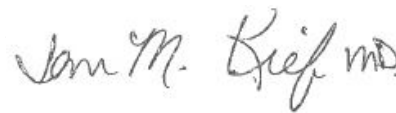
As the academic year concludes, I want to share a few additional highlights:

- Last August, we celebrated 184 members of the Class of 2021 at the Matriculation & White Coat Ceremony, where they received their white coat and a new stethoscope branded with the Medical Alumni Association logo. These stethoscopes are provided by generous alumni supporters.
- Our Association provided medical students with lunches each quarter to help keep them going during their busy course schedule.
- Through the HOST (Help Our Students Travel) program, alumni welcome into their homes fourth-year medical students traveling out-of-state during their residency interviews. This year we had an increase of students taking advantage of this program.
- The annual Dean's Circle Dinner, thanking alumni for supporting the School of Medicine, took place last December. We are incredibly fortunate to have your support and pride in our school.
- Twenty-one alumni participated as a facilitators working with first- or second-year medical students to review cases and practice clinical problem-solving in Problem-Based Learning classes.

- In January, the Association participated by providing lanyards for interns and residents during the Housestaff Appreciation week to show appreciation for all our residents and interns.
- We continue to help support the student population with the Stethoscope Program and the Medical Alumni Association Scholarship Fund that provides scholarship support to medical students based on merit and financial need.

These are just some of the many fantastic things we have accomplished. As we look to the future, our mission is to help advance and influence the interest of our beloved alma mater, to support current medical students on their journey to becoming physicians, and to provide programs and opportunities for alumni to connect with each other and the School of Medicine. We hope that you will become involved to help further advance the work of the School of Medicine. We are recruiting members for our Board of Directors and if you would like information, or to get involved with the Medical Alumni Association, visit our website or contact the Office of Alumni Relations at 303-724-2518 or email [healthalumni@ucdenver.edu](mailto:healthalumni@ucdenver.edu).

I look forward to seeing you at any of our upcoming events. Feel free to contact me with any ideas on alumni engagement at [janmd@comcast.net](mailto:janmd@comcast.net).



Jan Kief, MD | Class of 1982  
President, Medical Alumni Association  
University of Colorado School of Medicine



Sally Peach

### “The HOST program helped out a lot!”

“The Neuwelts in Portland were my first hosts and were absolutely fantastic. They took me out to dinner the night before my interview and dropped me off at OHSU the morning of the interview. They frequently host international students and fellows, and have a warm welcoming home for guests.” - *Fourth-Year Medical Student Sally Peach*

“I stayed with Dr. Stephen Cohen in Tucson and had a wonderful experience. He was easy to contact and coordinate with and provided a lot of insight into practicing medicine for 20+ years. Additionally, he even took time out of his day to drive me to my interview!” - *Fourth-Year Medical Student Bill Quach*

## Volunteer for Problem Based Learning (PBL)

“I started doing the PBL program this year and have really enjoyed it. I wanted an opportunity to teach and interact with medical students. I have loved being a physician and as I see that role drawing to a close for me, it seemed important to pass on what I have learned. The group meetings are fun, energetic interludes that have allowed me to observe ‘my’ students growing and changing over the year. They are going to be great physicians and I’m already proud of them.”

-*Dr. Elizabeth Regan, Residency 1985*

“Problem-Based Learning sessions have been a critical part of learning how to reason through clinical issues, consider complex social influences on patients’ health, and develop skills related teamwork. Beyond these skills, my PBL facilitator has also been an incredible role model and resource for me as I navigate the process of becoming the best physician I can be for my future patients. I am so grateful for that.”

-*Mackenzie Garcia, Class of 2020*

*Medical Alumni Association Student Board Representative*



## Top NCI Researcher Joins School of Medicine Faculty

The University of Colorado School of Medicine announced that Terry Fry, MD, has been recruited from the National Cancer Institute to join the faculty, effective February 2018.

Fry was among the first scientists to investigate the potential to insert modified genes into a child's own T-cells to target CD19, a surface protein found on nearly all cells affected by acute lymphoblastic leukemia. The first product using this technology, called chimeric antigen T-cell (CAR-T cells), was approved by the FDA for pediatric use in August 2017 and achieved an 80 percent remission rate in children with highly refractory leukemia resistant to all other therapies including conventional bone marrow transplant.

Fry has led several major studies to improve treatments for people with leukemia. In November, the journal *Nature Medicine* published an article that outlined a new treatment that genetically alters a patient's cells to fight cancer. Fry is the first author of the study. His work has been highlighted in the Discovery documentary *First in Human*, which aired last August, and in a recent *New York Times* article and *Washington Post* feature.

"Treatment for autoimmune diseases involves manipulating the same cells we're manipulating for cancer treatment," said Fry. "There are ways to use these same procedures to turn these cells off instead of on. This absolutely has potential beyond cancer."

Fry will be joining the Human Immunology and Immunotherapy Initiative as its co-director. The Human Immunology and Immunotherapy Initiative is part of the School of Medicine's Transformational Research Funding program, which provided five grants totaling \$80 million to research projects on campus. Funding for the program comes from clinical earnings of the faculty, from annual financial support from UCHHealth, and philanthropy, including a commitment by The Anschutz Foundation.

## Improving Health Status for People with Heart Failure

Patients with chronic heart failure face related health problems, such as depression and fatigue, that could be relieved by an expanded model of care, according to the study, "Improving Health Status for Patients with Chronic Heart Failure," published in *JAMA Internal Medicine*.

David B. Bekelman, MD, MPH, associate professor of medicine who practices at the Eastern Colorado Health Care System for the U.S. Department of Veterans Affairs, and colleagues evaluated 314 patients, with half of them enrolled in a program that addressed those related health status concerns.

The Collaborative Care to Alleviate Symptoms and Adjust to Illness intervention, also called CASA, offered 157 of the patients a nurse and social worker in addition to usual team of a primary care provider, cardiologist, and palliative care physician addressing the patients' needs. The CASA trial is the first clinical trial of such a collaborate intervention in heart failure and it included patients from VA, academic and safety-net health systems in Colorado who received

care between August 2012 and April 2015.

The CASA intervention did not result in significant changes in overall symptom distress, pain, shortness of breath or number of hospitalizations. The rate of death was similar—10 of the patients in the CASA trial died, while 13 of those receiving the standard of care died.

Still, the improvement in cases of depression and fatigue are important results because they are both difficult symptoms to treat in heart failure, Bekelman said.

## New Chair of Physical Medicine and Rehabilitation

Venu Akuthota, MD, was named chair of the Department of Physical Medicine and Rehabilitation effective January 1.

Akuthota has been on the School of Medicine faculty since 2002 and has served as vice chair and professor of the department and medical director of the Spine Center at the University of Colorado Hospital. He has also served as the department's residency program director.

"Venu brings exceptional talent and experience to this leadership role," said School of Medicine

## Improved understanding of color vision in mice

CU scientists, led by Maureen Stabio, PhD, assistant professor of anatomy and neurobiology at the University of Colorado School of Medicine, have discovered a new property of a little understood cell called the M5.

They knew that mice possessed light-sensitive proteins called opsins that allowed them to detect a limited range of colors. But as they investigated the role M5 cells played in this, Stabio discovered that the mice also had neurons that could compare signals from the different opsins and then send those color signals to the brain for interpretation.

"We are the first to discover this particular color vision circuit in mice," Stabio said. "We

knew they had opsins but we didn't know they possessed the other two requirements for color vision."

Stabio's work focuses primarily on the cells and circuits of the retina, including a group called intrinsically photosensitive retinal ganglion cells or ipRGCs which includes the M5. These cells are primarily involved in a kind of vision known as non-image forming vision.

The discovery that color vision in mice is far more complex than originally thought, opens the door to experiments that could potentially lead to new treatments for humans. The study was published in December in the journal *Neuron*.

Dean John J. Reilly, MD.

Akuthota is author of more than 90 publications, author/editor of two textbooks, and has spoken and chaired national and regional conferences. He is a founding senior editor of the PM&R journal and has held leadership positions in the North American Spine Society and Musculoskeletal Council Chair for the American Academy of PM&R.

Akuthota succeeds Dennis Matthews, MD, who became chair in December 1996 and who has had a distinguished and pioneering career. Matthews is recognized as a leader in care for patients with pediatric muscle disease and cerebral palsy.

## CU Researchers Identify Potential Treatment for Diastolic Dysfunction in Heart Failure

Researchers at the University of Colorado School of Medicine have identified a potential treatment target for patients with diastolic dysfunction, which is a heart relaxation abnormality.

According to a study published in the February 7 issue of the journal *Science Translational Medicine*, the researchers tested the effect of an investigational drug called givinostat in treating diastolic dysfunction, an abnormality that contributes to heart failure with preserved ejection fraction (HFpEF).

HFpEF refers to cases where the heart can pump blood normally, but is not able to fill as efficiently as a healthy heart. Millions of people worldwide suffer from HFpEF, which can be caused by hypertension, diabetes, aging or other conditions. To date, there have been no effective drugs identified to treat this form of heart failure.

Studying of the hearts of patients with diastolic dysfunction and HFpEF, the research team found that fibrosis, the commonly suspected culprit in these cases, is not the sole cause of diastolic dysfunction. Instead, their findings indicated that there was a defect in the ability of the muscle cells of the heart to relax.

Mark Y. Jeong, MD, assistant professor of medicine, and Timothy A. McKinsey, PhD, associate professor of medicine, tested whether givinostat might improve the heart's ability to relax in the face of hypertension or aging. They found that the investigational drug, tested in rat and mouse models, helped the heart relax properly.

"These are exciting findings because we may be able to help patients with a form of heart failure that has been recalcitrant to standard-of-care therapies," said McKinsey. "Givinostat is currently in clinical development for the treatment of muscular dystrophy. Our data suggest the possibility that givinostat could be 'repurposed' for the treatment of HFpEF."

Further study is needed to determine whether it could be an effective treatment, said McKinsey, who is also director of the Consortium for Fibrosis Research & Translation (CFReT), which is one of the programs supported through the CU School of Medicine's Transformational Research Funding initiative ([www.cfret.org](http://www.cfret.org)).

## Green Vegetables are Hard to Find in Baby Food

Convincing children to eat green vegetables might be difficult in part because their tastes often aren't nurtured in infancy to accept the bitterness of dark green vegetables.

The inability to foster a taste for those vegetables isn't simply because parents shy away from them due to infants' reaction. It's likely related to the lack of commercially prepared single-vegetable

products available to parents and caregivers to offer their infants and toddlers, according to a study by researchers from the University of Colorado School of Medicine on the Anschutz Medical Campus.

The study, published this spring in *The American Journal of Clinical Nutrition*, is the first study to examine the prevalence and types of vegetables in infant and toddler food manufactured and sold in the United States.

The researchers compiled a database of 548 infant and toddler foods sold by more than 20 U.S. companies. They then examined the ingredients and nutrients using the U.S. Department of Agriculture's vegetable categories.

Of the foods in the database, only 52 were single-vegetable products and none of those were dark green vegetables or beans/peas. In baby food that had multiple ingredients, fruits were listed as the first ingredient in 37.8 percent of the products, more commonly than all vegetables. Red/orange vegetables, such as carrots and sweet potatoes, were the first ingredient in 23.7 percent of products, while dark green vegetables were listed first in only 1.1 percent of products.

"The commercial infant and toddler foods market in the U.S. does not appear to provide caregivers with an adequate type and selection of products to facilitate children's later acceptance of the kinds of vegetables they will encounter and be encouraged to consume once they have transitioned to table foods," writes Kameron J. Moding, PhD, postdoctoral fellow in the Department of Pediatrics, and her co-authors.

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CU Medicine Today will keep alumni and others knowledgeable about and connected with the School of Medicine and the University of Colorado by writing truthful and relevant articles and providing a forum for news and comments from alumni.

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## RAIN

By Vishnupriya Krishnan

I remember the day her family brought her in, from their village several miles away, because rain was falling so thickly outside that it looked like a curtain. The medics laid her down on one of the beds in the trauma room, and immediately the doctors began rolling up her sleeves to poke for veins. Her wrinkled skin was dotted by so many different colors of lesions that it looked as though Monet's water lilies were blooming on her swollen belly, but her face was young and bright, like the moon. She must not have been more than thirteen.

"This is something you'll never see in the States," the doctor said to me, "An advanced case of tuberculosis." I wrapped the blood pressure cuff around her emaciated arm, slid the pulse oximeter onto her limp index finger, while medical students and residents swarmed around her, whispering words like "critical" and "fascinating," and then her eyes, previously fluttering with delirium, flickered open and looked straight at me.

Her pain hit me like a thunderclap. She squeezed my hand white as a medical student struggled to insert a catheter for the first time. I thought of the sacrifices patients' bodies endure for us to learn so much, and I squeezed back.

I smoothed her hair away from her sweaty forehead. I don't remember exactly what I said to her—phrases like "cavitary lesions" and "hematogenous spread" were buzzing around in my head—but I told her she



was brave, that everything would be okay. The doctors put more lines in and she looked at me and squeezed my hand some more.

Later that day, I came back to sit with her. Faint anguished whispers escaped her mouth. From the smell in the room, I could tell that she had soiled her sheets. The medical students and doctors were at the next trauma bed, for an elderly man with pesticide poisoning had been brought in, and no X-rays could be taken for our patient anyway until it stopped raining, for the imaging building was across the street.

I lifted each of her legs slowly—each movement was excruciating—and slid the dirty sheet out from underneath her, averting my eyes to siphon away some of the shame, replacing the bedding with a fresh sheet. When I had finished, her face was wet with tears. That evening,

she was wheeled to the ICU – the last time I would see her.

I had complained about the language barrier over dinner a couple nights ago with my friends, how it was difficult to learn about patients beyond the few sentences and lab values we read in their charts. But this pain in my patient's cracked lips and brimming eyes I understood. I understood.

I understood, too, the pain that comes with witnessing pure suffering without knowing how to predict the outcome. Patients come into our lives and leave footprints on our hearts, and we are never the same for it. Maybe part of being a healer is simply committing to being a witness. Listening to your patient. Holding their hand. Journeying with them across the uncharted waters of their illness. Affirming their human dignity.

*Vishnupriya Krishnan, a second-year medical student, wrote this essay for the "Literature, Art and Medicine" elective. She is on the editorial board of The Human Touch, an anthology of poetry, prose, photography and graphic art from the Anschutz Medical Campus community.*

## The Why and What of Sex and Cancer

by Saketh Guntupalli, MD

The impetus for *Sex and Cancer* was a study on sexual function that originated with our own Department of Obstetrics and Gynecology here at CU.

Completed in 2015, the groundbreaking study is called “Sexual & Marital Dysfunction in Women with Gynecologic Cancer,” which was published in the *International Journal of Gynecologic Cancer* and presented at the 18<sup>th</sup> biennial meeting of the International Gynecologic Cancer Society in Lisbon, Portugal in 2016.

The purpose of the study was to put issues related to gynecologic cancer patients and sexual functioning front and center and to unearth some answers that could help other women—and their partners—rediscover and sustain intimacy. It was groundbreaking because no study to date had examined in great detail the effect that gynecologic cancer has on marital and domestic partner relationships.

When we saw the study results, my co-author and I knew we needed to do two things.

First, we felt compelled to tell women who had experienced breast or gynecologic cancers that they had *a lot* of company if they had big disruptions in their intimate relationships after diagnosis and treatment.

Second, we needed to tell them how to establish a “new normal” in sexual functioning—one that could be even better than before cancer entered their life.

With that latter goal in mind, we interviewed therapists who work with women, and in some cases couples, who have struggled with sexual functioning or just wanted to kick their love life into a higher gear. We also talked

with many of my patients and, whenever possible, their partners or spouses.

My co-author, Maryann Karinch, and I knew each other well before starting work on this book. I’m her physician here at UHealth. We wanted to make that clear so that you know this isn’t “just” a physician and an author teaming up to write a book. This is the deeply personal mission of a team with day-to-day experience—from the perspective of oncologist and patient—of sexual dysfunction after cancer diagnosis and treatment.

We divided the book into two parts, with the first being focused on understanding why cancer and its treatments are bound to affect sexual functioning. There’s no way around the challenges, but understanding the various causes of them will go a long way to helping you use the menu of solutions, which are the focus in the second part of the book.

Our entire discussion in the book on “issues and answers” centers on the study conducted here and carried out at four locations, including two UHealth facilities, Columbia University Medical Center in New York and Loma Linda University Medical Center, which is about sixty miles east of Los Angeles. We also refer to other complementary studies to give readers a sense of what kinds of test instruments have been used to ascertain the extent to which sexual function or dysfunction occurs in populations affected by cancers of different kinds.



Considered together, the studies helped us get a better understanding of the nature of the dysfunctions and how to address them. They also illuminate how the medical community might avert problems for new patient populations.

When you add to that the contributions of other CU physicians, nurses, and technicians, as well as physical therapists, sex therapists, and other relevant experts, we were able to offer a doable and practical approach to overcoming sexual dysfunction after gynecologic and breast cancers.

*Saketh Guntupalli, MD, is an associate professor of obstetrics and gynecology in the Division of Gynecologic Oncology and co-author of “Sex and Cancer: Intimacy, Romance, and Love after Diagnosis and Treatment.”*

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