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Cover photo: David Bentley, PhD, and Richard Davis, PhD, lead the RNA Bioscience Initiative, one of the five major projects funded by the Dean’s Transformational Research Funding program.

Photo by Trevr Merchant.
Improving Lives in Changing Times

The University of Colorado School of Medicine’s success depends on the sustained effort of everyone associated with it to build and maintain a vibrant community of educators, clinicians, scientists, staff and other valued contributors.

In ordinary times, that requires a level of dedication and coordination unmatched in many professional endeavors. The lives of our patients, the future of the healthcare system, breakthroughs in laboratories demand constant, unyielding attention. We are fortunate to have so many talented people at our school working together to benefit our community and the world.

These, however, are far from ordinary times. During the past year, we have witnessed proposals that would take health insurance away from millions of people, that would limit entry to scholars seeking to join our community, and that would make devastating cuts to the budgets of federal agencies that provide crucial funding for biomedical research.

The actions of our elected leaders will undoubtedly have a significant impact on health care over the upcoming years and we will need to adapt our tactics for this changing environment. We are already doing so by bolstering the school’s investments in research, by adding clinical sites in our community, by re-evaluating the curriculum for medical students and by advocating for the programs that have made valuable improvements in the lives of so many people.

In this issue of CU Medicine Today, we have articles about five Transformational Research Funding projects receiving substantial support from the school. We are investing in teams exploring the promise of immunotherapy, the search for common targets in fibrotic disease, productive uses of big data in caring for patients, a better understanding of the role of RNA in human health, and expanding discovery of innate immunity and the vast landscape of the microbiome.

Such programs will be crucial to the future of medicine and to our campus. The leaders of these projects are already recruiting faculty, managing resources that promote collaborative science, organizing training and educational programming and sponsoring pilot research projects. While the projects vary in topic and scope, they all have one common element: They are investments in people.

While times change, our calling is to improve the lives of others. We will remain steadfast in fulfilling our fundamental missions of providing world-class health care to all in need, advancing science to improve our understanding of biology and translating that understanding to improved prevention and therapy, and educating the next generation of researchers and health care providers.

We also will not change our commitment to embracing diversity as a core component of our strategy. We will continue our efforts to recruit and support a diverse student body, faculty and staff and to leverage their skills to meet the needs of the diverse population we serve. We will continue to support a diversity of ideas, respectful and civil dialogue among those with differing points of view, and a tolerant environment for all.

With warm regards,

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.

**Huntington Potter, PhD**, director of the Rocky Mountain Alzheimer’s Disease Center and professor of neurology, in February told 9News, the NBC affiliate in Denver: “We found so far that Leukine is safe in people with Alzheimer’s disease. That means that it doesn’t have the side effects that so many other Alzheimer’s drugs have had, which are swelling in the brain and bleeding into the brain.”

**Kenneth Tyler, MD**, chairman of neurology, explained to the San Francisco Chronicle the significance of a research article, published in February, based on findings by his laboratory team: “A lot of people were dubious about Enterovirus D68 because they said, ‘Gosh, this virus isn’t known to be neurotropic and we’re not finding it in the spinal fluid. We asked, ‘Would these (strains) produce a neurologic disease in mice, and would it be similar to what we saw in humans?’ And the answer was a resounding yes.”

**Kennon Heard, MD**, professor of emergency medicine and section chief of medical toxicology, was quoted in February by the CBS affiliate in Colorado Springs, that she is training to compete in curling at the 2018 Paralympic Winter Games. “I got online and looked around and said, ‘This wheelchair curling sounds kind of interesting. I think I’ll give it a try.’”

**Torri Metz, MD**, assistant professor of obstetrics and gynecology, warned against marijuana use during pregnancy in a February New York Times article: “There is an increased perception of the safety of cannabis use, even in pregnancy, without data to say it’s actually safe.”

**Virginia Borges, MD**, associate professor of medicine, explained the benefits of cold cap treatments to reduce hair loss due to chemotherapy, on CBS This Morning in February. “They have more energy,” she said. “They really feel like a return to themselves, their sense of themselves, much faster because they don’t have to wait for their hair to regrow.”

**Pam Wilson, MD**, associate professor of physical medicine and rehabilitation, told the NBC affiliate in Denver: “We found so far that marijuana occurs and the number of medical (marijuana) licenses in the state to do with this wave of people who are using marijuana: “Ingestion of edible products contains a little arm or cheek rash, “These are kids with a decent percentage of their bodies covered despite good moisturizing, bathing and increasing topical prescriptions.”

**Erica Wymore, MD**, assistant professor of pediatrics, was quoted in a New York Times article in February about pregnant women using marijuana and the risks of birth defects: “Just because they don’t have a major birth defect or overt withdrawal symptoms doesn’t mean the baby’s neurological development is not impacted.”

**Matthew Greenhawt, MD**, assistant professor of pediatrics and chair of the food allergy committee of the American College of Allergy, Asthma and Immunology, explained in a Washington Post article in January why new National Institutes of Health guidelines are closely tied to eczema. “[S]evere eczema is not a kid with a little arm or cheek rash,” he said. “These are kids with a decent percentage of their bodies covered despite good moisturizing, bathing and increasing topical prescriptions.”

**Thomas Inge, MD**, chief of pediatric surgery and director of adolescent metabolic and bariatric surgery, discussed with The New York Times his study of outcomes for children who get bariatric surgery. Many more could have reached a normal weight, he said in the February article, if they had had the operation when they were younger, before they got obese.
Jessica Cataldi, MD, a fellow in the Pediatric Infectious Diseases fellowship, appeared on 9News, the NBC affiliate in Denver, in February, to discuss the importance of the HPV vaccine: “This vaccine is about cancer prevention. It can prevent almost 80 percent of cervical cancer...and many cancers of the throat and the mouth.... We give it to children around age 11 or 12 because that’s when their immune system responds the best.”

Stephen Daniels, MD, PhD, chair of pediatrics, was quoted in the Chicago Sun-Times in March, explaining reasons that parents struggle to keep junk food away from children: “Families and kids are busy, and they often want convenience as part of their choices.”

Andrew Freeman, MD, assistant professor of medicine, told ABC News in February that the most heart-healthy diet includes foods like extra-virgin olive oil, antioxidant-rich berries, green leafy vegetables and plant-based proteins. “There is sort of mass confusion about what foods are healthy or not healthy,” he said. “When you take the time to weigh through the data and the evidence it becomes clear. Human beings haven’t changed all that much in the last many, many years.”

Karyn Goodman, MD, associate director of clinical research for CU Cancer Center and visiting professor of radiation oncology, told the Coloradoan newspaper in January about research that focuses on shorter radiation treatments for cancer patients. “We hope this is the first of many clinical trials we are able to open across the UCHealth system,” she said. “This is a major step toward expanding access to oncology trials, and we hope to continue to bring these leading-edge treatment options to Coloradans outside of the Denver metro area.”

Abraham M. Nussbaum, MD, MTS, chief education officer at Denver Health and an associate professor of psychiatry, wrote an op-ed in December for the Washington Post about Medicaid. “Over the past few weeks, there has been talk both of funding infrastructure projects and defunding Medicaid, at least in part. I recently saw a patient who reminded me that Medicaid itself provides an essential kind of infrastructure.”

Lilia Cervantes, MD, associate professor of medicine, told the Denver Post in November that Denver Health’s Center for Health Equity plans to expand its recruitment efforts to include middle schoolers and graduate students. “The idea is that when patients have a doctor who is culturally congruent,” she said, “they better understand their options and are more likely to make an appointment.”

Thomas Bak, MD, associate professor of surgery, was quoted in a November report on 9News, the NBC affiliate in Denver, about the first kidney donation to travel over an ocean to Colorado. “We fly organs all across the country pretty frequently for this program, so it’s definitely becoming more common,” he said. “A flight to Hawaii is really not much different than a flight to New York, but the concept of flying organs over the ocean is neat.”

Jennifer Honda, PhD, a postdoctoral fellow in medicine, was mentioned in an article in The New Yorker in December because the author asked her to determine whether nontuberculous mycobacteria, a pathogen that can cause lung disease in individuals with weakened immune systems, could be found in the author’s showerhead.
Teach Your Children Well

Jill Landsbaugh Kaar seeks to unravel mysteries of healthy lifestyles for kids

By Cynthia Pasquale

Childhood obesity and rates of Type 2 diabetes are rising across the country. While researchers know some of the main culprits — sugary foods and inactivity — there is still much to learn.

Jill Landsbaugh Kaar, PhD, an assistant professor of pediatrics at the School of Medicine, is one of those dedicated researchers contributing to the effort. She recently helped draft a guideline for the American Heart Association emphasizing that children should consume no more than six teaspoons of added sugar per day. Kaar’s research aims to unravel patterns of behavior that are optimal for a healthy body.

She and her husband, a chemical engineering professor at CU Boulder, came to Colorado in 2010, after post-doctoral studies at the UK Medical Research Council in Cambridge, England. As a mother of a toddler, Kaar strives to model healthy behavior that her two-year-old daughter, Zoe, will learn. Her leisure time is spent playing with Zoe, reading books, going for walks (with Zoe) and spinning classes when she has some weekend time to herself.

“When I started this journey, I wanted to help people by learning how nutrition affected obesity, but now I know that there are so many other variables we need to consider, like the amount of time you are active, your screen time and sleep,” she said. “If you exercise for the recommended 60 minutes most days of the week, but your job or school requires you to sit for eight hours, five days a week, are you living a healthy lifestyle? It’s one of the questions I want to unravel.”

How did you choose this career and area of research?

I always was interested in why some people are at a healthy weight, but others struggled with their weight. I wanted to help them. I always thought the issue was a matter of diet and physical activity. After obtaining my nutrition degree, I decided to apply to graduate school and focused on the other side of the energy balance equation, physical activity.

My master’s degree is in exercise physiology and my PhD is in physical activity epidemiology. My postdoc work looked at maternal and child health epidemiology, which helped me understand that the issues don’t always begin with kids, but with parents, who are the decision-makers.

As I learned more and more about obesity, the sleep component came to the forefront, and that is a new direction I am taking with my research. It’s not just what you eat or how you exercise, metabolism is also an outcome of how you sleep. If you aren’t getting enough sleep, you might not be getting the benefits of eating healthy and exercising during the day.

What are the biggest roadblocks to restructuring not-so-healthy lifestyles into healthy ones?

When I was growing up, it was more of the norm...
that you had one parent who stayed at home, but that is rare now: Most families need two incomes. This often means that the entire family is not home at the same time and that together time may be very short. We still want that important family meal, even if it is fast, so one thing we can do is educate people and give them the tools they need to plan ahead. Even if you only have 45 minutes for a meal, you can get a healthy, affordable meal on the table in 20 minutes and still get out the door on time with a bit of prep earlier in the week.

Kids learn from their parents, so it is about role-modeling. You can teach them that dinnertime is an event where you have a well-balanced meal and all check in with each other. You teach them that this is a nice time and you make it enjoyable as a family event.

**What happens when a child is no longer under your roof and you don’t have a say when it comes to eating healthy or balancing life?**

Perhaps think of it as if you are teaching kids values and morals. From the time they are young, you teach them to say “please” and “thank you.” Your child knows they have to say these things, and while they might not always do it, they have learned the importance of manners. The same goes for diet.

I don’t believe in counting calories for any age group because it is an unrealistic thing to ask families to do. It’s very time-consuming, and it’s not a lifestyle you are going to be able to maintain. Instead, I try to instill healthy eating. For breakfast, for instance, we eat yogurt and fruit and maybe a piece of toast or cereal. My daughter eats the same thing. I don’t give her sugared cereal or cookies; I chose healthier options for her to eat. I feel kids will have enough opportunity for all of the other sugary stuff, and as a parent, I want to provide her with good tasting, healthier options at home when it is more in my control. I am sure if I offered my daughter yogurt or a cookie, she would take the cookie, so I give her more limited choices: strawberry or vanilla yogurt, apple or orange slices.

Physical activity is the same idea. My daughter doesn’t see me sitting on the couch and watching TV. We keep the television off and play with her. We go outdoors whenever we can. At bedtime, we read books. As I delve deeper into sleep research, I understand the importance of not having blue light – computers or other screen time – before bedtime. A person needs more calm time then, and this is a behavior that a parent can monitor and change for a child.

**You recently co-authored new recommendations for the American Heart Association saying that children ages 2 to 18 should consume less than six teaspoons of added sugars each day. How did you and your colleagues reach this figure?**

There is not a lot of literature on how much sugar is linked to certain outcomes like obesity or diabetes. This was an invited article by the American Heart Association, which convened a group of researchers – both medical doctors and PhDs – to comb the literature and find out what we know now, where the research gaps are, and where does research need to move forward. The idea was to recommend a number that will improve child health.

My contribution was related to childhood obesity and diabetes. There’s not a lot of literature about the exact amount of sugar consumed that leads to obesity. So, for instance, nothing out there says that if you consume X number of sugary beverages, you are twice as likely to become obese. But what we do know is how much sugar kids are eating today from detailed food records. We know that preschoolers have about 12 teaspoons of sugar a day. We also know that obesity and Type 2 diabetes are increasing, and so we know that 12 teaspoons may be too much.

We don’t want kids to have more than one sugar-sweetened beverage, which contains 10 to 12 teaspoons of sugar, each week. The average kid probably has one of these beverages each day.

**You mentioned that your current research deals with how many behaviors affect obesity. What does your research entail?**

I have a scientist development award from the American Heart Association to study health behavior patterns of children. These behaviors include diet, screen time, sleep and activity. I am trying to unravel these patterns.

Let’s assume that you have some kids with healthy behaviors in all of those categories. They get adequate sleep and physical activity and have limited screen time and they eat well. Other kids don’t do any of those things well – or at least what we think they should be doing to maintain good health. Kids with healthy lifestyles are going to have a good BMI (body mass index), while the poor health behavior pattern group will most likely be linked to a higher BMI and therefore have a higher risk of obesity.

We don’t know how unhealthy the patterns are in-between, those mixed lifestyles of kids that have some healthy and some unhealthy behaviors. What about a child who eats OK, and gets some physical activity every day, but has six hours of screen time? Are they at risk of obesity equivalent to the child with poor or unhealthy lifestyle behaviors? We need to know the combinations that lead to the child having an increased risk of obesity.

The second part of the study is what happens if you have a healthy lifestyle pattern – you eat right and you exercise – but you have poor sleep. Does this mean you have a higher risk of obesity? My hypothesis for the research is that if you have poor sleep, you don’t get the same benefits of having that healthy lifestyle pattern.
Learning Outside the Walls of Medical School
Introducing students to the personal experiences of patients

By Tonia Twichell

When Jackie To came to the University of Colorado, she committed to four years’ intense study at the School of Medicine, then augmented her training by joining C-STAHR.

Through research, education and advocacy, C-STAHR (Community-Students Together Against Healthcare Racism) offers Anschutz Medical Campus students a deep dive into the health concerns of neighboring communities to learn about health disparities.

“I have never heard of a group that works this closely with the community at every step of the decision-making process,” said To, who graduates in May from the CU School of Medicine. “It was very appealing that we would be forming relationships at a very grassroots level.”

A group of medical students began C-STAHR after hearing Salud Clinic Director Tillman Farley, MD, a CU School of Medicine alumnus of the class of 1987, give a presentation about health disparities. The students partnered with 2040 Partners for Health, a health care advocacy group representing Northwest Aurora, East Montclair, greater Park Hill, Northeast Park Hill and Stapleton neighborhoods. C-STAHR members use community-based participatory research techniques to ensure residents are involved in all aspects of the research process.

“I immediately fell in love with the idea that we could actually go about making some sort of difference in the way doctors interact with patients,” To said. “But the reason I kept coming back to C-STAHR was the community members, quite honestly. I felt like I had never really had that kind of exposure before.”

In addition to conducting research, C-STAHR students created the Health Esteem futuRe pOwer Encouragement Speak up (HEROES) program, which educates minority high school students about health-care careers. Others are involved in addressing the CU School of Medicine’s curriculum so that it reflects more diversity.

Meanwhile students initiated other projects using the C-STAHR model under the umbrella of 2040 Community-Based Student Program including research focused on maternal-child health, teen obesity and alcohol use in the Burmese refugee community.

Now in its sixth year, 2040 Community-Based Student Programs, which includes C-STAHR, has 61 students (and 19 graduates) from the schools and colleges of medicine, pharmacy, nursing and public health. The projects ask for a four-year commitment from medical students, who receive training in leadership, grant writing and research, said Janet Meredith, MBA, senior clinical instructor in the Department of Family Medicine and director of student programs at 2040 Partners for Health.

“They really get to know people who are different from themselves,” Meredith said. “When they hear a woman talk about her experience with segregation … (or) a community member who lost two sons at the hands of Denver police and a daughter who died of pneumonia because it was too expensive to go to the hospital, they get an education in a way that they will never pick up in a book.”

Maternal Child Health Project

Megan Kalata, a second-year medical student, became interested in pediatrics because of research showing that children who are healthy when they begin school at age 5 are likely to continue in good health.

“It’s a lot harder to catch up later on,” she said.

When casting around for a project, she was concerned by studies showing that babies born to African-American women are three times as likely to die compared to those born to white mothers.

The studies showed that the results were not affected by age, education or socio-economic factors, but rather indicated that levels of stress-
related cortisol are higher in African-American women.

In February 2016, she organized focus groups to ask African-American women about their health-care experiences during pregnancy.

“Every time we met I learned something different, and I started hearing a lot of things repeated that I wouldn’t have thought about.”

One theme that emerged was the reception African-American women received in their first prenatal visit. About half the women said their health-care provider recommended an abortion.

“Now, some were young – teens even – but others were in their 30s, engaged to be married, and had a stable life. Some were in graduate school.

“Another common theme was their personal level of comfort talking to a provider and feeling judged and not feeling like they can ask good questions. We’re trying to tease out if that happens with all providers including doulas, doctors and midwives.”

Improving Patient-Provider Communication

When Jackie To’s father had a stroke during a family vacation, he encountered verbal abuse from the emergency doctor.

The family had been vacationing in Nevada when the stroke occurred, but their insurance only covered him in California. To and her parents knew that quick treatment was important for her father’s recovery, but they also knew they couldn’t afford treatment without insurance.

“When we showed up at the emergency room in California, the doctor started screaming at us about how we shouldn’t have waited. He said we should have just gone to the first emergency room we found. It was terrifying. I was 19, and I spoke up for my dad and told the doctor that would have bankrupted us so we intentionally made that decision. We took a chance.”

The physician’s demeanor changed when he realized that, unlike her immigrant parents, she could speak English well. He asked her about school, and she told him she was a freshman at Stanford University.

“After that I was treated differently than my parents. If I hadn’t been there, I expect the encounter would have gone very differently. I think about all the other families out there who don’t have a daughter accompanying them to an emergency room; a daughter who speaks excellent English and is going to Stanford.”

Her research project at C-STAHR is meant to help people like her parents. Students and community members decided to focus on patient-provider communications after hearing patients complain about doctors ignoring them during visits.

To is sympathetic to both patients and providers. “Physicians have a specific agenda to get through and a limited amount of time to do it. That can make them curt and impatient. In that encounter you might feel the doctor is rushing you through and not addressing the things you’re actually concerned about. That makes you feel like you have no power. So the time crunch causes miscommunication and perceived discrimination.”

Using a survey tool, the team asked patients to prioritize their concerns so they can be mentally prepared for their visit. Team members also encouraged the patients to be assertive. “You have the right to speak up!” she said.

Through focus groups, To learned how important a doctor’s language and communication style can be.

“Working with community members made me hyper-aware that things you say can be misinterpreted.”

Benefits for Students

2040 Community-Based Student Program research will continue after To, Kalata and other students have graduated because other students will advance the studies with the help of community members.

“What’s valuable and noteworthy is that the students really own the program,” says Frank DeGruy, MD, MSFM, chair of the Department of Family Medicine. “Faculty help navigate things like Institutional Review Board policies, but students set the agenda.”

The program has proved to be an important recruiting tool for incoming students interested in community work, said Shanta Zimmer, MD, associate dean for the Office of Diversity and Inclusion. And participants tend to experience successful residency matches, Meredith said. Between 2014 and 2016, all but one graduating medical student placed in their first choice for residency.

“One of the things that the institution gets out of this is that we as faculty have these students who are role modeling incredible commitment to advocacy and community engagement,” Zimmer said. “Being a physician is more than the facts they are learning in medical school. It’s a lifelong commitment to service. The partnership comes from the community and reminds us all again that it’s not just the things we’re studying but also what we’re learning from patients. They teach us well.”
CLINICAL CARE

Using Technology to Combat Opioid Epidemic

Pilot project makes state prescription database more accessible

By Michael Davidson

Doctors should be able to fight opioid misuse by relying on online computer databases, but so far, existing systems such as online databases that track prescriptions have failed to live up to their promise.

So Jason Hoppe, DO, an associate professor of emergency medicine, and a team of physicians and software developers have developed a pilot project that links the Colorado Prescription Drug Monitoring Program and University of Colorado Hospital’s electronic medical records system.

The federally funded project is an example of how CU Anschutz faculty and researchers could have a national impact on the opioid abuse epidemic, possibly leading to improved software that helps doctors and hospitals across the country ensure patient safety, identify people vulnerable to addiction, and stop prescription medication misuse.

Diagnosing a digital disconnect

Software that tracks prescription medications has been available for years. Since 2008, Colorado has had an online statewide database recording when a pharmacy dispenses controlled substances including opioids such as Vicodin and OxyConti, and other potentially addictive medications, such as stimulants like Adderall and benzodiazepines.

Such software allows providers to review a patient’s history before writing a prescription. Hoppe said the databases also could be effective tools for identifying people who visit multiple doctors in an attempt to get prescriptions for opioids or addictive medications.

Providers can use information stored in the database to determine whether patients should be referred for addiction treatment. Databases also can warn doctors if a patient takes a dangerous combination of medications, and in the future, software could perhaps create risk profiles that identify patients susceptible to addiction.

“I think there are positives, and there is evidence that shows they improve patient safety,” Hoppe said. “But there are a lot of barriers to using it.”

Hoppe noted that statistics show that nationally doctors check the databases in their states only 12 percent to 20 percent of the time before writing a prescription for a controlled substance.

“We would like to get that number a lot higher,” said Hoppe, who is co-chair of the Colorado Consortium for Prescription Drug Abuse Prevention’s working group focused on improving the database.

A critical element for providers is time. Doctors need to quickly diagnose and treat patients while simultaneously reading and updating electronic medical records (EMR). Switching to a different software program to check the state database takes several steps and distracts both doctors and patients.

“If you’re in a busy primary care clinic or emergency department, and you’re seeing patients for only five minutes, and it takes you five minutes to load the system, you’re unlikely to use it,” Hoppe said. If doctors think a patient needs an opioid painkiller and do not see signs that raise concerns about possible misuse or abuse, they often write prescriptions without checking the state’s database.

An obvious solution would be to integrate the state database and EMR systems. To overcome technical problems, Hoppe and the team worked with Epic, the software company that sells one of the most widely used EMR systems. UCHealth uses Epic’s software and is part of the project.

The initial pilot project is small, Hoppe said, with doctors in the SOM’s Emergency Medicine Department and the University of Colorado Hospital being the first users.

“We have to see how it does, how people like it, and if we can make it solvent in terms of cost,” Hoppe said. The U.S. Department of Justice funded the pilot project, and the software will have to show results before receiving more financial support.

Users at CU Anschutz like the system so far, Hoppe said, and it already has made his job easier. “I use it for 90 percent of patients now that it’s just one click,” he said.
Research Programs Boosted with Major Investment

School of Medicine awards grants to promising initiatives

By Mark Couch

In January 2016, Dean John Reilly, Jr., MD, announced five recipients of Transformational Research Funding awards.

These awards are major investments in programs that will position the University of Colorado School of Medicine as a leader in cutting-edge and emerging fields, attract extramural funding, help recruit and retain outstanding faculty, enhance education and training, and positively impact human lives and society in Colorado, the nation and the world.

These investments are funded by the Dean’s Office with a portion of clinical earnings by the faculty, from annual financial support from UCHealth, and from philanthropic contributions, including a commitment of $15 million by The Anschutz Foundation. No state-appropriated funding or student tuition or fees are being used for the Transformational Research Funding awards.

The awards were selected with the assistance of a committee of external reviewers who considered about 40 proposals submitted by faculty teams. The initiatives that were selected are expected to catalyze:

- **Innovative scholarship** that makes significant contributions to knowledge and science in areas of strategic importance to CU, and that has potential to improve human lives, society, the environment, or the economy, will enhance culture and community, or provide other public benefit;
- **Multidisciplinary collaboration** that positions CU as a national leader in these selected areas;
- **Faculty teamwork** across career stages to provide mentorship, support professional advancement, and position CU faculty as leaders in key fields; and
- **Training opportunities** in cutting-edge interdisciplinary or multi-disciplinary research.

Each project has a five-year budget totaling between $10 million and $20 million.

During the past year, the leaders of the initiatives have been recruiting faculty, managing resources that promote collaborative science, organizing training and educational programming and sponsoring pilot research projects.

Each project is profiled on the following pages of this issue of CU Medicine Today. The five projects are

- **Consortium for Fibrosis Research & Translation (CFReT)** – Investigators in this program are working to discover the mechanisms that govern pathological fibrosis and to develop treatment for patients with diverse fibrotic diseases.
- **Data Science to Patient Value (D2V)** – This initiative focuses on Big Data methods, their applications to medicine and health care delivery, and ultimately, the achievement of high value, patient-centered health care.
- **GI and Liver Innate Immune Programs (GALIIP)** – Researchers are addressing the unmet need in diagnosis, treatment and understanding of many gastrointestinal and liver diseases, including fatty liver disease, eosinophilic esophagitis and inflammatory bowel disease.
- **Human Immunology & Immunotherapy Initiative (HI³)** – HI³ is working on experimental models for the preclinical testing of therapeutics, reliable immunotherapeutic production, consistent clinical trials research support, and organized immune monitoring capabilities.
- **RNA Bioscience Initiative** – While modern biology has been revolutionized by the discovery that many processes of fundamental importance are regulated by RNA molecules, major knowledge gaps remain in the basic, diagnostic and therapeutic areas of RNA bioscience.
Strengthening Connections Between Fibrosis Researchers

Consortium aims to address unmet need for anti-fibrotic therapies

By Mark Couch

The Consortium for Fibrosis Research & Translation aims to unify campus researchers and clinicians who, due to their concentrated focus on a particular organ, may not have recognized similarities of their work.

"This is a group that is focused on fibrosis, which is essentially excessive scarring," said Tim McKinsey, PhD, professor of medicine and director of the Consortium for Fibrosis Research & Translation (CFReT). "Fibrosis is a wound-healing process that can be beneficial, but it can also be very deleterious," he said. "If your internal organs become scarred, they become dysfunctional. It’s estimated that about 45 percent of the deaths in the Western world are due to some form of fibrosis."

The goal of the CFReT is to investigate and understand the common elements about fibrosis in different organ systems, and ultimately develop therapies that could address those deleterious effects.

"Unfortunately there really are no treatment options for people with fibrosis," McKinsey said. "There are a couple of drugs used to treat a lung fibrosis disorder called idiopathic pulmonary fibrosis or IPF, which is a deadly condition. There are two FDA approved drugs for IPF, but neither are very effective. So there’s really a huge unmet medical need for the development of novel anti-fibrotic therapies."

What do the molecular pathways in cardiac fibrosis, for example, tell researchers that might be useful in understanding progressive scarring in lung, liver, or kidney?

"One of the goals of our center to define novel biochemical pathways that commonly regulate fibrosis in diverse organ systems because we feel that those will be crucial drug targets," he said.

"The CFReT is unique in that it brings together experts in the basic science and the clinical treatment of people with fibrotic diseases," McKinsey said. "There are centers of excellence in fibrosis that are related to a particular organ scattered around the country, but this is the first consortium of its kind where experts in fibrosis across organ systems are under one roof."

Mary Weiser-Evans, PhD, professor of medicine and co-director of CFReT, said the approach to research that might consider fibrosis has traditionally been focused on specific organ systems.

"While the CFReT is a unique multidisciplinary approach, there is an underlying complication because many of the other organ-specific centers across the country are NIH-funded and at the NIH there are individual institutes that would fund a liver fibrosis center or a pulmonary fibrosis center. So our goal is to bring together multiple institutes to get this funded, which will be complicated."

Such an approach creates a natural tendency for specialists to flock together. For CFReT investigators, the goal is to find the common ground between the hepatologists, cardiologists, pulmonologists and others. While initially focused on heart, lung, liver, and kidney fibrosis, an unexpected, but welcomed result of the CFReT has been increased interest from investigators from other disciplines, including neuroscientists, scleroderma specialists, and researchers focused on eye fibrosis.

"In putting this application together, we had an opportunity to talk to a diverse group of investigators, including liver experts and lung experts. It turns out we have a lot in common, but we tend to talk to just the heart or vessel experts," said McKinsey, who runs a laboratory focused on molecular mechanisms of heart failure.

One of the key duties of the leaders of the Transformational Research Funding initiatives will be to establish centers of excellence on the Anschutz Medical Campus that can continue after the initial funding awards wind down.

"A main focus of ours is sustainability," McKinsey said. "After five years of funding, we want to make sure we can continue to maintain and grow this very special consortium."

To that end, the CFReT has established the Fibrosis Innovation Group (FIG) and hired Keith Koch, PhD, who has held research and leadership roles in the private sector, to lead the effort. The FIG is modeled after structures used by successful biotechnology companies and nonprofit research institutes with units that provide useful services to other researchers and that can help advance the ongoing work of the members of above and right, Timothy McKinsey, PhD, and Mary Weiser-Evans, PhD. Photos by Trevor Merchant.
CFReT.

At this start-up stage, the CFReT has been investing directly in work of campus researchers, whether they are well-established faculty members or promising graduate students.

“We have an internal granting system where we provide pilot funds to investigators, and we have now funded six distinct investigators with these pilot funds,” said McKinsey. “The goal is to generate preliminary data that will lead to new grant applications and industry collaborations.”

For example, Michel Chonchol, MD, professor of medicine and director of the polycystic kidney disease program in the Division of Renal Diseases and Hypertension, received a CFReT grant that will support imaging work with patients.

“We have funded a clinician, Michel Chonchol, to perform a study in humans with something called polycystic kidney disease, which is a genetic disorder that has a severe fibrotic component, and he's using an imaging method called MRE (magnetic resonance elastography) to quantify fibrosis in these patients. Such a study would not have been possible without funding from the CFReT.”

So far, two graduate students in existing programs on campus – one in Pharmacology and another in Integrated Physiology – have been funded through CFReT, Weiser-Evans said. “One is working on iPS (induced pluripotent stem) cells in heart regeneration and fibrosis.”

Such research is crucial because fibrosis can interfere with normal organ structure and function.

“Organ regeneration is inhibited by fibrosis,” McKinsey said. “So this student is looking at the interplay between fibrosis and cardiac regeneration.”

In addition, the funding is supporting a lecture series and additional faculty recruitment efforts. A seminar series started last November with guest speakers already scheduled throughout 2017. Furthermore, Maggie Lam, PhD, from UCLA will be joining the CFReT as an Assistant Professor starting May 1.

In addition to building a community of researchers on campus, the leaders of CFReT also want to raise awareness of the impact of fibrosis on day-to-day life.

“I think when talking to lay public, it's important to convey some common examples of how fibrosis can affect your life,” McKinsey said. “I have a friend who has a form of eye fibrosis. He is essentially blind because he had surgery and as the wound healing response occurred, it never resolved. That means his eye became progressively fibrotic and scarred over. So that's an example of how fibrosis is not going to kill you but it can significantly affect your quality of life.”

He cited another example.

“A colleague of mine has a friend who's a singer and unfortunately she has this rare disorder where her vocal chords become fibrotic and she can't sing any more. She's not going to die from that, but she can't do what she loves. So it's not just that fibrosis is deadly. It certainly is deadly, but it can also can significantly affect your quality of life.”
Maximizing Technology’s Impact in the Doctor-Patient Relationship

Data Science to Patient Value initiative tries to personalize big data, improve experiences

By Michael Davidson

When Jean Kutner, MD, MSPH, provides care for patients, she wishes she could spend more time talking with patients about their health and the care they want to receive—and not spending her time on a computer, trying to sort through volumes of health records.

“That’s probably not a good use of our valuable and limited time together,” said Kutner, a general internist and palliative care specialist, chief medical officer of University of Colorado Hospital and associate dean for clinical affairs at the University of Colorado School of Medicine.

Despite her occasional frustration, Kutner is not against technology—far from it. She wants to unlock its potential to create effective care personalized for each patient.

Kutner co-leads the Data Science to Patient Value (D2V) initiative, a new multidisciplinary program at the University of Colorado Anschutz Medical Campus. The initiative, supported with a $20 million grant from the School of Medicine’s Transformational Research Funding program, has big ambitions.

“Our work could revolutionize how we think about how health care is provided, the patient experience, and how we make decisions,” Kutner said. “Our goal is to make CU Anschutz a leader in the intersection between data and value and the application of cutting-edge data science to the value equation.”

Personalizing big data

Right now, the volume of clinically relevant data in health records and from other sources can be overwhelming. Initiatives like D2V could fix that and develop technologies that create a new era in health care. Kutner thinks in the future supercomputers will help diagnose and treat patients, and that will lead to real improvements in their health and maximize the doctor-patient relationship.

“This is personalized medicine focused on a patient’s goals and values, and not necessarily on their genome,” Kutner said.

She gives the hypothetical example of a patient just discharged from the hospital. In a few years, a doctor could use an activity tracker like a Fitbit to see if the patient exercises and gets out of the house. The doctor would look for signs the patient is not recovering or has developed other health problems.

Kutner said the clinical team could see the data and reach out to patients, checking on their status and, if necessary, asking them to come in to be evaluated. Before the visit, a supercomputer could analyze a patient’s data and compare it to data collected from tens of millions of other people. The analysis could create a personalized risk profile with suggestions for a custom treatment plan based on proven therapies. At the start of the next appointment, a doctor could see that information in single user-friendly dashboard.

“With all that data already synthesized, I could get the most value out of face-to-face time with a patient and help them make decisions about their treatment,” Kutner said. “That would be my ideal world.”

Physicians would still have important roles, Kutner said. The doctor and patient would use their time together to talk about what problems are arising and focus on their patient’s priorities. They would work together to get back on track.

Value from the patient’s perspective

While D2V is working on technological innovation in fields such as medical informatics, biostatistics and data visualization, Kutner said it also will address the more philosophical question of how to define value. It is not a simple question.

“If I’m a patient, I might define value differently than an insurer or a health care provider,” Kutner said. Patients can have unsatisfactory experiences despite being what doctors might consider success stories.

D2V will address that disconnect by including stakeholders such as patient advocates and experts in public health and the insurance industry. Kutner believes that will keep the project focused on the ultimate goal, which is improving care.

Building technology and a team

D2V started work in 2016 by recruiting experts from across CU Anschutz. Kutner wants to take advantage of CU Anschutz’s collaborative
environment and current faculty members, researchers and staff.

“We have unique expertise here. We have outstanding data scientists. We have people who do world-leading work in care decision making and understanding stakeholder perspectives,” Kutner said. “We need to connect them behind a common goal.”

D2V also recruits researchers from around the world, with more people hired each month. Guest speakers from other leading institutions have given seminars to spark ideas.

Eight pilot projects are underway. They include a team trying to improve the databases that track children who have severe asthma attacks. That project’s goal is to test whether risk profiles can help create personalized predictions of when children might suffer attacks.

D2V will fund an additional six pilot projects in 2017.

Left, Jean Kutner, MD, is one of the leaders of the Data Science to Patient Value initiative. Photo by Glenn Asakawa/University of Colorado.

### D2V Scientific Cores

Data Science to Patient Value (D2V) consists of six cores which accelerate rigorous cutting-edge data science methods and applications to address pressing health problems, advance the science of person-centered high value health care across the care continuum by integrating different stakeholder perspectives including the UCHealth System as a learning and innovations partner.

The six cores and their missions are:

**Patient & Systems Value Core** - To focus on the science of value from multiple perspectives across the macro health care system.

**Data & Informatics Core** - To create and sustain investigators’ access to high-value data assets that are discoverable, accessible, and reliable to facilitate research in data sciences and discovery by providing ‘bleeding edge’ informatics expertise and tools.

**Analytics Core** - To be a multidisciplinary, collaborative analytic and computational research environment that catalyzes research resulting in innovative applications of complex analytic approaches, and development of novel analytic and computational approaches, methods, and tools.

**Stakeholder Engagement & Governance Core** - To become the most trusted resource on how best to engage diverse stakeholders in the work of research, implementation and dissemination in health care.

**Training & Education Core** - To train and mentor the next generation of scientists who can advance and integrate the methods of person-centered, high-value data science and health systems innovation.

**Dissemination & Academic Industry Collaboration Core** - To disseminate and showcase the work of D2V investigators and increase potential collaborative opportunities with external stakeholders that ultimately lead to increased scientific impact and sustainability of D2V.

### Three Goals of D2V

Michael Ho, MD, PhD, professor of medicine, co-director of the Center for Innovation at Denver and Seattle VA Medical Centers and co-leader of D2V, said the initiative has three primary goals:

- Advance the science of health care value that will impact patients, providers, the health care system and the community as a whole.
- Advance the science in data and informatics, and ultimately how we inform patients and deliver health care to improve value.
- Train the next generation of scientists in both areas.

Michael Ho, MD, PhD
Innate Immune Program Builds From Strength

Understanding the world of microbes inside the body

By Mark Couch

The GI and Liver Innate Immune Program (GALIIP) plans to build on strengths already on the CU Anschutz Medical Campus to expand understanding of some of the fastest-growing diseases facing society.

Costing the U.S. health system nearly $500 billion annually, gastrointestinal and liver-related diseases are significant burden, yet there is an unmet need in diagnosis, treatment and understanding of conditions such as fatty liver disease, eosinophilic esophagitis and inflammatory bowel disease.

A common element of these diseases is dysfunction of the immune system, particularly the innate immune system. The innate immune system is a first line of defense against infection by microorganisms and it plays a critical role in resolving inflammation after injury or infection. The innate immune system presents physical and chemical barriers to infectious agents, recruits immune cells to sites of infection, and identifies and removes foreign substances present in organs, tissues, blood and lymph.

“The concept of innate immune response is that it happens much sooner than adaptive response,” said Hugo Rosen, MD, professor of medicine and immunology, head of the Division of Gastroenterology and Hepatology and one of the leaders of GALIIP. “They’re kind of the first line of defense against a pathogen infection.

“Where an adaptive or T cell response takes four to eight weeks, this happens in hours to days,” he said. “And organs like the gut and the liver are characterized by a very high frequency, or what we call an enrichment, of these innate lymphocytes and nowhere else in the body do you find such concentration.”

In recent years, scientists have focused their attention on gaining a better understanding the concentrated microbe population living in the human intestines.

Sean Colgan, PhD, professor and vice chair for research in the Department of Medicine and one of the leaders of GALIIP, said, “The GI tract and the liver are termed mucosal tissues and a mucosal tissue is one that interacts with the environment, the outside world.”

“In particular, think about the gut,” he said. “The gut interacts with more bacteria, more microbes than any other organ in the body. And in fact one of the great strengths we have here on this campus is the microbiota work that’s going on.”

One of the leaders in that effort, Colgan said, is Catherine Lozupone, PhD, in the Department of Medicine's Division of Biomedical Informatics and Personalized Medicine. Using state-of-the-art, high-throughput gene sequencing and a groundbreaking algorithm she designed, Lozupone has published more than 50 papers, laying a foundation for a field believed to hold great promise for yielding more personalized treatments and prevention strategies.

GALIIP also draws on a rich legacy. Work by Norman Pace, PhD, who now is a Distinguished Professor of the University in CU Boulder’s Department of Molecular, Cellular and Developmental Biology and who previously held faculty positions at National Jewish and the University of Colorado Health Sciences Center, informs the program. Pace’s laboratory led the development and use of molecular methods to study microbial ecosystems.

“We have a very large footprint in microbiota analysis,” Colgan said.

The next step is to expand into new areas of discovery, outlined by GALIIP as:

• Mucosal innate immunity. Accumulating evidence indicates that the unique anatomy and complex architecture of the GI tract and liver provide cues that contribute significantly to both disease progression and resolution of mucosal disease. Compartmentalized tissue and microbe populations within the intestine, for example, result in significant metabolic shifts within these tissue microenvironments. During active inflammatory disease, metabolic demands often exceed supply, resulting in localized areas of metabolic stress.
• Microbiota. Advances in DNA sequence-based technologies now permit genetic analysis of complex microbial populations without
the need for prior cultivation. These molecular methods of culture-independent microbiology and their recent application to studies of the human GI tract in health and disease have served as a paradigm shift in understanding of host-microbe interactions. Upwards of 40,000 bacterial species are estimated to comprise the collective gastrointestinal microbiome, most of which have not been characterized.

- **Hepatic diseases and innate immunity.** Innate immunity is critical to the health of the normal liver and central to the pathogenesis of common hepatic disorders, such as non-alcoholic fatty liver disease (NAFLD). Given the epidemic of obesity in our society, NAFLD and subsequent liver fibrosis have emerged as a major morbidity risk. Innate immunity is central to the development of NAFLD.

Among the advantages for researchers at the CU Anschutz Medical Campus are existing repositories of specimens for research and the proximity of clinical centers for adults and children.

“We have been building repositories of human specimens. So in addition to murine models of disease, we have human models of disease,” said Rosen. “In my lab, we started a repository in 1999 and we now have over 60,000 specimens.

“Using those samples, researchers can look at the populations of cells residing over the liver and ask how many of these cells are autoimmune liver conditions, viral conditions, fibrotic-scar-forming conditions, and interestingly in the liver the predominant population is actually innate lymphocyte population,” he said.

With such knowledge, GALIIP researchers building a better understanding of the vast landscape of the microbiome and why it manifests differently in particular populations.

“One of our big pushes is to understand the differences between liver disease and gut disease in kids and in adults,” Colgan said. “So being on this campus and having Children’s Hospital and University Hospital here and the basic science is a big advantage.”

With the combined insights, GALIIP researchers hope to improve the understanding of the vast landscape of the microbiome.

“You get this genetic foundation in terms of what's known about certain receptors, or certain pathways, that are regulated genetically, but there is so much more going on within the microenvironment,” Rosen said.

*Left, Sean Colgan, PhD, and Hugo Rosen, MD. Below, Hugo Rosen, MD, with researchers in his laboratory. Photos by Trevr Merchant.*
Harnessing the Power of the Human Immune System

Building a strong base for immunology and immunotherapy research

By Mark Couch

Treating disease by harnessing the power of the human immune system has emerged in recent years as a critical area of inquiry in medical science.

On the CU Anschutz Medical Campus, the Human Immunology and Immunotherapy Initiative (HI3), one of the five Transformational Research Funding projects funded by Dean John Reilly, MD, has been organized to provide focus and resources for such an effort.

Immunotherapy, which was described by Science magazine as the Breakthrough of the Year in 2013, has led to major changes in the standard of care for some diseases and is particularly useful in infectious disease, autoimmunity, allergy and asthma and has been widely recognized for its potential in treating cancer.

"Immunotherapy is important because, first of all, it represents a sea change in how we approach therapy in cancer," said John Cambier, PhD, chair of the Department of Immunology and Microbiology and one of the directors of HI3.

"As a field we've been working for decades to understand enough about cellular interactions in the immune system to get to a place where we can intervene and almost all of those studies have been in the mouse. It's really only in the last 10 years or so that we've gotten to the point where we can take all that basic knowledge and formulate it into therapies."

During its initial year, the leaders of HI3 have targeted their efforts on assembling the scientific and clinical infrastructure needed to boost the impact of researchers working on and recruited to campus.

"We made a conscious decision to take a go-slow approach, putting together all of our infrastructure pieces in a thoughtful and careful manner," Cambier said.

"Any and all new recruits who are clinical scientists, who have translational as well as clinical delivery interests and intent, are going to need a certain infrastructure that doesn't really exist on the campus, so we're putting our money right now into building that essential infrastructure.

In addition to recruitment, our main focus was to establish resources to test and monitor the state of the immune system in research studies aimed at discovery or in clinical trials aimed at monitoring patient care."

To that end, HI3 has established the Human Immune Monitoring Shared Resource (HIMSR) to fill in gaps between clinical and basic science research, providing sample preparation and immune-based assays. Equipment for sample processing, cell sorting, cytometry, cutting-edge imaging, and data analysis are among the pieces obtained or managed by HIMSR.

"It'll probably be over $1 million worth of equipment in the end," Cambier said. "We've taken delivery of what we had the space to accommodate. There are a number of investigators across campus, as well as external investigators, who have expressed interest in using the HIMSR for their studies. So there is already a queue to use this share resource. HIMSR is already working with more than 20 groups on campus that want access to these services."

In addition, HIMSR offers free initial project consultation regarding research endpoints, the selection of appropriate assays. The HIMSR also offers coordination of investigators with available statisticians and bioinformaticians to assist in study design and data analysis, and will continue to ask the scientific community for ideas related to testing and development of new technologies for immune monitoring.

The equipment and services – scientific and clinical infrastructure – are essential to building a strong foundation for the future of immunology research and immunotherapy on campus and to fulfilling HI’s mission. The foundation of the initiative – an all-inclusive facility providing experimental models for the preclinical testing of new candidate therapeutics, reliable immunotherapeutic production, consistent clinical trials research support, and organized immune monitoring capabilities – is fundamental for any future HI efforts. The ultimate goal is to establish preeminence in human immune system-targeted therapies on the CU Anschutz Medical Campus.

From there, HI3 plans to train future scientific leaders and recruit exemplary faculty.

"One of the purposes of bringing in really strong mid-to-senior faculty is that we'll bring in people who have a history of innovation, who have shown in the past that they can do that part of it," Cambier said.
HI³ is already recruiting high-profile researchers in partnership with other programs on campus, such as with the pediatric oncology program at Children’s Hospital Colorado. Internationally renowned recruits will help attract other faculty to campus.

“They will be important in doing the second-level of recruiting of people, who will probably be younger,” Cambier said.

There are other HI³ searches underway.

“We have three standing search committees: one looking for basic scientists who are focused on human immunology and translation, one in the autoimmunity space and that will be for clinician scientists and then one in the cancer immunotherapy area,” Cambier said.

One of the challenges of recruiting the top specialists in immunology and immunotherapy is that many other institutions are targeting this area of research.

“The reality is that everybody is trying to find these same people, so competition is keen,” said Cambier, who added that one potential recruit was interested in joining CU and then his home institution received a $150 million philanthropic contribution to support immunotherapy research. Each area requires a specific approach, akin to building a baseball team through free agency and by developing talent on the farm-team system.

“There are different strategies to recruiting faculty and in basic science departments, we do it very differently than normally its done in clinical departments,” Cambier said.

“In clinical departments, at least in the context of these searches, we want to find targets of opportunity. People who we think would add significantly to the expertise in the place.

“Whereas in the basic sciences, we are primarily interested in people who are early in their career. So you approach it in a different way, by advertising to see who shows up. So on the clinical side, you grow your own, meaning you have fellows in your program that you eventually bring on to the faculty or you find targets of opportunity.”

Andrew Fontenot, MD, professor of medicine in the Division of Allergy and Clinical Immunology and one of the directors of HI³, agreed that the goal is to bring in people who are “programmatic builders” who will help increase the number of RO1s on campus.

The potential benefits of immunotherapy, the demand for innovative care, the need to pick up the pace in comparison to some other institutions and to take advantage of the opportunities to serve patients will be driving forces for HI³ in the years ahead.

“We have a huge catchment area in terms of patients and we have nobody in the region who’s trying to serve it on the scale that the demand would dictate,” Cambier said. “So the idea is to get us up to speed, not only on the delivery of the therapies that are out there, checkpoint inhibitors and CAR T-cells, but also to innovate and develop the next generation of therapeutics.”

Left, John Cambier, PhD. Photos by Trevr Merchant.
RNA Bioscience Initiative Off to Fast Start

New program has productive first year

By Mark Couch

As Richard Davis and David Bentley explain it, the RNA Bioscience Initiative is the center of universe, the theory of everything and the best way to improve our knowledge of life on Earth.

“RNA is associated with every cell. It doesn’t matter what disease. It doesn’t matter what topic. It’s relevant to virtually every cell in everything,” said Davis, PhD, director of the RNA Bioscience Initiative and professor in the Department of Biochemistry and Molecular Genetics.

Davis’ fellow director of the RNA Bioscience Initiative, Bentley, PhD, professor of biochemistry and molecular genetics, is similarly expansive.

“RNA biology is a very inclusive field because it has really expanded so much, it’s sent its tentacles out in so many directions,” Bentley said. “It’s got applications that go far beyond basic science. It’s an ideal initiative in a medical school because it’s something that clinicians and basic scientists can unify around and share common interests.”

The RNA Bioscience Initiative is one of the five Transformational Research Funding projects funded by Dean John Reilly, MD, and in its first year, Davis and Bentley have sprinted out of the gate with a far-reaching community-building, faculty-recruiting, apprentice-training, grant-making, technology-testing program.

The excitement of being scientists in charge of crafting an influential new campus program has been focused by the administrative responsibility of the task.

“It’s very exciting and it’s a lot of work” said Davis.

“I feel good about the fact that we’re spreading money for RNA biology kind of far and wide and diffusely about the campus,” Bentley said. “I would also say I feel rewarded that there’s such good interaction with people in medicine, with clinicians. I think we’re making some headway in getting them integrated. We will continue to do that.”

In its first year, the RNA Bioscience Initiative has

• Provided seed grants to nine campus investigators to support research projects, selected from about three dozen applications;
• Supported four graduate students for a year as RNA Scholars;
• Hired a new faculty member and continued to recruit others;
• Created an RNA Club where students, postdocs and faculty give 45-minute chalk talks about their research;
• Purchased a controller for generating single-RNA sequencing libraries that will be available for researchers through the campus Genomics Core;
• Sponsored a seminar series, branded by the RNA Bioscience Initiative, bringing distinguished lecturers and emerging leaders to campus.

The scope and pace of activity are intended to expand the RNA expertise in the campus research community and to make crucial connections with clinicians and educators. Understanding the basic biology is a necessary step to establishing diagnostic capabilities and therapeutic breakthroughs that will improve the human condition.

“It’s really pretty much all-encompassing,” Davis said. “It spans the whole thing. Probably more than any other field, there have been more surprises in how pervasive RNA is in its regulation of different things and its different functions than in almost any other field.”

Making that point clear is the list of seed grant recipients who are researching kidney disease, breast cancer, ovarian cancer, embryonic cells in neural development and myelodysplastic syndrome. The applications for grants up to $50,000 came from “endocrinology, pathology, infectious diseases, pharmacology, rheumatology, anesthesiology, neuro, I mean it’s everything,” Davis said. “And it really spans a very broad spectrum.”

While the reach of the program is wide, Davis and Bentley are attentive to the details in how the RNA Bioscience Initiative manages interactions of participants.

For example, the RNA Club speakers are specifically instructed to engage in “chalk talks” rather than to present projected images on a screen.

“They’re not supposed to use slides,” Davis said. “They’re supposed to draw. It’s designed to be informal, to engage, and to have more interaction and more discussion.”
And they practice what they preach. In presentations about the RNA Bioscience Initiative to the School of Medicine's Faculty Senate and Executive Committee, Bentley wrote on a whiteboard rather than using the PowerPoint presentations that are usually presented.

The initiative’s community-building endeavors have extended beyond the boundaries of the Anschutz Medical Campus. The leaders have chartered buses to take members of the RNA Bioscience Initiative to meetings of the long-established RNA Club at CU Boulder.

The initiative has also established relationships between beginners and experts. A summer internship program welcomed six undergraduate students, who were paired with faculty mentors, as they sought to gain laboratory experience.

The undergraduates attend lectures on RNA by Davis and on how to design experiments by senior faculty. “Every mentors’ lab had to have someone come in and talk about research and give a presentation,” Bentley said. “There was an educational component.”

“These are kids in college who want to get exposure to research because they want to find out what it is,” Davis said. “Maybe they know they want to go to graduate school and they know they have to have that experience. If they want to go to medical school, it also won’t hurt to have that experience.”

“And maybe we’ll attract them later,” Davis said.

The RNA Scholars, who are four graduate students on the Anschutz Medical Campus, get a stipend and a small discretionary fund – $2,000 – to support their work. They can use it for a computer or to attend a meeting. In addition, the leaders have created the RNA Bioscience travel award, which supports students who got to meetings and present posters or give talks.

While strengthening the campus community, the RNA Bioscience Initiative is also investing in support services for those conducting RNA-related research, evaluating sequencing equipment and hiring Kent Riemondy, PhD, as an informatics fellow.

That expertise is critical for researchers because the amount of data can overwhelm the capacity to understand it, so improving the ability to conduct the analysis is paramount. “Many people consider it the rate-limiting step in analysis today,” Davis said.

All the while, the program has also been actively looking to hire rising stars in the field, posting ads and bringing prospective faculty members to campus. The RNA Bioscience Initiative recently announced that Olivia Risland, PhD, assistant professor of molecular genetics at the University of Toronto, will be joining the School of Medicine faculty this fall.

Left, David Bentley, PhD, and Richard Davis, PhD. Below, Richard Davis, PhD. Photos by Trevr Merchant.
Exercise Expert Offers His Take on Lactate

CU physiologist studies connection to cancer

By Lisa Marshall

For decades, lactate has been studied largely in the context of exercise, painted as a nagging metabolic byproduct that accumulates in the tissues and blood during workouts, stiffening muscles and hindering performance.

Now a new paper, published in February in the journal *Carcinogenesis*, paints the complex, often misunderstood, molecule in a more sinister light—as a key driver in the development and spread of cancer.

Its authors say the paper could help explain why people who exercise tend to have lower rates of cancer—because their bodies are able to more effectively process the lactate we all produce when we metabolize sugar. It also could lead to new treatments.

"With this paper, we open a whole new door for understanding cancer, showing for the first time that lactate is not only present, but mandatory for every step in its development," said lead author Iñigo San Millán, director of the sports performance department and physiology laboratory at the CU Sports Medicine and Performance Center at CU Boulder.

San Millán, also an assistant professor in the School of Medicine’s Department of Physical Medicine and Rehabilitation, spent two years working on the paper with University of California Berkeley professor and renowned lactate researcher George Brooks. The team applied lessons learned from dozens of exercise physiology and muscle metabolism studies conducted at CU Boulder, the CU Anschutz Medical Campus, the University of California and elsewhere to try to answer a century-old question: How does a normal cell become a cancer cell and then what happens?

As far back as 1923, German Nobel laureate Otto Warburg observed that cancer cells take in exponentially more sugar, or glucose, than normal cells. They also inefficiently convert far less of it into ATP, or energy, converting about 70 percent of it to lactate as a byproduct. The phenomenon—the first sign of a normal cell turning cancerous through abnormal cell metabolism—is known as the “Warburg effect.” The paper seeks to explain why it happens.

With heightened focus on genetics in recent decades, many researchers moved away from studying cancer metabolism, and the role of lactate became overshadowed, San Millán said. He hopes to help swing the pendulum back.

The paper illuminates the role lactate plays in fueling angiogenesis (the formation of new blood vessels in tumors); how it interferes with the body's immune response to cancer; and how it creates an acidic microenvironment (the space outside the cancer cell) supportive of cancer metastases, or spread. The paper also theorizes how three major transcription factors, or proteins, involved in most cancers (HIF-1, cMYC, and p53) kick-start and perpetuate lactate deregulation in cancer.

The paper draws parallels between what happens in the muscles of an athlete in training, and what happens in a developing cancer.

“During high-intensity exercise, working muscles display many of the same metabolic characteristics as cancer cells,” explains San Millán, a former pro cyclist and physiologist to Tour de France cyclists. Muscles take up large amounts of glucose, turning it to energy inside the mitochondria and churning out more lactate than the body can immediately clear.

In a healthy person, Brooks' research has shown, the body then recycles that lactate for beneficial use—turning it into a key source of fuel for the brain, muscles, and organs, preventing it from building up.

In cancer, the authors suggest, that recycling system breaks down.

San Millán hypothesizes that while people who exercise regularly are at less risk of cancer—in part due to their body's ability to clear lactate more efficiently—a sedentary lifestyle, combined with excess sugar intake may fuel lactate accumulation and kick-start the metabolic misfiring that can lead to cancer.

The authors hope cancer researchers will use the paper as a starting point for further studies. Already, San Millán is studying breast cancer cell lines, and this summer he will team up with University of Colorado Hospital to study the impact of personalized exercise programs on cancer patients.

Ultimately, he hopes the paper could lead to new exercise and dietary prescriptions for cancer patients, new diagnostic tools that could use deregulated lactate signaling as a marker of a brewing cancer, or new drugs which target MCT Transporters, which are responsible for transporting lactate from cell to cell.

“We hope to sound the alarm for the research community that to stop cancer you have to stop lactate,” he said. “There are many ways to do that.”
Caring for Saddam Hussein

Joseph Horam assigned to treat former Iraqi dictator

By Tonia Twichell

By 2006, a desert deployment did not faze Col. Joseph Horam, MD.

Horam had already deployed twice to the Middle East, including serving in Saudi Arabia during Desert Storm. After he transitioned from the active Army in 1994 and joined the Wyoming National Guard, he assumed deployments abroad were behind him.

“I thought ‘That’s the last I’ll see of this. That’s the once-in-a-20-year event,’” said Horam, a 1987 graduate of the CU School of Medicine. “Little did I know this kind of deployment would be recurring.”

When Horam received a call in early spring 2006 asking him to come a month early to Iraq, he was experienced enough to suspect a high-level assignment was in the cards.

Upon arrival in Baghdad, the commander of special missions asked if he’d like to learn more about his new patient, VIC.

“Vic?” Horam asked.

Very Important Criminal, aka Saddam Hussein.

At that point, the former Iraqi dictator had been in custody for three years, facing multiple charges of crimes against humanity and a likely death sentence for atrocities that included the massacre of more than 140 people in the town of Dujail after an assassination attempt in 1982.

Horam arrived in Iraq at a particularly fraught moment. The Abu Ghraib torture and abuse scandal, in which members of the U.S. Army and Central Intelligence Agency committed a series of human rights violations against detainees and which led to the deaths of at least two people, remained in the news.

“Memories of the atrocities were fresh. I learned that Saddam was to be kept in optimal health to allow for justice to prevail – or the show could go down,” he said. “No pressure!”

Horam knew the job overseeing the health of the combative former dictator would be far more complicated than ordering lab tests, reviewing medicine and performing physicals.

Care included building trust, which meant smoking cigars together in the evening, enduring Hussein’s rage when Horam wouldn’t help mediate a pardon for him, and nursing him through two hunger strikes.

Hussein’s charisma was notable, but Horam knew not to put much stock in it.

“I always recognized him for being a brutal dictator.”

Always in a Medical Setting

A lifetime of patient care had prepared Horam for this unusual assign-
Being a pediatrician was never an obstacle. “When you look at the statistics, about 40 percent of soldiers are 24 years old or younger. Plus, pediatricians are pretty good with infectious disease, mental health and comprehensive team management of complex patients.”

While there, he again had medical encounters with enemy combatants.

“Regardless who comes in, there is a moral obligation to provide humane care. You’re not going to win hearts and minds. That’s not going to happen when you take care of the enemy. You do it because it’s the humane thing to do.”

Treating Saddam Hussein

Hussein’s body had taken a beating over the years, and treatment included care for old shrapnel wounds, hypertension with adrenal adenoma and other issues common for a 67-year-old man.

Upon arrival, Horam was handed a foot-tall stack of papers documenting Hussein’s medical care under coalition forces.

Horam also cared for several members of Hussein’s cabinet, many other high-level detainees, and U.S. soldiers at Golby Troop Medical Clinic. But as Horam expected, the forceful, narcissistic former dictator had a way of insisting he was patient No. 1.

“He knew I was going to be his advocate for his medical care. But he started believing that I was also his advocate for his personal agenda. One thing I never bought into is that I would become sympathetic for his cause.”

Hussein was proud of his accomplishments as the country’s leader, often talking about improvements to the country’s education, military, government, medical care and economy, as well as promoting religious diversity in his administration.

Hussein knew that the U.S. was struggling in Iraq, and he believed he could serve as a mediator and leader in a new government.

“His agenda was basically that he was the one person to lead his country. He was willing to do it in partnership with the U.S. government. Ultimately he was angry with me for not having the level of influence to get the political and military leadership to meet with him and bring his issues forward.

“He threatened to fire me at least three times.”

To show his frustration with his American captors and the Iraqi court proceedings Hussein went on two hunger strikes – the first was brief, the second was 19 days long.

Horam’s concern was Hussein’s mental condition.

“There was a point when he was less energetic, and the thing you have to realize is that we were coming up on the latter part of his court hearings. We risked acquittal if he appeared weak and in less than optimal health.”

Horam decided he needed some assurance that Hussein was not in danger of starving himself to death, so he asked a psychiatrist on staff for a set of questions.

“We needed to make sure we were not in a situation where his competency was compromised. So I asked the questions and the psychiatrist analyzed the answers. His opinion: It was not a hunger strike to the death. It was a hunger strike for protest and behavior manipulation.”

At that point, Horam was living in the prison that housed Hussein and his former cabinet, and he felt the heavy burden of his responsibility. “I was always a little more intimidated by the process than by my patient.”

While there were always guards nearby, Horam was often alone with Hussein and the other incarcerated detainees.
"I did feel at times that if he had a weapon of choice, he would not have hesitated taking me out. There was a certain rage sometimes ...."

But there were quieter moments. Hussein liked to host his American captors for dinner and Cuban cigars, which were provided by the Red Cross.

“He talked about his family and religion. He was interested in different philosophies, and sometimes just liked to sit and listen to our discussions when we would talk about our own issues. He could be very contemplative.”

Hussein often wrote poetry and read Hemingway, Horam said. Sometimes he would gather with his former cabinet.

“When they would get together he was in his element. He was still in charge.”

Horam once asked Hussein about U.S. intelligence reports during the first Gulf War that indicated Iraqi forces were prepared to use Scud missiles armed with chemical warheads against U.S. troops. In response, hospitals had been set up and 12,000 beds readied for casualties.

“I asked Saddam what actually happened in Desert Storm when we were getting pretty high alerts about chemical threats. He said, ‘There was too much consequences.’ He had cancelled the bombardment. Reading between the lines, I think he had a sense that there were some limits on what he could do.”

Keeping a Secret

Horam left Iraq about four months before Hussein’s execution. Their parting was respectful.

“He commented that I had a personal interest in him, not as a prisoner, but as a person. That I had cared.”

Horam introduced Hussein to his new doctor, and admits to worrying a bit about Hussein’s care. (“The new doctor did fine,” Horam said with a smile.)

For 10 years Horam kept quiet about his patient due to non-disclosure restrictions imposed by the military. He returned to his medical practice at Cheyenne Regional Medical Center, grateful for partners who had cared for his patients during deployments, and is medical director of Blue Cross Blue Shield of Wyoming. (He deployed one more time - to Kosovo in 2009 as part of a multinational task force.)

He still thinks about the man he now describes as his “easiest patient ever.”

A few years ago, he was at a gathering with other physicians, some of whom had also cared for Hussein during his incarceration. Horam’s wife, Carol, was talking with the other wives.

“One of the other spouses came over and said, ‘You never told Carol about being Saddam Hussein’s doctor?’”

Carol Horam wasn’t upset about being kept in the dark, but, with a laugh, Horam said she now understands why he didn’t call home to talk with her and their three children very often during that particular deployment. Plus, “Carol always knew there was more to my story about receiving a Bronze Star,” he said.

Horam has since retired from the military after 27 years of service and has a lifetime of stories about his adventures abroad.

“I miss it,” he said. “I really do. I would do it again. The experience gave me a sense of purpose and allowed me to fulfill service to state and nation as a medical officer assigned to the U.S. Army that was unique.

“I felt I did an excellent job as a military doc.”
Cultural events hosted by the Medical Alumni Association have been popular with our alumni.

Last October, A Night at the Ballet brought together more than 350 alumni, students, and residents, who made new connections and enjoyed the Colorado Ballet’s presentation of Tchaikovsky’s Swan Lake. The evening offered enjoyable conversation, delicious food, and breathtaking performances.

Past Medical Alumni Association programs have included behind-the-scenes tours at art museums, superb performances by renowned symphony orchestras, and themed evenings at the opera.

The Association is enthusiastic about the steady interest in the cultural programming. We appreciate those who supported the event and we hope to see you soon at future alumni outreach events.

Medical Alumni Association members are now eligible for discounted tickets to some of the most masterful performances in Colorado including those by CU Presents, Opera Colorado, the Colorado Symphony, and the Colorado Ballet. Take advantage of these discounts, reconnect with fellow CU School of Medicine alumni, and join our efforts to grow appreciation for the arts.

To learn more or suggest other partnership opportunities in your area, please contact the Office of Alumni Relations at 303-724-2518 or email healthalumni@ucdenver.edu.
Dear Alumni,

At the University of Colorado’s Medical Alumni Association, we are celebrating spring. It is when prospective medical students visit us on campus and are amazed by the opportunities offered by our School. Our spring tradition is to join fourth-year medical students for Residency Match Day and celebrate their recent academic achievements. This is also the time of year when we put the finishing touches for the upcoming Alumni Weekend and Reunion that is May 25-27, 2017.

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

• Last August, we welcomed 184 first year medical students and presented each of them with a new stethoscope branded with the Medical Alumni Association logo.

• Our Association provided first-and second-year medical students with quarterly connections, including a Halloween breakfast, a December lunch, and a Valentine Dessert party. Each event is a bonus to a busy, rigorous week of coursework.

• Through the HOST (Help Our Students Travel) program, alumni from across the United States provided travel and housing accommodations to fourth-year medical students as they interviewed with some of the country’s best residency programs.

• Expanded our annual all-alumni event. A Night at the Ballet brought out more than 350 people- 33% Student; 33% Residents, Interns, and Fellows; and 33% alumni and faculty.

• Hosted two Medical Alumni Association regional events – one in Washington, D.C. and the other in Grand Junction.

• The Association awarded the $5,000 Medical Alumni Association Scholarship recognizing a student for outstanding academic performance and commitment to the work of the Medical Alumni Association.

• We offered significant benefits to the student population with the Stethoscope Sponsorship Program, and the Medical Alumni Association Scholarship Fund, just to name a couple.

Now, imagine what we can accomplish next year and beyond. The mission of our Association 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. This past year has been a testament to effectively meeting this charge, but we cannot do this important work without you!

There are numerous ways to help advance the work of the Association and the School of Medicine, and our incredible network of alumni do so each and every day. Take a moment to contact us and share a recent, exciting achievement. If you graduated in a year ending in a 2 or 7, consider becoming an ambassador and invite your classmates to Reunion Weekend 2017. Perhaps you would like to join our board of directors and help form the strategic direction of the Association. Your ongoing participation is vital to the Association’s success.

If you would like to participate in any of our programs, support our efforts, or update your contact information, please contact our alumni office at healthalumni@ucdenver.edu or call 303-724-2518.

We would love to hear from you!

With Appreciation,
Wag Schorr, MD ’63
President, Medical Alumni Association
All in the Family

Four generations of CU School of Medicine physicians

By Chris Casey

The Kenagy-Vance family line of physicians stretches across states, continents and generations, but a common thread connects them: the University of Colorado School of Medicine.

Four generations of men in the Kenagy-Vance family have cared for patients in Switzerland, Pennsylvania, Idaho, Minnesota and points beyond after earning medical degrees from the University of Colorado.

John Brough “JB” Kenagy started it all in 1906 when he graduated from the School of Medicine – then located in Boulder.

The next two physicians in the family – Fayre H. Kenagy (class of 1920) and J. Corwin (Corky) Vance (class of 1971) – attended the medical school in Boulder and then the CU Health Sciences Center in Denver, respectively.

The gap between medical school graduates Fayre and Corky is because Corky’s father, Edward Pershing Vance, who married Barbara Eloise Kenagy, chose a different path: He pursued a successful career in natural resource stewardship in the Pacific Northwest.

Karl Kenagy Vance, son of Corky and Karen Vance, extended the family’s black-and-gold bond into the 21st century by attending medical school at the CU Anschutz Medical Campus from 2005 to 2009. Karl had applied to about 10 medical schools, but chose CU.

“The combination of the high-quality education at the medical school and the lifestyle of being in Colorado factored in,” said Karl, who is an avid cyclist and skier. “Also, it was something I thought would be cool – that I would be the fourth generation of my family to go to the CU School of Medicine.”

Before CU

The history of physicians in the family dates back to Bern, Switzerland, where Corky’s sixth great-grandfather, Hans Gnage, practiced medicine before fleeing the country at a time when Mennonites faced religious persecution.

“Family legend has him seeing a patient when the police came to arrest him for draft evasion,” Corky said. “His wife had the policeman sit down to wait for him and offered food and drink, but then sent their son to tell his father to leave the country instead of coming home. His family joined him later.”

Hans arrived in Pennsylvania in 1742, joined the Amish community, and resumed work as a physician. It would be several generations later when JB Kenagy, born and raised in a Mennonite community in Ohio, and already established in a career as an educator would carry on the family tradition of medicine.

JB studied at the Kansas Normal School in Fort Scott, then moved to Colorado to teach, first in Buena Vista for four years, then for three years in Gunnison, where he was the principal. He then decided to become a physician, moved to Boulder and entered CU medical school and graduating in 1906 at age 43. He moved to Rupert, Idaho, to practice internal medicine.

JB’s son, Fayre Kenagy, aspired to become a doctor like his father. Though he was drafted into the military during World War I, he received a deferment to finish his medical degree.

Keeping the CU tradition going

Fayre delivered J. Corwin Vance in August 1945, starting a lifelong bond with the boy who went by the nickname Corky.

“I was in awe of my grandfather and wanted to follow in his footsteps. I therefore also attended the CU medical school,” Corky said. “When Karl was born, we named him Karl Kenagy Vance, after his great-grandfather. He later decided to attend the CU medical school as well, having heard how great it was.”

Corky Vance is now retired, but Karl worked with his father during the final year of his practice in Minneapolis. Karl now works with several of Corky’s longtime staff members, though in a different dermatology practice.

The Twin Cities are a fitting home for the father and son because they have paired interests in fine food and wine and in international travel. When Corky and Karl aren’t pursuing culinary interests, you might find them on their bicycles or in planes traveling the world. Sometimes they’re globetrotting and cycling – as they did on a family trip to Italy last fall.

Both father and son met their wives while attending the CU medical school. Corky met his wife, Karen, while she was a lab technician, and Karl connected with Pamela while out on the town with classmates.

Just as Corky was inspired to pursue medicine by his grandfather, Karl looked up to his father, who became the first dermatologist in the Twin Cities to perform Mohs surgery – a microscopic procedure that removes skin cancers.

“He found it rewarding. Growing up around medicine, you get an understanding of the process, the responsibilities and the ups and downs of it,” Karl said. “Mostly, it’s a fulfilling career because it’s a daily opportunity to help people.”
Camaraderie with CU classmates
Karl enjoyed the camaraderie with his classmates at CU Anschutz after struggling to connect with pre-med classmates at Stanford University. He excelled in chemical engineering, and it wasn’t long before he connected that discipline to a growing interest in wine. After graduating from Stanford, he became an assistant wine maker in Northern California and Australia. A few years later, however, he realized that winemaking couldn’t quite match the fulfillment of medicine.

At CU Anschutz, Karl loved his classmates. “It was hard to find people who weren’t into skiing and biking,” he said.

While in school, he was influenced by J. Ramsey Mellette, MD, the faculty member who trained him on Mohs surgery. Back in the 1970s when Corky first performed Mohs, it was a new and innovative procedure. “Now, this procedure is pretty widespread,” Karl said. “I like it because of the precision in which we take the cancer out, and I enjoy the creativity involved in the reconstruction (of the tissue).”

Mohs is usually performed on a patient’s face, so the reconstruction of the skin requires utmost precision to minimize scarring.

Finding a mentor
Corky was inspired to pursue dermatology by Robert Goltz, MD, who in the late 1960s served as head of the Department of Dermatology in the medical school. Corky so enjoyed Goltz’s teaching that he took the professor’s early-morning class on public health.

“Dr. Goltz noticed that I was a hard worker, that I liked dermatology and was good at it,” Corky said. “I was good at visual learning, and that’s why dermatology appealed to me. You have to be able to memorize what rashes and other conditions on the skin look like.”

Goltz proved to be the catalyst for Corky’s career in Minnesota. Goltz, who had just accepted a job as chair of dermatology at the University of Minnesota, suggested Corky pursue his residency in the Land of 10,000 Lakes.

Now, as Corky and Karen settle into retirement, they watch their progeny carry on the Kenagy-Vance caregiver tradition. Karl has established his own thriving practice in Minneapolis, while his sister Chardonnay, who attended medical school at Wake Forest University, is a family practice doctor.

“The most important thing is your job,” Corky said. “If you have a miserable job, you’ll be miserable wherever you are. If you have a rewarding job – as we are lucky enough to have – you’ll be happy.”

MISSION STATEMENT
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Geneticist Pushes Limits in Lab and in Life

Vitiligo expert Richard Spritz races cars, hikes Himalayas while doing groundbreaking research

By Michael Davidson

Richard Spritz, MD, likes to be on the edge. Spritz, director of the Human Medical Genetics and Genomics Program, loves the rush of pushing his vintage Porsche 911 around a racetrack. He hikes in the Himalayas, and spent his most recent vacation trekking across a remote island, following the footsteps of famous Antarctic explorer Ernest Shackleton.

A career spent in a laboratory might seem less exciting, but not for Spritz. While he once was an accomplished mountain climber and survived two avalanches while backcountry skiing, he says his passion is not for taking risks—it is for the thrill of doing something new.

“I think that science is an incredibly adventurous thing. You’re always pushing beyond what’s known,” Spritz said. “I’m not an adrenaline junkie. Other people might call me that. I’ve just always been attracted to adventurous things.”

In Spritz’s eyes, there have been few bigger adventures in recent decades than the quest to understand genetics and use that knowledge to cure diseases.

Fateful decisions

Spritz, 66, is one of the world’s leading vitiligo researchers. For almost two decades, he’s been conducting groundbreaking work understanding the genetics behind the skin pigmentation disorder that causes white patches to appear on the face, body and hair. An estimated 50 million people worldwide have the condition, and Spritz has worked closely with international vitiligo organizations.

Spritz is from Philadelphia, but feeling the mountains’ call, he became an accomplished mountain climber in his youth. Successful ascents in the Alps, including the notoriously dangerous north face of the Eiger, earned him the respect of the climbing elite, and in the 1970s an invitation to climb Mount Everest.

Spritz declined because he was in medical school and did not want to disrupt his career. “I absolutely made the right choice,” he said.

“It’s mostly out of my system,” Spritz said. But he’s not through going on adventures, and last fall he hiked across South Georgia, an island near Antarctica. Peter Hillary and Jamling Tengzin Norgay, the sons of the first two men to climb Everest, were on the trek. They were filming a documentary for National Geographic about Shackleton, who had to cross the mountainous island to rescue his stranded crew.

Spritz made a career-defining decision “literally one day while walking down the street,” he said. He had planned to become a surgeon, but realized genetic research was a better fit for someone seeking to push scientific boundaries.

“I was incredibly lucky, because I did that at exactly the right moment in history, at the beginning of recombinant DNA research,” Spritz said. “I was lucky to get in on the ground floor.”

In the late 1970s, researchers were just discovering how to isolate, identify and sequence human genes. The biggest early discovery Spritz was part of was finding and sequencing a mutation that affects hemoglobin, the molecule that carries oxygen in the blood. It was the first time a mutation had been sequenced.

Still making discoveries

In October, Spritz and his lab published a paper in Nature Genetics finding 23 genes linked to susceptibility for vitiligo. The lab tested 4,680 people with the condition and 39,586 control cases. The study attracted the attention of pharmaceutical companies, which Spritz said is good news because a medication to treat vitiligo could be a major step forward from the current steroid and ultraviolet light treatments.

“Despite the fact that vitiligo has been known for hundreds of years, there’s never been a drug developed for it,” Spritz said. “That might change in the near future.”

People with other conditions might benefit as well. In the mid-2000s, Spritz established that vitiligo was an autoimmune disease, in which the body attacks its own skin pigmentation cells. Research has shown people susceptible to vitiligo have increased odds of other autoimmune conditions such as Type I diabetes, rheumatoid arthritis and Addison’s disease.

Vitiligo research could lead to progress understanding those conditions, and vice versa.

That would be the next chapter in an ongoing scientific adventure.

“It’s amazing to me how far we’ve come, how naïve we were and yet how prescient we were at the same time,” Spritz said. “We are asking and answering the kinds of questions we couldn’t have imagined when I was a student. I think that’s incredibly inspirational – and we’ve hardly started.”
Honoring a Patient

By Lilia Cervantes, MD

I am a Latina physician who had been a full-time clinician until 2014 when I began pursuing a research career. I am driven by a passion to change local and national policy to improve access to care for undocumented immigrants with end-stage renal disease (ESRD).

As a physician at Denver Health, I became closely acquainted with an undocumented Mexican patient who had ESRD with severe symptoms. In Colorado, undocumented patients can only receive dialysis when they arrive critically ill in the emergency department.

My patient was homeless. She had two boys in elementary school. She had previously suffered three cardiac arrests. Her goal was to be comfortable. She asked to withdraw from dialysis, to have a natural death.

I gathered a multi-disciplinary team. Together, we found her a temporary home while we worked with an adoption agency to find a family that adopted her children. We then sought assistance from the Mexican consulate, securing her a passport to return home to Mexico. She wanted to pass away in her father’s home.

My patient’s story has inspired me to help others like her and her experience continues to ground my research vision.

Soon after she passed away, and while I was working as a full-time clinical hospitalist, I wrote a research proposal to improve palliative care in Latinos with ESRD. I was awarded a four-year Harold Amos Medical Faculty Development stipend from the Robert Wood Johnson Foundation.

My transition from full-time clinician to a practicing physician with a research portfolio has been both challenging and exciting. My childhood shaped how I respond to challenges. I grew up in the Valverde neighborhood on Denver’s west side and I faced food insecurity, homelessness, and learned English as a second language.

With each challenge we faced as a family, my parents taught me to be tenacious, to use education to empower myself to change the well-being of my community, and to believe that the impossible is possible.

Many thought it would be impossible for me to switch from a clinical to a research track after working as a full-time hospitalist for six years. It has now been two years since I received the Harold Amos Medical Faculty Development award. I am determined to succeed and become an independent researcher.

My research to shape public policy and change access to care for undocumented immigrants with ESRD has informed others of the experiences of patients whom they might have not noticed previously. These studies have included qualitative interviews of patients describing their illness experiences, which was published earlier this year in JAMA Internal Medicine; a retrospective analysis looking at mortality differences between emergency-only and routine thrice weekly hemodialysis among undocumented immigrants, which is currently in review for publication; and qualitative interviews of healthcare professionals who provide care for undocumented immigrants with ESRD to describe their perspectives, which is currently a work in progress.

My patient passed away three years ago now. I have remained in touch with her boys and the people who surrounded her during her last weeks in Colorado.

This past year, we all came together for Day of the Dead at the Denver Botanic Gardens to celebrate her life by creating an altar in her honor. We all reflected on how her life had inspired and changed us for the better.

Lilia Cervantes, MD, is an associate professor of medicine and a hospitalist at Denver Health and Hospital Authority.
The University of Colorado School of Medicine strives to provide veterans with the resources they need to complete a high-quality medical education and receive the exceptional patient care they deserve. You can fuel our efforts by supporting scholarships for student veterans and help them transition from combat to classroom to career.

Support our student veterans with a gift to the Colorado Military Medical Heritage Fund at giving.cu.edu/military-heritage or contact Travis Leiker at travis.leiker@ucdenver.edu or 303-724-2754.

“I am proud to be part of a university with such an incredible track record of supporting student veterans and veterans’ health care. It is important to continue this momentum with scholarship and programmatic support.”

- Capt. Jan Kief, MD (retired)
CU School of Medicine Class of 1982
Vice President, Medical Alumni Association