# 2019 Annual Report

## The Gates Center

Gates Center for Regenerative Medicine

UNIVERSITY OF COLORADO **ANSCHUTZ MEDICAL CAMPUS**

CU President Mark Kennedy toured the Gates Center's affiliated Gates Biomanufacturing Facility on Monday, July 1, 2019 – one of two stops at the CU Anschutz Medical Campus during a whistle-stop tour of four CU campuses marking his first day in office. Shown with Gates Center Chief Financial Officer Tim Gardner on his left, President Kennedy heard about Charles Gates' belief in the hope and benefit stem cell research promised for so many people in the world, along with our collective dedication to accelerate the transition of scientific breakthroughs into clinical practice as quickly as possible.

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**Cover photo: For Eileen and Brady Attar, Epidermolysis Bullosa means a lifetime commitment for care and searching for a cure.*

Hope is most sustainable when it soars from a foundation of real progress.

At the Gates Center for Regenerative Medicine, the progress we worked for in 2019 is the basis for new hope that the most promising concepts in our field will help transform medicine and bring treatment to patients who have long looked for answers and relief.

We enter 2020 on the verge of human clinical trials initiated by Gates Center member researchers on the University of Colorado Anschutz Medical Campus. With colleagues throughout the campus, we have established a joint clinical and research center of excellence in a debilitating and scientifically challenging disease that begins to show symptoms in adolescence, greatly impacting patients and their families. We've also refined our strategy and honed our focus in a planning process we called Gates Center 3.0. And we were honored with expanded national funding for key projects and announced a groundbreaking sponsored research agreement with a private company in one of our areas of focus.

These advances toward potential treatments encourage and motivate us as we spend more time in trial recruitment and clinical settings, along with families looking to regenerative medicine with their own hopes. For the first time ever we have decided to include cover photos of a patient along with some stories in this report, which remind us of the spirit of our namesake, philanthropist Charles C. Gates, and the Gates family leadership whose funding both launched and helps sustain the Gates Center. The family's success in entrepreneurship, business and community building has never lost sight of making real improvements in human lives.

Hope backed by progress was on display when the Epidermolysis Bullosa (EB) iPS Cell Consortium, a unique collaboration of research teams from the Gates Center, Stanford and Columbia universities, received an $800,000 grant from the National Institutes of Health 21st Century Cures Act. The award was immediately doubled by a required match from a group of private foundations united to back research into EB – a disease from which their founders' children sadly suffer. Notably, the Consortium was the only hopeful in a group of eight research applicants funded in 2017 to be awarded a second round of funding by the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) – one of twelve institutes within the NIH participating in the 21st Century Cures Act Regenerative Medicine Innovation Project.

The growing endorsement of the Consortium's research, evidenced by additional grant funding from a variety of sources, has already resulted in a 24-fold "return on investment," with the initial $500,000 NIAMS grant in 2017 sparking more than $12 million in total research funding; even before the newest award. The EB Research Partnership in New York and the California-based EB Medical Research Foundation co-founded the Consortium in 2016 to create this multi-institutional partnership, and they along with the London-based Cure EB Charity have generously matched both NIAMS awards.

We believe the continuing endorsement from the 21st Century Cures Act second round of funding underlines that what we're doing here is leading-edge, and that we're competitive with the best institutions in the country for acquiring federal funding.

Our work in finding a cure for epidermolysis bullosa, from which 3½-year-old Brady Attar shown on our cover suffers, also opens doors for the kind of partnerships between universities and private enterprise that Charles C. Gates envisioned for his family's philanthropy. The core science and expertise of academia can be infused with the urgency and organizational skills of entrepreneurs to more quickly advance discoveries toward human applications. In November, AVITA Medical, a regenerative medicine company with a technology platform positioned to address unmet medical needs in therapeutic skin restoration, and scientists at the Gates Center announced a preclinical research collaboration to establish proof-of-concept and explore further development of a spray-on treatment of genetically modified cells for EB patients. The technology holds promising potential applicability to other genetic skin disorders, as well.

The partnership will pair AVITA Medical's patented and proprietary Spray-On Skin™ Cells technology and expertise with the Gates Center's innovative, patent-pending combined reprogramming and gene-editing technology to allow cells to function properly.

In the meantime, a strategic planning process we called Gates Center 3.0 kept us on track in 2019 while also putting us on a path for continuing growth and results in 2020. In collaboration with Peter Buttrick, M.D., senior associate dean for academic affairs at the University of Colorado School of Medicine, we worked hard to align our priorities with our Anschutz colleagues. This process helped identify gaps in our offerings and our most promising areas of expertise, and delineated which specialties may not be a priority without a new source of funding or a key recruitment of research talent. As part of this renewed focus, our Gates Center communications and administrative team collaborated with University of Colorado School of Medicine IT colleagues on a new web site to highlight our work and priorities.

Among those with whom we had the opportunity to share our work and priorities were two important visitors to Gates facilities in 2019. Recently-named University of Colorado system President Mark Kennedy toured the Gates Biomanufacturing Facility (GBF) as the first stop along his high-profile tour of all four CU campuses on his first day on the job. At the GBF, Kennedy heard from top researchers, including Terry Fry, M.D., a professor of pediatrics and Gates Center member, who works with GBF experts to produce materials for his groundbreaking CAR-T cell therapies. Dr. Fry was among the first scientists to investigate the potential to insert modified genes into a child's own T-cells to target CD19, a surface protein found on cells damaged by acute lymphoblastic leukemia. The new CAR-T cell techniques have produced life-saving results in pediatric cases previously considered nearly hopeless. As described in our GBF section, Dr. Fry and others will employ the GBF's expertise in state-of-the-art and efficient Good Manufacturing Practice (GMP) manufacturing in clinical trials in the coming year – another major milestone for the Gates Center and its research members.

U.S. Rep. Diana DeGette, a key architect of expanded federal research funding in regenerative medicine, toured the GBF in November (see photo) and put a spotlight on Gates Center programs that successfully competed for 21st Century Cures

Dennis Roop and others hosted U.S. Rep. Diana DeGette (D-CO) on a tour of the Gates Biomanufacturing Facility on November 6.

grant awards. DeGette said the second-round awards are clear signs that the Anschutz Medical Campus along with its partners at Stanford and Columbia are answering the call to help patients with no other options.

The past year also saw a tremendous advance in our efforts to integrate research, clinical care and academic advancement on the Anschutz Medical Campus. Spurred on by stories of patients suffering from Ehlers-Danlos Syndrome (EDS), a collection of rare, difficult-to-treat and debilitating connective tissue disorders described in one of this report's stories, the Gates Center, Children's Hospital Colorado and the CU School of Medicine joined together to elevate our national leadership in research, innovation and care. Enabled by generous funding, the campus is now focused on a three-year initiative to create an Ehlers-Danlos Syndrome Center of Excellence to address an immediate and critical national need for patient-centered, coordinated EDS care and education, while fostering leading-edge research into novel therapeutics for new, highly effective treatments for the future. Ellen Roy Elias, M.D., professor of pediatrics and medical director of the Special Care Clinic at Children's Hospital Colorado, and we at the Gates Center are charged with building this comprehensive center – with Dr. Elias and her multispecialty colleagues overseeing the coordinated patient care and education and the Gates Center leading the development of future treatments. We are grateful for the generous $2.1 million commitment from The Sprout Foundation, funded by

Suzanne and Bob Fanch, along with support from Wagner Schorr, M.D. '63 and Annalee Schorr, and Diane and Marshall Wallach, that make this initiative possible. And we are hopeful that our combined clinical and research efforts will advance our ability to bring the finest care to patients of all ages suffering from EDS in Colorado and beyond.

Importantly, our annual report gives us an opportunity to focus on people. We highlight the accomplishments of a number of our 118 members whose grants, publications and honors are testament to the talent and contributions of our membership advancing the regenerative medicine field. We profile and congratulate those members specializing in a variety of our Center's areas of focus as well as in other specialties who benefit from our efforts to help commercialize their discoveries through the Gates Grubstake Fund and Startup Toolbox. Watching on and off-campus researchers' progress toward clinical trials, we marvel at the growth, ability and accomplishment within our affiliated Gates Biomanufacturing Facility and its team of over 40 people. Similarly, we thank those who so ably manage our Core Facilities and provide our members access to the latest equipment and counsel that would be otherwise too expensive or inaccessible.

As we look to the future, we are inspired by the college undergraduates who benefit from our Gates Summer Internship Program and the graduate program we support, the interest shown by those who come to visit and learn about our operation and research, as well as by the new faces that have joined our Gates Center ranks during 2019. Finally, we are grateful for the leadership, support and hope provided by members of our Gates Center Advisory Board and our donors, who sustain and encourage our efforts to accelerate therapies and cures to patients in need. We gathered together to celebrate all this in August 2019 at Charlie's Picnic and look forward to doing so again in the years to come.

With great appreciation,

Dennis R. Roop, Ph.D.
Director, Gates Center for Regenerative Medicine
Charles C. Gates Endowed Chair in Regenerative Medicine and Stem Cell Biology

## GATES ADVISORY BOARD

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*"The charm of fishing is that it is the pursuit of what is elusive but attainable, a perpetual series of occasions for hope."*

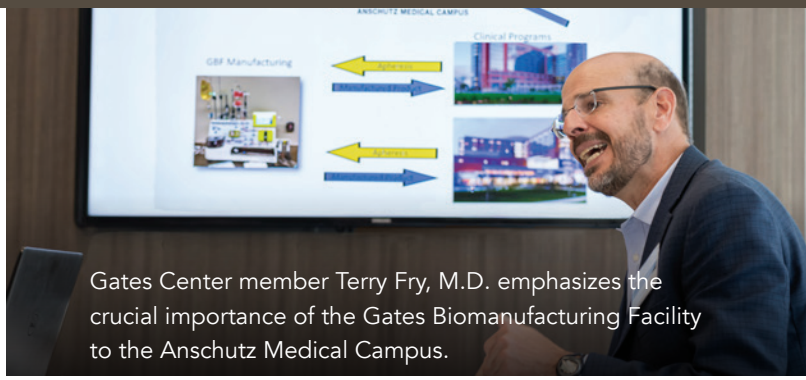
*~John Buchan*

The Gates Center for Regenerative Medicine was made possible by the generosity and philosophy of Charles C. Gates, who championed innovation, creativity and teamwork in building his family company into a worldwide leader for industry and technology. Late in his life, Charles Gates began talking to his family about the hope and benefit stem cell research promised for so many people in the world. Suffering from macular degeneration, Charles Gates started doing research on his own condition only to be introduced to the world of stem cells by his doctor, a family friend. He was amazed to learn about a science that had the potential to be leveraged across many diseases while also allowing for personalized therapies. Through his family's philanthropy, Charles Gates sought to extend his focus on innovation and collaboration in a world-class research center and support the transition of scientific breakthroughs into clinical practice as quickly as possible.

Charles C. Gates May 27, 1921, to August 28, 2005

# WHO WE ARE

Gates Summer Internship Program students



Gates Center member Terry Fry, M.D. emphasizes the crucial importance of the Gates Biomanufacturing Facility to the Anschutz Medical Campus.

Investigators work in Gates Center labs.

Tsion Habte, an undergraduate from Ethiopia, and Jill Cowperthwaite on right visit on the last day of Tsion's summer internship in Dr. Roop's Laboratory.

The Gates Center for Regenerative Medicine brings together and supports brilliant researchers and clinicians in stem cell biology and regenerative medicine in order to accelerate discoveries from the lab through clinical trials to therapies and cures.

The center was established in 2006 on the University of Colorado Anschutz Medical Campus with a generous gift in the memory of business entrepreneur and philanthropist Charles C. Gates. The Gates Center works across campus and with many other research partners, bringing together and fostering world-class research and clinical talent, regulatory and intellectual property expertise, commercial partners and diverse funding. Our facilities and member benefits include core labs, patented cell production platforms, the best-in-class Good Manufacturing Practice (GMP) production center at the Gates Biomanufacturing Facility, business development and commercial guidance, affiliation with undergraduate and graduate education programs, and more.

The Gates Center strategic plan embraces the following value drivers:

- Frontier Spirit: Fostering research with an entrepreneurial approach, balancing risks, opportunities and resources to minimize barriers to success and staying focused on producing tangible patient benefits.
- Talent: Pursuing, retaining and developing accomplished, passionate, and innovative change agents in both research and clinical settings.
- Collaboration: Serving as an indispensable resource, connector and shepherd of groundbreaking ideas and solid science, coordinating and optimizing outcomes for all of our partners and customers. Charles C. Gates said it: "No one does their best work alone."
- Patient Outcomes: Accelerating discoveries from the lab through clinical trials that lead to effective therapies and cures for those most in need of scientific breakthroughs.

Although the Gates Center is always open to new opportunities through discoveries or funding, its primary areas of research focus are both targeted and opportunistic –

where the potential for impact from lab bench to bedside has the most promise and speed. Current areas of focus include the following:

**Cardiology** – Gates Center researchers investigate regenerative solutions to heart disease, including the 50 percent of heart attack cases that result in heart failure. One potential treatment is exploring a method for converting cardiac fibroblasts into new heart muscle cells.

**Ehlers-Danlos Syndrome** – The Gates Center is the research arm of the Ehlers-Danlos Center of Excellence, created in partnership with Children's Hospital Colorado and the Dean of the School of Medicine John Reilly, Jr., M.D., and dedicated to moving bold research ideas from the lab into the clinic to deliver the finest care for people living with this rare group of connective tissue disorders.

**Epidermolysis Bullosa** – World-leading research into the development of a cure for this devastating, inherited group of skin diseases is anchored at the Gates Center, which helps lead a consortium including University of Colorado Anschutz Medical Campus, Stanford University School of Medicine and Columbia University Medical Center.

**Induced Pluripotent Stem (iPS) Cells** – The Gates Center is an international pioneer in launching multi-dimensional research projects using induced pluripotent stem cells (iPSCs) with its unique, safe and efficient combined gene editing and cell reprogramming approach that raises hopes for future clinical trials and potential cures for critical illnesses.

**Oncology** – The Gates Center and the Gates Biomanufacturing Facility are key to revolutionary advances in CAR-T cell treatment for cancer developed by Dr. Terry Fry, M.D., and others. Advances in CAR-T and other materials are already improving patient lives in previously hopeless cases.

**Ophthalmology** – The promise and wonder of regenerative medicine is evident in Gates Center member labs where researchers are growing new retinas in the CellSight laboratories to potentially reverse loss of sight and develop new therapies for millions of Americans suffering from macular degeneration and inherited retinal diseases.

**Orthopedics** – While the public hears misleading marketing claims about stem cells and joint repair, Gates Center researchers are conducting gold-standard clinical trials measuring the effectiveness of patient treatments and developing new scaffolds for joint and limb repair through 3D printing and cartilage regeneration.

**Wound Healing** – Gates Center members are producing groundbreaking results through various investigations, testing potential treatments that could speed tissue regeneration in debilitating skin wounds, reducing the chronic inflammation suffered by diabetes patients and treating side effects from radiation and chemotherapy.

Dennis Roop, Ph.D., recruited from the Baylor College of Medicine in 2007, is the Center Director and coordinates a talented array of 118 multi-institutional researchers from the Anschutz Medical Campus, CU Boulder, CU Denver, Colorado State University, Colorado School of Mines and National Jewish Health, as well as private industry. The Gates Advisory Board, comprised of community leaders and clinicians, provides counsel and additional support [see page 6-7].

Key to the success of the Gates Center is the partnership with the Gates Biomanufacturing Facility, a state-of-the-art manufacturing facility that works with on and off-campus investigators to translate innovative research discoveries into safe and effective cell therapy and protein biologic products for human clinical trials. The GBF operates under FDA "Good Manufacturing Practice" guidelines with a trained staff of more than 40 people within a 20,000 sq. ft. facility. The GBF has proven essential in engagement of research talent present on the Anschutz Medical Campus as well as in talent recruitment nationwide.

*Regenerative medicine includes research into the uses of adult stem cells, which can be reprogrammed into embryonic-like stem cells and then differentiated into virtually any cell type in the body. These core tools are referred to as induced Pluripotent Stem Cells (iPSCs). The long-term goal is to return iPSC-derived adult stem cells to the patient from whom they were derived in order to regenerate cells, organs and key bodily functions. Other research includes production and manipulation of key proteins in the body to fight or correct disease, and the alteration of a patient's own T cells to produce CAR-T cells for immunotherapy to combat cancer.*

# WHAT WE DO

## Gates Center for Regenerative Medicine

**Where leading-edge research comes to life.**


**BENCH RESEARCH** → **REGULATORY & COMMERCIALIZATION AID** → **FUNDING** → **CLINICAL TRIALS** → **PATIENT BENEFIT**

### MISSION

The Gates Center for Regenerative Medicine brings together and supports brilliant researchers and clinicians in stem cell biology and regenerative medicine in order to accelerate discoveries from the lab through clinical trials to therapies and cures.

### GATES CENTER BENEFITS

- Core laboratories
- Gates Biomanufacturing Facility
- Business development, regulatory & commercialization support
- Research finance assistance
- Recruitment of top talent
- Education and outreach
- Clinical trials

### RESEARCH CONSORTIUM

The Gates Center is a world-class consortium of 118 researchers, clinicians and private industry members from:

Boulder · Denver CU IN THE CITY · University of Colorado Anschutz Medical Campus · Colorado State University · School of Medicine 1874 Colorado · uchealth · National Jewish Health · Children's Hospital Colorado

*"No one does their best work alone."* – Charles C. Gates

# LIST OF MEMBERS

| NAME | DEGREE(S) | POSITION | ACADEMIC INSTITUTION/AFFILIATES | PRIMARY (AND SECONDARY) APPOINTMENT(S) |
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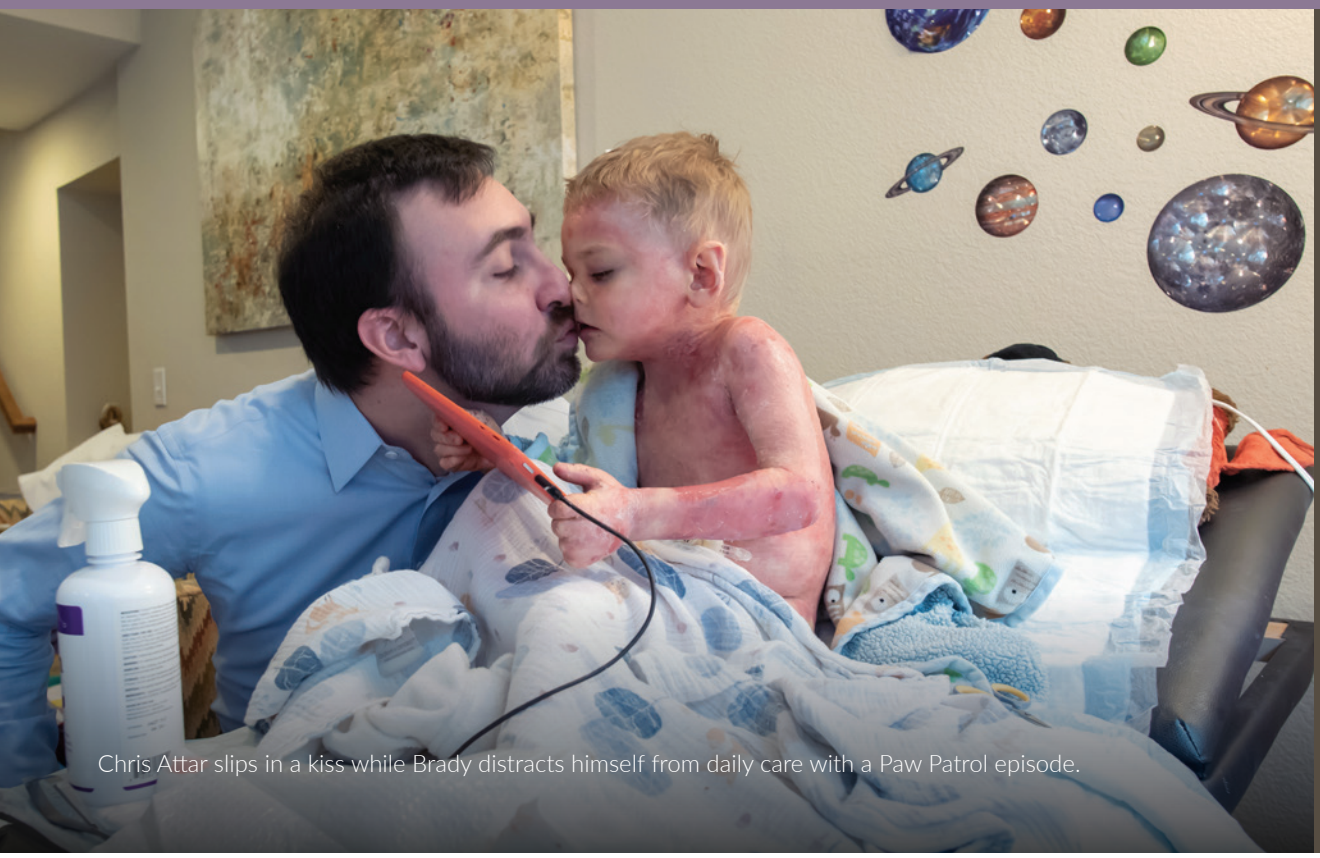
| Rozhok, Andrii* | Ph.D. | Research Instructor | University of Colorado, Anschutz Medical Campus | Department of Dermatology |
| Russ, Holger Andreas | Ph.D. | Assistant Professor | University of Colorado Anschutz Medical Campus | Barbara Davis Center for Diabetes Microbiology and Immunology Department |
| Salinas, Branden | Ph.D. | Director of Protein Development and Manufacturing | University of Colorado Anschutz Medical Campus | Gates Biomanufacturing Facility |
| Sartorius, Carol | Ph.D. | Associate Professor | University of Colorado Anschutz Medical Campus | Department of Pathology |
| Seefeldt, Matthew | Ph.D. | Director of Cell Therapy | University of Colorado Anschutz Medical Campus | Gates Biomanufacturing Facility |
| Serban, Karina | M.D. | Assistant Professor | National Jewish Health | Department of Medicine, Division of Pulmonary and Critical Care Medicine |
| Shellman, Yiqun | Ph.D. | Associate Professor | University of Colorado Anschutz Medical Campus | Department of Dermatology |
| Sherk, Vanessa | Ph.D. | Instructor | University of Colorado Anschutz Medical Campus | Department of Medicine/Endocrinology |
| Song, Kunhua | Ph.D. | Assistant Professor | University of Colorado School of Medicine | Department of Medicine, Division of Cardiology |
| Soranno, Danielle | M.D. | Assistant Professor | University of Colorado Anschutz Medical Campus | Department of Pediatrics |
| Stenmark, Kurt | M.D. | Professor | University of Colorado Anschutz Medical Campus | Department of Pediatrics/Critical Care |
| Sussel, Lori | Ph.D. | Professor Sissel and Findlow Family Chair | University of Colorado Anschutz Medical Campus | Barbara Davis Center for Diabetes/Pediatrics (Cell & Developmental Biology) |
| Terzian, Tamara | Ph.D. | Assistant Professor | University of Colorado Anschutz Medical Campus | Department of Dermatology |
| Thamm, Douglas | V.M.D. | Assistant Professor | Colorado State University | Department of Clinical Sciences |
| Torchia, Enrique | Ph.D. | Assistant Professor | University of Colorado Anschutz Medical Campus | Department of Dermatology |
| Verneris, Michael | M.D. | Professor The Barton Endowed Chair of Pediatric Bone Marrow Transplant | University of Colorado Anschutz Medical Campus | Department of Pediatrics/Hematology, Oncology and Bone Marrow Transplantation |
| Vladar, Eszter | Ph.D. | Assistant Professor | University of Colorado Anschutz Medical Campus | Division of Pulmonary Sciences, Department of Cell & Developmental Biology |
| Wagner, David | Ph.D. | Associate Professor | University of Colorado Anschutz Medical Campus | Department of Neurology |
| Walker, Lori | Ph.D. | Associate Professor | University of Colorado Anschutz Medical Campus | Department of Medicine/Cardiology |
| Wang, Xiao-Jing | M.D., Ph.D. | Professor John S. Gates Endowed Chair in Stem Cell Biology | University of Colorado Anschutz Medical Campus | Department of Pathology |
| Wang, Zhijie | Ph.D. | Assistant Professor | Colorado State University | Department of Mechanical Engineering |
| Williams, Trevor | Ph.D. | Professor | University of Colorado Anschutz Medical Campus | Department of Craniofacial Biology, School of Dental Medicine/Department of Cell and Developmental Biology, SOM |
| Wilusz, Carol | Ph.D. | Professor | Colorado State University | Department of Microbiology, Immunology and Pathology |
| Wilusz, Jeff | Ph.D. | Professor | Colorado State University | Department of Microbiology, Immunology and Pathology |
| Yi, Rui | Ph.D. | Associate Professor | University of Colorado Boulder | Department of Molecular, Cellular and Developmental Biology |
| Zamora, Martin | M.D. | Professor | University of Colorado Anschutz Medical Campus | Division of Pulmonary, Critical Care Medicine |
| Zhou, Wenbo | Ph.D. | Associate Professor | University of Colorado Anschutz Medical Campus | Department of Medicine/Clinical Pharmacology and Toxicology |

* New members in 2019

# HOPE FOR PATIENTS INSPIRES OUR WORK



Chris Attar slips in a kiss while Brady distracts himself from daily care with a Paw Patrol episode.

From the moment of Brady Attar's arrival into this world, as a beautiful baby boy who somehow had startling skin lesions covering his body even before his cord was cut, his family had much to learn.

Eileen and Chris Attar had their second boy at one of the best children's hospitals in Texas, and yet the expert who could teach them the most about extremely rare Epidermolysis Bullosa was hundreds of miles away in Austin. It would be days and weeks before they fully understood, still in shock, that "EB" was a genetic disorder that in severe versions weakens skin and soft membranes to the point where patients like Brady have new raw wounds every day.

And with no cure, EB doesn't end.

In those first weeks, Eileen says now, "I couldn't believe it, such denial. There's just no way this could exist, that it could be this hard. How will I do this every day of my life from here on out?"

Three and a half years later, the Attars are themselves teaching some of the top clinicians and stem cell researchers in the world how families live with EB and where the first treatment breakthroughs might come. Having uprooted their family to Colorado in search of expertise, they spend a lot of time sharing their own knowledge with Gates Center researchers and Dr. Anna Bruckner, director of the Children's Hospital Colorado EB Center of Excellence and her team. The Attars and other EB families from a multistate region visit the clinic regularly for treatment because it's one of the few of its kind in the nation.

On any given day, Eileen might tell Dr. Bruckner that Brady's EB leaves him longing to taste ice cream, but unable on some days to even swallow water. Hours later, Eileen and Chris might sit at a table for an update with Gates Center Ph.D.s working assiduously toward EB cures, and explain how EB lesions close up the throat.

"We are so thankful," Eileen said of the research meeting, "that they keep us in their brains while they do what they are doing."

The close integration and interaction of basic scientific research, treatment development and production, and world-leading clinical knowledge are what has come to distinguish the Gates Center and the Anschutz Medical Campus from many other academic hubs in the nation. In rare and highly specialized disciplines such as EB, only a few locations can offer families and researchers the combination of hands-on treatment and exploration of the underlying causes.

Three Gates Center researchers are at the forefront of EB exploration, including Gates Center Director Dennis Roop, Ph.D.; Ganna Bilousova, Ph.D., assistant professor of Dermatology at the School of Medicine; and Igor Kogut, Ph.D., also an assistant professor of Dermatology at the School of Medicine. The Gates Center is one anchor of an EB iPS Stem Cell Consortium along with Stanford University and Columbia University, a consortium that has received multiple rounds of funding from the National Institutes of Health 21st Century Cures Act. They also receive generous matching private funds (a requirement of this funding mechanism) from the EB Research Partnership in New York and the California-based EB Medical Research Foundation, which co-founded the Consortium in 2016 to create the multi-institutional partnership, and the London-based Cure EB Charity. The Colorado Team has additionally received funding from the U.S. Department of Defense, the Dystrophic Epidermolysis Bullosa Research Association (DEBRA) International, the King Baudouin Foundation's Vlinderkindje Fund and the Gates Frontiers Fund.

Elsewhere in the Annual Report, you can read about how the integration of basic research discoveries, on-campus production of treatment materials, and clinical capacity for on-site clinical trials in CAR-T cell cancer therapy will advance this model in 2020. This is the kind of real-world academic and clinical progress accelerating discovery from the lab to therapies and cures envisioned by Charles C. Gates and other generous funders when the Gates Center was originally founded.

The reason Eileen Attar gave birth to Brady in a room where few people knew anything about EB is that it impacts only about 20 in 1 million live births. Researchers estimate about 25,000 to 50,000 families in the U.S. are living with EB patients.

With the Attar family now in Denver, after moving north from Houston to find Brady the best possible care, researchers can learn from Brady and dozens of other families at the Children's specialty clinic just how the rare disease shows up every day. Eileen would welcome the company – she absorbs information, encouragement and support from every possible source.

"When I think about it too much, it's too daunting," she said. "How is this sustainable?  That's when it really hit me. It's bigger than me."

EB is an inherited skin and soft-tissue disorder that causes blisters and peeled skin with even light touches. It also can create sores and scar tissue in the mouth, esophagus, lungs, muscles, eyes, nails and teeth. There are multiple forms of EB, and Brady has the most severe kind, dystrophic EB.

Straight from the womb, Brady was born with sores and abraded lips from kicking in-utero and from descending the birth canal. Children with severe cases need hours of bandaging and wound care each day, like severe burn victims, and everyday movement such as crawling or walking can cause pain and more damage.

Brady often has throat wounds and scarring that make him not want to swallow, and nearly all his feeding is done through a GI portal in his stomach. Eileen and Chris carry around a worn notebook full of reminders about his nutrition, his wound care, his medications and appointments. Kristina Byrne is a full-time RN who also accompanies Brady to school, and has become so embedded in the family she's often told she can never quit.

Kristina touches Brady affectionately on the leg, and tells his Children's Hospital medical team, "I hope his wife likes me," waiting for them to get her joke about her serious commitment.

There is no current treatment or cure for EB, only attention to its symptoms. Research has focused on both external applications of materials that could restore skin cells, or injections of modified cells that might eventually override the patient's damaged cells.

The Gates Center has grants to work in both areas and more. In its second 21st Century Cures Act award, the Center said "the funds will advance innovative Consortium research and expansion of treatment in areas including a potential "Spray-On Skin™" application of regenerative cells, and a promising treatment of internal diseased tissue with systemically targeted-delivery cells."

Spray-on delivery of new cells "has the potential to revolutionize treatment" for kids with EB, Roop said.

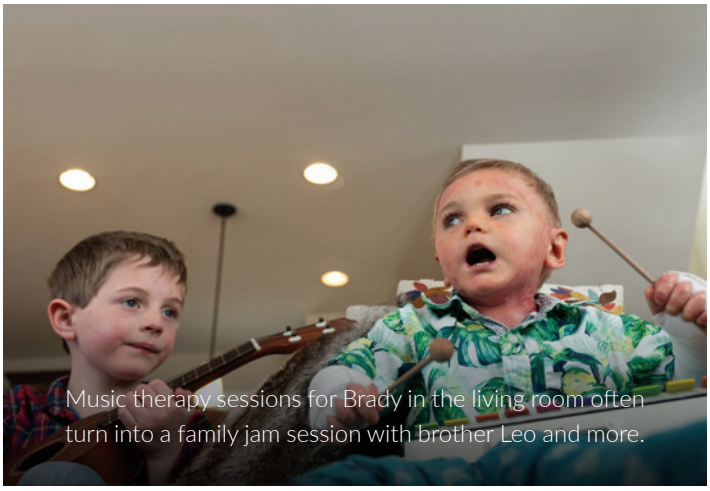
Still, even if proven successful, transforming significant portions of skin will be time-consuming. That's why researchers also are zeroing in on internal delivery of modified cells that would travel through the blood stream to damaged cells and replace them.

"We're going for the moon shot, we're going for the complete cure," Roop said. Moreover, knowledge gained in EB research has already and will continue to inform other medical disciplines – new methods of skin growth and targeted cell delivery could help millions.

Preparing for meetings with EB parents, Roop sometimes has to temper those words in his own head. "You realize you have to be very very cautious, and very realistic. The FDA is very cautious. And it always takes longer than the parents want," Roop said. "We don't know exactly what the timeline is going to be to get FDA approval. I'm an eternal optimist by nature, and I'm sure it shows when I start talking, and parents get excited."

Human clinical trials of promising EB treatments are still some time away. The approval process may seem even slower than on other new drugs, as therapies that involve altering cells may need longer observation times to ensure there are no unwanted cell mutations.

At the Attars' meeting with Gates researchers and their primary EB clinician, Dr. Bruckner, Chris Attar mentioned that at their last research update, they had looked into a



Music therapy sessions for Brady in the living room often turn into a family jam session with brother Leo and more.

Brady shows off his improved walking skills with caregiver Kristina Byrne, RN, in between clinic exams.

microscope and watched altered healthy cells move in to replace damaged cells, a process called homing. He asked if that method was closer to approval.

Bilousova responded, “We see cells going into the tissue, but it’s relatively few cells. So one ongoing issue is making the homing more efficient.” That will require complex production machinery to be set up in new Gates research laboratories in 2020. Researchers must avoid mistakes or rushing that can set back promising lines of investigation.

“If we don’t do it right, not only do we fail the patient, we fail the whole field,” she told the Attars.

Eileen and Chris understand all this, and accept it on one level, as supporters of science and research. On another level, where they are parents of a beautiful boy who loves Paw Patrol and wrestling his older brother, Leo, and the family jam sessions that erupt when Brady has his music therapy in the living room, they would do anything to lessen his daily agonies.

Around the conference table, Eileen said, “So much of hope depends on how Brady is doing day to day. On good days when he’s doing well, this all makes sense. And on days when things are not going well or something new has happened, it’s ‘We needed this yesterday already.’ ”

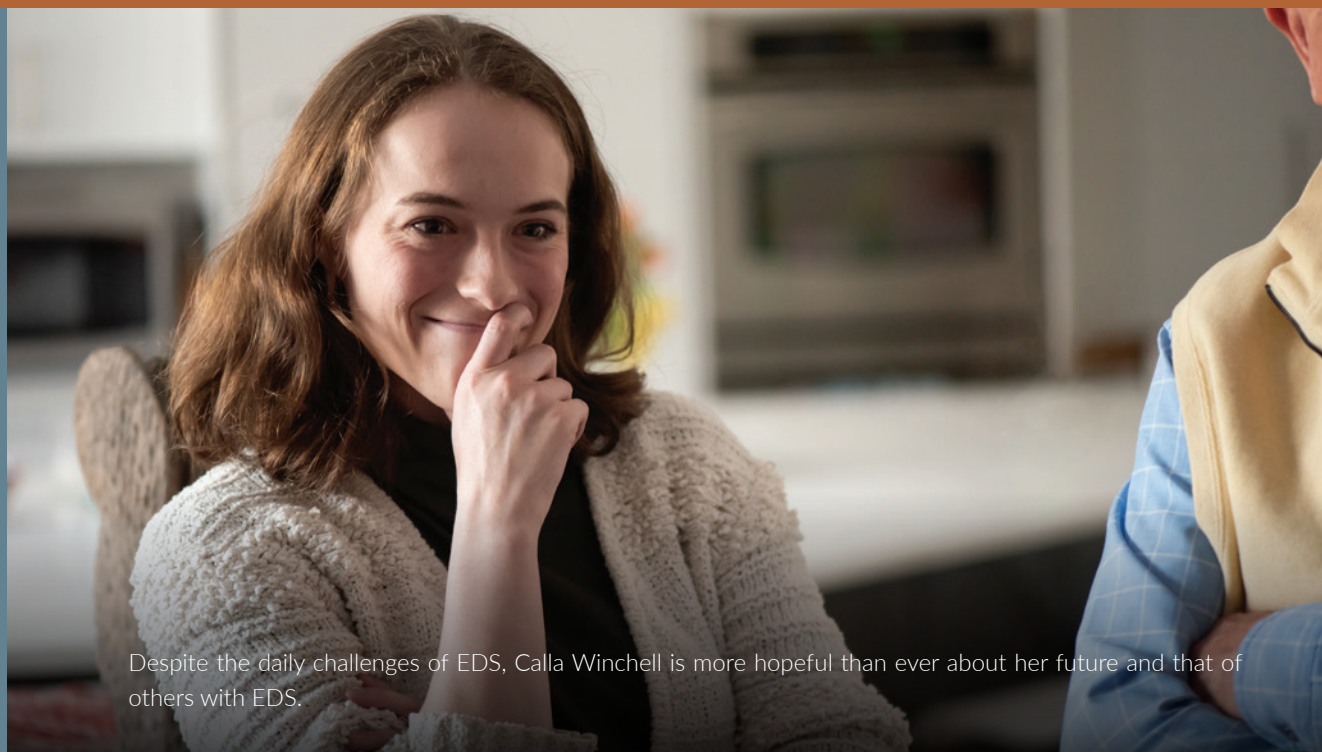
Roop listens and nods. These are the sorts of tensions and contradictions that flow constantly around the Anschutz Medical Campus, between the research towers and the clinics. The families inform and motivate and inspire the professionals.

“I see a parent like you and I have to try not to oversell it,” Roop said. “But we are in fact very optimistic about so many things.”


Brady talks with his doctors while Kristina Byrne, RN, offers encouragement; compression bandages helps soothe his abraded skin and prevent further damage.

# HOPE REALIZED

## EHLERS-DANLOS SYNDROME CENTER OF EXCELLENCE ADVANCES RESEARCH, CARE



Despite the daily challenges of EDS, Calla Winchell is more hopeful than ever about her future and that of others with EDS.

She's a bright and motivated young woman with an infectious smile. She's seemingly the picture of perfect health. But, at 25 years old, she wears support braces on her wrists and knees. And sports pain patches, too. Her condition is so painful, in fact, that she can't sleep. She takes pills for that, she said.

Calla Winchell has Ehlers-Danlos Syndrome (EDS). It's a rare group of genetic disorders that affects the elasticity of her connective tissues – the "glue" that holds the body together. There are 14 distinct types of EDS and the hypermobile form is the most common, impacting an estimated 1 in 5,000 people, with the majority of symptomatic patients being women. In hypermobile EDS, the symptoms and severity can vary greatly from person to person, with some patients only moderately impacted while others, like Calla, face pain and inconveniences on a daily basis.

The culprit of EDS is the body's inability to process collagen protein correctly, which harms the connective tissue's ability to provide support and structure to the body. It can cause hypermobile joints, stretchy skin and fragile tissues. In other words, parts of the body that should be stable, are not. The ligaments and tendons supporting the joints are loose, causing the muscles to pick up the slack. All day long, the muscles must contract just to keep the body together.

It's a painful and debilitating disease that can affect many of the body's systems at once, causing problems with digestion, breathing, movement and balance, and even mental health. People with EDS face the difficulty of finding an optimal plan for their treatment and care, often inhibited by the severity and complexity of the disorder. In addition, poor awareness of EDS in the medical community means that it regularly goes undiagnosed or is misdiagnosed.

Not unlike many others with EDS, Calla must navigate through a daunting array of physicians, specialists and healthcare providers across multiple agencies, each with differing perspectives and points of view.

Not anymore.

Thanks to significant philanthropic support from The Sprout Foundation, a Denver-area foundation funded by Suzanne and Bob Fanch, and gifts from others including Wag and Annalee Schorr, the Ehlers-Danlos Syndrome Center of Excellence was launched in 2019. The goal of the center is to eventually develop a cure for EDS at the Gates Center for Regenerative Medicine, while better addressing the clinical needs of patients today through specialty care at Children's Hospital Colorado. The clinical components of this new center address the critical need for patient-centered, coordinated EDS care where physicians come together to agree on the treatment plan, rather than leaving the patient and their family to determine the course of action.

Simultaneously, the Gates Center for Regenerative Medicine scientists are conducting leading-edge research with the ultimate goal of finding a cure. Today, this research is aimed at discovering the genetic underpinnings of hypermobile EDS and leveraging this information to develop future therapies for patients like Calla.

The Fanches said, "Sprout Foundation has funded research and the outstanding staff at the Gates Center for Regenerative Medicine to accelerate the cure for this life-changing disorder and also for clinical care to patients through the EDS Center of Excellence."

Joining in this effort are Calla's own grandparents, Wag Schorr, an accomplished nephrologist and 1963 CU School of Medicine alumnus, and his wife, Annalee.

An essential component of the EDS Center of Excellence is a translational research program, which leverages existing campus resources and partnerships, including the Gates Center for Regenerative Medicine and the Colorado Center for Personalized Medicine.

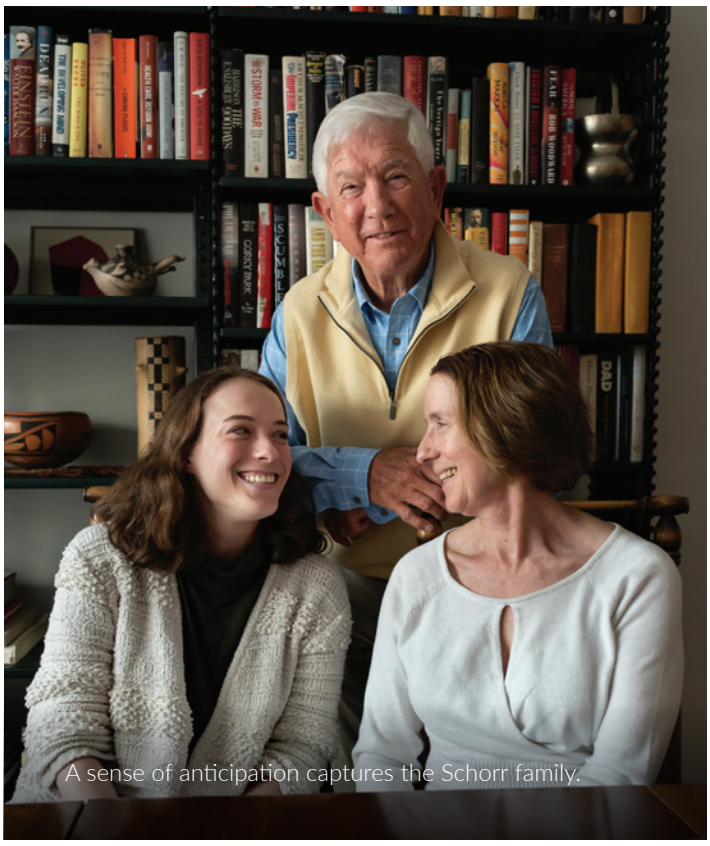
The research program at the Gates Center is led by Dennis Roop, Ph.D., director of the Gates Center, in partnership with Ganna Bilousova, Ph.D., and Igor Kogut, Ph.D. The program brings EDS patients' genetic information from clinical visits to the Gates Center where researchers are working on future treatments for the condition. In this virtuous cycle, patients inform future therapies in the lab that, in turn, could ultimately change lives back in the clinic.

Calla is one of those patients. She is motivated by the possibility of improving EDS research.

In preclinical models, scientists are collecting stem cells from Calla and other patients that indicate a possible mutation. These studies, using multiple patients, allow for a more accurate portrait of the errors in DNA. Early findings at the Gates Center suggest that a possible mutation for the hypermobile form of EDS may have been identified. The hope is that this research will lead to a potential treatment in the coming years.

Scientists are growing skin cells in the lab using Calla's stem cells, with the EDS gene mutations removed. If successful, the modified stem cells will hook onto sites of inflammation and grow new cells – restoring function to damaged tissues and organs. It sounds like science fiction, but it could be a reality at the CU Anschutz Medical Campus in the years to come.

The research advances taking place at the Gates Center will ultimately mean incredible hope and healing for people like Calla, and others with rare genetic disorders, who are eager to regain their health and their independence.



A sense of anticipation captures the Schorr family.

"I'm thrilled," she said. "I'm excited to receive coordinated care and treatments that will help me get back to my life. What if I could go to the grocery store and not have to use a wheelchair anymore?"

By bringing research together with clinical care, the EDS Center of Excellence is helping turn such possibilities into realities.

Calla's care plan is coordinated by a team of experts at the EDS multidisciplinary clinic at Children's Hospital Colorado, led by the Medical Director of the Special Care Clinic Ellen Roy Elias, M.D., in close collaboration with Kourtney Santucci, M.D.

The clinic places the patient at the center of care, and brings forward all of the right health professionals required to determine a comprehensive care plan. In this model, the patient is seen by a team of specialists in a single day, with the goal of having a treatment plan at the end of the visit.

Calla's grandfather, Dr. Schorr, says no more will Calla and others like her have to create a "center of excellence" for themselves as they traverse a complex and fragmented healthcare system to ensure their needs are met.

The pioneering work taking place at the EDS Center of Excellence began with Dr. Schorr's vision. In 2016, as a member of the Gates Center for Regenerative Medicine Advisory Board, Dr. Schorr approached director Dennis Roop and began laying the groundwork for research efforts in EDS, which he and Annalee funded later that year. Dr. Schorr's vision and commitment made it possible to develop the EDS Center of Excellence as a place to realize scientific advances in EDS research (see page 59 to learn more about Dr. Schorr's long and prolific career).

"CU is poised for another breakthrough in medicine," said Dr. Schorr. "I believe that EDS patients will soon have access to effective treatments, and possibly even a cure. If we are precise with our research and resources, we can resume our place at the forefront of the medical world. That's our responsibility."

Another must, said Dr. Schorr, is to empower visionaries in their fields to pave the path toward new discoveries and major medical advances.

Leading this charge is CU School of Medicine Dean and Vice Chancellor for Health Affairs John Reilly, Jr., M.D. Dean Reilly said, "One of the great advantages of having our pediatric hospital partner, Children's Hospital Colorado, and a research entity like the Gates Center on campus is the opportunity to collaborate. By bringing some of the best minds together to lead the next generation in EDS research, we get remarkable innovation, and leading-edge treatments and care. What our philanthropic partners have built here is inspiring, and together we are determined to bring hope to patients and their families. It has been exciting to see two families with a long friendship come together with a shared goal to create a center that will have a positive effect on so many patients and families."

With each new discovery at the EDS Center of Excellence, lives will improve through better care and better health. Each new discovery brings new opportunity for people with EDS to live lives they never knew they could have.

Suzanne and Bob Fanch
*Photo Courtesy of Devil's Thumb Ranch*

> ***We chose to support this center because we envision a future where there is a cure for EDS. As donors, we understand the power that philanthropy can have to accelerate research discoveries and transform patient care through collaborations like this one.***
> ***~Suzanne and Bob Fanch***

# SELECT MEMBER PUBLICATIONS AND HONORS*

**Bruce Appel, Ph.D.,** *Professor,* Department of Pediatrics

In this manuscript, Dr. Appel describes signaling interactions between neuronal axons and glial oligodendrocytes that determine how axons are wrapped by insulating myelin membrane (Hughes and Appel, Nat Commun. 2019). These signaling interactions might mediate how myelin is formed on axons in response to brain activity, thereby contributing to learning and memory.

**Joseph Brzezinski, Ph.D.,** *Associate Professor,* Department of Ophthalmology

Dr. Brzezinski and colleagues show that mouse retinas and human retinal organoids can be treated to become cone photoreceptor-dominant (Kaufman et al., Dev Biol, 2019). They go on to profile the transcriptional changes that occur as stem cells differentiate into cones. These findings are being used to probe the mechanisms that control cone photoreceptor development.

**Andrii Rozhok, Ph.D.,** *Instructor,* Department of Dermatology

**James DeGregori, Ph.D.,** *Professor,* Department of Biochemistry and Molecular Genetics

Drs. Rozhok and DeGregori report computational studies demonstrating that aging-dependent changes in selection for cancer-causing mutations is sufficient to explain the late-life increases in cancer risk (Rozhok and DeGogori, eLife, 2019). Importantly, this paper overturns dogma in the cancer field that posits that aging-associated cancer risk is due to the time-dependent accumulation of mutations. Instead, they show that physiological changes in our tissues associated with old age dramatically alter selection for oncogenic mutations.

**Santos Franco, Ph.D.,** *Assistant Professor,* Department of Pediatrics

Dr. Franco and colleagues define the role of a gene in the brain whose function was previously uncharacterized (Gutierrez, et al., eNeuro, 2019). They determined that this gene, Csmd2, is a component of synapses—the connections between brain cells. They show that it interacts with other proteins at synapses and determine that Csmd2 is required for normal development of neurons.

**James Hagman, Ph.D.,** *Professor,* Department of Immunology, National Jewish Health

In this paper, Dr. Hagman and colleagues show that CHD4, a protein that opens or closes chromosomes, which in turn allows genes to be turned on or off, respectively, is essential for transcriptional repression and lineage progression in B lymphopoiesis (Arends et al., Proc Natl Acad Sci USA, 2019).

**Jeffrey Jacot, Ph.D.,** *Associate Professor,* Department of Bioengineering

In this article, Dr. Jacot and colleagues show that an engineered cardiogenic material can be implanted to replace part of the heart wall in a rat and provides better heart function than commercial patches (Tao et al., Acta Biomaterialia, 2019).

**Kenneth Liechty, M.D.,** *Professor,* Department of Surgery

Dr. Liechty and colleagues report that the use of cerium oxide nanoparticles conjugated with microRNA-146a can correct impaired wound healing in diabetic wounds (Zgheib, et al., J Am Coll Surg, 2019).

Traci Lyons, Ph.D. and her lab

**Traci Lyons, Ph.D.,** *Associate Professor,* Department of Medicine

Dr. Lyons and colleagues (see photo) reveal that immunosuppression during postpartum involution is mediated by PD-L1 expression on lymphatic endothelial cells and macrophages and PD-1 expression on T-cells (Tamburini et al., Frontiers in Immunology, 2019). Using PD-1 blockade during involution, they reveal that the tumor promotional effects of postpartum involution are due in large part to this mechanism of immune suppression.

**Chelsea Magin, Ph.D.,** *Assistant Professor,* Department of Medicine

**Ganna Bilousova, Ph.D.,** *Assistant Professor,* Department of Dermatology

In this manuscript, Drs. Magin and Bilousova optimize hydrogel biomaterials to better maintain human skin cells in culture outside of the body for longer periods of time (Davis-Hall et al., Advanced Biosystems, 2019). These materials have the potential to improve the number of cells available for high-impact research in regenerative medicine.

**Ram Nagaraj, Ph.D.,** *Professor,* Department of Ophthalmology

In this paper, Dr. Nagaraj and colleagues tested a product, developed in their own laboratory named Peptain-1, for its ability to prevent retinal ganglion cell death in two animal models for glaucoma (Stankowska et al., Cell Death and Discovery, 2019). In both models, they find that Peptain-1 can efficiently prevent ganglion cell death. They were able to duplicate these findings in cultured retina and retinal ganglion cells that were exposed to glaucoma-related stress.

**Lee Niswander, Ph.D.,** *Professor,* Department of Molecular, Cellular, and Developmental Biology, CU Boulder

Dr. Niswander and colleagues report the development and testing in an animal model of a hydrogel that can be injected into the uterus and used to protect delicate neural tissue in the case of the neural tube defect spina bifida (Bardill et al., Journal of Surgical Research, 2019).

**Karin Payne, Ph.D.,** *Assistant Professor,* Department of Orthopedics

**Ganna Bilousova, Ph.D.,** *Assistant Professor,* Department of Dermatology

In this study, Drs. Payne and Bilousova and their colleagues evaluated chondrogenesis of induced pluripotent mesenchymal progenitor cells (iPS-MPs) encapsulated in a cartilage-mimetic hydrogel under different culture conditions: free swelling versus dynamic compressive loading and different growth factors (TGFβ3 and/or BMP2) (Aisenbrey et al., Biomater Sci, 2019). These authors report a promising cartilage-mimetic hydrogel for iPS-MPs that when combined with appropriate biochemical and mechanical cues induces a stable chondrogenic phenotype.

**Mark Petrash, Ph.D.,** *Professor,* Department of Ophthalmology

In this paper, Dr. Petrash and colleagues demonstrate that pharmacological inhibition of aldose reductase, an aldo-keto reductase, resulted in enhanced regeneration of lens tissue in a mouse model of cataracts
(Zukin et al., Chem Biol Interact, 2019).

**Eric Pietras, Ph.D.,** *Assistant Professor,* Department of Medicine

Dr. Pietras and colleagues demonstrate that blood-forming hematopoietic stem cells (HSC) remain quiescent and retain their long-term repopulating potential during chronic inflammatory insult (Experimental Hematology, 2019). A rigorous surface marker combination as well as a fluorescent reporter system were used to identify and characterize the molecular features of these cells. This study helps to resolve long-standing confusion in the hematology field relating to how the molecular and functional characteristics of HSC are impacted by chronic inflammatory disease.

**Robert Plenter, B.S.,** *Senior Professional Assistant,* Department of Medicine

**Martin Zamora, M.D.,** *Professor,* Department of Medicine

In this publication, the authors clarified the class(es) of C-kit-derived cell(s) required for heart transplant survival prolongation (Plenter et al., Cell Immunol, 2019). Their results suggest that alloimmunity is a major signal for trafficking of C-kit-derived cells to the allograft and demonstrate that C-kit+ derived cells expressed CD11b early after arrival and that these cells are required for survival prolongation. Co-therapy studies demonstrate near complete blocking of acute rejection when combined with existing immunosuppressives. These results demonstrate the potential therapeutic application of autologous C-kit+ progenitor cells as possible co-therapeutics for durable graft survival.

**Jennifer Richer, Ph.D.,** *Professor,* Department of Pathology

In this study, Dr. Richer and her colleagues discover that tumor metabolism is changed to support tumor cell anchorage independent survival during metastasis and that tumors co-opt a program of immune suppression used by trophoblasts during pregnancy to suppress the maternal immune system (Rogers et al., Mol Cancer Res, 2019).

**Dennis Roop, Ph.D.,** *Professor,* Department of Dermatology

**Xiying Fan, Ph.D.,** *Instructor,* Department of Dermatology

Drs. Roop and Fan and their colleagues have developed a novel mouse model that provides the first-ever direct visualization of the clonal development of non-melanoma skin cancers from single stem cells in a live mouse (Kubick et al., J. Invest Dermatology, 2019). This model also allows the visualization of immune cells and the evasion of immune detection by pre-malignant cancers. The ability to visualize pre-malignancies with immune-evasive properties will now allow screening for drugs and immunotherapies that eliminate cancers at an early stage of development prior to progression to malignancy.

**Holger Russ, Ph.D.,** *Assistant Professor,* Department of Pediatrics

Dr. Russ is a co-author of this paper, which identifies a novel regulatory mechanism that controls the maturation of stem cell derived beta cells (Zhou et al., Stem Cell Reports, 2019). These findings have important implications for current efforts to provide a cell replacement therapy for patients suffering from diabetes.

**Lori Sussel, Ph.D.,** *Professor,* Department of Pediatrics

Dr. Sussel and her colleagues report that the long noncoding RNA (lncRNA), Paupar, modulates PAX6 regulatory activities to promote alpha cell development and function in the pancreas (Singer et al., Cell Metab, 2019). These findings illustrate a distinct mechanism by which a pancreatic lncRNA can coordinate glucose homeostasis by cell-specific regulation of a broadly expressed transcription factor.

**Michael Verneris, M.D.,** *Professor,* Department of Pediatrics

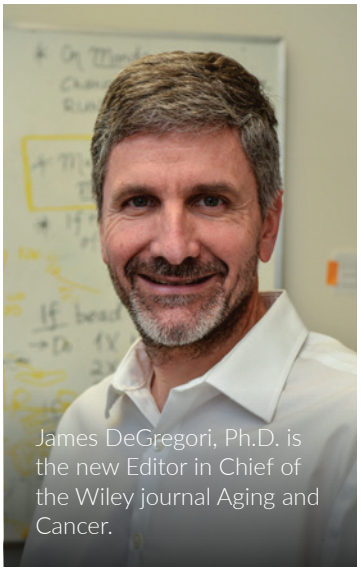
Dr. Verneris and his co-authors show that in myelodysplastic syndrome there are inhibitory monocytes that impair NK cell function, which has implications for blood and marrow transplantation (Sarhan et al., JCI Insight, 2019).

**Lori Walker, Ph.D.,** *Associate Professor,* Department of Medicine

**Kurt Stenmark, M.D.,** *Professor,* Department of Medicine

Drs. Walker and Stenmark and their colleagues report the novel finding of dedifferentiation of adult cardiac myocytes (Burns et al., PloS One, 2019). Historically, cardiac myocytes were thought to be terminally differentiated, however they describe factors that induce these cells to dedifferentiate and re-enter a more proliferative state. This breakthrough is a first step in harnessing the plasticity of cardiac myocytes.

# *HONORS*



James DeGregori, Ph.D. is the new Editor in Chief of the Wiley journal Aging and Cancer.

**James DeGregori, Ph.D.,** *Professor,* Department of Biochemistry and Molecular Genetics, is the new Editor in Chief of the Wiley journal Aging and Cancer (see photo). He explains, "As the newest member of the Wiley family of scientific journals, Aging and Cancer will provide an important forum for new results and ideas that improve our understanding for how old age influences many different facets of cancer, from incidence, to its development and pathology, to treatment outcomes."

**Kathleen Gavin, Ph.D.,** *Assistant Professor,* Department of Medicine/ Division of Geriatric Medicine received one of four 2019 University of Colorado Department of Medicine Rising Star Awards. Her citation reads in part, "During her relatively short tenure, Kathleen Gavin has received multiple awards for her research including being named a Boettcher Investigator in 2018, published extensively and developed an innovative independent line of investigation. She has certainly had a tremendous impact on our Department and our entire campus."

**Chelsea Magin, Ph.D.,** *Assistant Professor,* Department of Medicine/Medical Oncology, was named Colorado Bioscience Association Educator of the Year 2019. Magin is an active mentor in the Colorado BioScience Institute's Research Experience for Teachers program and the principal investigator of the Bio-inspired Pulmonary Engineering Laboratory at the Anschutz Medical Campus. Additionally, Magin serves as the director of product development for Sharklet Technologies, Inc., where she led a research and development team that designed medical devices that use the Sharklet surface texture to control biological adhesion.

Mark Petrash, Ph.D. was the 2019 ARVO Foundation Honoree recognized for commitment to the Association for Research in Vision and Ophthalmology.

**Vikas Patel, M.D.,** *Professor and Vice Chair,* Department of Orthopedics, was named the inaugural Endowed Chair in Orthopedic Spinal Innovation in October 2019. The chair was established thanks to a $2 million gift from a family grateful for the patient-centered care on the CU Anschutz Medical Campus. With this endowed chair, the benefactors hope "to accelerate leading-edge research initiatives, build the foundation for a translational innovation center, and spark discovery and development in spinal care in the CU Department of Orthopedics." Dr. Patel previously served as chief of orthopedic spine surgery.

**Mark Petrash, Ph.D.,** *Professor,* Department of Ophthalmology, was the 2019 ARVO Foundation Honoree recognized for commitment to the Association for Research in Vision and Ophthalmology (ARVO) and the ARVO Foundation including financial support, exemplary leadership of a Foundation initiative or dedication to endeavors that represent the mission of the ARVO Foundation. Dr. Petrash served on the ARVO Foundation Board of Governors during 2013-2019, including three years as Foundation Board Chair (see photo).

Eric Pietras, Ph.D. received the Division of Hematology's 2019 Outstanding Innovator Award.

**Eric Pietras, Ph.D.,** *Assistant Professor,* Department of Medicine/ Hematology, who is the Cleo Meador and George Ryland Scott Endowed Chair in Hematology, received the Division of Hematology's 2019 Outstanding Innovator Award (see photo).

**Jennifer Richer, Ph.D.,** *Professor,* Department of Pathology, was chosen to serve as the 2021 Basic Science Chair on the Annual Meeting Steering Committee of the Endocrine Society (see photo).

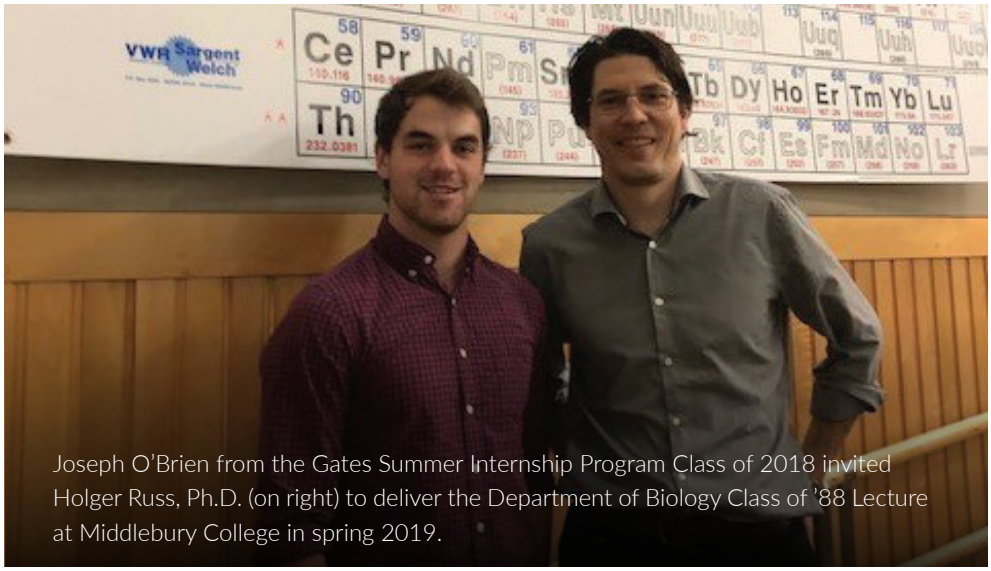
**Paul Rozance, M.D.,** *Professor,* Department of Pediatrics and Integrative Physiology, was named the Frederick Battaglia State of the Art Speaker at the Annual Meeting of the Western Society for Pediatric Research and elected Secretary Treasurer of the Society for Reproductive Investigation (see photo).

Jennifer Richer, Ph.D. will serve as the 2021 Basic Science Chair on the Annual Meeting Steering Committee of the Endocrine Society.

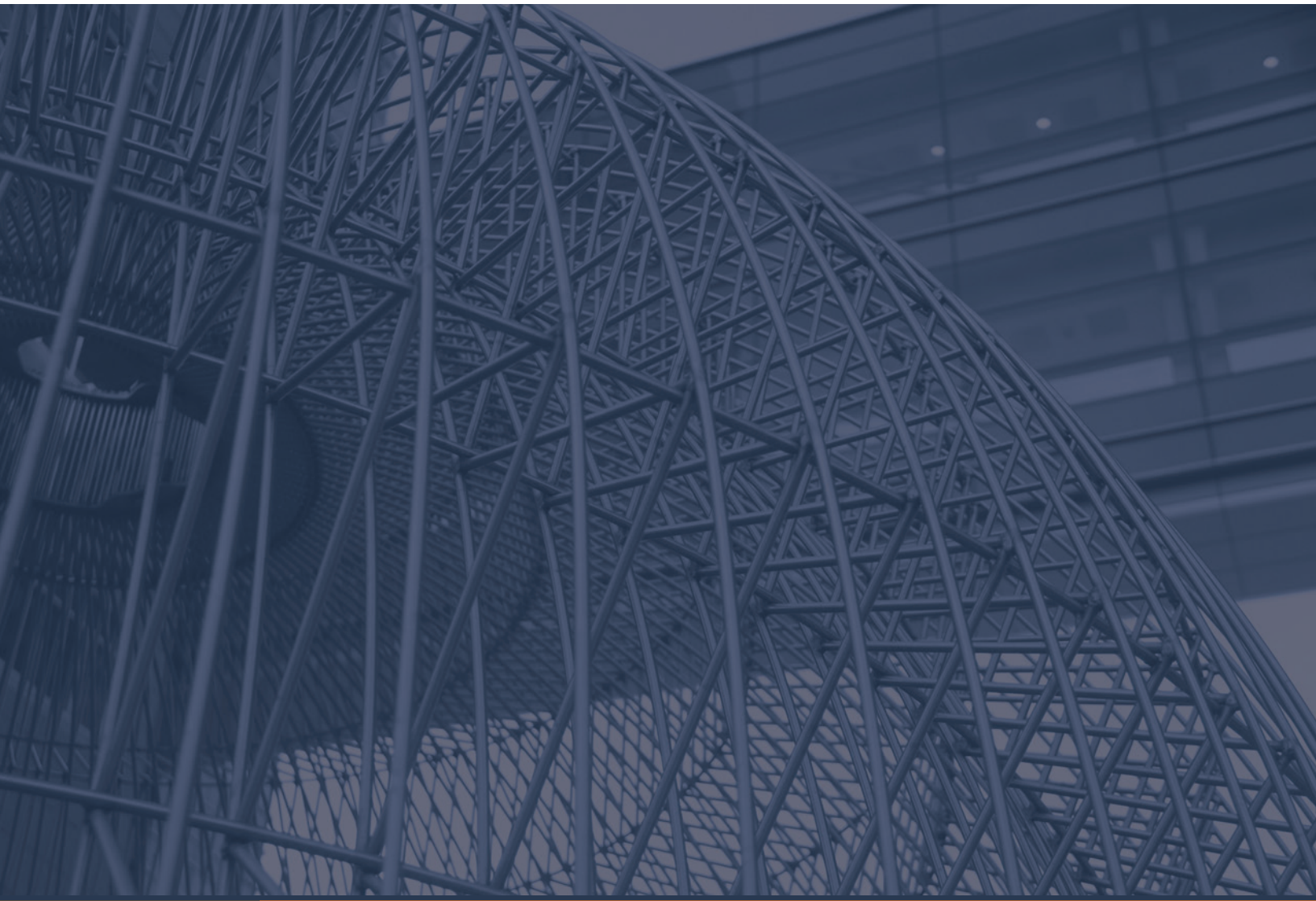
**Holger Russ, Ph.D.,** *Assistant Professor,* Barbara Davis Center for Diabetes, was session chair for the Western Regional Islet Meeting, Victoria, BC, Canada, and the invited speaker for the following: 3rd Joint EASD Islet Study Group & Beta Cell Workshop in Oxford, England; Department of Biology Class of '88 Lecture, Middlebury College, VT (see photo); TUM Technical University Munich, Germany; MCDB Graduate program, University of Miami, Miami, FL; CDMD Seminar Series, Indiana University School of Medicine, IN; and Colorado Café Scientifique, Denver, CO.

**Lori Sussel, Ph.D.,** *Professor,* Barbara Davis Center for Diabetes, Pediatrics (Cell & Developmental Biology), received the "2019 Grodsky Award" and delivered a keynote at the West Coast Regional Islet gathering in Victoria, British Columbia. She also presented the Stefan S. Fajans Lecture in Diabetes at the University of Michigan.

Paul Rozance, M.D. was named the Frederick Battaglia State of the Art Speaker.




Joseph O'Brien from the Gates Summer Internship Program Class of 2018 invited Holger Russ, Ph.D. (on right) to deliver the Department of Biology Class of '88 Lecture at Middlebury College in spring 2019.



# GRANT AWARDS

| PRINCIPAL INVESTIGATOR(S) | AGENCY/SPONSOR | AMOUNT AWARDED | TITLE | FUNDING PERIOD |
|---|---|---|---|---|
| Benam, Kambez | National Institutes of Health | $1,974,712.00 | A Microphysiological Mimicry of Human Lung-Bone Marrow Organ-Organ Crosstalk On-a-Chip | 09/17/19 - 06/30/24 |
| Benam, Kambez | Department of Defense | $306,663.00 | Computed Tomography-Guided 3D-Bioprinted Living Human Lung for Precision Medicine | 12/15/19 - 12/14/21 |
| Bentley, David<br>Russ, Holger | National Institutes of Health | $348,430.00 | Trisomy 21 and RNA polymerase II function | 10/01/19 - 09/30/24 |
| Bilousova, Ganna | National Institutes of Health | $376,310.00 | MicroRNA-based purification of keratinocytes derived from pluripotent stem cells for the treatment of skin diseases | 03/01/19 - 02/28/21 |
| Brzezinski, Joseph | National Institutes of Health | $1,728,302.00 | Mechanisms of cell fate specification and competence regulation in photoreceptors | 08/01/19 - 07/31/23 |
| DeGregori, James | National Institutes of Health | $234,000.00 | Understanding and circumventing aging-dependent changes in the bone marrow microenvironment that promote leukemogenesis | 04/01/19 - 05/31/21 |
| DeGregori, James | Veteran's Administration | $1,846,940.00 | Dissecting the Role of Inflammation in Smoking and Aging Associated Lung Cancers | 04/01/19 - 03/31/23 |
| DeGregori, James | National Institutes of Health | $1,550,000.00 | Determining how aging-associated changes in the microenvironment contribute to leukemogenesis | 10/01/19 - 09/30/24 |
| DeGregori, James | National Institutes of Health | $593,000.00 | Aged tissue environments as drivers of oncogenic adaptation in hematopoiesis | 01/01/20 - 11/30/24 |
| Lanning, Ryan<br>Lyons, Traci (Co-PIs) | CCTSI: Novel Clinical and Translational Methods | $25,000.00 | Optical Lymphangiography of Murine Mammary Tissue during Involution and in Postpartum Breast Cancer | 05/01/19 - 04/30/20 |
| Liechty, Kenneth<br>Grayck, Eva<br>Sudipta, Seal | National Institutes of Health | $2,750,952.00 | Modulation of inflammation and oxidative stress in diabetic wound healing | 04/01/19 - 03/31/23 |
| Magin, Chelsea | National Science Foundation | $501,767.00 | CAREER: Spatiotemporally Addressable Hydrogel Biomaterials as Tools for Investigating Fibroblast Mechanobiology | 02/01/20 - 01/31/25 |
| Magin, Chelsea<br>Bilousova, Ganna | Department of Defense | $311,000.00 | 3D models of pulmonary fibrosis to facilitate precision medicine | 01/01/20 - 06/30/21 |
| Niswander, Lee | National Institutes of Health | $2,760,342.00 | Non-coding RNA regulation of early neural development | 12/01/19 - 11/30/24 |
| Patel, Vikas | OMeGA Medical Grants Association | $15,000.00 | 2019-2020 Spine Fellowship | 08/01/19 - 07/31/20 |
| Payne, Karin<br>Bryant, Stephanie<br>Ferguson, Virginia<br>Miller, Nancy | National Institutes of Health | $1,125,718.00 | Treatment of pediatric physeal injuries using a 3D printed biomimetic of growth plate cartilage | 03/01/19 - 02/28/22 |

| PRINCIPAL INVESTIGATOR(S) | AGENCY/SPONSOR | AMOUNT AWARDED | TITLE | FUNDING PERIOD |
|---|---|---|---|---|
| Phiel, Christopher | National Institutes of Health | $466,500.00 | The Regulation of mRNA Methylation by Glycogen Synthase Kinase-3 | 07/01/19 - 06/30/22 |
| Pietras, Eric | Department of Medicine Outstanding Early Career Scholar Program | $75,000.00 | Inflammation-induced hypoxia as a metabolic trigger of leukemogenesis | 07/01/19 - 06/30/22 |
| Pietras, Eric | National Institutes of Health | $243,500.00 | Impact of IL-1 signaling on HSC function and emergence of clonal hematopoiesis | 02/01/19 - 01/31/24 |
| Roop, Dennis<br>Bilousova, Ganna | National Institutes of Health | $807,981.00 | Exploring Alternative iPS Cell Therapies for Recessive Dystrophic Epidermolysis Bullosa | 08/01/19 - 06/30/21 |
| Roop, Dennis<br>Bilousova, Ganna | EB Charities (The EB Research Partnership,<br>The Los Angeles-based EB Medical Research Foundation,<br>The London-based Cure EB Charity | $807,981.00 | Exploring Alternative iPS Cell Therapies for Recessive Dystrophic Epidermolysis Bullosa | 08/01/19 - 06/30/21 |
| Roop, Dennis<br>Bilousova, Ganna<br>Kogut, Igor | EB Charities | $276,254.00 | Delivering keratinocytes derived from gene-edited RDEB iPSCs by Spray on Skin | 01/01/19 - 12/31/19 |
| Roop, Dennis<br>Bilousova, Ganna<br>Kogut, Igor | EB Charities | $281,489.00 | Systemic delivery of MSCs derived from gene-edited RDEB iPSCs | 01/01/19 - 12/31/19 |
| Roop, Dennis<br>Bilousova, Ganna<br>Kogut, Igor | EB Research Partnership,<br>EB Medical Research Foundation | $518,638.00 | Delivering keratinocytes derived from gene-edited EB Simplex iPSCs by Spray on Skin | 07/01/19 - 06/30/20 |
| Roop, Dennis<br>Bilousova, Ganna<br>Kogut, Igor | Sprout Foundation | $1,970,000.00 | Research Program Ehlers-Danlos Syndrome Center of Excellence | 07/01/19 - 06/30/22 |
| Russ, Holger | UCAMC-RNA Bioscience Initiative | $10,000.00 | Elucidating AIRE dependent expression of tissue-restricted antigens in stem cell derived organotypic thymus cultures from healthy and autoimmune patients | 05/01/19 - 04/30/20 |
| Russ, Holger<br>Davidson, Howard | National Institutes of Health | $432,500.00 | Stress induced changes to the human beta cell proteome | 04/01/19 - 03/31/21 |
| Russ, Holger<br>Phelps, Edward | Juvenile Diabetes Research Foundation | $440,000.00 | Localized Immune modulation in Beta Cell Replacement | 06/01/19 - 05/31/21 |
| Shellman, Yiqun | University of Colorado School of Medicine | $50,000.00 | University of Colorado Academic Enrichment Fund | 01/01/19 - 01/30/20 |
| Shellman, Yiqun<br>McCarter, Martin | Cancer League of Colorado Team Award | $60,000.00 | Targeting anti-apoptotic pathways to improve immunotherapies for melanoma | 07/01/19 - 06/30/20 |
| Walker, Lori | Chernowitz Medical Research Foundation | $412,500.00 | Elucidating the Mechanisms Underlying Cannabinoid-mediated Changes in Smooth Muscle Contractility | 11/01/19 - 10/31/22 |
| Xu, Junwang<br>Liechty, Kenneth | National Institutes of Health | $1,555,000.00 | The role of long non-coding RNA GAS5 in diabetic wounds | 05/01/19 - 04/30/24 |
| | **TOTAL AWARDS =** | $24,855,479.00 | | |

# COMMERCIALIZATION

## GATES CENTER COMMERCIAL EFFORTS FUEL STARTUPS

It tends to be a bit more complicated than a chocolate-in-the-peanut-butter moment, but every Gates Center-related medical startup has that instant where a break in mindset led to promising discovery.

For eye surgeon Jeffrey Olson, M.D., and what would soon become AmpVision LLC, the "a-ha!" moment came as he was researching treatment for an entirely different part of the body – kidneys. Olson and other eye specialists spend a large amount of their time dealing with macular degeneration and diabetic retinopathy, affecting more than 10 million people in the U.S. alone.

Both conditions produce too much protein inside the eye. Olson's team had been studying the possibility of "cell encapsulation," which puts therapeutic materials inside tiny polymers for long-term release. As they looked at different membranes, they stopped suddenly on kidney dialysis, which relies on a sophisticated external pump-and-filter system to clean the bloodstream.

"We saw reports of kidney patients being inflammatory-deficient," Olson said. "For them, it was an unwanted side effect." The dialysis process filtered out "good" inflammatories. "For us, there's too much protein in the eye, and it causes inflammation. So, why not use the side effect as the treatment?"

The result of the epiphany is a manufactured device the diameter of a pencil eraser that is meant to be implanted in the eye and filter out excess proteins over time. The device is modeled to last for years, eliminating monthly needle-stick injections in each eye – "that's 700 needle sticks in a lifetime," Olson notes.

"It's like putting an air filter in the room instead of spraying in an air cleaner," he said.

Even with his third startup, Olson can't take the next steps alone, he said.

"The toughest thing we run into every time is the 'valley of death' – you've got a great idea, you pitch it, they love it, and they say, 'If you can raise $500,000 or $1 million to get it into patients, we'll fund the $4 million clinical trial,'" Olson said. Neither Olson, an associate professor of ophthalmology at the School of Medicine who practices at UCHealth and the VA, nor his colleagues have that kind of walking-around money.

That's where the Gates Center, the CU Innovations Office, the Grubstake Awards and the Gates Startup Toolbox enter the picture for the 118 Gates-member researchers hoping to take their technology toward patient treatment. Most researchers – many of whom are also busy clinical providers – need seed money, legal and regulatory expertise, and business advice to move their ideas along.

"The focus of doing research is for the betterment of humanity," said Heather Callahan, Ph.D., J.D., EMBA, who is Entrepreneur in Residence at the Gates Center and CU Innovations. "If you just research it and never translate it into a product and get it on the market, it doesn't have all the value it could have. It's just the way our society has set this up. The commercial component is the critical piece to connect bench research to making patients better."

Olson received help from the Gates Grubstake Fund, which provides three or four annual awards up to $350,000 to support the translational development of regenerative medicine projects into patented, clinic-ready products. AmpVision has employed some of that funding for a regulatory consultant to navigate FDA procedures, and to investigate how to start up clinical-grade manufacturing if the device is approved for human trials.

The presentations and persuasion that come with fundraising are "not my favorite part," Olson said. "Gates Grubstake has really gotten us through some of that." The Gates funds are less restricted, for example, and therefore easier to direct where needed, than other sought-after funding such as federal Small Business Innovation Research grants, Olson said.

Through Grubstake and the Startup Toolbox, Callahan said, the variety of assistance available for researchers is unparalleled. "We connect them to law firms, lawyers who are used to working with inventors who help them form a company and license the technology; we help them assemble a management team; we help them obtain non-dilutive funding…those are the things that make a difference in the success of a company."

Gates Center research members have launched a number of promising startups to help translate their discoveries into products for treating patients. Each is at a different stage of fundraising, regulatory approval, and steps remaining to clinical trial. Here is a partial list:

**Allander Biotechnologies, LLC –** Gates member Xiao-Jing Wang, M.D., Ph.D., leads this startup bringing to the clinic a protein-based therapeutic that can be topically applied to treat inflammatory disorders with unmet medical needs such as oral mucositis (a side-effect of cancer treatment) and chronic non-healing wounds (frequently seen in diabetics). Allander has received one of the first Grubstake Awards, two Phase 2 NIH Small Business Innovation Research (SBIR) awards and investment funding. Allander's goal over the next year is to file for pre-Investigational New Drug (IND) status, a critical step in the FDA approval process for new drug therapies.

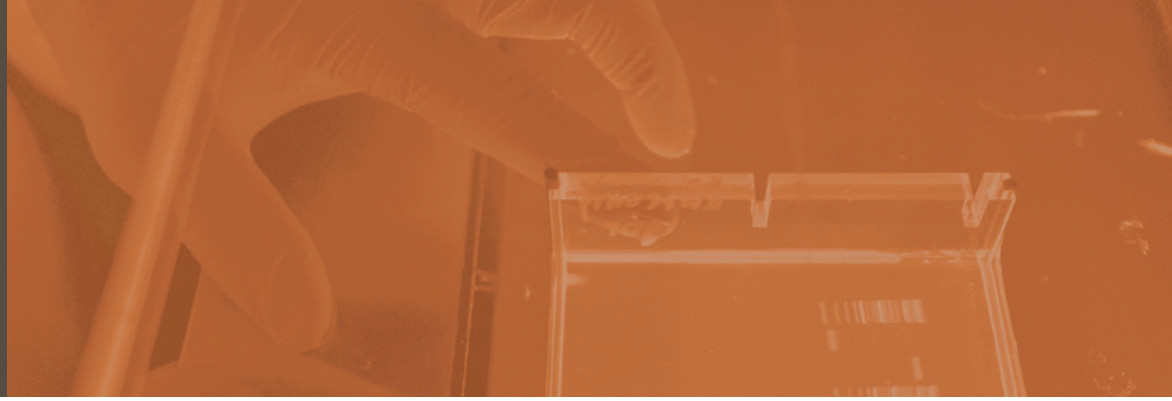
**Ceria Therapeutics, Inc. –** Ken Liechty, M.D., has received two Grubstake Awards to develop a therapeutic cerium oxide nanoparticle conjugated to miRNA (CNP-miR146a) designed to treat inflammatory disorders with unmet medical needs such as diabetic ulcers and acute lung injury. Dr. Liechty's startup, Ceria Therapeutics, Inc., filed a pre-IND through the University of Colorado before the company was even formed. Ceria has received investment funding from Children's Hospital. Ceria is currently assessing whether its therapeutic, CNP-miR146a, might be helpful in treating acute respiratory distress symptoms in patients with serious cases of COVID19.

**Omix, LLC –** is led by Kirk Hansen, Ph.D., an associate professor at the School of Medicine. Omix has technology that characterizes the tissue scaffolds that allow regeneration to happen in situ. Such tissue scaffolds require meticulous FDA approvals of their manufacturing for safety and efficacy.

**Op-T, LLC –** David Wagner, Ph.D., an Associate Professor in the Department of Medicine and Department of Neurology at the School of Medicine, is developing diagnostics for autoimmune disease and therapeutic approaches to control autoimmune inflammation. Op-T plan to file an IND for a drug product in early 2020 and to start clinical trials later in the year. Their focus is on the immune cascade, useful for type 1 diabetes, atherosclerosis and multiple sclerosis

**SummitDx, LLC –** Shi-Long Lu, M.D., Ph.D., an Associate Professor at the School of Medicine, is developing saliva liquid biopsy tests for the early detection of Head and Neck cancer. The company is built on the research discoveries of Dr. Lu and John Song, M.D., from the University of Colorado Anschutz Medical Campus. The company's lead product in development is HNKlear, the first saliva test for Head and Neck cancer recurrence following front-line treatment.

**Validus Cellular Therapeutics, Inc. –** Validus researchers, including Steve Dow, Ph.D., Director of the Center for Immune and Regenerative Medicine at Colorado State University, have discovered that through special activation of mesenchymal stem cells, drug resistant infections become more treatable. In clinical veterinary studies to treat animal infections, activated cells seek out resistant infections and enhance the body's natural immune system. Validus has a new CEO, Ethan Mann, and is applying for SBIR funding as well as investment capital.



# 2019 GATES GRUBSTAKE FUND

With new solutions in mind, the Gates Grubstake Fund is an initiative of the Gates Frontiers Fund and a key component of the Gates Center for Regenerative Medicine's commercialization strategy for projects and teams affiliated with the Gates Center. Through a process overseen by the Gates Center with significant support from CU Innovations, Grubstake Fund investment decisions regarding three to four annual awards of up to $350,000 are made on a competitive basis by a Scientific Investment Advisory Committee comprised of subject matter experts and institutional investors with a focus on biotechnology:

## GATES GRUBSTAKE SCIENTIFIC INVESTMENT ADVISORY COMMITTEE

- Mark Brunvand, M.D., Field Medical Director, CAR T-cells, Bristol-Myers Squibb
- William Hiatt, M.D., Professor, Division of Cardiology, University of Colorado Anschutz Medical Campus; Past President and now Chief Science Officer, CPC Clinical Research
- Ryan Kirkpatrick, Partner, Colorado Impact Fund
- David L. Lacey M.D., Biopharmaceutical Consultant, former SVP, Head of Research, Amgen
- Mark Lupa, Ph.D., Principal, High Country Ventures
- Kimberly Muller, J.D., Managing Director, CU Innovations, University of Colorado Anschutz Medical Campus
- Mark Petrash, Ph.D., Professor and Vice Chair, Department of Ophthalmology, Associate Director, Gates Center for Regenerative Medicine, University of Colorado Anschutz Medical Campus
- Matthew Seefeldt, Ph.D., Director of Cell Therapy, Gates Biomanufacturing Facility
- Geoff "Duffy" Solich, Executive Vice President, E & P Resources LLC; member, Gates Center Advisory Board
- Ann Sperling, Senior Director, Trammell Crow Company; member, Gates Advisory Board
- Robert Traver, J.D., Patent Attorney, Sheridan Ross

## 2019 GATES GRUBSTAKE AWARDEES:

**Terry Fry, M.D.**
***Optimized manufacturing of CD19xCD22 CAR expressing T cells for the clinic***

Refractory cancers are an increasing cause of early death in adults and children. Recent breakthroughs in cell based immunotherapeutic treatments (primarily CAR-T cell therapy) are changing that rapidly, with hundreds of trials ongoing in the U.S. and around the world. Although some patients may be cured with current monovalent CAR-T cell therapy (that targets only CD19), relapses shorten remissions in a majority of patients. Dr. Terry Fry and his team are developing a next generation bicistronic CAR-T cell therapy (that targets both CD19 and CD22) designed to prolong remissions in patients, improving patient well-being and decreasing healthcare costs. The Grubstake Award will allow them to develop the manufacturing process at the Gates Biomanufacturing Facility.

## Holger Russ, Ph.D.

***Generation of functional, patient specific thymi for cell therapy***

One of the challenges following bone marrow transplants for cancer therapy is often lethal complications including bacterial pneumonia and graft versus host disease. Although reconstitution of blood forming cells is rapid following transplantation, T cell reconstitution is very slow and incomplete due to the lack of a functional thymus in the patient. To resolve this, Dr. Russ and his team are generating functional, patient specific thymi for co-transplantation into bone marrow transplant recipients. Dr. Russ's approach can also be used to treat patients with a congenital absence of a thymus. The Grubstake Award will allow them to transfer the technology to the Gates Biomanufacturing Facility for manufacturing scale up and to prepare for pre-IND filing with the FDA.

## Ram Nagaraj, Ph.D.

***Therapeutic peptide for neuroprotection in acute closed angle glaucoma***

Glaucoma is the leading cause of irreversible blindness, with an estimated 80 million people worldwide affected by 2020. Retinal ganglion cell death (RGC), a hallmark of the disease, leads to degeneration of the optic nerve, resulting in visual field loss. RGC death correlates with increased intraocular pressure (IOP) due to defects in the drainage of fluid from the anterior chamber of the eye. In acute angle closure glaucoma, there is a sudden rapid rise in IOP with damage that requires immediate medical attention, typically surgery. Despite immediate care, RGC continue to die and cause a permanent reduction in vision within three months. Dr. Nagaraj and his team are developing a peptide-based therapy designed to prevent the rapid loss of RGC from acute angle closure glaucoma. The Grubstake Award will allow them to assess treatment schedules to assess whether additional formulation work is required.

## Raj Kumar, Ph.D.

***Production of Efficacious Recombinant hypo-glycosylated FSH Glycoform for Clinical Applications***

Artificial reproductive technology (a $1.5 billion market) may be used when women do not produce sufficient Follicle-Stimulating Hormone (FSH) for optimal ovarian follicle growth and estrogen production to support pregnancy. Currently, the response rate to standard FSH is very poor. Dr. Kumar and his team have discovered that reason appears to be the glycosylation pattern (location sugars are added to the protein) of the FSH. Dr. Kumar has shown that FSH21, expressed in women with normal reproductive cycles, is also more biologically active in animal models. He plans to use funds from the Gates Grubstake Award to begin the process of developing the tools needed for manufacturing FSH21 for clinical testing.

Gates Grubstake Fund Scientific Investment Advisory Committee members and 2019 awardees indicated by * (left to right) William Hiatt, Mark Brunvand, Mark Petrash, Kimberly Muller, Mike Verneris*, Kenneth Liechty*, Duffy Solich, Kunhua Song*, Ryan Kirkpatrick, Ann Sperling, Matt Seefeldt and Mark Lupa

## Gates Grubstake Fund awards have benefited an array of focus areas and departments:

| AREA OF FOCUS | DEPARTMENT | AWARDEE | PROJECT NAME | AWARD YEAR |
|---|---|---|---|---|
| iPSC's (induced pluripotent stem cells) | Department of Dermatology | Ganna Bilousova, Ph.D., and Igor Kogut, Ph.D. | Induced pluripotent stem cell services as a platform for clinical research | 2015 |
| Ophthamology | Department of Ophthamology | Jeffrey Olsen, M.D. | Intraocular device to potentiate retinal stem cell transplantation in macular degeneration | 2016 |
| Ophthamology | Department of Ophthamology | Valeria Canto-Soler, Ph.D. | Stem cell-derived retinal transplant to treat dry- AMD | 2017 |
| Ophthamology | Department of Ophthalmology/ School of Pharmacy | Ram Nagaraj, Ph.D. | Therapeutic peptide for neuroprotection in acute closed angle glaucoma | 2019 |
| Orthopedics | Department of Orthopedics | Karin Payne, Ph.D., and Vikas Patel, M.D. | Structural living bone allografts to enhance bone formation in orthopedic surgery | 2015 |
| Orthopedics | Department of Orthopedics | Karin Payne, Ph.D. | Bioresorbable 3-D printed personalized implant for cartilage regeneration in pediatric growth plate injuries | 2017 |
| Oncology | Department of Medicine/ Medical Oncology | Antonio Jimeno, M.D., Ph.D. | Proprietary humanized mouse model to assess cancer treatments | 2014 |
| Oncology | Department of Pediatrics/ Hematology, Oncology and Bone Marrow Transplantation | Mike Verneris, M.D. | Generation of Engraftable Hematopoietic Stem Cells from Induced Pluripotent Stem Cells | 2018 |
| Oncology | Department of Pediatrics/ Hematolory and Immunology | Terry Fry, M.D. | Optimized manufacturing of CD19xCD22 CAR expressing T Cells for the Clinic | 2019 |
| Oncology and Wound Healing | Department of Pathology | Xiao-Jing Wang, M.D., Ph.D. | Human Smad7-based proteins combined with a cell permeable peptide called Tat. Tat-Smad7 and its derivatives can be used via topical application to treat at least four diseases: oral mucositis, psoriasis, chronic wounds, and fibrotic diseases. | 2014 |
| Wound Healing | CSU Department of Clinical Services | Steven Dow, D.V.M., Ph.D., and Mary Ann DeGroote, M.D. | Antimicrobial stem cell therapy for infected diabetic foot ulcers | 2015 |
| Wound Healing | Department of Surgery/ Pediatric Surgery | Ken Liechty, M.D. | A platform technology useful for treating a variety of diseases where inflammation and oxidative stress are pathognomonic in the progression of the disease; initial focus is treatment of diabetic ulcers, where compelling in vitro and animal model data exists showing that treatment results in closure rates of diabetic wounds equal to nondiabetic wounds | 2016 |
| Cardiology | Department of Medicine/ Cardiology | Kunhua Song, Ph.D. | Heart regeneration by conversion of non-myocytes into functional cardiomyocytes | 2018 |
| Diabetes | Barbara Davis Center for Diabetes | Holger Russ, Ph.D. | Generation of functional, patient specific thymi for cell therapy | 2019 |
| Neurology | Department of Neurology | David Wagner, Ph.D. | A 15-amino acid peptide to potentially stop demyelination and restore myelin production in multiple sclerosis | 2016 |
| Obstetrics | Department of Obstetrics and Gynecology | Raj Kumar, Ph.D. | Production of Efficacious Recombinant hypo-glycosylated FSH Glycoform for Clinical Applications | 2019 |
| Pulmonary | Department of Surgery/ Pediatric Surgery | Ken Liechty, M.D. | Prevention and treatment of pulmonary fibrosis | 2018 |
| Transplantation | Department of Pulmonary, Critical Care Medicine | Martin Zamora, Ph.D. | Clinical development of autologous CD117+ progenitor cell therapy for solid organ transplantation | 2017 |

# CORE FACILITIES

Near the end of 2019, the Directors of several Gates Center Core Facilities informed Gates Center leadership of their transition plans for 2020. Dr. Peter Koch, director of the Bioengineering Core and Dr. Maranke Koster, director of the Morphology and Phenotyping Core, announced their plans to accept offers from the Brody School of Medicine at Eastern Carolina University as Professor and Chair Department of Anatomy & Cell Biology (Peter) and Full Professor with Tenure (Maranke). We thank Peter and Maranke for ten outstanding years of service to the Gates Center as directors of these cores and wish them much success in their new positions.

After 27 years of service to the University, Karen Helm announced that she will be retiring in June 2020. Karen has served as director of the Flow Cytometry Core for the last 12 years. Because of the outstanding service that she has provided to so many members of the Gates Center, we decided to highlight her career and partnership with the Gates Center in this year's annual report.

These transitions have provided an opportunity for Gates Center leadership to reassess the core facilities supported by the Center and make the following changes for 2020. Many of the services previously provided by the Bioengineering Core will be now be offered by the Stem Cell Biobank and Disease Modeling Core. Dr. Igor Kogut has agreed to direct the Morphology and Phenotyping Core and will expand the services provided by this Core (see next page). In the meantime, a search committee comprised of several stakeholders in the Flow Cytometry Core selected Lester Acosta as the new Core director effective July 1, 2020. Lester is currently the leader of the Core cell sorting staff and has worked under Karen Helm's supervision for over 11 years. Although Lester has "big shoes to fill," we look forward to working with him and anticipate that the Core will continue to provide outstanding service to Gates Center members as was the case under Karen's leadership.

Following a presentation made to the Gates Advisory Board at its September meeting by Dr. Bruce Appel, Professor and Head, Section of Developmental Biology, Department of Pediatrics and Diane G. Wallach Chair of Pediatric Stem Cell Biology, Gates Center leadership made a decision to support the new Organoid and Tissue Modeling Core Facility established by Bruce and Dr. Peter Dempsey, Associate Professor, Department of Pediatrics. Bruce made a strong argument for establishing this new core, which he and Peter believe will fill a void on campus and provide Gates Center members with opportunities to develop and utilize powerful human organoid and tissue models that will enhance their research capabilities and improve competitiveness for external grant funding (see next page).

## *FLOW CYTOMETRY CORE*

### KAREN HELM: A FRIEND, COLLABORATOR AND EXPERT OPERATOR

"I think everyone loves her!"

Karen Helm has worked for the University of Colorado for 27 years and managed the Gates Flow Cytometry Core and its impressive evolution over the last 12. She exemplifies the professional expertise, dedication to science, commitment to helping and teaching colleagues and clients – and friendliness – that have helped propel this core to be renown on campus and beyond for its first-class service. After all, how many people on an academic campus are actually loved by everyone?!

When Gates Center Director Dennis Roop, Ph.D. arrived on the CU Anschutz Medical Campus in 2007 to begin a program in stem cell biology and regenerative medicine, he spoke to Karen's core director Christopher Hogan about gaining access to equipment. Dr. Roop's decision to contribute Gates Center funds ($1 million) toward the Flow Cytometry Core then and since rather than starting a separate core was seminal and according to Karen, "really jumped us ahead."

Cores enable all investigators access to expensive state-of-the-art equipment and expertise with which to generate preliminary data to make their grants and publications more competitive. The Flow Cytometry Core has been very successful in weaving together Gates Center, Cancer Center, Dean's Academic Enrichment Fund and NIH grants to expand its services – efforts spearheaded by Karen. "We've really grown," says Karen. Starting from one sorter/analyzer and Karen as the sole employee, they now have four sorters, four analyzers, a mass cytometer, many pieces of ancillary equipment and six on staff who work with customers at CU Anschutz, National Jewish Health, CU Boulder, CU Colorado Springs, CSU and CSU Pueblo. Although the fragility of cells precludes their operating outside the state, they provide protocols and expertise to many researchers outside of Colorado because of the unique methods developed at CU with Karen and her staff's help. Some of these include sorting for side population cells and live adipocytes. Karen has also given many presentations at professional society meetings on these and many other topics, significantly moving the field of flow cytometry forward.

Prior to coming to the University, Karen worked at Swedish Hospital in flow cytometry and, when CU needed a flow cytometrist to manage the Cancer Center Flow Cytometry Core in 1993, Karen was hired. In 1997 CU purchased a MoFlo, the highspeed sorter that was based on a Lawrence Livermore National Laboratory instrument developed to facilitate the sorting of human chromosomes as part of the Human Genome Project. The University's brand new MoFlo that operated five times faster than the equipment it replaced, was the 24th in the world. Not surprisingly, Karen has given substantive cytometry lectures over the years at the request of Cytomation (original manufacturer of the MoFlo).

Karen explains the core's current operation and significance for Gates Center members and others engaged in stem cell research:

- Flow cytometry (FC) is an essential tool for stem cell research, allowing the examination of cells at the single-cell level by using cell surface, internal, and nuclear labels. We also have more specialized equipment, which can rapidly isolate and collect unique types of cells.
- Traditional flow cytometers use laser beams and fluorescent tags to identify the presence or absence of cell markers, however the number of easily identifiable labels is limited to 10 to 15 in conventional systems. Recently, with funding provided by the Gates Center and other campus sources, the core purchased a mass cytometer. This instrument uses rare-earth metal tags to easily identify up to 45 different markers on each cell.

Karen's expertise goes well beyond having the skills to use newly designed equipment. She is one of a small, tight-knit group of operators that has grown up since the development of the first cell sorter by a CU Boulder graduate student studying the effects of radiation at Los Alamos, which was patented in 1967. Her theoretical curiosity and tenacity have driven her not just to obtain equipment to use, but also to maintain it beautifully and get the absolute most out of it. The original #24 upon which she worked in 1997 has been upgraded but is surprisingly still in use. Additionally, she is regularly called upon to perform beta tests for Propel Labs in Fort Collins, which uses its customers from around the world as their design team. This includes flying

Flow Cytometry Manager
Karen Helm

potential Propel customers to visit Karen's core facility at the Anschutz Medical Campus or Fort Collins for demonstrations.

Most important to Karen are her staff and customers. She believes that people in her position need to have 50% science and technology ability and 50% people skills to deal with a lot of people and to interact and teach them in a friendly manner. Judging on comments such as "Honestly, she is responsible for the quality of experimental data for many people at CU!!!" and "Without her and her expertise my career in rare events would have stalled and likely halted," she and her staff have succeeded beyond measure.

Karen Helm announced in fall 2019 that she would retire in June 2020. She has trained a fantastic group by example over the past 15 years and leaves the core in very capable minds and hands.

Karen Helm will be greatly missed as a friend, collaborator and expert operator.

## *MORPHOLOGY AND PHENOTYPING CORE*

The Morphology and Phenotyping Core is now being operated under new leadership with Dr. Igor Kogut serving as director. It provides a full set of histology services including the following:

- Paraffin and OCT embedding.
- Sectioning of frozen and paraffin blocks.
- Routine (H&E) and special staining for all types of tissues.
- Consultation to optimize tissue isolation and fixation procedures.

Beginning in 2020, this core will be expanded to provide accelerated access to ultrastructure analysis by electron microscopy. The ultrastructural analysis of grafts generated with skin cells isolated from Ehlers-Danlos Syndrome (EDS) patients has proven essential for characterizing a novel in vivo skin xenograft model that faithfully recapitulates the skin phenotype seen in EDS patients.

## *STEM CELL BIOBANK AND DISEASE MODELING CORE*

The Stem Cell Biobank and Disease Modeling Core was established in 2017 on the basis of the development of a more efficient approach for reprogramming a patient's diseased skin cells into stem cells by a team of scientists at the Gates Center, Ganna Bilousova, Ph.D., assistant professor of dermatology, Igor Kogut, Ph.D., assistant professor of dermatology, and Gates Center Director Dennis Roop, Ph.D. The process, which was described in a paper published in Nature Communications in February 2018, reports a clinically safe approach that consistently reprograms healthy and disease-associated patient's skin cells into induced pluripotent stem cells (iPSCs) with an unprecedented efficiency.

This core is co-directed by Drs. Bilousova and Kogut and offers complete services related to the production of high-quality human iPSCs from patient-derived somatic cells at one-third the cost charged by others. In addition to reprogramming services, the core provides genome engineering services using CRISPR/Cas to modify genes of interest in human iPSCs including the following:

- The development of iPSC-based lineage tracing models.
- The correction and introduction of disease-associated mutations in human iPSCs.
- The generation of isogenic pairs of genetically corrected and unmodified iPSCs by simultaneous reprogramming and gene editing of patient's somatic cells.
- The production of custom-made modified mRNAs encoding a variety of factors for transient transfection into cells.

This core continues to provide services for numerous clients on the Anschutz Medical Campus and at CU Boulder, as well as national and international external clients.

## *THE ORGANOID AND TISSUE MODELING CORE FACILITY*

### Background:

Recent advances in adult stem cell 3D organoid cultures, induced pluripotent stem cells (iPSCs) and genome editing technologies have created unprecedented potential to investigate and treat human disease. However, progress toward effective therapies has been slowed by lack of in vitro models that recapitulate the complex tissue environments in which cells differentiate and function. Despite great strengths in cell and animal models, the University of Colorado Anschutz Medical Campus (AMC) has had a critical need for experimental systems that better represent human development, homeostasis and disease. The development of an Organoid and Tissue Modeling Core Facility will provide investigators with a wide array of opportunities to develop and utilize powerful human organoid and tissue models that will enhance their research capabilities and improve competitiveness for external grant funding.

### Generation of intestinal 3D Organoids and Tumor Organoids:

In July 2016, an Enteroid Stem Cell Core was established within the Gastrointestinal and Liver Innate Immunity Program (GALIIP), which was funded through the Dean's Transformational grant mechanism. This core was directed by Dr. Peter Dempsey and its primary goal was to generate mouse and human intestinal 3D organoids. In addition to generating intestinal 3D organoids, Dr. Dempsey collaborated with Dr. Wells Messersmith, head of the Division of Medical Oncology, to successfully generate tumor organoid lines from patients with colorectal cancer, pancreatic ductal adenocarcinoma, esophageal cancer and cholangioma. Other investigators have expressed an interest in generating organoids from the following tumor types: bile duct, liver and head and neck cancers.

### Generation of Organoids from Other Patient-derived Tissues and Diseases:

With continued advances in methodologies to grow other adult stem cells, there has also been tremendous interest from CU Anschutz investigators to establish organoids from a wide variety of patient-derived tissues, including: taste buds, salivary gland, thymic epithelium, lung, brain, heart and pancreas.

Investigators have additionally expressed interest in generating organoids from patients who suffer from osteoarthritis, obesity, immunodeficiencies, polyposis syndromes, inflammatory bowel disease, HIV and aging, and from pediatric patients with intestinal failure and monogenic diarrheal diseases.

### Core Facility Goals:

The Organoid and Tissue Modeling Core Facility aims to provide CU Anschutz investigators the ability to overcome the barriers to organoid and tissue experimentation. The facility will be equipped to culture and store tissue and organoid samples and to stock consumable materials, and will be staffed by scientists providing investigators with training and technical assistance. Specific offerings will include:

- Training and expertise in organoid culture techniques.
- Experimental design consultation and novel protocol development.
- Access to consumable, specialized reagents at reduced cost.
- An automated live cell imaging platform to increase the scale and information content of organoid experiments.
- Development of new bioengineering technologies and new platforms for drug discovery.
- A repository of in vitro grown primary human tissues that are accessible to the research community.
- Access to well characterized cell and tissue lines.
- Organoids derived from normal and diseased tissues.

## Collaboration and Impact:

A major goal of the Organoid and Tissue Modeling Core Facility is to complement and synergize with the Gates Center for Regenerative Medicine. For example, the Core will build on the services and expertise of Drs. Ganna Bilousova and Igor Kogut, who co-direct the Gates Center's Stem Cell Biobank and Disease Modeling Core to derive, genetically modify and differentiate patient iPSC lines. The Core will also foster new collaborations by coordinating interactions with the Bioengineering Department, the new AMC Neurotechnology Center and the Biofrontiers Institute in Boulder.

## Administration, Leadership and Implementation:

Peter Dempsey, Ph.D., Associate Professor of Pediatrics, will serve as Director of the Core Facility and Bruce Appel, Ph.D., Professor of Pediatrics, will serve as Director of Training and Education. Together, they will function as Co-Directors of the Organoid and Tissue Modeling Core Facility. A Steering Committee will consist of faculty representatives from participating departments and centers. This committee will meet annually to evaluate Core Facility finances, operations and productivity, as well as goals and directions.

The Core Facility will be located on the third floor of the Barbara Davis Center. The space will include a separate tissue culture facility with 3 biosafety hoods, 1 clean bench, 2 double stacked CO2 incubators, phase microscopes with imaging, centrifuges, water baths, etc. Adjacent to the tissue culture facility will be a designated room for the Olympus IX83 automated spinning disk confocal microscope. Additional lab bench space (1 bay) will be adjacent to Dr. Dempsey's own laboratory space.

To promote Core Facility use, a website will be established that will have detailed descriptions of training and services provided and access to iLabs for reservations and purchasing. Additionally, a series of on-campus seminars will be offered to interested parties to describe the application of organoid technologies and the services provided by the Core. The Core will also partner with the Graduate Training Program in Cell Biology, Stem Cells and Development to develop graduate curricula. A new two credit hour course was initially offered in fall 2019. Working with the Department of Bioengineering, the Core will also engage bioengineering students as research interns, which should catalyze new technology development. Additionally, semi-annual workshops will be held to showcase Core Facility capabilities, and an annual research symposium will feature external and AMC investigators engaged in organoid and tissue-based research.

Peter Dempsey, Ph.D. will serve as Director of the Organoid Core Facility.

Bruce Appel, Ph.D. will serve as Co-Director of the Organoid and Tissue Modeling Core Facility and as Director of Training and Education.

# GATES BIOMANUFACTURING FACILITY

## Charles C. Gates Biomanufacturing Facility

UNIVERSITY OF COLORADO **ANSCHUTZ MEDICAL CAMPUS**

The Gates Biomanufacturing Facility (GBF) worked seamlessly with the Gates Center for Regenerative Medicine and clinical and regulatory colleagues across the CU Anschutz Medical Campus in 2019 to make remarkable progress toward initiating a fully integrated clinical trial in the coming year.

We are now producing the first cell-based immune therapy for which the basic science, regulatory approval, clean manufacturing process and infusion of patients will all have been done on the Anschutz Medical Campus. As a Good Manufacturing Practice (GMP) facility, the GBF is proud and honored to be a key link in this loop. We believe our ability to support on-campus clinical trials will lead to multiple similar efforts in the near future by other researchers and clinicians in a variety of disciplines and continue to bolster the reputation of the GBF and Anschutz as a leader in combined academic research and clinical translation.

"It's an actualization of what we've been working on for years," said Thomas Flaig, M.D., an oncologist and vice chancellor for research on the Anschutz Medical Campus. "This is a new space for us to get into. It's one thing to have an idea, it's another thing to figure out how to actually make the product, and then to deliver it. And we'll have all that in the loop."

The past year delivered a number of milestones at the GBF that similarly culminated years of organization, refinement of methodology and infusions of the right people in the right positions to carry out the complex process of an Investigational New Drug (IND). Among our team's accomplishments:

- Quadrupling the capacity to deliver clinical grade materials.
- Producing clinic-ready materials in protein biologics, natural killer cells, reprogrammed CAR-T cells, and a combination of a protein reagent and a cell therapy.
- Hiring 12 key staff members, boosting our team by 30 percent, including new supply chain and project management teams.

"We've made a sustainable nonprofit business here, where we have enough infrastructure and capability to move clinical trials forward at a relatively fast pace," said Christopher Garbe, director of quality. "Now we can take on more academic clients at the University and get them into their clinical trials." It's extremely rewarding and exciting to picture that in 2020, the GBF will hand-deliver across campus modified CAR-T cells for injection into clinical trial patients at University of Colorado Hospital and Children's Hospital Colorado. That work is led by initiating investigator and Gates Center member Terry Fry, M.D., Director of Cancer Immunotherapy on the Anschutz Medical Campus, and a leading national cancer researcher recruited from the National Cancer Institute.

Fry was one of the first investigators to genetically modify a patient's own CAR-T cells to become cancer-fighters when reintroduced into the same patient's body. The treatment

is FDA-approved for leukemia and lymphoma patients who have not responded to any other treatment and has remarkable results in past trials: 50 percent of lymphoma patients enter sustained remission. In leukemia, 90 percent enter remission, but half of those relapse within a year, Fry said. Researchers want to improve those odds and also take on more cancers—including solid tumors that represent a new level of complexity in targeting.

Fry and his team plan to begin infusing patients with cells attacking CD19 antigens on campus in the summer of 2020. The next iteration of an Anschutz Medical Campus trial, Fry said, will be infusions targeting two antigens at once, CD19 and CD22. "The goal of the next trial we open is a true, novel, first-in-human trial conducted using the infrastructure being enabled by the current trial," he said.

"This puts us on the map as one of the few centers in the U.S. that are not just participating in other peoples' trials, but running our own, and with novel therapies that have potential to take us beyond b-cell malignancies such as leukemia and lymphoma," Fry said. "It's really important, given the investment the campus has made in cell therapy that we can be part of that dialogue.

"The long-term vision is that we can produce drug product and run trials of investigators targeting cancers outside the area of hematology. We're already having conversations about new treatments for solid tumors such as colorectal and pancreatic cancer."

We're proud to play our part in this new era of CU-led research and treatment. Delivering innovations in cell-based immune therapies from the minds of our research members into treatments for patients in need has always been the vision for the GBF. And now we are there.

GATES FRONTIERS FUND

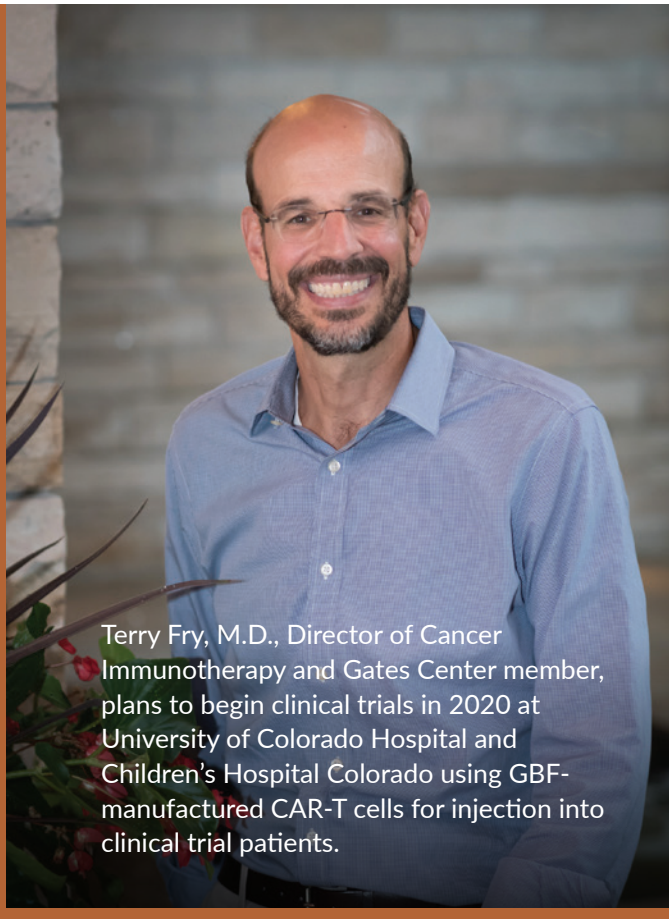
uchealth

Children's Hospital Colorado

School of Medicine
UNIVERSITY OF COLORADO
ANSCHUTZ MEDICAL CAMPUS

University of Colorado
Anschutz Medical Campus

The GBF will manufacture modified CAR-T cells for injection into clinical trial patients at University of Colorado Hospital and Children's Hospital Colorado.



Terry Fry, M.D., Director of Cancer Immunotherapy and Gates Center member, plans to begin clinical trials in 2020 at University of Colorado Hospital and Children's Hospital Colorado using GBF-manufactured CAR-T cells for injection into clinical trial patients.

# EDUCATION

## THE GATES SUMMER INTERNSHIP PROGRAM

Row 1 (Seated): Austin Schoppe, Kaleb Todd, Emily Thomas, Micaela Roy
Row 2 (Middle): Anit Tyagi, Kavya Ganuthula, Drew Harrahill, Anna Martch, Ryan Tseng, Griffin Hampton
Row 3 (Standing): Marina Schlaepfer, Kevin Winkler, Maggie Jewett, Isabella Martus, Sukriti Bhattarai, Iryna Chelepis, Khoa Nguyen, Christopher Schaff, Aiden Jacobs, Madison Kraus, Elizabeth Golding, Kelley Coakley (absent: Stefan Marasligiller)

Hope such as that expressed by our 2019 intern Kelly Coakley in her quote on the top of the facing page has permeated the Gates Summer Internship Program (GSIP) from the beginning.

Inspired by years of positive experiences allowing young people to work under them as summer interns in Gates Center laboratories, Drs. Tamara Terzian, Neil Box and Enrique Torchia (see photo) thoughtfully conceived of an official internship program they hoped would inspire outstanding young college undergraduates to pursue careers in stem cell biology and regenerative medicine. Their hope and initiative proved to be a great catalyst, inspiring the heartfelt and generous support of Gates Center friends Rhondda and Peter Grant (see photo), whose 2014 gift enabled the launch of the GSIP program in the summer 2015 with 12 students. Five years later this program has attracted increased and widespread visibility, ignited professional careers, gained additional supporters along with the Grants and become a signature of the Gates Center's educational efforts.

Recruiting the best and brightest undergraduates is key to the quality of the GSIP, and the number and quality of the applications received speak to the program's growing reputation. Having expanded substantially in offerings and demand since the initial class of 12 students, the program attracted a record number of 230 applicants from 42 states in 2019, and the 23 interns and affiliates accepted were assigned to Gates Center members' laboratories across campus to work on specialized research topics and therapies. They also assembled regularly for 24 bi-weekly seminars on research, clinical subjects, and professional development, and gathered for social and volunteer activities on campus, in Denver and across Colorado. The program concluded with a Closing Day Ceremony on August 9, 2019, featuring guest speaker and CEO of Avita Medical Dr. Mike Perry talking about the vast array of career possibilities available within the field of regenerative medicine and a presentation of the interns' work at a poster session and reception for family, friends, donors, mentors and the wider campus community.

*Those at the Gates Summer Internship Program believed that I would be able to thrive in your scientific community, and I can only hope that I can substantiate these beliefs throughout the rest of my career. I will always be thankful for the opportunity and believe that this program has the capability to invigorate the passion for science, medicine, and technology in the future professionals in their chosen fields.*

*~Kelley Ann Coakley, 2019 GSIP Intern*

The Gates Center joins these students in thanking those who have made this transformative program possible. We have had Drs. Tamara Terzian, Neil Box and Enrique Torchia devote five years as founding directors and Peter and Rhondda Grant and other donors who have reveled in playing a formative role in talented young peoples' lives by way of their generous support. We have had dedicated Gates Center member mentors and their lab staff who have taken these students under their professional wings for the summer, and often beyond as they pursue their studies and apply and are accepted to graduate and medical schools. And we have had lecturers open our students' eyes to a myriad of possibilities beyond their individual lab experiences and projects.

Anecdotal news of our past interns is particularly heartening, especially regarding interns who have elected to pursue studies on the Anschutz Medical Campus. From our very first class of 2015, for example, Emily Paton (see photo with her former mentor on page 61) and Weston Ryan entered the University of Colorado School of Medicine in fall 2018, and their classmate Madison Baker matriculated in the Anschutz Medical Campus's Cell Biology, Stem Cells and Development Graduate (CSD) Program in the fall of 2017. Madison was described just this year by CSD's former Director Bruce Appel as "a fabulous graduate student, the likes of whom we might never have been able to recruit had she not first been a GSIP intern." Finally, 2017 GSIP Intern Alisha Eskew entered CU School of Medicine in fall 2019 (see note to her mentor Curt Freed, M.D. below). Getting news such as this along with other messages and stories included in this Education section gives us great hope for the future of this program and its participants.

Effective January 1, 2020, Assistant Professor in the Department of Ophthalmology Joe Brzezinski, Ph.D. and Director of Marketing and External Relations Jill Cowperthwaite will take over as co-directors of the program. Joe is a longtime GSIP and CSD mentor (see his bio on page 55), and Jill has been involved in marketing and fundraising for the program since its beginning. They are most grateful for the inspired leadership and generous support that have contributed to the program's strong foundation and look forward to cultivating it in the years to come.

*While I expected the Gates Center Summer Internship Program to change the way I look at research, I did not anticipate how it would impact my self-perception. From the moment I started in the lab, I felt like a scientist. My ideas were valued, my contributions were validated, and my presence, especially as a woman in science, was affirmed. The program helped me find the confidence I needed to continue pursuing a career in research.*

*~Ellie Macintosh, Davidson College, GSIP Class of 2018, winner of a 2019 Goldwater Scholarship – an award founded by the U.S. Congress in 1986 to encourage scientific research.*

*Dear Grants and Gracious Donors who made this program possible,*
*This summer that I spent with the Gates Summer Internship program was challenging scientifically, methodically, and professionally but also extremely rewarding in that each of these challenges pushed me to grow to be a better member of the scientific community. I developed technical skills learning laboratory protocols that were handcrafted by my colleagues themselves and learned how to ensure the data collected and analyzed was always fair, sound, and ethical. We networked and got to witness the ground-breaking research projects from synthesis of lung capillaries to decoding the genetic basis of obesity. I'm thankful for the opportunity to be exposed to so many applications of science through the workshops and lectures, but I'm also thankful for the peers I got to grow with and witness their journey, as well, as we connected our summer projects with our future goals. We pondered about the immense amount of experiments that goes into that one graph that can change everything. Or about the creativity manifested in our mentors and colleagues that we hope to achieve one day. This summer was filled with science, miracles, and inspiration and I am so fortunate to carry the things I learned from this internship as I pursue medicine and hope to become a physician. Working with an M.D./Ph.D. this summer who worked in the lab and saw patients, I saw the invaluable connection that helped bring patient needs into the lab and innovation into delivering quality care. Thank you for the endless support of this program and for motivating a generation of scientists with a never-ending drive.*

*~Kavya Ganuthula*

Founding Gates Summer Internship Directors Drs. Enrique Torchia, Tamara Terzian and Neil Box (left to right) shepherded the program and its students alongside Gates Center member mentors for five years.

*Thank you for organizing this GSIP program for years. It has improved every year, and interns enjoy the program including social activities because the experience enhances their bonds, networking and career plans. And, my intern was one of the best students I have ever had. I greatly enjoyed the opportunity.*

*~2019 GSIP Mentor Survey*

*I want to thank you with the utmost gratitude for your contribution toward my acceptance into medical school. Not only was your letter invaluable, but also your teaching and mentorship during my summer research project for GSIP were priceless. I appreciate your support throughout the process, and I cherish you and your contribution to my current and future success.*

*~From a message to Curt Freed, M.D. from GSIP Class of 2019 intern Alisha Eskew who entered CU Medical School in Fall 2019*

(left to right) Peter Grant, Diane Wallach and Rhondda Grant visit at the Gates Summer Internship Program Closing Ceremony.

| *INTERN* | *UNDERGRADUATED INSTITUTION* | *MENTOR* | *DEPARTMENT* |
|---|---|---|---|
| Sukriti Bhattarai | University of Southern Mississippi | Shi-long Lu, M.D., Ph.D. | Department of Otolaryngology |
| Iryna Chelepis | Utah Valley University | Neil Box, Ph.D. | Department of Dermatology |
| Kelley Coakley | Regis University | Nidia Quillinan, Ph.D. | Department of Anesthesiology |
| Kavya Ganuthula | University of Colorado Denver | Stanca Birlea, M.D., Ph.D. | Department of Dermatology |
| Elizabeth Golding | Tulane University | Tania Reis, Ph.D. | Department of Medicine<br>Division of Endocrinology, Metabolism and Diabetes |
| Griffin Hampton | Colorado School of Mines | Kristin Artinger, Ph.D. | Department of Craniofacial Biology |
| Drew Harrahill | University of Nebraska | Curt Freed, M.D. | Department of Division Head and Professor of Medicine |
| Aiden Jacobs | University of Wisconsin, Madison | Holger Russ, Ph.D. | Department of Pediatrics |
| Maggie Jewett | University of Dayton | Jeffrey Jacot, Ph.D. | Department of Bioengineering |
| Madison Kraus | University of Nebraska | Beth Tamburini, Ph.D. | Department of Medicine and Immunology |
| Stefan Marasligiller | Vanderbilt University | Tamara Terzian, Ph.D. | Department of Dermatology |
| Anna Martch | Colorado Christian University | Enrique Torchia, Ph.D. | Department of Dermatology |
| Isabella Martus | Middlebury College | Mark Petrash, Ph.D. | Department of Ophthalmology |
| Khoa Nguyen | University of Colorado Boulder | XJ Wang, M.D., Ph.D. | Department of Pathology & Cancer Research Program |
| Micaela Roy | Middlebury College | Angelo D'Alessandro, Ph.D. | Department of Biochemistry and Molecular Genetics |
| Christopher Schaff | Colorado Mesa University | Joseph Brzezinski, Ph.D. | Department of Opthalmolology |
| Marina Schlaepfer | Caldwell University | Lori Walker, Ph.D. | Department of Cardiology |
| Austin Schoppe | University of Texas, San Antonio | Karin Payne, Ph.D. | Department of Orthopedics |
| Emily Thomas | University of Oklahoma | Chelsea Magin, Ph.D. | Department of Pulmonary Sciences and Critical Care Medicine |
| Kaleb Todd | Fort Lewis College | Yiqun Shellman, Ph.D. | Department of Dermatology |
| Ryan Tseng | University of Colorado Denver | Mayumi Fujita, M.D., Ph.D. | Department of Dermatology |
| Anit Tyagi | University of Denver | Antonio Jimeno, M.D., Ph.D. | Department of Medical Oncology |
| Kevin Winkler | University of Colorado Boulder | Michael Verneris, M.D. | Department of Pediatrics |

# A FORMER GSIP INTERN FINDS HOPE IN HANGING UP HER SHEARS

After five years working as a professional hairstylist, Renee Woods came to the conclusion that she liked her job, but didn't love it. She had always enjoyed science growing up and decided to hang up her shears to enroll as an undergraduate at the University of Colorado Denver. As a CU student, Renee found that "little things kept pushing me towards medicine." In particular, a vacation encounter in Mexico with a poor man. He was "shoeless and begging for money to pay for surgery" on his necrotic foot, resulting from diabetes. This experience had a profound effect on her. "I think about him a lot," and how he wasn't able to get help because he couldn't afford it. Renee realized that she wanted "to work in areas that need healthcare."

Renee's pre-med advisor at CU passed along a GSIP brochure to her, and she saw the value of the opportunity. Working as an intern in Michael Verneris, M.D.'s laboratory, Renee was immediately impressed by the thoughtfulness and organization of the program. Laboratory experience for an undergraduate can be hard to secure, and she was surprised by the scope of the research projects and the amount of responsibility given to the interns. It is "hard work being in a lab," there is a "period of learning, requiring lots of hours," and it is all packed into a summer program. In addition to her research experience, Renee really enjoyed the chance to get to know her fellow interns, attend seminars, and meet other scientists and physicians. GSIP gave Renee "a clearer picture of my path." Upon graduation, Renee returned to work in the Verneris lab and maintains that it definitely guided her to pursue further education.

Renee is now a first-year medical student at St. Georges University in Grenada. She feels that her time as a GSIP Intern has helped her in countless ways. From her research experience in the Verneris laboratory and the introduction to many different scientific concepts, to the friendships she made along the way, GSIP was "hard work, but worth it." Renee described a group whitewater rafting trip she took that summer as an intern as exemplifying her GSIP experience. It was "a great day, perfect," and "they were all joking about falling in" to the water. As it turned out, Renee did fall in. It was "only knee-deep, but it was very cold." Renee immersed herself in the whole experience: she was soaked, but full of excitement and hope for her future.

Former GSIP intern Renee Woods at her last day party given by former mentor Mike Verneris, M.D.


Mike Verneris, M.D. instructs former GSIP intern Renee Woods in the use of her last-day gift of a stethoscope.

Graduate Program in Cell Biology, Stems Cells and Development (CSD) Program Retreat was held in Breckenridge, CO, in October 2019.

# GRADUATE PROGRAM IN CELL BIOLOGY, STEM CELLS AND DEVELOPMENT (CSD)

On June 31, 2019, Bruce Appel, Ph.D., Gates Center member and Diane G. Wallach Chair in Pediatric Stem Cell Biology, stepped down as director of the Graduate Program in Cell Biology, Stems Cells and Development (CSD). In acknowledging and thanking all the students, faculty, administrators and others who have contributed toward the program's remarkable growth in size and the quality of the graduate training it provides, Dr. Appel concluded, "Finally, the investment made by the Gates Center for Regenerative Medicine has been a wonderful catalyst for our growth, by allowing us to recruit more students and to support the academic and research efforts of all our members."

Since 2016, the Gates Center has supported this combined program, which helps attract and train talented candidates in the regenerative medicine field. The program is based on the premise that although medical use of stem cells holds great promise for treatment of human diseases and birth defects, to advance the use of stem cells in the clinic, scientists must continue to pursue fundamental discoveries as to how cells function and how cells in embryos form the different tissues of the body.

On July 1, 2019, former CSD Associate Director Jeff Moore, Ph.D. stepped in as the new Director. In the 2019 CSD Newsletter, he reflects, "Since arriving from Washington University to start my lab here in 2012, CSD has provided an important part of my experience – stimulating research collaborations, supporting new education efforts, meeting new friends and always learning. CSD has grown quite a bit in that time, both in terms of numbers of students and faculty and also our reputation and the scope of our training program." He noted that this growth and progress led to the most successful recruitment season yet in which the program recruited nine out of the program's top ten applicants to matriculate in Fall 2019. Outgoing Director Bruce Appel described it as "by far the largest, most diverse and perhaps most accomplished group of students we have recruited, which the Gates Center helped make possible."

Dr. Moore is a dedicated teacher and scientist and is excited to step into the role of CSD Director. He looks forward to the opportunities that lie ahead fueled by support from and collaboration with the Gates Center and the Gates Summer Internship Program, which is proving to be a terrific training ground and potential source of program applicants.

During the year, the Gates Center helped support a wide variety of training activities in the CSD program. Student Adam Almeida received support to travel to the MDI Biological Laboratory in Bar Harbor, Maine, to attend a workshop on quantitative fluorescence microscopy. Student Zeke Thomas received support to travel to the National Institutes of Health in Bethesda, MD to attend a workshop on computational modeling and simulations of protein dynamics. In addition, 22 students and postdocs received support to travel and present their work at national and international conferences, including: Society for Developmental Biology, Boston, MA; American Society for Cell Biology, Washington, D.C.; Society for Neuroscience, Chicago, IL; North American Cystic Fibrosis Conference, Nashville, TN; American Heart Association's Scientific Sessions, Philadelphia, PA; Keystone Symposium on Islet Biology: From Gene to Cell to Micro-organ, Santa Fe, NM; Southwestern Regional Meeting of the Society for Developmental Biology, Denver, CO; Gordon Research Conference on Craniofacial Morphogenesis and Tissue Regeneration, Barga, Italy; Western Region Islet Study Group, Victoria, Canada; EMBO Workshop on Emerging Concepts of the Neuronal Cytoskeleton, Villarrica, Chile.

Teaching and outreach is a core value of the CSD program, and Gates Center support helped support programs for 7th grade students from Slavens Middle School to learn about cell biology and careers in biomedical research; a Bootcamp Program to teach fundamental techniques in cell and molecular biology to summer research interns at the high school and undergraduate levels; a recruitment trip to Fort Lewis College in Durango, CO; and a guest speaker at the first-ever Colorado Science Policy Summit, which brought together scientists, science policy advocates and policy makers from the Colorado legislature and U.S. Congress.

The Gates Center looks forward to continuing to help support, grow and promote this superb program.

# OUTREACH

(Left to right) Chancellor Don Elliman and Debbie and President Mark Kennedy tour the Gates Biomanufacturing Facility in July 2019.

While overall Gates Center activity progressed on campus during 2019, extensive time and effort focused on expanding our reach – particularly introducing ourselves and our services to the public, researchers, elected officials and students. As we worked to prepare for relocating our Gates Center offices and labs to an adjacent building in 2020, many of these activities took place in our affiliated and increasingly humming Gates Biomanufacturing Facility (GBF).

Highlights of 2019 included having CU President Mark Kennedy and his wife Debbie honor us with their presence for a briefing and tour of the GBF on President Kennedy's first day on the job (see photos on the inside cover of this report and in this section). One of only two stops on the Anschutz Medical Campus included in the President's whirlwind four-campus visit, the facility provided an appropriate backdrop for Professor of Pediatrics Terry Fry, M.D. to explain cell-based therapies for children with cancer. Terry, who has been working closely with the GBF to prepare for clinical trials planned to start in 2020 (see article on page 42), joined the School of Medicine from the National Cancer Institute in 2018, as one of the first scientists to investigate the potential to insert modified genes into a child's own T-cells to target CD19, a surface protein found on nearly all cells affected by acute lymphoblastic leukemia.

In addition to hosting on-and-off campus researchers and clinicians who might benefit from the Gates Center and the GBF's efforts to accelerate research toward clinical trials and patient benefit, the Gates center welcomed a far-flung group of Deans from five Indonesian universities. Guests of the Center of Global Health at the University of Colorado's School of Public Health, they are involved in a project geared toward improving Indonesian academic faculty capacity through training to initiate and conduct high-quality research and to link Indonesian and CU Anschutz faculty to carry out collaborative studies. They are also our long-distance-award winners for 2019 (see photo).


Dean John Reilly, Director of Quality Chris Garbe and Congresswoman Diana DeGette observe the bioreactor in which protein biologics are manufactured for human clinical trials.

We were also pleased to have several of our elected officials visit the Gates Biomanufacturing Facility. U.S. Representative Jason Crow (D-CO), whose district includes the Anschutz Medical Campus, and his staff stopped by during a visit to campus in July, and U.S. Representative Diana DeGette (D-CO) and her District Director Joeana Middleton arranged for a Gates Center update and tour in November. Given the Congresswoman's long interest and involvement in stem cell research and her co-sponsorship of the seminal 21st Century Cures Act that included regenerative research provisions, she was enthused to hear about a hot-off-the-press $800,000 grant from the National Institutes of Health 21st Century Cures Act. This award to the Epidermolysis Bullosa (EB) iPS Cell Consortium, which includes research teams from the Gates Center, Stanford and Columbia universities, was particularly notable as the Consortium was the only entity in a group of eight research applicants funded in 2017 to receive a second round of funding. DeGette was quoted in a November 26, 2019 Gates Center press release,

> In drafting 21st Century Cures, our goal was simple: we wanted to find ways to safely speed up the development of new treatments and cures for some of the world's most vexing medical challenges. And now, just three years later, we are seeing the real-world impact that this legislation is having and the promising new treatments it's funding – like those here at the Gates Center.

Additionally, we were joined by various school groups and teachers who seek to augment classroom study with real-world insight into leading-edge research. Finally, off-campus outreach opportunities included an evening presentation to the Broomfield Rotary Club and Gates Center Director Dennis Roop's introduction and presentation as the 2018-2019 Honoree at the Colorado Chapter of the Achievement Rewards for College Scientists (ARCS) Spring 2019 Gala at the Museum of Nature and Science. As of September 2018, the hard-working 42-year-old ARCS Foundation's Colorado Chapter had celebrated the award of $6,500 to 46 young scientists enrolled in Colorado universities for a cumulative total of over $4.6 million.

The Gates Center ended the 2019 year having created a brand new website at gatescenter.org with which to disseminate information about its efforts to bring together and support brilliant researchers and clinicians in stem cell biology and regenerative medicine in order to accelerate discoveries from the lab through clinical trials to therapies and cures. We greatly appreciate having the opportunity to share our work and our resources both in person and virtually and are tremendously grateful for the interest and support that comes our way.


*Thank you for the picture. We would like to thank you again for your kind hospitality during our visit to the Research Center. We were happy that we could visit such impressive Center for Research, and the most current Cells and Protein treatment. We learned a lot. Please send our thanks and regards to Prof Dennis Roop, Ph.D. and the others.*

*With kind regards,*
*Cissy (the one in yellow in the picture)*
*Cissy B. Kartasasmita, Professor of Paediatrics, Faculty of Medicine/Hasan Sadikin General Hospital, Indonesia*

# NEW FACES AT THE GATES CENTER

**Steven Bono:** Steven Bono started working at the Gates Center on January 15, 2019, as a research service professional. Originally from Reading, Pennsylvania, where he maintains there is nothing like a Philly Cheesesteak – his favorite food, Steven grew up in a Cuban/Sicilian family with five brothers and two sisters. Eventually, the mountains, scholarships and grants all brought him to Colorado to obtain his B.S. in Business Administration from the University of Colorado, with a minor in Finance. In February 2017, Stephen went to work as a billing specialist for the Grants and Contracts Office on the CU Anschutz Medical Campus and looks forward to the prospect of working here on campus until retirement. He now works with the business manager primarily on issues related to financial activity at the affiliated Gates Biomanufacturing Facility. Loving numbers, Stephen grew up practicing math as if it were the only subject. As a result, he enjoys reconciling and working in Excel to reach financial goals, along with networking and building relationships across the University to allow him to develop professionally and provide everyone the level of care they deserve on behalf of the Gates Center.

Having started skating at the age of one and played ice hockey since the age of two, Steven is passionate about the outdoors. He also loves fishing, having developed into a great trout fisherman since coming to the Rocky Mountains, and golfing to relax the mind and enjoy the type of course Colorado's beautiful terrain has to offer. Running, traveling and cooking are his other favorite pursuits. Though many people like to stay active, as he does, he maintains he would pick sleep over anything. We are consequently grateful for his wonderful financial and interpersonal skills and dedication to the Gates Center during his waking hours!

**Joseph A. Brzezinski IV, Ph.D.:** Joe Brzezinski was appointed co-director of the Gates Summer Internship Program (GSIP) in December 2019 (see page 44), having been involved in this program as a mentor since 2016. Joe grew up in the Niagara Falls region of upstate New York and attended college at SUNY Fredonia, graduating with a B.S. in Recombinant Gene Technology. In 1999, he went to the University of Michigan for graduate school where he studied retinal development with Dr. Tom Glaser in the Department of Human Genetics. In 2006, he went to Northwestern to study cortical development with Dr. Anjen Chenn and subsequently joined Dr. Tom Reh's lab at the University of Washington in 2007. There, he continued his studies of retinal development prior to joining the Department of Ophthalmology on the CU Anschutz Medical Campus in 2012. He is now Associate Professor of Ophthalmology and Director of the CellSight Laboratory of Developmental Genetics. His goal is to understand how genetic programs control retinal development and to apply this knowledge to the production of cone receptors from stem cells, which may restore vision in patients with diseases like AMD (see CellSight). Joe is an active mentor in the Cell Biology, Stem Cells and Development (CSD) Graduate Program.

We are grateful to have someone of Joe's experience, enthusiasm and dedication to help further the GSIP's efforts to encourage outstanding undergraduates to consider careers in stem cell biology and regenerative medicine.

**Cathey McClain Finlon:** Cathey Finlon joined the Gates Advisory Board on July 1, 2019 after several years of intense courtship.

Cathey retired as CEO/owner of 26-year-old McClain Finlon Advertising, ranked as one of the top independently owned advertising agencies in the U.S. and consistently ranked as a top woman-owned business. She served as President of the Denver Art Museum during an important transition period, and retired once again. She continues to serve on the board of the Denver Art Museum.

A community leader, she has chaired the boards of Children's Hospital Colorado, Denver Metro Chamber of Commerce, Rocky Mountain Junior Achievement, History Colorado, Denver Advertising Federation, and Denver Scholarship Foundation. Her past and present board service also includes Denver Public Schools Foundation, University of Denver Daniels College of Business Advisory Board, Colorado Outward Bound, National Repertory Orchestra and the American Association of Advertising Agencies (NYC).

She was inducted into the Colorado Business Hall of Fame and has received many advertising awards but is proudest of the Del Hock Lifetime Achievement award from the Metro Denver Chamber of Commerce and lifetime achievement awards from the Denver Advertising Federation and the Denver Art Museum.

She is an avid sportswoman who has cycled all over the world and has been married to Dick Finlon since 1978. Given her lifetime of professional accomplishment and service, we are particularly honored and grateful to have her join our Gates Center family.

**Terri Foote:** Terri Foote is an example of the Gates Center's affiliated Gates Biomanufacturing Facility's (GBF) tremendous success in recruiting superb staff from all over the country. Arriving in May 2019 as Director, Program Management and Supply Chain, Terri brings over 20 years of experience in the pharmaceutical industry, holding various leadership positions in supply chain, program management, operations, sales and business development, and engineering. Terri is the former Vice President of Technical and Business Operations at Tolmar, Inc., a pharmaceutical company with a legacy and pipeline in extended release dosage forms commonly used in oncology and urology, along with an extensive portfolio of dermatology products. Living in Austria and Switzerland, she was previously the Head of Global Manufacturing Supply Chain for Sandoz (the generic division of Novartis Pharmaceuticals Inc.) with responsibility for establishing harmonized global supply chain organizations, processes, and performance across 25 internal manufacturing sites, 10 global 3rd party suppliers, and 65 different Sandoz/ Novartis country sales and marketing organizations. This post involved over five years of international pharmaceutical and supply chain experience in Europe, Africa, South America, and Asia (India and Bangladesh).

Terri was born in Omaha, Nebraska, and grew up in Lincoln. Having excelled in math and science in high school and received encouragement from a teacher and advisor, she decided on Industrial Engineering as a good combination of working with people (which she truly enjoys), and processes to help businesses improve their planning, throughput, and quality of products. Terri went on to receive her B.S. in Industrial Engineering from University of Nebraska and her Executive M.B.A. from the University of Colorado. She is also a Certified Project Management Professional (PMP) with over 10 years project and program management that includes multiple Phase 1 and software implementation projects, as well as a certified executive coach, leadership trainer and speaker and a mentorship member through The John Maxwell Team.

Terri says Gates is a phenomenal place to work! While the inspirational work toward phase one clinical trials to which the GBF contributes – both in the academic and commercial environments – is what originally lured her to the position, she says it is the amazing people with whom she gets to work every day that keeps her wanting to do more for the GBF and their clients. She says her hope for the future is that "our efforts will have a significant impact on the introduction of many medical therapies that greatly improve and save people's lives" and "that my daily efforts will encourage and over time, have a significant and positive impact on the lives of my colleagues, our clients, and their patients."

As a Division 1 NCAA scholarship college gymnast, Terri loves participating in or being a spectator for a variety of sports and to have fun both inside and outside of work. Terri and her real estate investor husband live in Denver and have two grown children who constitute her pride and joy: Branden in the on-line human resources/benefits services industry in Denver and Mikayla as a manager/producer in the music and gaming industries in Los Angeles. Since supply chain management represents one of the greatest risks in manufacturing, we feel fortunate to have attracted someone of Terri's exceptional caliber and dedication to our midst.

**Deysy Piedra:** Deysy Piedra began working as a post grant administrator at the Gates Center in January 2019. She grew up in Denver where she attended Johnson & Wales University and obtained her B.A. in hospitality. Prior to the Gates Center, she began her career at the CU Anschutz Medical Campus' Human Medical Genetics & Genomics Program as the program coordinator. In her spare time, she enjoys traveling, cinema, and spending time with her family. She is ecstatic to be part of the administrative team for the Gates Center, an organization at the forefront of leading-edge medical research.

# FINANCIAL OVERVIEW

The following financial statement reflects the operations of the Gates Center for Regenerative Medicine, which has been the recipient of funding from a number of sources including the University of Colorado Foundation, the University of Colorado President's Office, the CU Anschutz Chancellor's Office, the Gates Frontiers Fund, our hospital partners and private donors. We continue to collaborate with other centers, departments and divisions on campus, as well as our hospital partners, and in many cases funding flows through these other entities in such a manner that our financial statement does not fully capture the extent of our activities and philanthropic support. Likewise, research performed by individual Gates Center members is funded directly through federal and state research grants, private foundations and individual donations, along with targeted support from the Gates Center.

Overall, Gates Center expenditures are designed to fuel the research of the future. In addition to providing research support to its members, the Gates Center operates four core laboratory facilities (Flow Cytometry, Morphology and Phenotyping, Bioengineering, and Stem Cell Biobank & Disease Modeling), and it provides laboratory infrastructure to members for work done outside of the core facilities. The Gates Center's affiliation with the Gates Biomanufacturing Facility is a critical strategic asset in both moving therapies into clinical trials and promoting the retention and recruitment of top talent. Commercialization support, education and outreach, and marketing and development activities are also provided as part of the overall Gates Center mission.

## GATES CENTER OPERATIONS

Fiscal Year 2019 was the fourth year of operations under a five-year funding agreement between the Gates Frontiers Fund, the University of Colorado Foundation, the University of Colorado President's Office and the CU Anschutz Chancellor's Office. Additionally, the Gates Center was a critical partner in garnering over $3,653,475 in new philanthropic support for key initiatives described in more detail throughout this report.

Consistent with our mission and past priorities, center research program support of $730,619 was the largest expense category, totaling 29% of all spending for 2019. This amount was below our 5-year average of $850,000 as we have fulfilled long-term commitments made to key campus investigators. Investments in equipment and operations of the core facilities and the Gates Center laboratories totaled $576,000 (23% of expenses) in 2019, which was consistent with prior years. The balance of our expenses was for marketing and development totaling $563,000 (23% of expenses), center enrichment, educational activities and commercialization support totaling $375,000 (15% of expenses), and center administration totaling $235,000 (9% of expenses).

The Gates Center net of sources of income less expenditures was $80,391 for the fiscal year ended 6/30/2019 leaving a fund balance $96,000 for this period.

Our current funding is sufficient to meet our expenses and research funding obligations through December 2020, and we have new funding commitments in place to cover Gates Center operations through December 2025.

| | 2015 | 2016 | 2017 | 2018 | 2019 |
|---|---|---|---|---|---|
| **Infrastructure and Operations Grants** | | | | | |
| Gates Frontiers Fund | $1,000,000 | $1,200,000 | $1,200,000 | $1,200,000 | $1,200,000 |
| University of Colorado Foundation | $1,000,000 | $600,000 | $600,000 | $600,000 | $600,000 |
| University of Colorado Presidents Office | | $600,000 | $600,000 | $600,000 | $600,000 |
| Philanthropy | $10,330 | $147,617 | $200,000 | $327,585 | $159,669 |
| **Infrastructure and Operations Grants** | **$2,010,330** | **$2,547,617** | **$2,600,000** | **$2,727,585** | **$2,559,669** |
| **Gates Center Expenditures** | | | | | |
| Center Research Program Support | $751,750 | $976,914 | $721,053 | $1,072,416 | $730,619 |
| Lab Operations and Core Facilities | $619,465 | $494,696 | $594,723 | $580,161 | $575,931 |
| Marketing & Development | $338,655 | $336,937 | $530,526 | $554,373 | $562,529 |
| Center Admin/Maint/Supplies | $336,792 | $376,593 | $389,380 | $474,671 | $235,213 |
| Center Enrichment, Education and Commercialization | $134,719 | $255,649 | $285,939 | $257,238 | $374,986 |
| **Total Expenditures** | **$2,181,381** | **$2,440,789** | **$2,521,621** | **$2,938,859** | **$2,479,278** |
| | | | | | |
| ***Center Sources - Expenditures*** | **($171,051)** | **$106,828** | **$78,379** | **($211,274)** | **$80,391** |

# ACKNOWLEDGEMENTS

## CHARLIE'S ANGELS

On August 22, 2019, at the fourth annual Charlie's Picnic, Wag Schorr, M.D., became the third recipient of the "Charlie's Angel" award. Initiated in 2017, the award honors special individuals who play unusual and often quiet roles, helping the Gates Center thrive.

After welcoming the partygoers on behalf of herself, husband Marshall, brother John Gates and his partner Julia Wrapp, Diane Gates Wallach conferred the award – the only item on the agenda aside from camaraderie and enjoying a relaxed evening on a surprisingly stormy summer night. Diane explained the award's genesis in her father Charlie Gates' love of the long running television series "Charlie's Angels," featuring gorgeous and athletic women solving the world's problems in creative ways. As strong, persistent individuals, they functioned even stronger as a team. They could surely make a splash when necessary but avoided publicity and rode quietly into the sunset after the good deed was done. Most importantly, these angels practiced what Charlie loved, which was stepping out, being bold, taking risks...and caring about making the world a better place.

Diane described Wag as adventurous and curious, traveling with his bride Annalee to all corners of the world; an aspiring golfer who pursues the perfect game while loving the walk and endless possibilities; a lover of young people, endlessly encouraging them toward medical and scientific careers; and a legendary doctor who pioneered kidney transplants internationally, having studied at the University of Colorado School of Medicine under transplant pioneer Thomas Starzl, M.D., Ph.D. who performed the first organ transplant in 1963. Finally, Wag recently took the initiative to create a new and unique research and clinical collaboration between the Gates Center, Children's Hospital Colorado and the Dean of the CU School of Medicine. This particular Angel, Diane explained, has graced himself in many ways over the years and on top of it has now assembled both the team and funding to breathe life and urgency into finding a cure for the rare disease of Ehlers-Danlos Syndrome – a disease from which his granddaughter Calla suffers (see article on page 20).

(left to right)
Wag Schorr's wife Annalee Schorr,
granddaughter Savannah Winchell,
daughter Kate Schorr,
son Wag Schorr-Ratzlaff and
Charlie's Angel Wag Schorr

**The Gates Center gratefully acknowledges the following individuals, foundations and organizations for supporting our research and mission through their gifts made during the 2019 calendar year:**

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To learn more about how you can play a role in accelerating research through philanthropic gifts, please reference the enclosed envelope, visit giving.cu.edu/gatescenter or contact Michael Tortoro at 303-724-7618 or Michael.Tortoro@cuanschutz.edu.

CU President Mark Kennedy, Bea Taplin and Nancy and Curt Freed, M.D.

John Gates and Julia Wrapp

Co-host John Gates addresses the partygoers

CU medical student Emily Paton reunites with GSIP mentor Antonio Jimeno

Dori Biester, Chancellor Don Elliman and Dean John Reilly

Janie and Rick Stoddard

Carolyn Baker, Dori Biester and Pamela Beardsley

Coe and Frank Atherton

Terry Fry, Cristina Cenciarelli and Richard Schulick

Betsy and Peter Mangone

Anthony and Ellen Elias

Marshall Wallach, Gretchen and Chuck Lobitz

Marcia and Dick Robinson

Brett and Raquel Miller

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For inquiries about the Gates Biomanufacturing Facility, please refer to the facility's website at www.gatesbiomanufacturing.com and/or contact Tim Gardner.


Brady Attar takes a break from clinical talk while his family trades information with the care team at Children's Hospital Colorado.