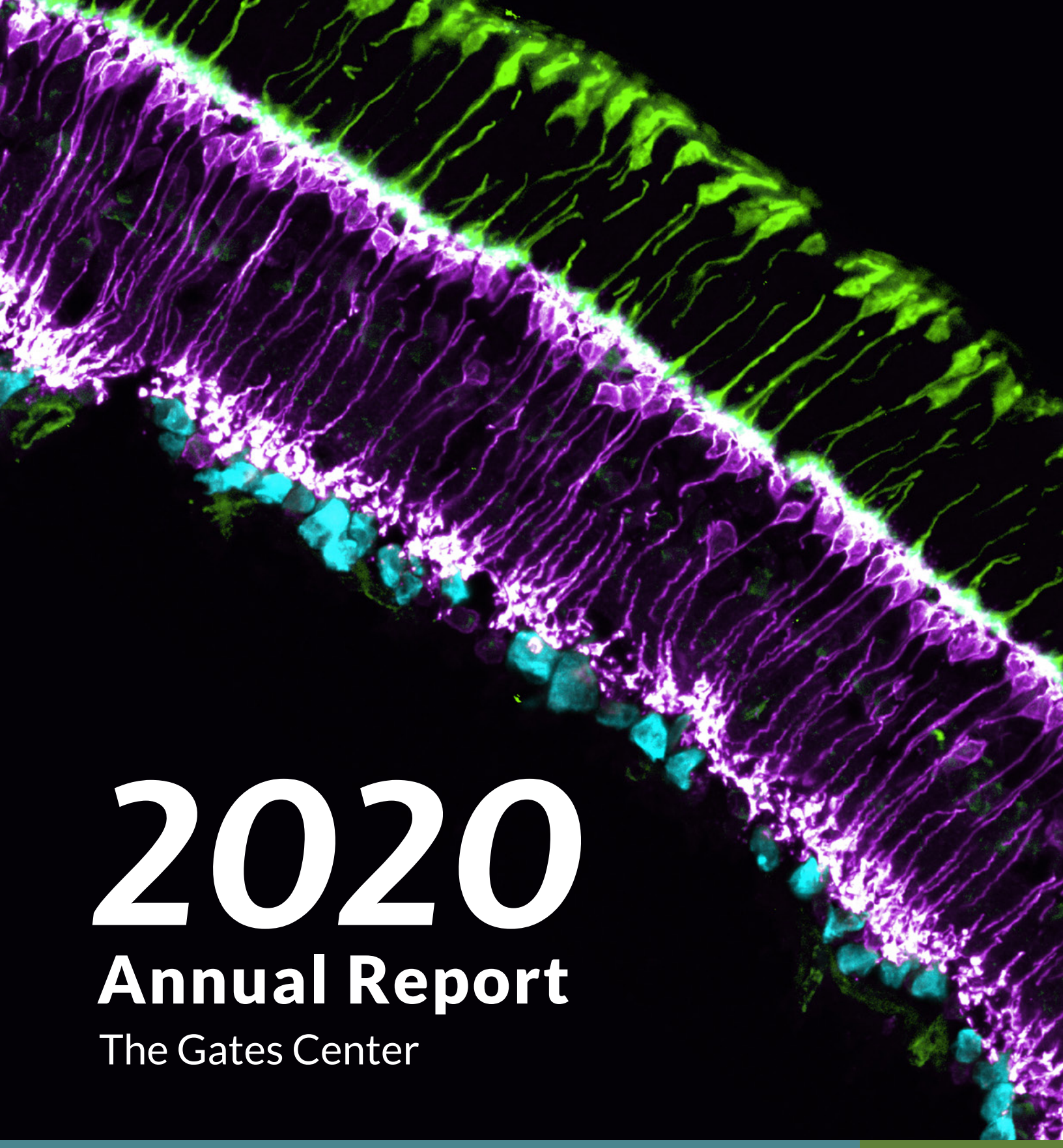
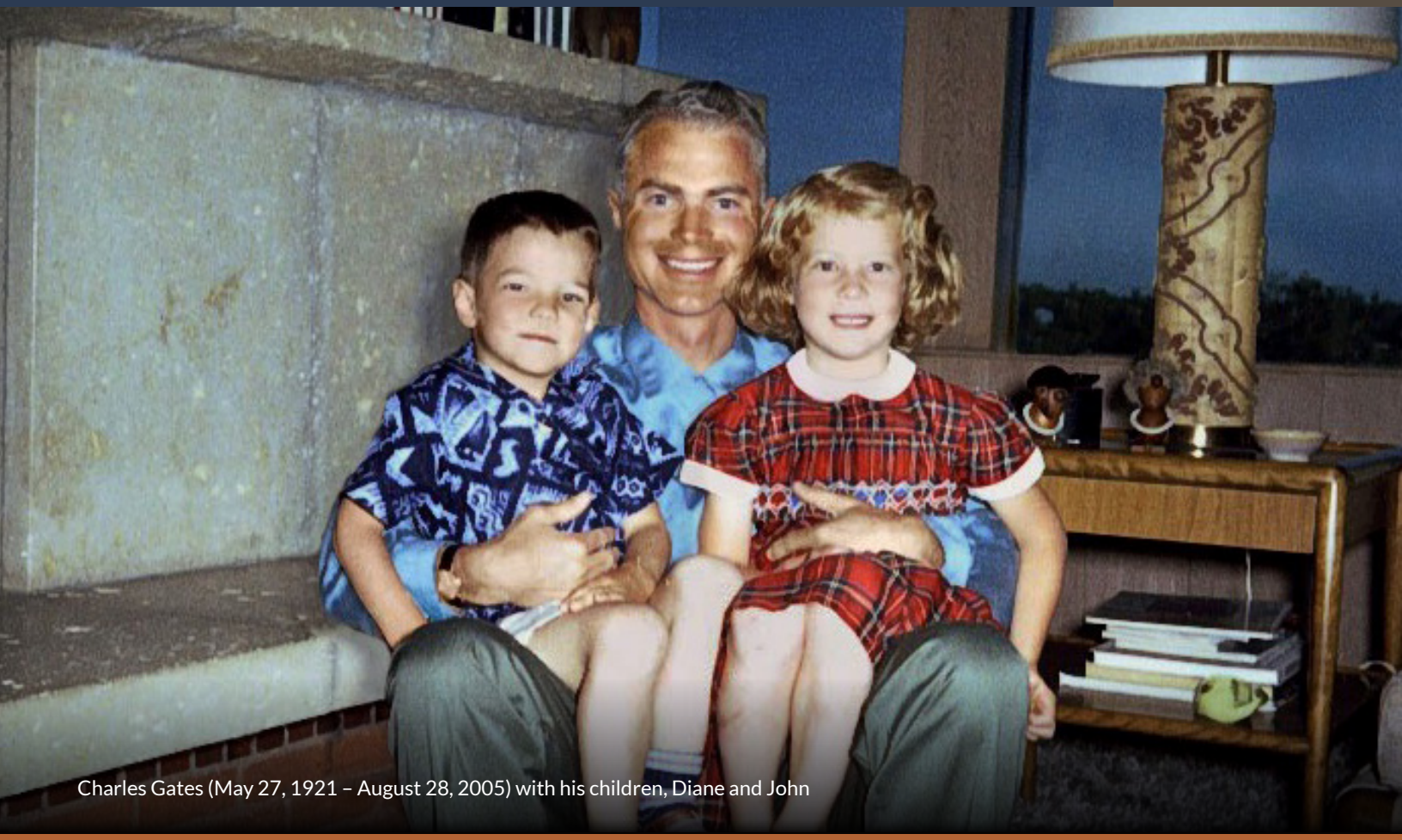


2020
Annual Report
The Gates Center

Gates Center for Regenerative Medicine
UNIVERSITY OF COLORADO **ANSCHUTZ MEDICAL CAMPUS**

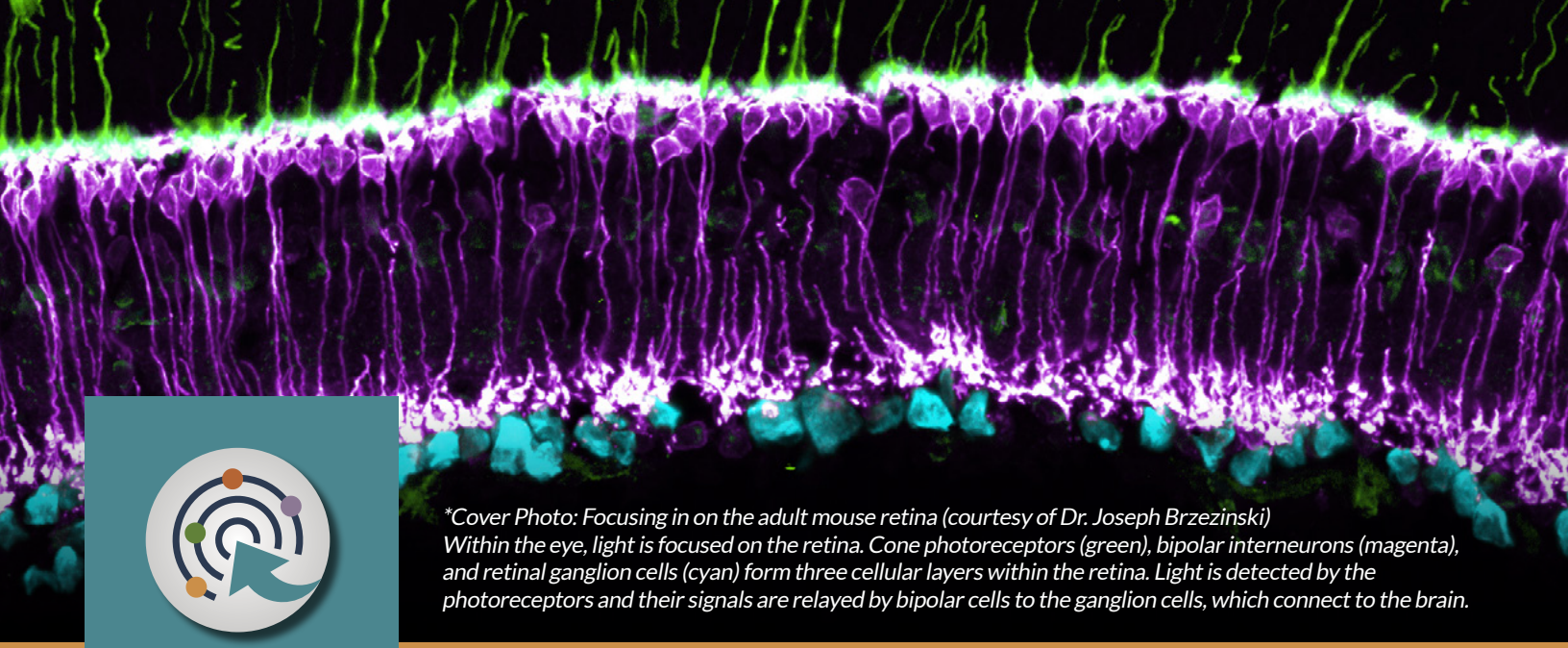
"The vision of Charlie Gates through Diane and John has led us as a campus to places we never would have traveled without them."

~Anschutz Medical Campus Chancellor Don Elliman's toast at the virtual Charlie's Picnic held on Wednesday, August 26, 2020



Charles Gates (May 27, 1921 – August 28, 2005) with his children, Diane and John

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's company, the Gates Rubber Company, into a worldwide leader for industry and technology. Late in his life, Charles Gates began talking to his daughter Diane Wallach and son John Gates (see photo) about the hope and benefit stem cell research promised for so many people in the world. Suffering from macular degeneration, Charles Gates had started doing research on his own condition only to be introduced to the world of stem cells and regenerative medicine by his doctor and family friend, the late Will Hiatt. "Charlie" 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 and leadership from Diane and John, Charles Gates sought to extend his focus on innovation and collaboration in a world-class research center and support the translation of scientific breakthroughs into clinical practice as quickly as possible.



*Cover Photo: Focusing in on the adult mouse retina (courtesy of Dr. Joseph Brzezinski)
Within the eye, light is focused on the retina. Cone photoreceptors (green), bipolar interneurons (magenta), and retinal ganglion cells (cyan) form three cellular layers within the retina. Light is detected by the photoreceptors and their signals are relayed by bipolar cells to the ganglion cells, which connect to the brain.

WEB EXTRAS
Look for this icon to focus in on Gates Center website links and additional content!

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LETTER FROM THE DIRECTOR

Dennis Roop, Ph.D., shared his journey in science with the Gates Summer Internship Program Class of 2020 during their Final Day Program, highlighting the press conference at which he accepted his appointment from the University of Colorado in 2006.

This was a year that was not easily controlled or directed. It was hard to shape or work with; and it was hard to treat, relieve or cure. For the world and for the Gates Center, this was the true definition of an "intractable" year. Yet this was a year of significant accomplishment.

We focused intensely and productively, inwardly and outwardly with our Gates Center members on basic science, advanced along the research continuum and moved toward clinical trials and patient benefit. One of our member's Joseph Brzezinski, Ph.D.'s visually stunning image of an adult mouse retina on this annual report cover demonstrates our emphasis on basic science.

Overall, in spite of collaborating via Zoom, virtual workspaces, and reduced-capacity laboratories, we never lost sight of Charles Gates' ambitious vision to work together to accelerate the translation of scientific breakthroughs into clinical practice. "I have never been prouder of our campus," University of Colorado Anschutz Medical Campus Chancellor Don Elliman said repeatedly throughout the year.

Because of previous groundwork, the Gates Center and the CU Anschutz campus achieved a remarkable milestone, years in the making. In 2014, the Center planned for the key missing link in the creation of the most robust biotech and healthcare ecosystem in Colorado history. As a result, thanks to our campus partners and private sector benefactors, we launched a state-of-the-art manufacturing facility in 2015. The establishment of the Gates Manufacturing Facility laid the foundation for working 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.

On July 30, 2020, the Gates Biomanufacturing Facility in collaboration with the CU Anschutz campus reached the milestone:

- we manufactured cancer fighting chimeric antigen receptor T cells (CAR-T cells) developed by faculty in the CU School of Medicine;
- we launched a clinical trial at UCHealth University of Colorado Hospital;
- and we enrolled patients with no other viable therapeutic options.

This UCD19 CAR-T trial represented the first cellular immunotherapy project in which the developmental science, the regulatory filing and approvals, the manufacturing process and the infusion of patients in clinical trials had all been done at the Anschutz Medical Campus. This made us one of the few academic medical campuses in the nation where bench science can move to manufacturing and on to patient treatments all within walking distance.

On top of this significant milestone, the campus established yet another entity specifically designed to facilitate on-campus trials. The Cellular Therapy Operations Program (CTOP), organized in 2020, provides a team of experienced clinical research professionals to focus on regulatory support, medical and scientific writing, and project management for trials designed to test products produced on campus at the Gates Biomanufacturing Facility. Vice Chancellor for Research Thomas Flaig, M.D. and key campus leaders worked to create the program, now led by Mike Verneris, M.D., as the Scientific and Medical Director. In less than a year, CTOP's team had already supported two Investigational New Drug (IND) applications to the FDA and helped prepare four clinical trials – including the landmark trial described here and within this report in which several patients have experienced 100% remission.

This annual report seeks to introduce the Center to those who might not be familiar with it and to describe this confounding year in which countless individuals stretched, learned, and achieved far more than we might ever have believed possible. We have included reflections on what proved a year of paradox for Calla Winchell, a patient we highlighted in last year's report. Given the social isolation of this pandemic period, we also feature an article written by a clinician colleague, Emily Warshauer, M.D., who explores how our bodies are wired for touch.

As always, we have listed our Gates Center members and are pleased to highlight a number of their publications, honors and grants. Progress was also made in the area of commercialization as additional funds secured through the Gates Grubstake Fund and Startup Toolbox fueled Gates Center members' research. Notably, David Wagner, Ph.D. ended 2020 as the first Grubstake awardee on the cusp of a human clinical trial scheduled for early 2021.

Funding for the Center's next five years was finalized through the continued generosity of the Gates Frontiers Fund, the Chancellor's Office, and the School of Medicine. Their amazing support has set the stage for ongoing acceleration of our operations. Among other offerings, we have negotiated additional benefits for Gates Center members. Through these, the Center will also offer subsidized access to other core facilities with new cutting-edge equipment, technology and expertise beyond what is now available in other Gates Center subsidized cores.

We are also proud to tell the inside story of the outstanding determination, talent and spirit that prevailed within the Center's affiliated Gates Biomanufacturing Facility, which made this year's milestone UCD19 CAR-T clinical trial possible, as well as other such trials involving on and off-campus investigators in the future.

Finally, it was a particularly intractable year for the Gates Center's educational and outreach efforts. Just as we had accepted another outstanding group of college undergraduates for the Gates Summer Internship Program, we had to pivot to providing a summer of virtual webinars to a dispersed group of appreciative young people. Similarly, our regular outreach to our members, students and the public, on which we place such importance, was delivered virtually and enabled us to reach across the country and world. Our year's highlight was being able to host a virtual Charlie's Picnic, referenced throughout this report, showcasing the talent, resiliency, pride – and even fun – that goes along with working for or being associated with the Gates Center.

As always, we are tremendously grateful to those who have helped support us throughout the year – whether they be members of our Gates Center Advisory Board, our donors, our volunteers or our friends on and off campus. Our loss of two beloved Gates Center volunteers in December was a poignant reminder of our Center's remarkable good fortune in attracting extraordinary individuals as our champions. On ***page 7*** we remember board member Will Hiatt who planted the seed of the Gates Center in his patient Charlie Gates's mind. And on ***page 54*** we also honor legendary Denverite Peter Grant, whose wisdom, guidance and generosity enabled a number of Center projects but was especially crucial in supporting the creation and sustainability of the Gates Summer Internship Program. We also wished a happy retirement to longtime Gates Center Chief Financial Officer Tim Gardner for his many contributions since 2013 to the growth of the Center and the Gates Biomanufacturing

Facility; and to Lab Manager Charlie Wall who joined the Center in 2014 ***(see page 56)***.

Echoing the sentiments of the Alliance for Regenerative Medicine's CEO Janet Lambert, the Gates Center concluded 2020 grateful for all we and our Anschutz Medical Campus have learned, achieved and received. We look particularly forward to the year to come, which will include welcoming Marc Bonaca, MD, MPH, FAHA, FACC, to our Gates Center Advisory Board. Marc serves as the executive director of CPC Clinical Research and Community Health and is the inaugural holder of the William R. Hiatt Endowed Chair in Cardiovascular Research.

Aspirationally and with great appreciation,

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

> *When COVID-19 struck, we joined the rest of the world in not knowing what 2020 would bring. Instead, not even a global pandemic could derail the scientific advancements, investor appetite, and maturing pipeline that made headlines for the regenerative medicine sector in 2020. For a once aspirational sector, the future is now.*
> *~Alliance for Regenerative Medicine CEO Janet Lambert*

LEADERSHIP

GATES ADVISORY BOARD

Janelle Blessing
Marilyn Coors, Ph.D.
Donald Elliman, *Co-Chair*
Cathey Finlon
Yvette Pita Frampton
William Hiatt, M.D.*
Kevin Reidy
Daniel Ritchie, *Co-Chair*
Dennis Roop, Ph.D.
Wagner Schorr, M.D.
Geoff "Duffy" Solich
Ann Sperling
Rick Stoddard
Diane Gates Wallach, *Co-Chair*

CU President Mark Kennedy joined the Gates Advisory Board Fall Meeting on September 15, 2020.

Will Hiatt

It was with great sadness that the Gates Center and many other people and organizations heard of Will Hiatt's passing in December 2020. Without Will and his abiding professional and personal relationships with Charlie Gates and the Gates family, the Gates Center might never have seen the light of day. Further, the Center would not have been blessed with a brilliant, dedicated, wise and influential friend as a member of the Gates Center Advisory Board and a guiding light for the Center's early, formative years.

At the virtual Charlie's Picnic held in August 2020, Will recounted meeting Charlie Gates many years before when he joined the board of the Colorado Outward Bound School of which Charlie was a founder. Will said,

William R. Hiatt, M.D.
June 1, 1950 – December 8, 2020

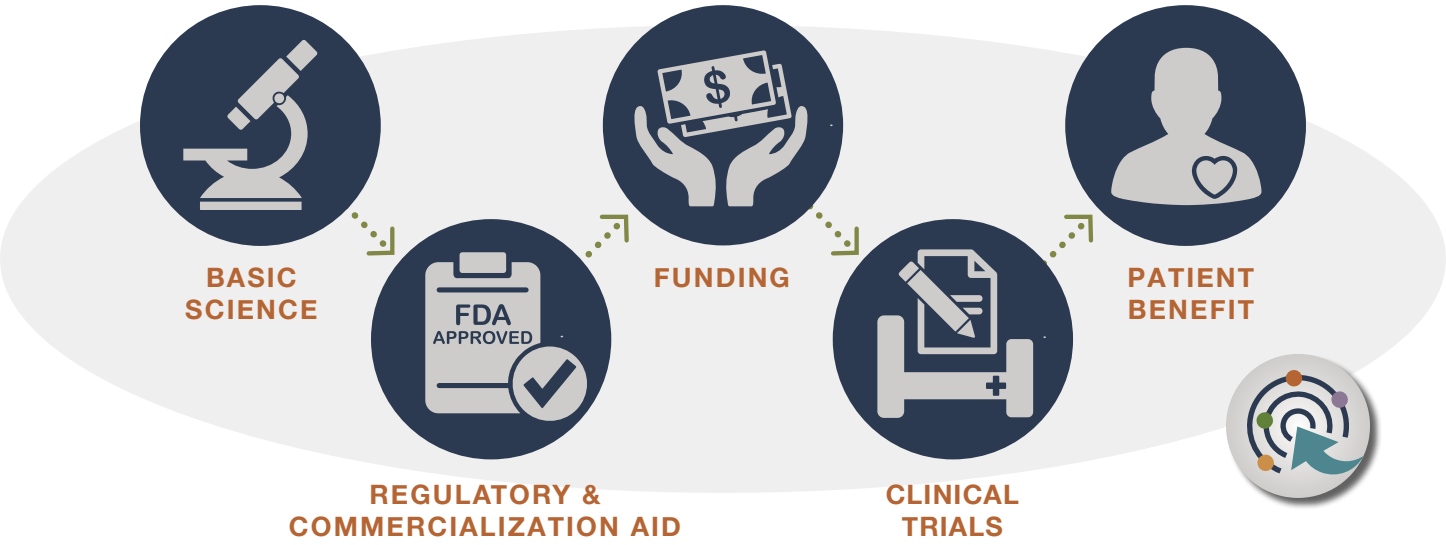
> *That experience and insight into Mr. Gates taught me the role of leadership with integrity, purpose and vision, which is fundamental to the Gates Center today. Suddenly, he was my patient, friend and mentor on how to live life to the fullest, which he knew a lot about. Charlie was committed to science and discovery and the potential of stem cell research to treat disease and restore function. The Gates Center was his idea, and he carried it forth to completion through the hard work of Diane Wallach, John Gates, Dennis Roop and others. Charlie used to say, 'throw your hat across the creek,' an expression that came from the old American West when crossing rivers and creeks was difficult for covered wagons. Pioneers sometimes threw their hats to the other side of the creek as an incentive to cross. Throwing your hat was a solid commitment to move forward. It also means embracing risk to create something bigger than yourself that benefits things like our health and function. This has certainly happened at the Gates Center, and I would note that it is a tremendous model for the future success of our university.*

We recognize and honor Will for all he contributed toward the genesis of the Center and our accomplishments to date.

ABOUT US

OUR 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.



OUR HISTORY

The Gates Regenerative Medicine Program 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.

In January 2007, Dennis Roop, Ph.D., was recruited from the Baylor College of Medicine to be the Program's founding director in order to establish the foundation necessary for it to be a leader in accelerating discoveries using stem cells and related technologies through clinical trials to patient benefit. In 2010, the Gates Regenerative Medicine Program achieved recognition as a center and is now known as the Gates Center for Regenerative Medicine.

Located on the largest new biomedical and clinical campus in the United States, the Gates Center is a vibrant component of the University of Colorado School of Medicine (SOM), surrounded by Children's Hospital Colorado (CHC), UCHealth's flagship University Hospital (UCH), and the five other schools and colleges on the University of Colorado Anschutz Campus. Ideally situated, the Gates Center has worked across campus and with community friends, campus partners (the CU Anschutz Chancellor's Office, SOM, CHC and UCH), and benefactors to establish the Gates Biomanufacturing Facility and a variety of additional partnerships and initiatives. It also promotes and provides benefits to its 124 multi-institutional research and clinical members that include access to core facilities and equipment, regulatory and intellectual property expertise, commercial partners, research funding and more.

OUR HIGHLIGHTS – Gates Center highlights include the following:

2015

Opened the Gates Biomanufacturing Facility (GBF), a state-of-the-art Good Manufacturing Practices (GMP) facility, which develops and manufactures investigational cell therapy and biologic products to support FDA-approved early phase clinical trials ***(see page 47)***

Created the Gates Summer Internship Program in regenerative medicine for college undergraduates ***(see page 51)***

Launched the Gates Grubstake Fund to finance promising research discoveries ***(see page 32)***

2016

Partnered with the Department of Ophthalmology and benefactors to establish the CellSight program to fuel research into the promise of stems cells for patients with age-related macular degeneration and launched the international recruitment of Valeria Canto-Soler, Ph.D. as director

2017

Established "Startup Toolbox" in partnership with benefactors and CU Innovations to provide Gates Center members with regulatory strategy, corporate formation and business development, and business models and financial plans to bridge the gap from academic research to clinical development ***(see page 37)***

2019

Established the Ehlers-Danlos Center of Excellence in partnership with Children's Hospital Colorado and the Dean of the CU School of Medicine

2020

Launched human clinical trials using cutting-edge CAR-T cells developed by faculty in the CU School of Medicine and created at the Gates Biomanufacturing Facility – the first cellular immunotherapy project where the developmental science, the regulatory filing and approvals, the manufacturing process, and the infusion of patients in clinical trials were all performed at the University of Colorado Anschutz Medical Campus

OUR VALUES – The Gates Center embraces the following:

INNOVATION	TALENT	COLLABORATION	PATIENT OUTCOMES
Fostering research with an entrepreneurial spirit espoused by Charles Gates: balancing risks, opportunities and resources to overcome barriers to success.	Pursuing, retaining and developing accomplished, passionate, and innovative change agents in both research and clinical settings.	Serving as an indispensable resource, connector, and shepherd of groundbreaking ideas and solid science, and coordinating and optimizing outcomes for all of our partners and customers. Charles C. Gates said it: "No one does their best work alone."	Accelerating discoveries from the lab through clinical trials that lead to effective therapies and cures for those most in need of scientific breakthroughs.

AREAS OF FOCUS

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 member 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 in the patient.

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. It is dedicated to developing a cure for EDS at the Gates Center and to better addressing the clinical needs of EDS patients through specialty care at Children's Hospital Colorado.

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 uses a novel iPSC approach (see below) to genetically correct skin cells that will be delivered to the same patient using Avita Medical's "Spray-on-Skin" device.

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 treatments for cancer developed by Gates Center members. 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.

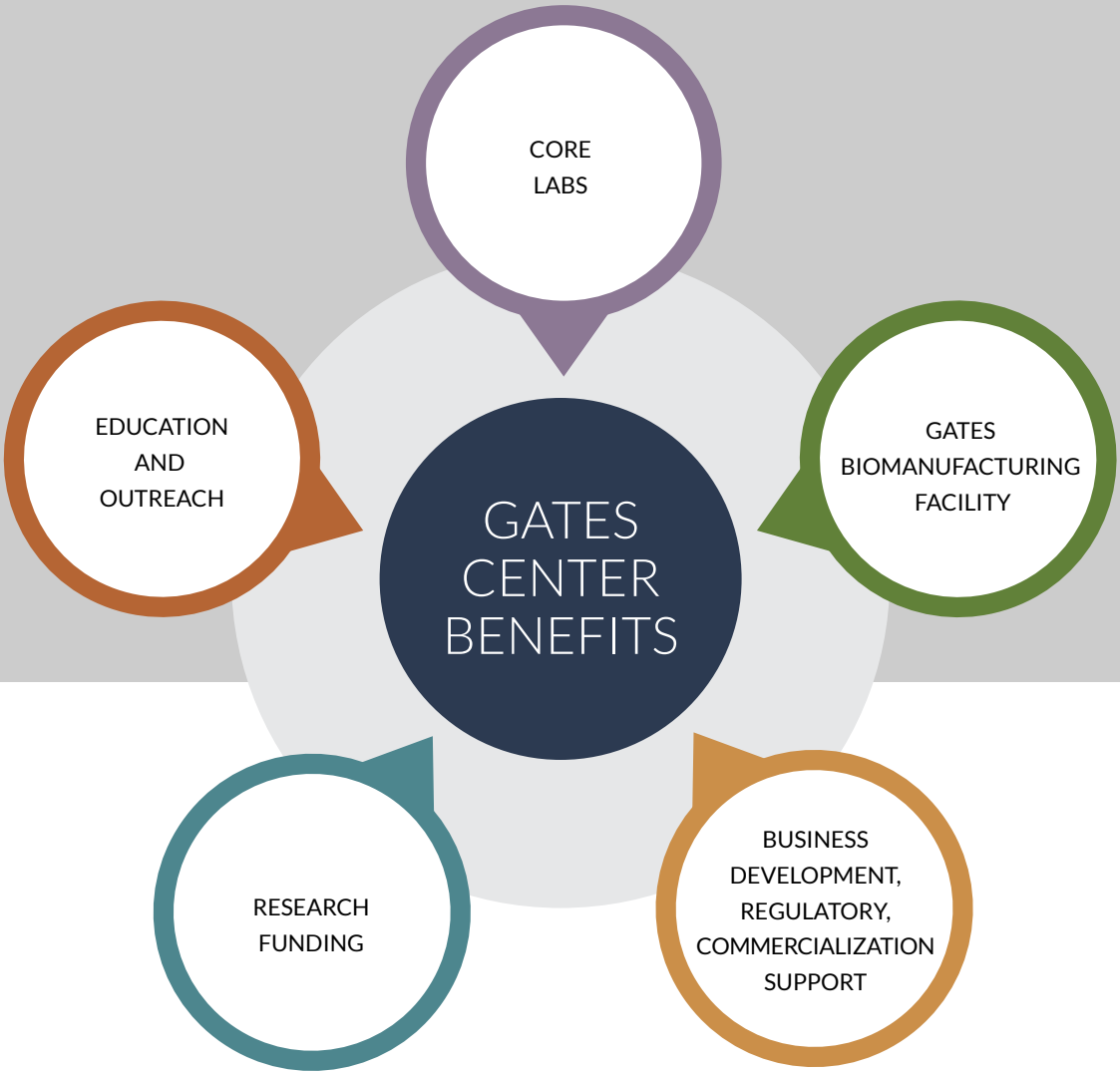
WOUND HEALING

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.

OUR GATES CENTER MEMBERS

The Gates Center is a world-class consortium of 124 researchers, clinicians and private industry members affiliated with the University of Colorado Anschutz Medical Campus (Children's Hospital Colorado and UCHealth), CU Boulder, CU Denver, Colorado State University, Colorado School of Mines, National Jewish Health, and Rocky Mountain Regional VA Medical Center.

The Gates Center aspires to move the world of stem cell research and regenerative medicine forward. We provide the following benefits in conjunction with our partners to serve and support our diverse members as they navigate each stage of the continuum from basic science to patient benefit:



GATES CENTER BENEFITS

- ***Core labs*** provide equipment and leading-edge scientific services that would not otherwise be available nor affordable to local, national, and international regenerative medicine researchers.
- ***Gates Biomanufacturing Facility*** features expertise in process development, manufacturing of cell- and protein-based therapeutics, and FDA Phase 1 clinical trial quality and control regulations to ensure that on- and off-campus research can progress into clinical trials as efficiently and cost effectively as possible.
- ***Education and Outreach*** include the ***Gates Summer Internship Program*** for college undergraduates and support of the ***Graduate Program in Cell Biology, Stem Cells and Development*** that move the field of regenerative medicine forward by developing a pipeline of highly skilled future scientists and physicians. Gates Center Seminar series and community outreach highlight advances in stem cell biology and regenerative medicine.
- ***Business Development, Regulatory, Commercialization Support*** include the ***Gates Grubstake Fund*** and ***Startup Toolbox*** that provide crucial funding to bring promising regenerative discoveries to the clinic, and to give innovators access to regulatory and business formation support.
- ***Research funding*** provides financing at critical stages for projects/teams affiliated with the Gates Center through direct grants and endowment distributions.

GATES CENTER MEMBERS

NAME	POSITION	ACADEMIC INSTITUTION/AFFILIATES	PRIMARY (AND SECONDARY) APPOINTMENT(S)
Bruce Appel, Ph.D.	Professor Diane G. Wallach Chair in Pediatric Stem Cell Biology	University of Colorado Anschutz Medical Campus	Department of Pediatrics/Developmental Biology
Kristin Artinger, Ph.D.	Professor	University of Colorado Anschutz Medical Campus	School of Dental Medicine Department of Craniofacial Biology
Reed Ayers, Ph.D.	Assistant Research Professor	University of Colorado Anschutz Medical Campus	Department of Orthopedics
Susan Bailey, Ph.D.	Professor	Colorado State University	Department of Environmental and Radiological Health Sciences
Christopher Baker, M.D.	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Pediatrics/Developmental Biology
James Bamburg, Ph.D.	Professor	Colorado State University	Department of Biochemistry and Molecular Biology
Linda Barlow, Ph.D.	Professor	University of Colorado Anschutz Medical Campus	Department of Cell and Developmental Biology
Jaime Belkind-Gerson, M.D., M.Sc.	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Pediatrics/Digestive Health Institute
Ganna Bilousova, Ph.D.	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Dermatology
Stanca Birlea, M.D., Ph.D.	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Dermatology
Petter Bjornstad, M.D.*	Assistant Professor	University of Colorado Anschutz Medical Campus Children's Hospital Colorado	Department of Pediatric Endocrinology and Nephrology
Neil Box, Ph.D.	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Dermatology
Kristen Boyle, Ph.D.	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Pediatrics
Jeffrey Brown, Ph.D.	Senior Scientist Research and Development	AlloSource	
Anna Bruckner, M.D., M.S.C.S.	Associate Professor	University of Colorado Anschutz Medical Campus Children's Hospital Colorado	Department of Dermatology/Department of Pediatrics
Justin Brumbaugh, Ph.D.*	Assistant Professor	University of Colorado Boulder	Molecular, Cellular and Developmental Biology
Joseph Brzezinski, Ph.D.	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Ophthalmology
Ellen Burnham, M.D., M.S.	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Medicine/ Pulmonary Sciences and Critical Care
Valeria Canto-Soler, Ph.D.	Associate Professor Doni Solich Family Chair in Ocular Stem Cell Research	University of Colorado Anschutz Medical Campus	Department of Ophthalmology
Sanny Chan, M.D., Ph.D.	Assistant Professor	National Jewish Health	Department of Pediatrics/ Division of Allergy and Immunology
Wallace Chick, Ph.D.	Assistant Professor	University of Colorado Anschutz Medical Campus	Department of Cell and Developmental Biology
Ryan Crisman, Ph.D.	Co-founder and Chief Technical Officer	Umoja Biopharma	
Angelo D'Alessandro, Ph.D.	Assistant Professor	University of Colorado Anschutz Medical Campus	Department of Biochemistry and Molecular Genetics/Division of Hematology
James DeGregori, Ph.D.	Professor Courtenay C. and Lucy Patten Davis Endowed Chair in Lung Cancer Research	University of Colorado Anschutz Medical Campus	Department of Biochemistry and Molecular Genetics
Peter Dempsey, Ph.D.	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Pediatrics
Steven Dow, D.V.M., Ph.D.	Professor	Colorado State University	Department of Clinical Sciences
Jason Dragoo, M.D.	Professor and Vice Chair of Academic Affairs Endowed Chair of Regenerative Medicine Head Team Physician Denver Nuggets Director UCHealth Steadman Hawkins Clinic Denver	University of Colorado Anschutz Medical Campus	Department of Orthopedics
Nicole Ehrhart, V.M.D., M.S., Diplomate ACVS	Professor	Colorado State University	Department of Clinical Sciences CVMBS School of Biomedical Engineering
Patricia Ernst, Ph.D.*	Professor Postle Family Chair in Pediatric Cancer and Blood Disorders	University of Colorado Anschutz Medical Campus	Department of Pediatrics
Xiying Fan, Ph.D.	Research Instructor	University of Colorado Anschutz Medical Campus	Department of Dermatology
Terri Foote, M.B.A.	Director Program Management and Supply Chain	University of Colorado Anschutz Medical Campus	Gates Biomanufacturing Facility
Heide Ford, Ph.D.	Professor David F. and Margaret Turley Grohne Endowed Chair in Translational Cancer Research	University of Colorado Anschutz Medical Campus	Department of Pharmacology
Santos Franco, Ph.D.	Assistant Professor	University of Colorado Anschutz Medical Campus	Department of Pediatrics/Developmental Biology

NAME	POSITION	ACADEMIC INSTITUTION/AFFILIATES	PRIMARY (AND SECONDARY) APPOINTMENT(S)
Brian Freed, Ph.D.	Professor	University of Colorado Anschutz Medical Campus	Department of Medicine/Allergy and Clinical Immunology
Curt Freed, M.D.	Professor Leopold Korn and Michael Korn Chair in Parkinson's Disease	University of Colorado Anschutz Medical Campus	Department of Medicine/ Clinical Pharmacology and Toxicology
Jed Friedman, Ph.D.	Professor	University of Colorado Anschutz Medical Campus	Department of Pediatrics
Terry Fry, M.D.	Professor Robert J. and Kathleen A. Clark Endowed Chair for Pediatric Cancer Therapies	University of Colorado Anschutz Medical Campus	Departments of Pediatrics/Hematology and Immunology
Mayumi Fujita, M.D., Ph.D.	Professor	University of Colorado Anschutz Medical Campus	Dermatology (Immunology & Microbiology)
Christopher Garbe, M.B.A.	Senior Director CMC and Allogeneic Cell Therapy Program	Umoja Biopharma	
Kathleen Gavin, Ph.D.	Assistant Professor	University of Colorado Anschutz Medical Campus	Division of Geriatric Medicine
Moumita Ghosh, Ph.D.*	Assistant Professor	National Jewish Health	Division of Pulmonary, Critical Care and Sleep Medicine
Laurie Goodrich, D.V.M., M.S., Ph.D.	Associate Professor	Colorado State University	College of Veterinary Medicine
Lia Gore, M.D.	Professor Ergen Family Endowed Chair in Pediatric Oncology	University of Colorado Anschutz Medical Campus	Department of Pediatrics/Hematology, Oncology and Bone Marrow Transplantation
Samuel Gubbels, M.D.	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Otolaryngology
James Hagman, Ph.D.	Professor	National Jewish Health University of Colorado Anschutz Medical Campus	Department of Immunology and Genomic Medicine, Department of Immunology and Microbiology, Program in Molecular Biology
Kirk Hansen, Ph.D.	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Biochemistry and Molecular Genetics
Paco Herson, Ph.D.	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Anesthesiology Neuronal Injury Program
William Hiatt, M.D.	Professor	University of Colorado Anschutz Medical Campus	Cardiology and CPC Clinical Research
Hua Huang, M.D., Ph.D.	Professor	National Jewish Health	Integrated Department of Immunology
Srividhya Iyer, Ph.D.*	Assistant Professor	University of Colorado Anschutz Medical Campus	Department of Orthopedics
Jeffrey Jacot, Ph.D.	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Bioengineering
Sujatha Jagannathan, Ph.D.*	Assistant Professor	University of Colorado Anschutz Medical Campus	Biochemistry and Molecular Genetics
William Janssen, M.D.	Associate Professor	National Jewish Health	Division of Pulmonary, Critical Care and Sleep Medicine
Antonio Jimeno, M.D., Ph.D.	Professor Daniel and Janet Mordecai Chair in Cancer Stem Cell Biology	University of Colorado Anschutz Medical Campus	Department of Medicine/Medical Oncology
Malik Kahook, M.D.	Professor Slater Family Endowed Chair in Ophthalmology	University of Colorado Anschutz Medical Campus	Department of Ophthalmology
Karen King, Ph.D.	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Orthopedics
Dwight Klemm, Ph.D.	Professor	University of Colorado Anschutz Medical Campus	Department of Medicine/Pulmonary Sciences
Igor Kogut, Ph.D.	Assistant Professor	University of Colorado Anschutz Medical Campus	Department of Dermatology
Melissa Krebs, Ph.D.	Assistant Professor	Colorado School of Mines	Chemical and Biological Engineering
Raj Kumar, Ph.D.	Professor Edgar L. and Patricia M. Makowski Family Endowed Chair	University of Colorado Anschutz Medical Campus	Department of Obstetrics and Gynecology
Katherine Lee, Ph.D.	Assistant Professor	University of Colorado Anschutz Medical Campus	Department of Pediatrics/Infectious Disease
Kenneth Liechty, M.D.	Professor The Sandy Wolf Chair in Maternal Fetal Surgery	University of Colorado Anschutz Medical Campus	Department of Surgery/Pediatric Surgery
Carlin Long, M.D.	Professor	University of Colorado Anschutz Medical Campus	Department of Medicine/Cardiology
Shi-Long Lu, M.D., Ph.D.	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Otolaryngology
Traci Lyons, Ph.D.	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Medicine/Medical Oncology
Chelsea Magin, Ph.D.	Assistant Professor	University of Colorado Denver | Anschutz Medical Campus	Department of Bioengineering/Pediatrics and Medicine
Susan Majka, Ph.D.	Professor	National Jewish Health University of Colorado Anschutz Medical Campus	Division of Pulmonary, Critical Care and Sleep Medicine
Naresh Mandava, M.D.	Professor Sue Anschutz-Rodgers Endowed Chair in Retinal Diseases	University of Colorado Anschutz Medical Campus	Department of Ophthalmology
Joanne Masterson, Ph.D.	Assistant Professor	University of Colorado Anschutz Medical Campus	Department of Pediatrics

NAME	POSITION	ACADEMIC INSTITUTION/AFFILIATES	PRIMARY (AND SECONDARY) APPOINTMENT(S)
Xianzhong Meng, M.D., Ph.D.	Professor	University of Colorado Anschutz Medical Campus	Department of Medicine/Cardiology
Ram Nagaraj, Ph.D.	Professor	University of Colorado Anschutz Medical Campus	Department of Ophthalmology/School of Pharmacy
Devatha Nair, Ph.D.	Assistant Professor	University of Colorado Anschutz Medical Campus University of Colorado Boulder	School of Dental Medicine
Corey Neu, Ph.D.	Associate Professor Donnelly Family Endowed Associate Professor	University of Colorado Boulder	Department of Mechanical Engineering
Lee Niswander, Ph.D.	Professor	University of Colorado Boulder	Department of Molecular, Cellular and Developmental Biology
David Norris, M.D.	Professor	University of Colorado Anschutz Medical Campus	Department of Dermatology
Jeffrey Olson, M.D.	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Ophthalmology
Bradley Olwin, Ph.D.	Professor	University of Colorado Boulder	Department of Molecular, Cellular and Developmental Biology
David Ryan Ormond, M.D., Ph.D.	Assistant Professor	University of Colorado Anschutz Medical Campus	Department of Neurosurgery/Translational Clinical Research
Vikas Patel, M.D.	Professor Endowed Chair in Orthopedic Spinal Innovation	University of Colorado Anschutz Medical Campus	Department of Orthopedics
Karin Payne, Ph.D.	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Orthopedics
Anne-Laure Perraud, Ph.D.	Assistant Professor	University of Colorado Anschutz Medical Campus National Jewish Health	Department of Biomedical Research/ Immunology and Microbiology
Mark Petrash, Ph.D.	Professor	University of Colorado Anschutz Medical Campus	Department of Ophthalmology
Christopher Phiel, Ph.D.	Associate Professor	University of Colorado Denver	Department of Integrative Biology
Eric Pietras, Ph.D.	Assistant Professor Cleo Meador and George Ryland Scott Endowed Chair in Hematology	University of Colorado Anschutz Medical Campus	Department of Medicine/Hematology
Robert Plenter	Senior Professional Research Assistant	University of Colorado Anschutz Medical Campus	Division of Pulmonary, Critical Care Medicine
Christopher Porter, M.D.	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Pediatrics/Hematology, Oncology and Bone Marrow Transplantation
Huntington Potter, Ph.D.	Professor Director CU Alzheimer's and Cognition Center	University of Colorado Anschutz Medical Campus	Department of Neurology
Yosef Refaeli, Ph.D.	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Dermatology
Mary Reyland, Ph.D.	Professor	University of Colorado Anschutz Medical Campus	Departments of Craniofacial Biology/Cell Developmental Biology/Pathology
Angeles Ribera, Ph.D.	Professor	University of Colorado Anschutz Medical Campus	Department of Physiology and Biophysics
Jennifer Richer, Ph.D.	Professor	University of Colorado Anschutz Medical Campus	Department of Pathology
James Roede, Ph.D.	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Pharmaceutical Sciences
Dennis Roop, Ph.D.	Professor Charles C. Gates Endowed Chair in Regenerative Medicine and Stem Cell Biology	University of Colorado Anschutz Medical Campus	Department of Dermatology
Paul Rozance, M.D.	Professor	University of Colorado Anschutz Medical Campus	Department of Pediatrics and Integrative Physiology
Andrii Rozhok, Ph.D.	Research Instructor	University of Colorado Anschutz Medical Campus	Department of Dermatology
Holger Andreas Russ, Ph.D.	Assistant Professor	University of Colorado Anschutz Medical Campus	Barbara Davis Center for Diabetes Microbiology and Immunology Department
Branden Salinas, Ph.D.	Senior Director Manufacturing Science and Technology	Umoja Biopharma	
Carol Sartorius, Ph.D.	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Pathology
Matthew Seefeldt, Ph.D.	Executive Director	University of Colorado Anschutz Medical Campus	Gates Biomanufacturing Facility
Karina Serban, M.D.	Assistant Professor	National Jewish Health	Department of Medicine, Division of Pulmonary and Critical Care Medicine
Yiqun Shellman, Ph.D.	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Dermatology
Vanessa Sherk, Ph.D.	Instructor	University of Colorado Anschutz Medical Campus	Department of Medicine/Endocrinology
Kunhua Song, Ph.D.	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Medicine Division of Cardiology
Danielle Soranno, M.D.	Assistant Professor	University of Colorado Anschutz Medical Campus	Department of Pediatrics
Kurt Stenmark, M.D.	Professor La Cache Endowed Chair in Pediatric Critical Care	University of Colorado Anschutz Medical Campus	Department of Pediatrics/Critical Care
Lori Sussel, Ph.D.	Professor Sissel and Findlow Family Chair	University of Colorado Anschutz Medical Campus	Barbara Davis Center for Diabetes/ Pediatrics (Cell and Developmental Biology)

NAME	POSITION	ACADEMIC INSTITUTION/AFFILIATES	PRIMARY (AND SECONDARY) APPOINTMENT(S)
Tamara Terzian, Ph.D.	Assistant Professor	University of Colorado Anschutz Medical Campus	Department of Dermatology
Douglas Thamm, V.M.D.	Assistant Professor	Colorado State University	Department of Clinical Sciences
Enrique Torchia, Ph.D.	Assistant Professor	University of Colorado Anschutz Medical Campus	Department of Dermatology
Ronald Vagnozzi, Ph.D.*	Assistant Professor	University of Colorado Anschutz Medical Campus	Cardiology/Consortium for Fibrosis Research and Translation (CFReT)
Maria Natalia Vergara, Ph.D.*	Assistant Professor	University of Colorado Anschutz Medical Campus	Department of Ophthalmology
Michael Verneris, 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
Eszter Vladar, Ph.D.	Assistant Professor	University of Colorado Anschutz Medical Campus	Division of Pulmonary Sciences, Department of Cell and Developmental Biology
David Wagner, Ph.D.	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Neurology
Lori Walker, Ph.D.	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Medicine/Cardiology
Xiao-Jing Wang, M.D., Ph.D.	Professor John S. Gates Endowed Chair in Stem Cell Biology	University of Colorado Anschutz Medical Campus	Department of Pathology
Zhijie Wang, Ph.D.	Assistant Professor	Colorado State University	Department of Mechanical Engineering
Trevor Williams, Ph.D.	Professor Timpte/Brownie Endowed Chair in Craniofacial/Molecular Biology	University of Colorado Anschutz Medical Campus	Department of Craniofacial Biology, School of Dental Medicine/ Department of Cell and Developmental Biology
Carol Wilusz, Ph.D.	Professor	Colorado State University	Department of Microbiology, Immunology and Pathology
Jeff Wilusz, Ph.D.	Professor	Colorado State University	Department of Microbiology, Immunology and Pathology
Rui Yi, Ph.D.	Associate Professor	University of Colorado Boulder	Department of Molecular, Cellular and Developmental Biology
Martin Zamora, M.D.	Professor	University of Colorado Anschutz Medical Campus	Division of Pulmonary, Critical Care Medicine
Michael Zaretsky, M.D.*	Associate Professor Medical Director Colorado Fetal Care Center	University of Colorado Anschutz Medical Campus Children's Hospital Colorado	Department of Obstetrics and Gynecology Maternal Fetal Medicine
Wenbo Zhou, Ph.D.	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Medicine/Clinical Pharmacology and Toxicology

* New members in 2020

SELECT MEMBER PUBLICATIONS AND HONORS*

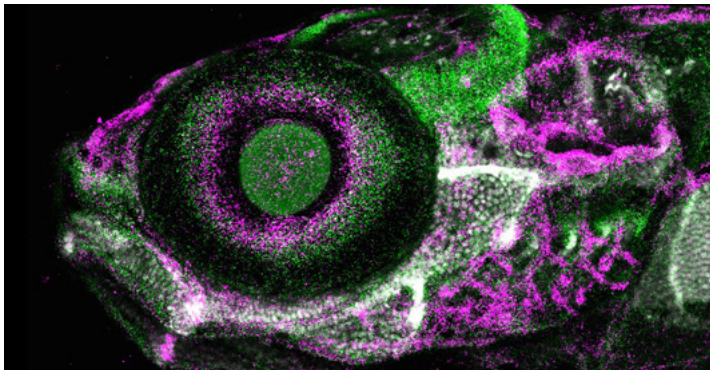
PUBLICATIONS

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

In this manuscript, Drs. Hughes and Appel describe how microglia modify myelin formation during development by phagocytosing individual myelin sheaths from axons (Hughes and Appel, Nature Neuroscience, 2020). This work contributes new information to our understanding of myelin plasticity and, potentially, myelin disease.

Kristin Artinger, Ph.D., *Professor,* School of Dental Medicine

In this manuscript, Dr. Artinger describes the role of two transcription and epigenetic regulators in the formation of the craniofacial skeleton in zebrafish and mice (Shull et al., Dev Biol, 2020). These factors regulate downstream gene expression and thus control specific developmental events required for the normal formation and may predict what happens during craniofacial birth defects.



The development of the zebrafish skull at 6 days (courtesy of Drs. Ezra Lencer and Kristin Artinger). Neural crest progenitor cells (white) give rise to the zebrafish jaw structures and express receptors (purple and green) that help the cells receive information about where they are located in the embryo. These receptors are also expressed in the eye and gills (purple) as well as brain (green). Understanding how these structures form may help in our understanding of craniofacial birth defects.

Susan Bailey, Ph.D., *Professor,* Department of Environmental & Radiological Health Sciences, Colorado State University

Dr. Bailey and her colleagues assessed telomere length dynamics and DNA damage responses before, during, and after one-year or shorter duration missions aboard the International Space Station (ISS) in a comparatively large cohort of astronauts [n = 11] (Luxton, et al., Cell Rep, 2020). Although generally healthy individuals, astronauts tended to have significantly shorter telomeres and lower telomerase activity than age- and sex-matched ground controls before and after spaceflight. During spaceflight, all crew members experienced oxidative stress, which positively correlated with telomere length dynamics. They proposed that in response to chronic oxidative damage in extreme environments, the telomerase-independent Alternative Lengthening of Telomeres (ALT) pathway is transiently activated in normal somatic cells.

Linda Barlow, Ph.D., *Professor,* Department of Cell and Developmental Biology

In this publication, Dr. Barlow and her colleagues describe in detail our modified protocol to generate lingual organoids from adult mouse taste stem cells, including refinement of specific culture media (Shechtman et al., JoVE, 2020).

Stanca Birlea, M.D., Ph.D., *Associate Professor,* **Dennis Roop, Ph.D.,** *Professor,* and **David Norris, M.D.,** *Professor,* Department of Dermatology

Drs. Birlea, Roop and Norris and their colleagues used biopsies from patients with vitiligo and laser capture microdissection to selectively harvest melanocytes and keratinocyte precursors from the hair follicle bulge of untreated vitiligo skin and vitiligo skin treated with narrow-band UVB (Goldstein et al., J. Invest Dermatology, 2020). The captured material was subjected to whole transcriptome RNA-sequencing and gene expression analysis. This strategy allowed them to characterize the pathways and signals in the hair follicle bulge that control the re-pigmentation process.

Kristen Boyle, Ph.D., *Associate Professor,* Department of Pediatrics

In this manuscript, Dr. Boyle and her colleagues describe the effects of the maternal fat-1 transgene on offspring skeletal muscle metabolism in a rodent model of maternal obesity (Boyle et al., Nutrients, 2020). The novel fat-1 transgene converts omega-6 to omega-3 fatty acids, resulting in a favorable inflammatory profile, even when dams are fed a high fat. This approach allowed them to distinguish the effects of maternal obesity from maternal inflammation on offspring outcomes. The maternal transgene protected offspring from impaired lipid metabolism and oxidative stress normally observed in offspring of obese dams.

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

In this paper, Dr. Brzezinski and colleagues determined that the fate choices of developing retinal neurons are flexible (Goodson, et al., Dev. Biol, 2020). In particular, they showed that the choice to become a bipolar cell neuron was plastic for just a brief time after the fate decision was made. This is less flexible than the decision to become a photoreceptor.

James DeGregori, Ph.D., *Professor,* Department of Biochemistry and Molecular Genetics and **Andrii Rozhok, Ph.D.,** *Instructor,* Department of Dermatology

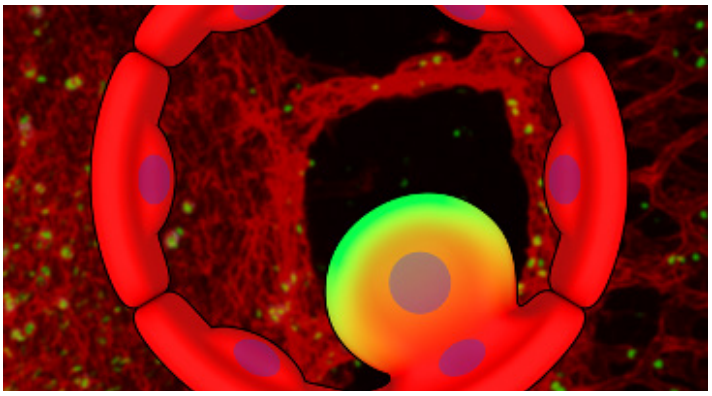
Drs. DeGregori and Rozhok and collaborators describe how blood stem cells with altered chromosomes can expand in the period after a bone marrow transplantation, which could increase the risk of secondary leukemias (Rozhok et al., Scientific Reports, 2020).

Jason L. Dragoo, M.D., *Professor,* Department of Orthopedics

In this article, Dr. Dragoo and his colleagues identify and quantify proteins in various blood products, including Platelet Rich Plasma (PRP), Platelet Poor Plasma (PPP), and Plasma alone (Miroshnychenko et al., Regenerative Therapy, 2020).

Patricia Ernst, Ph.D., *Professor,* Department of Pediatrics

In this article, Dr. Ernst and colleagues show that overexpression of wild-type, non-fusion MLL1/KMT2A increases the hematopoietic potential of ES-derived and embryonic progenitors (Yang et al., Stem Cell Reports, 2020). MLL1 expression selectively enhances hematopoietic commitment from hemogenic endothelium through an unexpected Rac/Rho/integrin signaling, adhesion-mediated mechanism.



Yang and colleagues show that increasing MLL1 levels enhances the production of hematopoietic cells from a hemogenic endothelial intermediate through an altered intracellular signaling state. This image shows a stylized endothelial-to-hematopoietic transition with a halo of green representing Rac signaling activity as the cells change shape. The stylized drawing is superimposed on a confocal image of MLL1-induced embryonic dorsal aorta immunostained with CD31 (red) and Runx1 (green) antibodies, performed by Elizabeth Howell in Nancy Speck's lab. Drawing by Donald Bakos.

Mayumi Fujita, M.D., Ph.D., *Professor,* Department of Dermatology

In this manuscript, Dr. Fujita and colleagues demonstrate for the first time that the NLRP1 inflammasome is involved in the development of acquired drug resistance of melanoma (Zili et al., Cancers, 2020). Because drug-tolerant cancer cells become cross-tolerant to other classes of cancer drugs, NLRP1 might be a suitable therapeutic target in drug-resistant melanoma, as well as in other cancers.

Celebrating after the thesis defense of a graduate student, Jenny Mae Samson, on August 12, 2020

Kathleen Gavin, Ph.D., *Assistant Professor,* Department of Medicine-Geriatrics

In this paper Dr. Gavin and colleagues describe that ovarian hormone suppression (a pharmacological model utilized to isolate the role of estrogen from that of aging) in premenopausal women approaching the age of menopause results in increased total and abdominal adiposity (Gavin et al., Obesity, 2020). However, ovarian hormone suppression does not result in a significant change in any component of free-living energy expenditure, although the magnitude of decrease in total and resting energy expenditure is similar to changes observed in previous studies. This study demonstrates that the mechanistic role of estrogen in the regulation of body composition and energy expenditure in women needs further research.

Lia Gore, M.D., *Professor,* Department of Pediatrics

In these publications, Dr. Gore and colleagues describe the outcomes of five large multi-institutional clinical trials examining four new treatments for acute leukemia and one treatment for children with brain tumors. In each case, several large academic medical centers worked together to define the best approach for children with difficult to treat cancers. The results of the clinical trials are reported in these papers and help define new treatment questions and new scientific insight, which will be the focus of future studies (Burke et al., Clinical Cancer Research, 2020; Salzer et al., Journal of Clinical Oncology, 2020; Winters et al., Pediatric Blood and Cancer, 2020; Wright et al., Pediatric Blood and Cancer, 2020; Carraway et al., Clinical Cancer Research, 2020).

James Hagman, Ph.D., *Professor,* and **Hua Huang, M.D., Ph.D.,** *Professor,* Department of Immunology and Microbiology, National Jewish Health

In collaboration with Dr. Huang, Dr. Hagman and colleagues determined the molecular mechanisms that control the differentiation of mast cells by epigenetic regulators (Li et al., Nat Commun, 2020).

Hua Huang, M.D., Ph.D., *Professor,* Department of Immunology and Microbiology, National Jewish Health

In this paper, Dr. Huang and his collaborators describe how IL-13 gene enhancers detect signals triggered by antigenic stimulation and how the induced enhancers cooperate with constitutively active enhancers to generate IL-13 gene transcriptional outputs in mast cells (Kamran et al., J Immunol, 2020).

T. Rajendra Kumar, Ph.D., *Professor,* Department of Obstetrics and Gynecology

In this manuscript, Dr. Kumar and his collaborators report the generation, structure, and function of a first-in-class, fully humanized, epitope-specific FSH blocking antibody (Gera et al., Proc Natl Acad Sci U S A, 2020). They perform fine mapping of the FSH-FSH receptor interface and confirm stable binding of the Fab domain to two of five receptor-interacting residues of the FSHβ subunit, which is sufficient to block its interaction with the FSH receptor. In doing so, the humanized antibody profoundly inhibited FSH action in cell-based assays, a prelude to further preclinical and clinical testing.

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

In this manuscript, Dr. Liechty and his colleagues assess the contribution of the long non-coding RNA GAS5 to the persistence of chronic inflammation in diabetic (Db) wounds, which is partly due to the prolonged presence of proinflammatory (M1) macrophages (Hu et al., J Invest Dermatol, 2020). Using in vivo and in vitro analyses, they found that the long non-coding RNA GAS5 is overexpressed in Db wounds. Knocking down the expression of GAS5 in Db wounds enhanced healing by promoting the transition of M1 macrophages to M2 macrophages. Their results suggest that targeting long non-coding RNA GAS5 may provide a therapeutic intervention for correcting impaired Db wound healing.

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

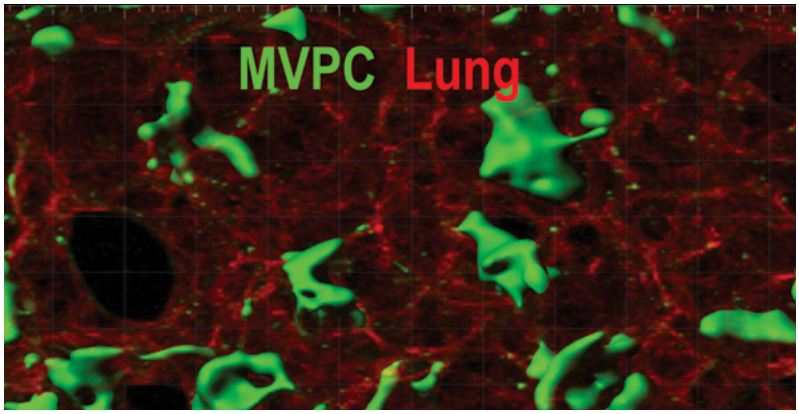
In this paper, Dr. Lyons and colleagues compared the proteomic content of extracellular vesicles (EVs) isolated from invasive breast cancer cell lines and plasma samples from young women's breast cancer (YWBC) patients and age-matched healthy donors using mass spectrometry, as well as functionally using two-dimensional tumor cell invasion assays (Jordan et al., Breast Cancer Res, 2020). They found that EVs from YWBC patients drive increased invasion of non-malignant cells via the Focal Adhesion Kinase pathway, thus elucidating the role of EVs in breast cancer progression.

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

In this manuscript, Dr. Magin and her colleagues used a hydrogel embedding process to maintain precision-cut lung slice viability ex vivo for up to 21 days in custom biomaterials (Bailey et al., American Journal of Respiratory Cell and Molecular Biology, 2020). They are using these viable lung slices as an ex vivo model for a variety of chronic pulmonary diseases.

Susan Majka Ph.D., *Professor,* Department of Medicine, National Jewish Health and **Dwight Klemm, Ph.D.,** *Professor,* Division of Pulmonary Sciences

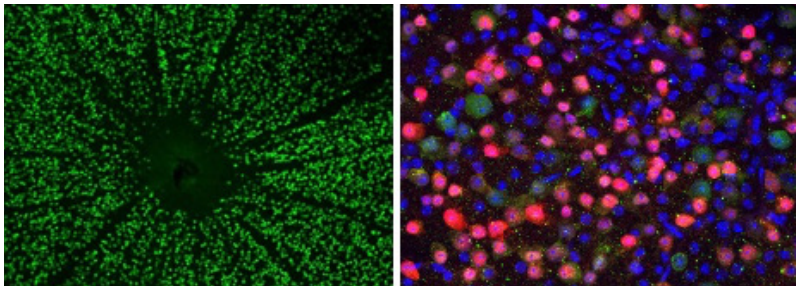
In these studies, Drs. Majka and Klemm and their colleagues demonstrate that lung mesenchymal vascular progenitor cells (MVPCs) modulate adaptive angiogenesis during tissue repair and genetic depletion of MVPCs reduces adaptive angiogenesis (Summers et al., FASEB J, 2020). Following vascular endothelial injury, Wnt activation in MVPCs was sufficient to elicit an emphysema-like phenotype. Their data suggest that lung MVPCs drive angiogenesis in response to injury and regulate the microvascular niche as well as subsequent distal lung tissue architecture via Wnt signaling.



Multiphoton image of MVPC in the Alveolar Capillary Network, Multiphoton image of MVPC in the Alveolar Capillary Network (Courtesy of Megan Summers M.S. and Susan Majka Ph.D.): Lung mesenchymal vascular precursors (MVPC; green) were localized in the distal lung (red). MVPC maintain the microvascular niche in distal lung. The microvasculature is necessary for efficient gas exchange and is remodeled or lost in disease.

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

In this paper, Dr. Nagaraj and his colleagues investigated lens protein modification by acylation in human lens proteins and found that malonylated and propionylated lysine modifications are widely distributed in the lens and their levels are maintained at certain levels during aging (Nahomi et al., Exp. Eye Res, 2020). They are now investigating how these modifications contribute to presbyopia.



Retinal ganglion cells (RGCs) stained for Brn3a (left) and RBPMS (right). Dr. Ram Nagaraj's laboratory is investigating mechanisms by which RGCs die in glaucoma and developing peptide and AAV2 mediated methods to prevent RGC death in glaucoma.

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

Dr. Niswander and her colleagues, utilize genomic information from patients to discover the genetics underlying neural tube defects in humans (Zou et al., Neural Dev, 2020).

Karin Payne, Ph.D., *Associate Professor,* Department of Orthopedics and **Melissa Krebs, Ph.D,** *Associate Professor,* Chemical and Biological Engineering, Colorado School of Mines

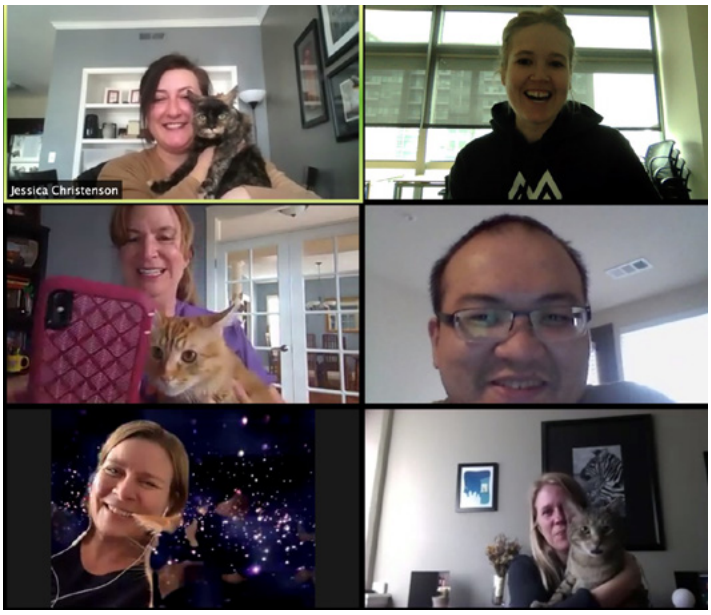
In this manuscript, Drs. Payne and Krebs and their collaborators studied the delivery of anti-VEGF antibody from alginate:chitosan hydrogels as a potential treatment strategy to prevent bony bar formation seen after physeal injury (Erickson et al., J Orthop Res, 2020). A quick release of anti-VEGF decreased bony bar formation and did not interfere with normal bone elongation. These results could have positive implications for children suffering from physeal injuries.

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

In this publication, the authors examined the pathways involved in the development of tubular cell injury and death before and after kidney transplantation (Jain et al., Transplantation, 2020). Their results suggest distinct therapies are needed at different times during organ preservation and transplantation. Prevention of apoptosis during cold storage is best achieved by inhibiting intrinsic pathways. In contrast, prevention of cell death and innate immunity after cold ischemia and transplantation requires inhibition of both the extrinsic death receptor pathway via TNFR1 and caspase-8 and inhibition of programmed necrosis via TLR4 and TNFR1.

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

In this study, Dr. Richer and her colleagues describe targetable alterations in estrogen receptor positive metastatic breast cancer that arise following estrogen-deprivation (Williams et al., Cancer Research, 2020). They find that biopsies that have mutations in the gene encoding the estrogen receptor may respond to immunotherapy due to elevated PD-L1 + macrophages.



Richer lab meeting during the time of Covid

James Roede, Ph.D., *Associate Professor,* Skaggs School of Pharmacy and Pharmaceutical Sciences

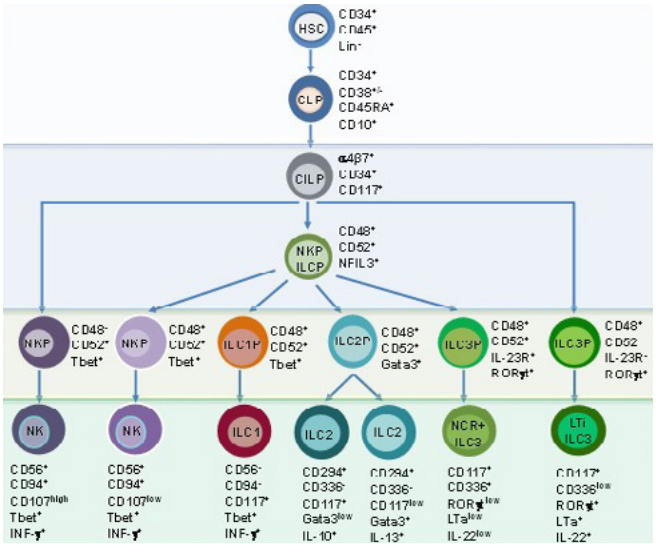
In this manuscript, Dr. Roede and colleagues examined whether exposure to simvastatin, a commonly used cholesterol-lowering drug, at a noncytotoxic dose would impair energy metabolism in human neuroblastoma cells (Kuzyk et al., Clin Transl Sci, 2020). Their results show that simvastatin induces delayed apoptosis in neuroblastoma cells through disruption of glycolysis and impairment of mitochondria. These findings provide mechanistic insight into the off-target effects of this therapy by the identification of molecular targets.

Yiqun Shellman, Ph.D., *Associate Professor,* **Mayumi Fujita, M.D., Ph.D.,** *Professor,* and **David Norris, M.D.,** *Professor,* Department of Dermatology

In these manuscripts, Drs. Shellman, Fujita and Norris and their colleagues investigate the therapeutic potential and mechanism of action for two different combinations to treat advanced melanoma in patients lacking options. They identified a subset of melanomas with a specific genetic makeup that may be good candidates for the combination of the MCL1 inhibitor plus venetoclax (Mukherjee et al., Cell Death Dis, 2020 and Mukherjee et al., Cancers, 2020).

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

Dr. Verneris and his co-authors describe the developmental steps that innate lymphoid cells take during development (Tufa et al., Sci Immunol, 2020). These findings have translational value considering that various groups are contemplating the use of induced pluripotent stem cell (iPSC)-derived, off the shelf natural killer (NK) cells for therapeutic purposes and an understanding of these developmental pathways may provide insight into strategies for increasing the yields of stem cell-derived NK cells.



In the publication from Science Immunology 20 Nov 2020, the Verneris laboratory used single cell RNA sequencing to decipher the developmental steps that a bone marrow stem cell takes to give rise to various innate lymphoid cell populations. These cells, newly discovered about 15 years ago, are tissue resident lymphocytes that facilitate tissue defense and repair. These studies pave the way for using bone marrow stem cells to create innate lymphoid cells for therapeutic purposes.

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

In this manuscript, Dr. Walker and her colleagues describe the isoform specific regulation of the HCN4 channel (Peters et al., Proc Natl Acad Sci U S A, 2020). The HCN4 channel is a critical pacemaker protein in the sinoatrial node of the heart and understanding its molecular regulation is critical in order to best understand cardiac rhythm disturbances.

Xiao-Jing Wang, M.D., Ph.D., *Professor,* Department of Pathology, **Dennis Roop, Ph.D.,** *Professor,* Department of Dermatology and **Antonio Jimeno, M.D., Ph.D.,** *Professor,* Division of Medical Oncology

Resistance to immunotherapy is a significant challenge, and the scarcity of human models hinders the identification of the underlying mechanisms. To address this limitation, Drs. Wang, Roop and Jimeno and their colleagues constructed an autologous humanized mouse model with hematopoietic stem and progenitor cells (HSPC) and tumors from two melanoma patients progressing to immunotherapy (Morton et al., Mol Cancer Res, 2020). Unlike mismatched humanized mouse models, generated from cord blood-derived HSPCs and tumors from different donors, the autologous humanized mouse model recapitulates a patient-specific tumor microenvironment. When these autologous humanized mice were treated with immunotherapies mirroring what the originating patients received, tumor growth accelerated, similar to the progression observed in the patients. Thus, autologous humanized mouse models represent an ideal experimental model to identify the underlying mechanisms leading to resistance of melanomas to immunotherapy.

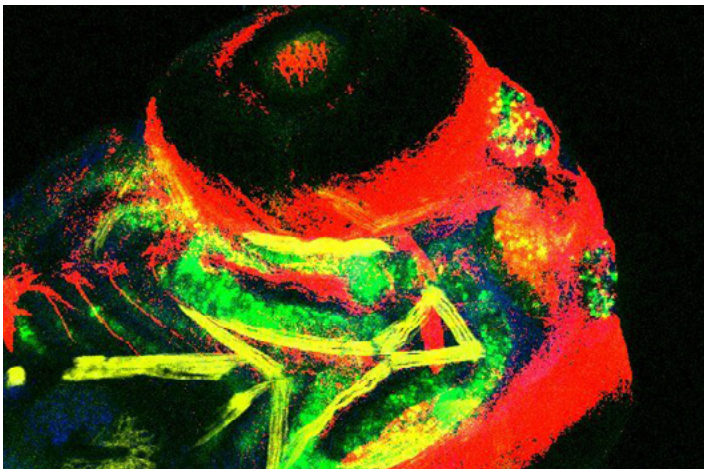
Trevor Williams, Ph.D., *Professor,* School of Dental Medicine

In this manuscript, Dr. Williams and his colleagues describe how a splicing factor involved in helping decide between an epithelial or mesenchymal cell fate regulates craniofacial clefting in the mouse (Lee et al., Development, 2020).

HONORS

Kristen Artinger, Ph.D., *Professor,* Department of Craniofacial Biology, was appointed as the new editor for *Birth Defects Research,* focusing on mechanisms of birth defects and developmental disorders. Beginning in January 2021, Dr. Artinger planned to work to attract cutting-edge research in developmental biology to the journal, and to develop several special issues on emerging topics and themes to advance science, understanding of mechanisms, and translation of basic science to clinical research and practice.

Maria Valeria Canto-Soler, Ph.D., *Associate Professor,* Department of Ophthalmology, was appointed Co-Chair of the Regenerative Medicine Strategic Planning Panel for the National Eye Institute Strategic Planning 2020 Vision for the Future plan. She was also invited as a thought leader for the NEI Audacious Goals initiative Roadmapping Workshop.



Zebrafish muscle, cartilage and neuron development are tightly connected. Neural crest progenitors (green) are developing very near cranial muscle (yellow) and forming neurons (red to the right in image). Cell nuclei are shown in blue. Understanding how these structures form may help in our understanding of craniofacial birth defects.

Patricia Ernst, Ph.D., *Professor,* Department of Pediatrics, served as President of the International Society of Experimental Hematology in 2020.

Sujatha Jagannathan, Ph.D., *Assistant Professor,* Department of Biochemistry and Molecular Genetics, received a Young Investigator Award from the FSHD Society. ***(https://www.fshdsociety.org/2020/08/17/2020-young-investigator-awards/)*** Facioscapulohumeral muscular dystrophy, or FSHD, is a genetic disorder with no effective cure that leads to the weakening of skeletal muscles. It typically begins in early teenage years with the loss of muscles in the face (facio), shoulders (scapula), upper arms (humerus), legs or core, and can spread to any muscle, resulting in 20% of patients needing a wheelchair by age 50 and over 70% experiencing debilitating pain and fatigue.

Chelsea Magin, Ph.D., *Assistant Professor,* Department of Bioengineering, received the Recognition of Early Academic Achievement Award from the Respiratory Cell and Molecular Biology Assembly of the American Thoracic Society.

Jennifer Richer, Ph.D., *Professor,* Department of Pathology, was named Basic Science Chair of the Annual Meeting Steering Committee for The Endocrine Society Annual Meeting 2021.

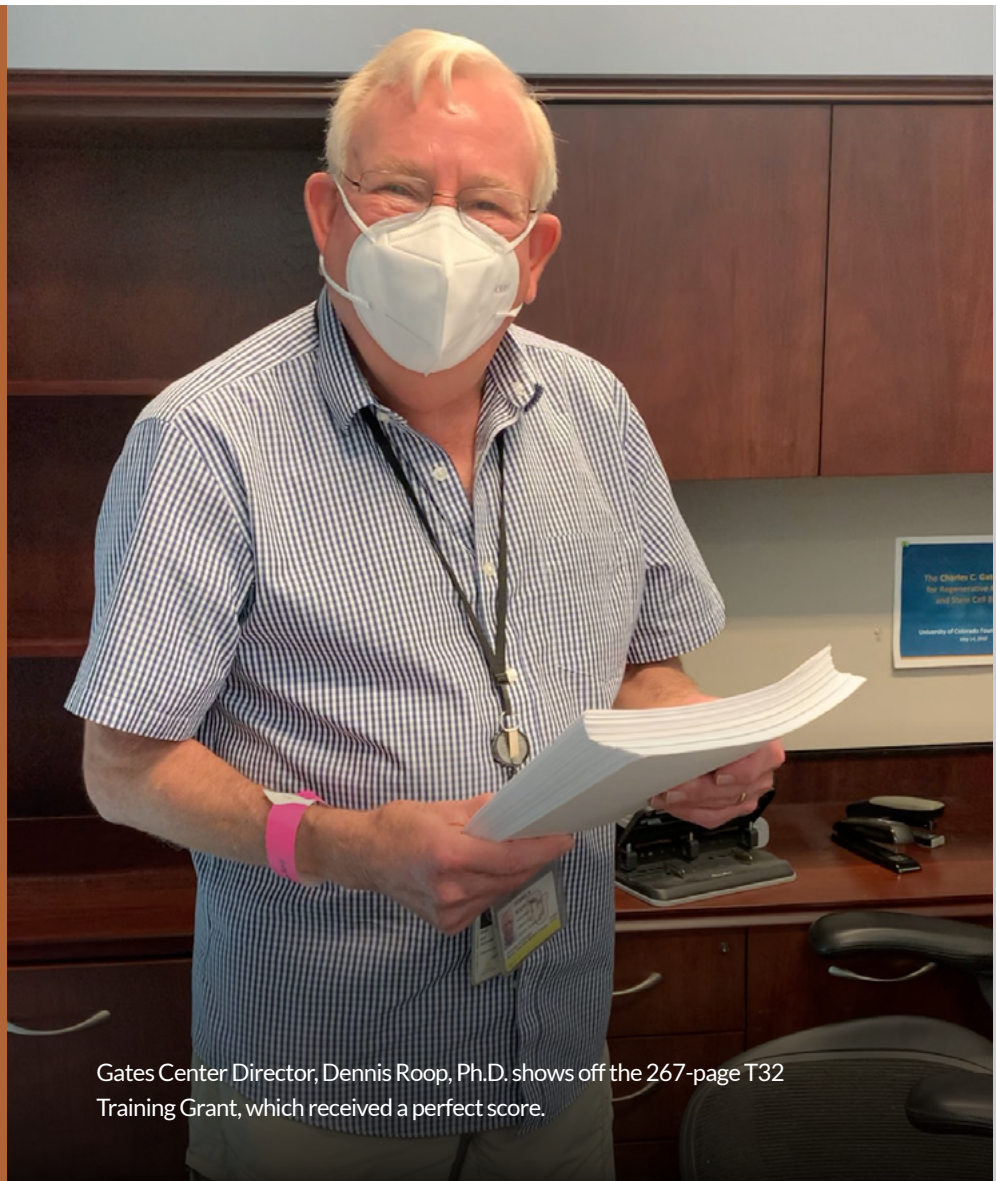
Natalia Vergara, Ph.D., *Assistant Professor,* Department of Ophthalmology, was announced as the winner of the National Eye Institute's 3D Retinal Organoid Challenge Award- Phase II: Reduction to practice. ***https://www.nei.nih.gov/about/goals-and-accomplishments/nei-research-initiatives/3-d-retina-organoid-challenge-3-d-roc/2017-ideation-challenge/2017-ideation-winner-and-honorable-mention***

*This list highlights only a few of numerous Gates Center members' publications and honors. Unless otherwise indicated, authors and honorees are from the University of Colorado's Anschutz Medical Center.

GRANT AWARDS

PRINCIPAL INVESTIGATOR(S)	AGENCY/SPONSOR	AMOUNT AWARDED	TITLE	FUNDING PERIOD
Appel, Bruce	National Institutes of Health (NIH)	$1,428,180.00	Mechanisms guiding axon selection for myelination in vivo	09/30/20 - 06/30/24
Barlow, Linda	National Institutes of Health (NIH)	$2,546,660.00	Characterization of progenitor populations in adult taste epithelium	07/01/20 - 06/30/25
Canto-Soler, Maria Valeria	Colorado Office of Economics Development & International Trade	$150,000.00	Advanced biomaterial systems for stem cell-derived retinal transplants	09/01/20 - 07/31/21
Canto-Soler, Maria Valeria Mathias, Marc	Department of Defense	$750,000.00	3D Retinal Transplants Derived from Human Induced Pluripotent Stem Cells to Treat Combat Laser-Induced Blindness	08/15/20 - 08/14/22
Ernst, Patricia Allen, Mary Ann	AB Nexus	$40,000.00	Identification of an embryonic cell-intrinsic cancer checkpoint: studying differential transcriptional effects of the proto-oncogene MLL1 versus MLL-ENL in an embryonic system	12/01/20 - 12/01/21
Fujita, Mayumi	National Cancer Institute	$345,034.00	Modulation of inflammasome-mediated cytokine activation by EGCG in human melanoma	03/01/20 - 02/28/21
Fujita, Mayumi	Veteran's Administration	$165,000.00	Autoinflammation in human melanoma	10/01/20 - 09/30/21
Fujita, Mayumi Dinarello, Charles	Cancer League of Colorado	$60,000.00	The role of alpha-1 antitrypsin in cancer immunotherapy	07/01/20 - 06/30/21
Jagannathan, Sujatha	Friends of FSH Research and Chris Carrino Foundation for Facioscapulohumeral Muscular Dystrophy (FSHD)	$197,753.00	Deciphering the role of aberrant protein synthesis in FSHD	02/01/20 - 01/31/23
Liechty, Ken Xu, Junwang, Malany, Siobhan	National Institutes of Health (NIH)	$2,627,897.00	Advancing small molecule CXCR4 agonists for diabetic wound healing	08/01/20 - 05/31/25
Magin, Chelsea	Colorado Clinical & Translational Sciences Institute	$30,000.00	Mechanically tunable hydrogel biomaterials to improve in vitro models of pulmonary fibrosis	09/15/20 - 04/30/22
Magin, Chelsea	National Institutes of Health (NIH)	$2,575,209.00	Hybrid Hydrogel Biomaterials Comprising Clickable Decellularized Extracellular Matrix for Engineering Dynamic 3D Models of Fibrosis	07/27/20 - 06/26/25
Magin, Chelsea	National Science Foundation	$501,768.00	CAREER: Spatiotemporally Addressable Hydrogel Biomaterials as Tools for Investigating Fibroblast Mechanobiology	02/01/20 - 01/31/25
Magin, Chelsea Tennis, Meredith	National Institutes of Health (NIH)	$275,000.00	Engineering ex vivo models of lung cancer and chemoprevention	07/14/20 - 06/13/22
Niswander, Lee Gleeson, Joseph Kitner, Chris	National Institutes of Health (NIH)	$6,979,481.00	Developmental Mechanisms of Human Meningomyelocele	12/01/20 - 11/30/25
Norris, David	Veteran's Administration	$66,000.00	Melanoma Resistance to Apoptosis: Mechanisms and Therapeutic Potential.	07/01/20 - 06/30/24
Osborne, Douglas Grant	American Skin Association	$60,000.00	Role of IL-37 in regulatory T cells and melanoma	04/01/20 - 03/31/21
Payne, Karin Bryant, Stephanie McLeod, Robert Vernerey, Franck Zuscik, Michael	AB Nexus	$125,000.00	Biophysical Cues Governing Growth Plate Organization: A Computational & Experimental Approach	12/01/20 - 11/30/21
Richer, Jennifer Slansky, Jill	Department of Defense (Breast Cancer Research Program)	$750,000.00	Targeting metastasis by inhibiting breast cancer metabolism and immune-suppression	04/01/20 - 03/31/23

PRINCIPAL INVESTIGATOR(S)	AGENCY/SPONSOR	AMOUNT AWARDED	TITLE	FUNDING PERIOD
Santoro, Nanette (PI) Kumar, T. Rajendra (PD) Sheeder, Jeanelle (PD)	National Institutes of Health (NIH)	$1,701,001.00	Colorado Women's Reproductive Health Research Career Development Center	07/30/20 - 06/30/25
Shellman, Yiqun	National Institutes of Health (NIH)	$1,954,091.00	Study of melanocyte lineage through SASH1 and associated proteins	04/13/20 - 03/31/25
Stenmark, Kurt R.	National Institutes of Health (NIH)	$13,954,835.00	Complement Mediated Remodeling in Pulmonary Vascular Disease	08/01/20 - 06/30/25
Stenmark, Kurt R.	American Lung Association	$200,000.00	Complement in endothelial cell injury in COVID-19	10/01/20 - 09/30/21
Stenmark, Kurt R.	Department of Defense	$1,866,000.00	Role of Mitochondrial/Metabolic Reprogramming in Controlling Aberrant Gene Expression in Pulmonary Hypertension	05/01/20 - 04/30/23
Thorburn, Andrew DeGregori, James (Multi-PI)	National Institutes of Health (NIH)	$1,668,600.00	Down syndrome as a systemic autophagy deficiency disorder	09/18/20 - 09/17/24
Vergara, Maria Natalia	ProQR Therapeutics- Collaborative Research Agreement	$272,021.00	Development an organoid based platform to assess drug efficacy that is predictive of clinical outcomes	4/15/2020 - 4/30/2021
Verneris, Michael	National Institutes of Health (NIH)	$3,038,439.00	Characterizing Innate Immune Dysregulation in Tonsils of Individuals with Down Syndrome	09/18/20 - 03/31/25
Williams, Trevor	National Institutes of Health (NIH)	$350,000.00	R21: Cellular and Molecular Analysis of Body Wall Closure	04/01/20 - 03/31/22
Young, Christian Wang, XJ	National Institutes of Health (NIH)	$1,680,879.00	Proprietary drug to treat radiodermatitis	09/24/20 - 08/31/22
	TOTAL AWARDS =	**$46,358,848.00**		



Gates Center Director, Dennis Roop, Ph.D. shows off the 267-page T32 Training Grant, which received a perfect score.

WHERE DO WE GO FROM HERE?
LIFE AFTER 2020

Calla Winchell is trained as a writer, researcher and a reader having earned a bachelor's degree in English from Johns Hopkins University and her Master of Humanities from the University of Chicago. She is also a friend of the Gates Center and one of the patients on whom our research is intensely focused. She suffers from Ehlers-Danlos Syndrome (EDS), a rare group of genetic disorders, which affect the elasticity of connective tissues. Last year's annual report profiled Calla and announced the launch of the Ehlers-Danlos Syndrome Center of Excellence, dedicated to developing a cure for EDS at the Gates Center and to better addressing the clinical needs of EDS patients through specialty care at Children's Hospital Colorado.

A PATIENT'S PATIENCE: THE YEAR OF PARADOX

A frequent comment that the sick and disabled have long hated is: "it must be nice to be able to stay home all day." Hopefully, the echo of the last year will be enough to put to rest such a sentiment. The able bodied have had a chance to live as the housebound do, and have found it to be among the most stressful experiences of their lives. This is no surprise to the chronically ill community. It is no vacation to stay in the same four walls for months at a time (even less so if you feel consistently ill). If I had one wish for what we learn from this year, it would be a greater empathy for those less able.

Indeed, the disabled community needs that empathy. Six out of ten deaths[1] from COVID-19 in the United Kingdom were disabled people of all ages, with a particular loss of our older community members. I suspect when all is said and done that will be similar in the United States. A whole generation of wisdom, humanity, love and happiness snuffed out because of bureaucratic incompetence and ableist policy decisions. It is a time for grim reflection, on why triage and medical rationing always coincidentally kills those less valued by society.

However, the chronically ill and the disabled have superpowers taught to them only by painful experience: how to find a life worth living no matter the restrictions. We have coping skills for days, because the social isolation that many had to deal with for the first time this year is a daily fact for many medically marginalized people. We can make joy in the smallest accomplishments, appreciate aspects of life that go completely unnoticed by others. To be clear, we are forced to be resilient by a non-inclusive world. I wish we had a world

[1] *"Covid: Disabled people account for six in 10 deaths in England last year" from the BBC https://www.bbc.com/news/uk-56033813*

that cultivated gentleness for the sick and disabled, but we do not live there yet. While it is not fair that we have to develop these coping methods, we do and they serve us well. What's more, this is a wisdom everyone can benefit from, regardless of ability, as long as they recognize they can learn from us.

And so this year has not been one solely of loss. For one, we had to get more intentional about our socializing, no longer able to rely on running into someone to spark a get together. Now, the disabled know all about that. Our lives are spent rationing energy, doing mental calculations about what each errand costs us. Socializing is approached with the same military discipline, for me at least. In the time before COVID-19, I'd spend most of a day that I had something scheduled conserving energy and napping strategically. I might also plan a day after to recover. And when I do not plan, it can set me back days. An ill-planned grocery run with too much running between aisles can have ripple effects on my energy and pain levels for days.

Beyond the intentionality forced on us all, because all of the socializing was remote, I could hang out with my friends, even in a lot of pain, because there was no travel time, no walking to get to the meet-up. This is a sentiment I've heard from many disabled friends, that in some ways our turn inward at the start of lockdown triggered reconnections with friends, both distant and close, old and new. And further, that it prompted creative ways to meet that happened to be low energy. Perhaps you were watching movies on Netflix over Zoom with friends, or turning to digital gaming platforms like Among Us for socializing. I've been able to attend my book club meetings, even when feeling awful, because all I need to do is open a screen. In that way, it has been a miraculous year and I hope this kind of inclusive creativity towards socialization continues even once the restrictions have lifted.

This year we also become unencumbered by geography, having entered the age of Zoom. Internships that were location specific have opened for anyone, academic fellowships that used to mandate presence on campus have gone global, and the way we work and where is changing. This widening of the world has been pure joy and it has prompted so much reconnection. I've personally had friends from a decade ago reach out, rekindled because we each no longer had so many distractions. I've joined three different reading groups, whose members are sprinkled liberally around the globe: Paris, Los Angeles, Madrid, Austin, Philadelphia, Rio de Janeiro. I fully expect these groups to persist, long after we've all gotten our booster shots and are frolicking maskless once again. And that is the contradiction of this year: the closing of the world has opened up time and interest in things that we typically get too busy to notice.

For accessibility, the paradox of this year again applies. On the one hand, there were countless things that disabled people had been fighting for, like the right to work from home or telehealth appointments (I was denied the ability to occasionally "Zoom" into classes in graduate school three years ago, because it would be too onerous for the professor) that have been achieved the second the able-bodied needed them. While the disabled and ill have been required to disclose medical information and provide proof for the necessity of their accommodations —with no guarantee that you will get those accommodations, as in my case – there has been no such requirement for accommodating the able-bodied. To be clear, this is not me asking that more bureaucracy be added; indeed, I'm of the opinion that we should believe people when they tell us their needs and work to accommodate them. Rather, I want to point to who is prioritized and who is believed, as well as who must overcome extra, unnecessary barriers. Accommodation is not entitlement; it is the bare minimum so that a space can be open to all. It is, in fact, in the very spirit of egalitarianism which we hold to be so virtuous.

All of this is understandably frustrating, for those who perhaps were forced to drop out of university because their administrations were unaccommodating, as a friend was forced to do a few years ago. However, it has undeniably opened up a world of possibility. Because now that we've demonstrated these accommodations can be achieved, there will be no excuse to not provide such accommodations to those meriting them. There is no going back and that is a very good thing.

Despite these positives though, it was without fail, the accessible entrances of buildings that were locked first, when the ordinance came down to limit entrance numbers. The closing of public restrooms is another troubling access issue, since they were often the only ones that had disabled stalls accessible. Most public seating areas are closed, which is absolutely an accessibility issue for those with mobility issues. The necessary switch to telehealth and the postponing of all elective procedures reduced quality of care. And one can recognize the necessity of these changes for public health and still be frustrated by them. There are too many instances

like this, of restriction and constriction of public space to those less able. Clearly, as certain forms of accessibility were achieved this year, so were others greatly restricted.

My hope as we come out of this peculiar year is that we don't return to normal, as so many are hoping: that we keep the cruel lessons learned in mind. We must begin valuing all humans, regardless of their ability. It will not be comfortable but we must investigate why "Do Not Resuscitate" orders were given to those with intellectual disabilities over "quality of life concerns," as was done in Texas and the UK (in clear breach of typical, legal DNR orders).[2] We must grapple with how easily we say the words "only the vulnerable should stay home," as if they have any less right to exist in public, as if ill people don't also have to go to the grocery store, hospital, pharmacy and so forth. If nothing else, I hope this year will teach the public more compassion for the housebound and mobility disabled, that being unable to work is not a holiday. I've always suspected that Leibniz was incorrect when he claimed that this was the best of all possible worlds: I don't think it is true yet but it can be, if we work towards a better one. Let us make that the goal. To focus on connection, rather than distance. And to value life, even when it looks very different from yours. There is no going back now, but we have a choice on how we move forward. Let us all hope we make the right one.

2"Austin Hospital Withheld Treatment from Disabled Man Who Contracted Coronavirus"
https://thetexan.news/austin-hospital-withheld-treatment-from-disabled-man-who-contracted-coronavirus/

The first DNR scandal in the UK, from last year:
"People with intellectual disabilities and the COVID-19 pandemic" ***https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7411434/***

The second DNR scandal in the UK:
"Fury at 'do not resuscitate' notices given to Covid patients with learning disabilities" ***https://www.theguardian.com/world/2021/feb/13/new-do-not-resuscitate-orders-imposed-on-covid-19-patients-with-learning-difficulties***

LOSING TOUCH DURING A PANDEMIC

Emily M. Warshauer, M.D. trained in Dermatology at the University of Colorado during the years 2015-2018. Research has always been important to Emily and as such, Emily became involved with the Gates Center early in her Dermatology residency. Her primary research focus has been investigating Sephardic ancestry in Recessive Dystrophic Epidermolysis Bullosa patients. Emily was proud to represent the Gates Center at conferences and events in Zermatt, Switzerland, Monterrey, Mexico and New York City. Currently, Emily works as a Dermatologist with her father, Bruce L. Warshauer, M.D., near her hometown in New Jersey. Emily continues to prioritize her ongoing research with Dennis Roop, Ph.D. and will always value her strong connection to the Gates Center.

Dr. Emily Warshauer meets with a young couple in Monterrey, Mexico in 2018, whose baby had been recently diagnosed with Epidermolysis Bullosa (EB). Dr. Warshauer met with patients in conjunction with her ongoing Gates Center project, in which genetic tests indicate that Colorado EB patients may be related to hundreds of EB patients in Mexico and throughout Latin America, who may also be descended from a group of Sephardic Jewish families who fled the Spanish Inquisition 300 to 400 years ago.

How essential is human touch? Tactile sensation is the earliest of our five senses to develop at just a few weeks of intrauterine life, and it is plausibly our first language acquired before we even enter the world. During 2020 when "physical distancing" and "social avoidance" became our mantra, the strong dynamic of human touch is facing unprecedented challenges. Interestingly, the acute focus on distancing inspired an interest to explore the essence of touch as it relates to how we understand the world and connect to each other.

Intrigue with the sense of touch transcends millennia and has been a great source of curiosity for many of the greatest human minds, including Aristotle. First highlighted in his work *On The Soul (Latin: De Anima)* written in 350 BC, Aristotle proclaimed touch to be essential for life and critical for survival. This strong framework written over 2000 years ago set the stage for further scientific investigation to better understand the complexity of mechanosensation. Heat, cold, pressure and pain receptors are delicately nurtured and protected in the skin, the largest organ in the human body, and empower the other senses of sight, sound, taste and smell[1].

Great progress has been made since the study of modern sensory physiology was initiated in the early 19th century. With Zoom now part of our vernacular and a critical mode of communication over the past year, let us take this opportunity to Zoom in on the intricate, specialized ultrastructural features that result in physiologically and functionally very different touch receptors[2].

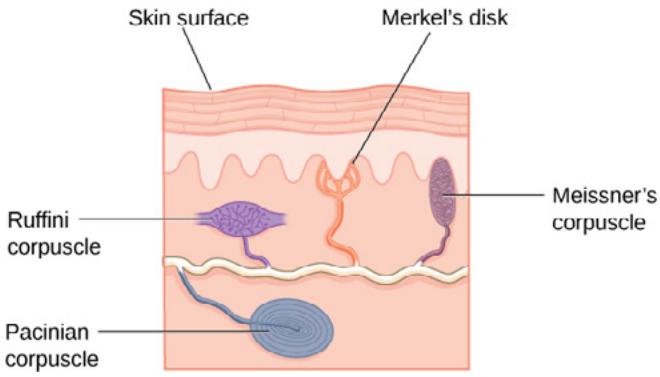
Pacinian corpuscles, Meissner's corpuscles, Merkel Cells and Ruffini corpuscles are specialized touch receptors that recognize and convert tactile stimuli into action potentials, delicately providing communication between the external and internal forces critical for mechanosensation. The Pacinian corpuscles are onion-shaped sensory organs located in the deep dermis. They detect deep pressure and vibration, and they are named after Filippo Pacini, the Italian anatomist who discovered *Vibrio cholera* as the causative bacterial agent during the Cholera outbreak in Italy in the 1850s[3]. Pacinian corpuscles are the largest corpuscles in the skin with their nerve endings encapsulated by inner lamellae derived from Schwann cells and the outer lamellae derived from fibroblasts[4]. These unique touch receptors are highly sensitive and are rapid adapters to environmental stimuli.

Similar yet smaller than the Pacinian corpuscles are the Meissner's corpuscles, which are concentrated in glabrous skin to sense vibration and dynamic motion. They consist of ellipsoid lamellar cells that have a sharp external surface and a smooth inner surface enabling them to connect to collagen fibers that cross the fibroblast capsule. They, too, are rapid adaptors to environmental stimuli[5].

In contrast to Pacinian corpuscles and Meissner's corpuscles, Merkel Cells are characteristically slow adapters to physical stimulation[6]. Originally described by Friedrich Merkel in 1875, the Merkel Cells represent a distinctive cell population of skin receptors sensing gentle touch. These are located at the dermal-epidermal junction. Composed of fast-conducting nerve fibers and specialized for high acuity sensation, Merkel Cells are attached to keratinocytes and desmosomes by cytoplasmic protrusions[5]. The last important skin receptors to highlight are the Ruffini corpuscles which are similar to Merkel Cells and slow adapters to pressure. These cells have spindle-shaped receptors located in the dermis and are especially sensitive to skin stretch.

Stretching across all sentient beings, touch is universal. The deliberate ability to reflect upon and appreciate the quality of touch, however, is a precious quality that distinguishes only human beings. During these times, the psychological manifestations of physical distancing and confinement have been profound. The prevalent feelings of isolation, intense loneliness and uncertainty for what might lie ahead deserve prudent consideration and great empathy.

In conclusion, touch is essential. The complex nature and intricacy of our skin receptor cells speak to their indispensability to our survival. As we Zoom out to a new world in which physical distancing has practically become dogma but look ahead, we may be in a position to be more aware, sensitive to and appreciative of the ultimate design and value of human touch than ever before. We have clearly been wired with intricate sensory tools not just for survival, but also to enable us to communicate and greatly enrich our daily existence.



A simple image outlining the touch receptors highlighted in Dr. Warshauer's article (Abraira VE, Ginty DD. The sensory neurons of touch. Neuron. 2013 Aug 21;79(4):618-39. doi: 10.1016/j.neuron.2013.07.051. PMID: 23972592; PMCID: PMC3811145.)

References

[1]*Kuhtz-Buschbeck JP, Schaefer J, Wilder N. Mechanosensitivity: From Aristotle's sense of touch to cardiac mechano-electric coupling. Prog Biophys Mol Biol. 2017;130(Pt B):126-131.*

[2]*Zimmerman A, Bai L, Ginty DD. The gentle touch receptors of mammalian skin. Science. 2014;346(6212):950-954.*

[3]*Shakeri A. Filippo Pacini-A Life of Achievement. JAMA Dermatol. 2018;154(3):300.*

[4]*Pawson L, Prestia LT, Mahoney GK, Guclu B, Cox PJ, Pack AK. GABAergic/glutamatergic-glial/neuronal interaction contributes to rapid adaptation in pacinian corpuscles. J Neurosci. 2009;29(9):2695-2705.*

[5]*Takahashi-Iwanaga H, Shimoda H. The three-dimensional microanatomy of Meissner corpuscles in monkey palmar skin. J Neurocytol. 2003;32(4):363-371.*

[6]*Winkelmann RK, Breathnach AS. The Merkel cell. J Invest Dermatol. 1973;60(1):2-15.*

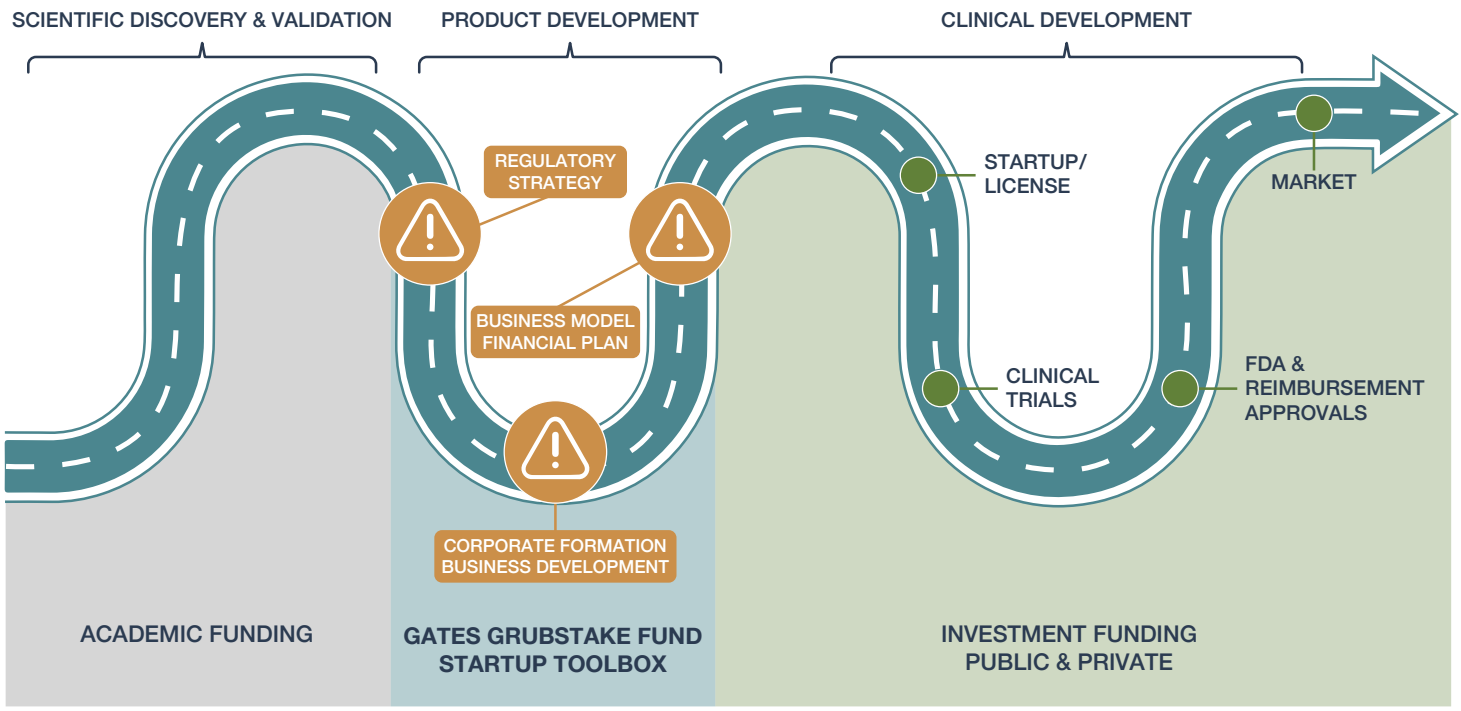
COMMERCIALIZATION

The path to commercialization has been a focus for the Gates Center from the very beginning. 2020 proved a seminal year as Gates Center member David Wagner, Ph.D., became the first Gates Grubstake Fund awardee at the starting gate to launch a clinical trial scheduled to begin in February 2021 ***(see Dr. Wagner's profile on page 36).***

Following the Gates Frontiers Fund's generous funding of two promising Gates Center members in 2014, the Gates Grubstake Fund (GGF) was incorporated as a private 501(c)(3) foundation in 2015 to advance innovative ideas with potential for commercial application in the field of regenerative medicine or stem cell technologies. Since then, funding has been awarded on a competitive basis to promising investigative teams whose research may lead to new therapies, commercial devices, technologies, or even spin-off companies.

The Gates Grubstake Fund's name comes from the Gold Rush, when investors would give prospectors seed money known as "grubstakes" to buy food and supplies while they searched for gold. Similarly, academic researchers focused on developing new therapies or devices with commercial potential are in critical need of gap funding while they work on product development.

THE PATH TO COMMERCIALIZATION



The Gates Grubstake Fund aspires to fill that funding gap for promising projects and has traditionally supported three to four annual awards of up to $350,000. That money can be spent on product development-related expenses, which would not be permissible with a traditional federal grant. And the Fund's success has been remarkable. Its initial investment of $6 million in Grubstake projects from 2014-2020 has resulted in seven pre-IND (investigational new drug) applications to the FDA and three IND/IDE (investigational device exemption) packages in preparation, in addition to Dr. Wagner's Phase 1a clinical trial scheduled for early 2021. Further, five companies have been spun out, and follow-on funding from grants, charities, or investment has exceeded $35 million.

The Gates Grubstake Fund owes its success not only to the Gates Frontiers Fund that has made these generous awards possible, but also to the impressive Scientific Investment Advisory Committee (SIAC), which makes investment decisions on a competitive basis through a process overseen by the Gates Center and CU Innovations. The SIAC is comprised of subject matter experts and institutional investors with a focus on biotechnology, and the list of members includes Sibylle Hauser and Mani Mohindru, whom we enthusiastically welcomed to the committee this fall. We have also included the late Will Hiatt, M.D., who served as a brilliant, dedicated and influential member of the Gates Center Advisory Board and this committee from the very beginning. Though Will sadly passed away in December, those present at the Grubstake pitch presentations in November may always remember his invaluable and rigorous participation in this year's award process, after which he wrote:

"I always learn a lot sitting on this committee – most prior grant reviews for NIH and others just focus on the science, but Grubstake represents a diversity of expertise on the committee that is quite extraordinary! Indeed - the whole Gates programs on campus are a real gift and opportunity!"

Members of the SIAC and 2020 Gates Grubstake Fund awardees are listed below.

GATES GRUBSTAKE FUND SCIENTIFIC INVESTMENT ADVISORY COMMITTEE:

- **Mark Brunvand, M.D.,** Field Medical Director, CAR T-cells, Bristol-Myers Squibb
- **Sibylle Hauser,** Strategic Advisor – Life Science, Richtr Financial Studio
- **William Hiatt, M.D.,*** Professor, Division of Cardiology, University of Colorado Anschutz Medical Campus; Past President and Chief Science Officer, CPC Clinical Research, member, Gates Center Advisory Board
- **Ryan Kirkpatrick,** Partner, Colorado Impact Fund
- **David L. Lacey M.D.,** Biopharmaceutical Consultant, former Senior Vice President, Head of Research, Amgen
- **Mark Lupa, Ph.D.,** Principal, High Country Ventures
- **Mani Mohindru, Ph.D.,** Senior Biotech Executive
- **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.,** Executive Director, 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 Center Advisory Board
- **Robert Traver, J.D.,** Patent Attorney, Sheridan Ross

It is an honor to be affiliated with the Gates Center for Regenerative Medicine. I look forward to working to help advance the Center's mission of accelerating innovative discoveries from the lab to therapies and cures. ~Mani Mohindru, Ph.D.

I am very honored to have been selected to serve on the Scientific Investment Advisory Committee in 2021 and will do my part to support advancing the most promising regenerative medicine projects which will potentially impact so many lives." ~Sibylle Hauser

2020 GATES GRUBSTAKES AWARDEES

Ulli Bayer, Ph.D.
"Pharmacological Restoration of Ischemic Spinal Cord Damage"

Dr. Ulli Bayer, a Professor in the Department of Pharmacology at the University of Colorado Anschutz Medical Campus, is also the CSO of Neurexis Therapeutics, a startup out of the University of Colorado. Dr. Bayer received a Grubstake Award to perform animal testing of an optimized peptide therapeutic in a mouse model of ischemic spinal cord damage. The therapeutic has already been shown to have activity in animal models of global cerebral ischemia and to have no apparent safety concerns at the highest doses tested. The number of patients at risk for ischemic spinal cord damage is 15,000 per year, while follow on indications of global cerebral ischemia and stroke are 550,000 and 800,000 per year, respectively. This funding will accelerate development toward pre-IND filing with the FDA.

Eduardo Davila, Ph.D.
"Manufacturing of Genetically Engineered Tumor Infiltrating Lymphocyte Therapy"

Dr. Eduardo Davila, a Professor in the Department of Medicine and the Amy Davis Chair of Basic Immunology Research, is the Director, Immunotherapy Medical Oncology and Director, Cancer Research Training and Education at the University of Colorado Comprehensive Cancer Center at the Anschutz Medical Campus and CEO of TrAMPoline, a startup company out of the University of Maryland. Dr. Davila received a Grubstake Award to develop the manufacturing process for next generation tumor infiltrating lymphocyte (TIL) therapy at the Gates Biomanufacturing Facility. TIL therapy fills an important unmet medical need for the treatment of the 1.5 million new cases of solid tumors each year as more than 50% of patients relapse or do not respond to current immunotherapy. This funding will accelerate development toward pre-IND filing with the FDA.

Michael Zuscik, Ph.D.
"Abaloparatide as the First Chondroregenerative Therapy for Osteoarthritis"

Dr. Michael Zuscik, the Mack Clayton Professor of Orthopedics and Vice Chair of Research, received a Grubstake Award to perform animal testing of a chondroregenerative peptide therapeutic for the treatment of osteoarthritis. Osteoarthritis is the most prevalent disease in the U.S., with 32 million patients diagnosed. The financial burden of disease is $185 billion, with lost wages and reduced productivity resulting in a financial toll of more than $300 billion. Dr. Zuscik's prior work with another peptide, Forteo, that binds to the same receptor has shown positive interim results in a prospective double blind clinical trial. The Grubstake funding will drive the decision of whether to develop abaloparatide for the treatment of osteoarthritis.

In 2020 the SIAC also recommended that additional available funding be deployed to accelerate translation to the clinic of previously funded projects that have made significant progress and that need additional funding to achieve a significant inflection point.

2020 2ND TRANCHE GRUBSTAKE FUNDING RECIPIENTS

Ken Liechty, M.D.
"Conjugated Nanoceria to Treat Inflammatory Disorders Including Pulmonary Fibrosis"

Dr. Kenneth Liechty is the Sandy Wolf Chair in Maternal Fetal Surgery and Director of the Colorado Fetal Care Center for Children's Hospital at the University of Colorado Anschutz Medical Campus. Dr. Liechty has received two Grubstake Awards to develop his conjugated nanoceria therapeutic for the treatment of diabetic foot ulcers and ARDS and has filed pre-IND applications with the FDA for both indications. The second tranche of funding is designed to enable further manufacturing at the Gates Biomanufacturing Facility in preparation for IND filing with the FDA.

Holger Russ, Ph.D.
"Generation of Functional Patient Specific Thymii for Cell Therapy"

Dr. Holger Russ is an Assistant Professor, Pediatrics in the Barbara Davis Center at the University of Colorado Anschutz Medical Campus. Dr. Russ used funds from the original Grubstake Award to develop and streamline his process for developing a patient specific thymus in the lab. His ground-breaking research has elicited interest from industry who have requested some final proof of concept studies. The second tranche of funding will answer the questions posed by industry and guide decision-making around patient benefit and commercialization.

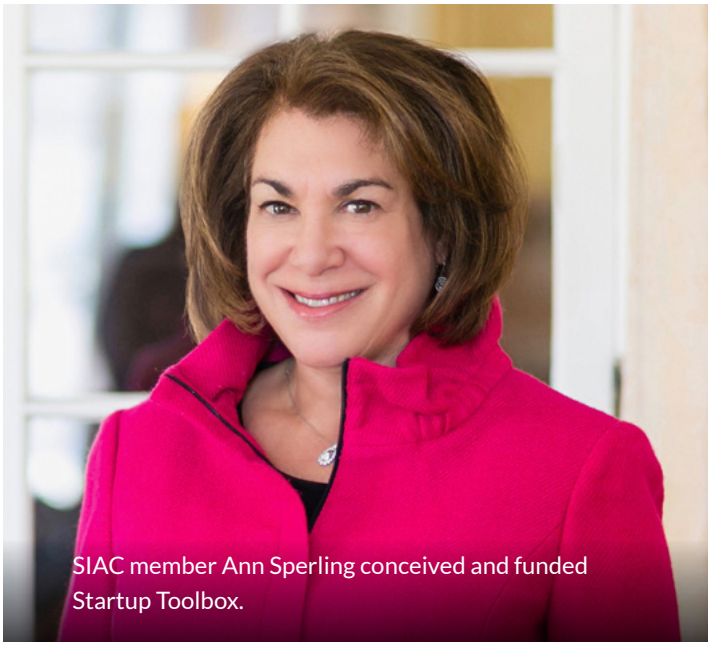
David Wagner, Ph.D.
"Therapeutic for Myelin Loss/Regeneration in Multiple Sclerosis"

Dr. David Wagner, an Associate Professor, Medicine – Pulmonary Sciences & Critical Care and Head, Immunology Section, is also the CSO of Op-T, LLC, a startup out of the University of Colorado Anschutz Medical Campus. Op-T, LLC is beginning a Phase 1 clinical trial at UC Health for the treatment of type 1 diabetes using a therapeutic peptide, OPT101, developed in part using the original Grubstake Award. The second tranche of funding is designed to develop the second-generation formulation of the therapeutic peptide and demonstrate its activity in animal models of type 1 diabetes and multiple sclerosis in preparation for additional IND filings with the FDA.

DEVELOPMENT STAGE		AWARDEE	PROJECT NAME	AWARD YEAR
In Vivo	Rodent	Michael Zuscik, Ph.D.	Abaloparatide as the First Chondroregenerative Therapy for Osteoarthritis	2020
		Holger Russ, Ph.D.	Generation of functional, patient specific thymi for cell therapy	2019
		Antonio Jimeno, M.D., Ph.D	Proprietary Humanized Mouse Model to Assess Cancer Treatments	2014
		Michael Verneris, M.D.	Generation of Engraftable Hematopoietic Stem Cells from Induced Pluripotent Stem Cells	2018
		Kunhua Song, Ph.D.	Heart Regeneration by Conversion of Non-Myocytes into Functional Cardiomyocytes	2018
		Eduardo Davila, Ph.D.	Manufacturing of Genetically Engineered Tumor Infiltrating Lymphocyte Therapy	2020
		Raj Kumar, Ph.D.	Production of Efficacious Recombinant hypo-glycosylated FSH Glycoform for Clinical Applications	2019
	Non-Rodent	Valeria Canto-Soler, Ph.D.	Stem Cell-Derived Retinal Transplant to Treat Dry-AMD	2017
		Karin Payne, Ph.D.	Bioresorbable 3-D Printed Personalized Implant for Cartilage Regeneration in Pediatric Growth Plate Injuries	2017
		Ulli Bayer, Ph.D.	Pharmacological Restoration of Ischemic Spinal Cord Damage	2020
Pre-Clinical	Pre-IND	Xiao-Jing Wang, M.D., Ph.D	Fusion Protein to Treat Chronic Wounds and Inflammatory Disorders	2014
		Steven Dow, DVM, Ph.D.	Antimicrobial Stem Cell Therapy for Infected Diabetic Foot Ulcers	2015
		Ganna Bilousova, Ph.D. and Igor Kogut, Ph.D.	Induced Pluripotent Stem Cell Services as a Platform for Clinical Research	2015
		Martin Zamora, Ph.D.	Clinical Development of Autologous CD117+ Progenitor Cell Therapy for Solid Organ Transplantation	2017
		Ram Nagaraj, Ph.D.	Therapeutic peptide for neuroprotection in acute closed angle glaucoma	2019
	IND/IDE	Kenneth Liechty, M.D.	Conjugated Nanoceria to Treat Oxidative Stress and Prevent Chronic Inflammation	2016
		Jeffrey Olson, M.D.	Intraocular Device to Potentiate Retinal Stem Cell Transplantation in Macular Degeneration	2016
		Kenneth Liechty, M.D.	Prevention and Treatment of Pulmonary Fibrosis	2018
		Terry Fry, M.D.	Optimized manufacturing of CD19xCD22 CAR expressing T cells for the clinic	2019
Clinical Trials	Phase 1	David Wagner, Ph.D.	A 15-Amino Acid Peptide to Potentially Stop Demyelination and Restore Myelin Production in Multiple Sclerosis	2016

STARTUP TOOLBOX BRIDGES CRUCIAL GAP

Similar to the Gates Grubstake Fund, the Startup Toolbox program was established to bridge a crucial gap for Gates Center members focused on moving discoveries from the lab into products and services that will impact patients. Gates Center Advisory Board member Ann Sperling has served on the Gates Grubstake Fund's Scientific Investment Advisory Committee from the beginning and as such, has reviewed and recommended awards for promising regenerative medicine opportunities. Nonetheless, she also recognized the need to help researchers when they need assistance outside of the science to build a business plan, or access intellectual property (IP), legal/regulatory help, pricing etc.

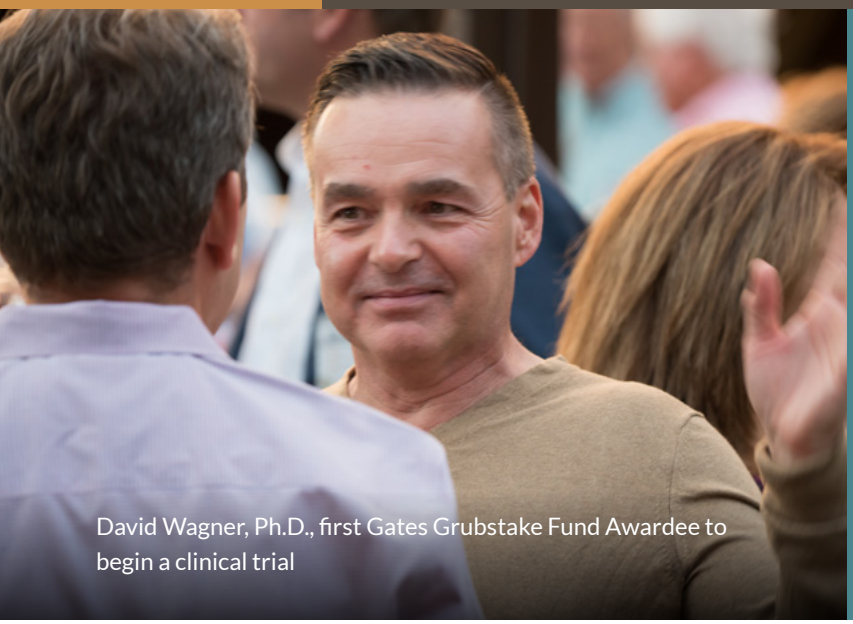


SIAC member Ann Sperling conceived and funded Startup Toolbox.

In 2017, Ann creatively conceived and generously funded Startup Toolbox as another partnership between the Gates Center and CU Innovations focused on commercialization. The novel platform contains services and resources that include corporate/legal, product development, regulatory, Small Business Innovation Resources (SBIR) consultants, as well as business plan and financial modeling support. Ann explains, "It attracts me because as a businessperson, I see the need to get these great scientific ideas into action through financial and organizational transformation, too, and access to this platform of services addresses this essential, non-scientific part."

To date, Startup Toolbox has been funded by Ann Sperling, Anita and Geoffrey "Duffy" Solich and others and has helped advance 16 projects that have received funding and pro bono support in regulatory strategy, corporate formation and business development. This has led to two new Colorado startups, and enabled researchers both to work with the Gates Center's affiliated Gates Biomanufacturing Facility and to plan for clinical trials at UC Health.

According to CU Innovations Executive Director Kimberly Muller, who also serves on the Gates Grubstake Fund's SIAC, "The Gates Center's success through the Gates Grubstake Fund and Startup Toolbox programs has showed us how we can support the very best ideas on their path towards clinical application. In fact, these programs have inspired CU Innovations to adopt similar models to support CU Anschutz researchers in areas outside of regenerative medicine as well."



David Wagner, Ph.D., first Gates Grubstake Fund Awardee to begin a clinical trial

GATES GRUBSTAKE FUND AWARDEE, DAVID WAGNER, LEADS THE WAY TO CLINICAL TRIALS

Dr. David Wagner's journey to the Gates Center and the University of Colorado Anschutz Medical Campus began in the far northeast corner of Tennessee where he grew up. On his way west, he lost his southern accent to present his impressive scientific findings, but he maintains close family ties and pride in his Appalachian roots. He now wears numerous hats he never envisioned. On the Anschutz Medical Campus, he is a Senior Investigator and Head Section of Immunology at the Webb-Waring Center and Associate Professor in the Department of Medicine - Pulmonary Science & Critical Care Medicine. He is also the Chief Scientific Officer for Op-T, LLC, a biotech startup he co-founded, developing diagnostics for autoimmune diseases and therapeutic approaches to control autoimmune inflammation. Recently, he joked that he now wears a pharmacologist's hat, as well, without the benefit of formal training. He is beginning first-in-human clinical trials with a drug he designed to benefit patients suffering from type I diabetes (T1D)—a drug that also has applications for multiple sclerosis (MS) and potentially atherosclerosis, along with severe cytokine responses in acute respiratory distress syndrome (ARDS) and COVID-19.

As a child, Dr. Wagner leaned towards medicine and science. He was born with an inguinal hernia only discovered when he was in third grade by a surprised doctor who promptly coordinated surgery to remedy the situation. This formative experience drew him towards medicine. However, once exposed to scientific research, he found his true calling. After receiving a Ph.D. from East Tennessee State University, Dr. Wagner moved to Colorado for a Postdoctoral Fellowship at National Jewish Health. He later received a Senior Postdoctoral Fellowship at the Barbara Davis Center for Diabetes followed by positions with Webb-Waring and the School of Medicine, where understanding how auto-aggressive T cells cause autoinflammation in T1D and other diseases has become his focus. In addition to his research, he has served as a board member and president on a regional community leadership board for the American Diabetes Association. In this capacity, he worked with doctors, nurses, physician assistants, and patients, and these interactions have kept the immediacy of patient needs and issues front and center.

Since 2014 when the Gates Center launched the Gates Grubstake Fund, 21 Grubstake awards have been directed towards talented scientists with promising research discoveries to accelerate the development of viable products and technologies for human benefit. In 2016, Dr. Wagner received a Grubstake Award to develop a platform technology licensed to his company Op-T, LLC and designed to treat autoimmune diseases by modulating aberrant immune signaling. Significantly, Dr. Wagner is the first Grubstake

awardee to advance his research and proprietary peptide to first-in-human Phase 1 clinical trials. Speaking of the Gates Center role in advancing his research toward this milestone, Dr. Wagner maintains,

> *The Gates Center really has been most valuable. One of the tricky parts for people like me is how to keep the academic lab work going while balancing the company work. The Gates Grubstake Fund grants have provided much-needed funds that facilitate that important bridge. The academic lab work is essential for the company's progress.*

Dr. Wagner will initially employ the Op-T, LLC drug, OPT101, (developed in part with Grubstake funding) in clinical trials for T1D. His 15 amino acid therapeutic peptide is a molecular interrupter. It targets and modulates cells that are highly inflammatory in autoimmune diseases. Some current clinical approaches to T1D involve monoclonal antibodies (MCAs), which can be effective. But MCAs target cells to die. When targeting immune cells, modulating (and in this case, down-modulating) can be more effective, allowing the immune system to regroup and reconfigure. There are many other diseases, like MS, that may also benefit from this approach. Pending positive results from this first clinical study, Dr. Wagner is eager to apply OPT 101 to MS. There is a real need for such a drug, and he notes that Colorado has a high incidence of MS. Through all of this, Dr. Wagner says he is "thrilled to be a member of the Gates Center." Funding from the Gates Grubstake award and assistance from the Gates Center has made a big difference, and seminars, coursework on business development, mentorship, and connections have been invaluable. He has also benefitted from having conversations with fellow members discussing how to navigate roadblocks and avoid potential pitfalls in drug development.

The COVID-19 pandemic added unexpected hurdles to launching his clinical studies. Early in 2020, Op-T, LLC filed an Investigational New Drug application (IND) with the FDA to use his proprietary peptide to treat T1D. At the onset of the pandemic, no one was willing to risk initiating clinical trials.

> *2020 was just a kick in the teeth. We received FDA approval, technically a "Safe to Proceed" letter on our IND (Investigational New Drug) application, on April 13, 2020. This was once Shut Down had commenced; this changed everything. Trying to schedule any sort of clinical trial was impossible … the only option was to wait … and wait.*

By the end of 2020, it was back to "all systems go" along with much hope and optimism. Phase 1a clinical studies were scheduled to begin in February 2021 with three patients, and Dr. Wagner was awarded "second tranche allocation funding" from the Grates Frontiers Fund directed toward improving his drug delivery method for the current clinical trials and expanding his studies to MS.

CORE FACILITIES

PROVIDE GATES CENTER MEMBERS WITH ACCESS TO STATE-OF-THE-ART EQUIPMENT, TECHNOLOGY AND EXPERTISE

In last year's annual report, we introduced the new Organoid Core, to which Gates Center members will have discounted access beginning in 2021. Drs. Bruce Appel and Peter Dempsey, co-directors of this core, anticipate that the core facility will be fully operational by late spring 2021.

During 2020, the Gates Center leadership team began discussions to provide Gates Center members with discounted access to two additional core facilities on campus, the Genomics Core and the Human Immune Monitoring Shared Resource. Both these cores are well established; the Genomics Core was launched in 1999 as one of the original shared resources in the University of Colorado Cancer Center, and the Human Immune Monitoring Shared Resource (HIMSR), was created in 2016 as part of the Human Immunology Immunotherapy Initiative supported by the University of Colorado School of Medicine. The Gates Center is very pleased to be able to leverage existing infrastructure so that members can have subsidized access to existing cutting-edge equipment and technology beyond what is now available in other Gates Center subsidized cores. For example, the Genomics Core recently purchased Visium Spatial Gene Expression technology from 10X Genomics for its facility. Visium Spatial Gene Expression is a next-generation molecular technology for classifying tissue based on total mRNA. This technology will allow Gates Center members to map the whole transcriptome with morphological context to discover novel insights into normal development, disease pathology and clinical translational research. Similarly, the HIMSR leveraged resources from across campus to obtain one of five IonPath's Multiple Ion Beam Imaging (MIBI) beta units in operation worldwide. Two commercial MIBI units have now been released, and the HIMSR unit received a commercial upgrade in January 2021. The MIBI allows single cell analysis *in situ* using antibodies tagged with isotopically pure metal reporters to image up to 100 target proteins or RNAs in fresh-frozen and fixed tissue, with a five-log dynamic range and 100 nanometer cellular resolution.

IMPACT OF THE COVID-19 PANDEMIC ON CORE FACILITIES

Gates Center Core Facilities were not "immune" from being impacted by the COVID-19 pandemic. To illustrate this, we have included some reflections from Lester Acosta, new manager of the Flow Cytometry Core:

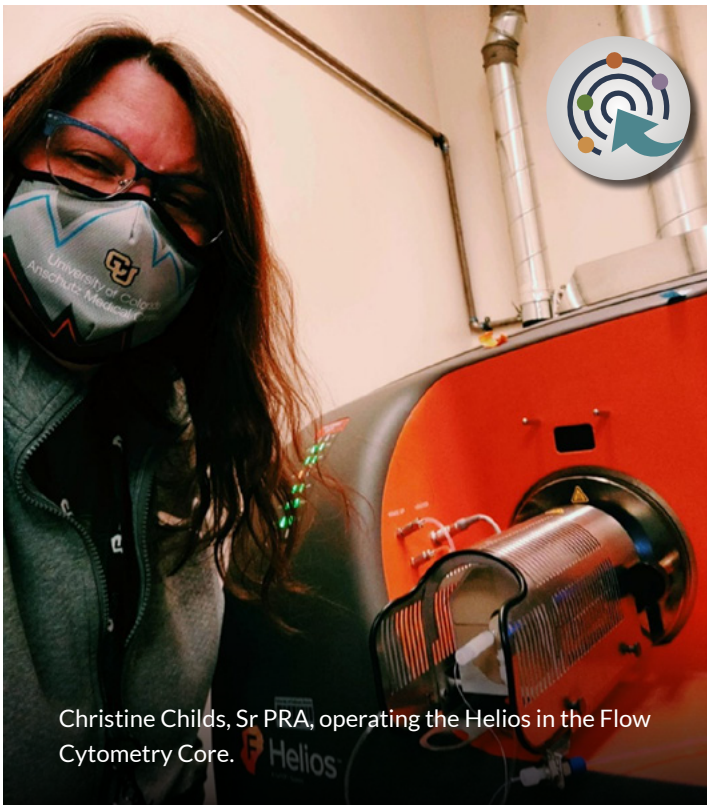
> *My first official day as manager was March 15, 2020 — a Sunday. My first day on the job was March 16, 2020, and my first official act was closing the core for the pandemic.*

> *We were able to re-open the lab in an abbreviated form to offer our services again on May 18, 2020. We used Zoom to interact with our customers, and we also started using TeamViewer software to allow remote access of our instruments by our trained self-run clients. Self-run clients could operate instruments from any computer, even from home.*

All Gates Center Core Facilities were forced to close on March 16, 2020 but were gradually allowed to open at reduced capacity by May 18, 2020.

Gates Center cores and shared cores include the following, and their descriptions are below:

CORE FACILITIES	CORE DIRECTORS	CORE LAB MANAGERS
Flow Cytometry Core (FCC)	Eric Clambey, Ph.D.	Lester Acosta
Genomics Core (GC)	Bifeng Gao, Ph.D., MBA	Katrina Diener
Human Immune Monitoring Core (HIMSR)	Jill Slansky, Ph.D. Kim Jordan, Ph.D.	N/A
Histology (Morphology And Phenotyping) Core	Igor Kogut, Ph.D	Laura Hoaglin
Organoid Core (OTMSR)	Peter Dempsey, Ph.D. Bruce Appel, Ph.D.	Sean McGrath, Ph.D.
Stem Cell Biobank And Disease Modeling Core (SCB&DM)	Ganna Bilousova, Ph.D Igor Kogut, Ph.D.	Michael Ferreyros



Christine Childs, Sr PRA, operating the Helios in the Flow Cytometry Core.

FLOW CYTOMETRY CORE

With the retirement of Karen Helm, the Flow Cytometry Core (FCC) is now being operated under new leadership, with Eric Clambey, Ph.D., continuing to serve as director and Lester Acosta as the new manager. The Flow Cytometry Core was established in 1999 as one of the original shared resources in the University of Colorado Cancer Center. Flow cytometry 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. The FCC has specialized equipment, which can rapidly isolate and collect unique types of cells. Specific cell types can be identified by cell surface antigen expression, cell cycle status, or by physiological properties of the cell that are unique amongst the general cell population. Often, these and other identification criteria can be combined simultaneously in a single experiment to yield a very powerful means of identifying and quantifying very specific cell populations. Historically, the FCC has only offered cell sorting done by staff during standard work hours. However, annual client surveys identified a growing need for cell sorting services that could be done by individual researchers, without staff assistance. Therefore, the FCC identified the Sony MA900 as a robust cell sorter, designed specifically with the intention to offer client-operated walk-up cell sorting. The FCC applied for and received institutional funds, along with additional funds provided by the Cancer Center Support Grant and the Gates Center, to purchase the Sony MA900. To ensure consistent training of researchers, all users interested in this service receive formal training by FCC staff. Once training is completed, users are granted increasing independence to perform self-run cell sorting. With these procedures in place, the FCC now offers cell sorting services on a 24/7 basis. The response to this new service has been robust and extremely positive, especially during the pandemic since self-run clients could operate instruments from any computer – even from home. In the past 12 months, nine clients booked 37 sorting appointments for 63 billable hours.

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. In 2018, with funding provided by the Gates Center and other campus sources, the core purchased a mass cytometer, the CyTOF (Helios). The Helios uses rare-earth metal tags to identify up to 45 different markers on each cell.

183 Years of Combined Biomedical/Genomics Laboratory Experience

Bifeng Gao, Ph.D., MBA, Director

Katrina Diener, B.S. Manager

Monica Ransom, Ph.D., Experimental Consultation, New Protocol Development

Brian Woessner, B.S., NGS, Single Cell Genomics

Okyong Cho, M.S., Single Cell Genomics, Arrays

An Doan, B.S., NGS, Spacial Genomics, Arrays

Colin Larson, B.S., NGS

Ted Shade, M.S., Bioinformatics Support

Megan Zapel, B.S., NGS

David Farrell, IT Support

GENOMICS CORE

Beginning in 2021, the Gates Center will offer members discounted access to cutting-edge next generation sequencing (NGS), single cell and spatial multi-omics and microarray technologies offered by the Genomics Core (GC). The GC was established in 1999 as one of the original shared resources in the University of Colorado Cancer Center under the direction of Mark Geraci, M.D., and Bifeng Gao, Ph.D., MBA, and has since provided nationally and internationally utilized next generation sequencing (NGS) and microarray research support and services. The GC initially offered microarray methodologies to investigate changes in gene expression. As microarray-based technology advanced, the GC quickly adapted by offering a broader range of microarray capacity including gene expression, genotyping, cytogenomics, and methylation analysis. In 2010, the GC gained its first NGS platform, Illumina HiSeq 2000, and continued to expand its services and expertise in NGS methodologies. In 2015, Dr. Geraci relocated to Indiana University to become the Chair of the Department of Medicine. With his departure, Dr. Gao assumed the directorship of the GC and has been instrumental in growing and developing the GC over the past 20 years. Since 2015, the GC has secured institutional support to upgrade its NGS technology and advance its genomic analysis to the single cell level, including spatial gene expression and single cell immune profiling. The GC also expanded its services and expertise in single-cell multi-omics solution that simultaneously detects SNV, CNV, and protein data from the same cell, providing Gates Center members with a platform to reveal biomarkers that help stratify patients, signal resistance, and predict relapse.

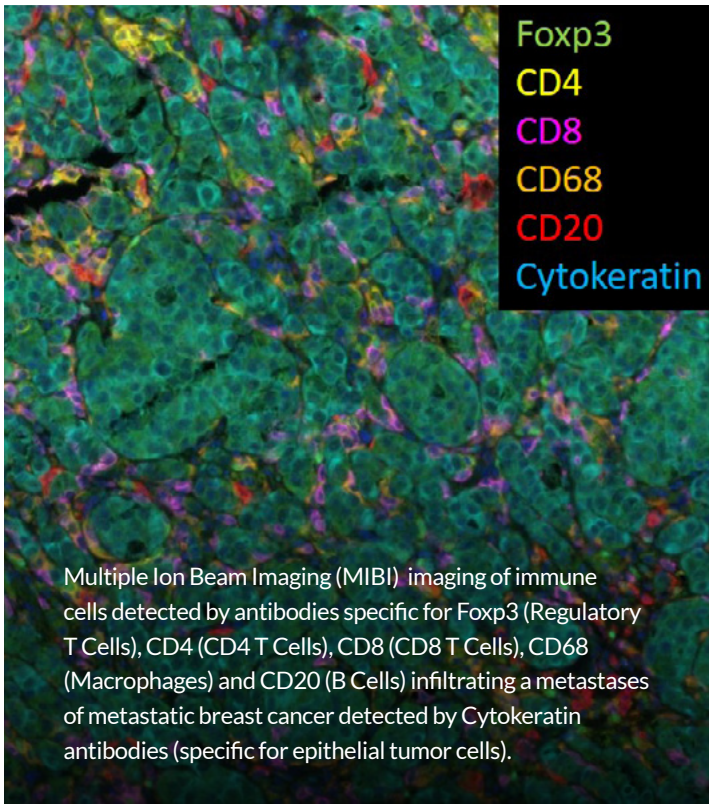
Recently, the GC purchased Visium Spatial Gene Expression technology from 10X Genomics for its facility. Visium Spatial Gene Expression is a next-generation molecular technology for classifying tissue based on total mRNA. This technology will allow Gates Center members to map the whole transcriptome with morphological context to discover novel insights into normal development, disease pathology, and clinical translational research.

HUMAN IMMUNE MONITORING CORE

Beginning in 2021, the Gates Center will offer members discounted access to the Human Immune Monitoring Shared Resource (HIMSR), which was established in 2016 as part of the Human Immunology Immunotherapy Initiative supported by the University of Colorado School of Medicine. The HIMSR is operated under the leadership of Director Jill Slansky, Ph.D., and Assistant Director Kim Jordan, Ph.D. The HIMSR leveraged resources from across campus to obtain one of five IonPath's Multiple Ion Beam Imaging (MIBI) beta units in operation worldwide. Two commercial MIBI units have now been released, and the HIMSR unit received a commercial upgrade in January 2021. The MIBI allows single cell analysis in situ using antibodies tagged with isotopically pure metal reporters to image up to 100 target proteins or RNAs in fresh-frozen and fixed tissue with a five-log dynamic range, and 100 nanometer cellular resolution. The HIMSR also operates state-of-the-art multiplex imaging instruments to visualize and quantify tissue microenvironments in human, humanized mouse, and mouse model tissues on the Vectra 3 and Vectra Polaris multispectral fluorescence imaging systems. The HIMSR has extended the capability of these detection systems beyond the standard commercially-available reagents to include goat, rat, biotinylated and humanized antibodies. Further, the HIMSR has developed novel assays for co-staining with RNA probes and proteins on the same tissue slide. The HIMSR's extensive IHC experience with the Vectra platform has also translated into new innovations on the MIBI platform, in which up to 27 antibodies have thus far been successfully imaged on a single slide. The HIMSR offers a standardized panel of 34 antibody targets for human tissue, with six metal channels available for customization for Gates Center members. The HIMSR offers full-service metal isotope antibody conjugations, titrations, and optimization of new antibody targets.

The HIMSR has also made many advancements in image analysis. It has developed novel scripts that pair with commercially available imaging analysis software for handling large whole-slide imaging datasets generated on the Vectra platform. Lacking commercially available software for the analysis of MIBI images, the HIMSR has additionally developed a novel workflow for cell segmentation and high parameter phenotyping algorithms to quantify cells in complex tumor microenvironments. Once MIBI data is converted to single cell data, it is compatible with the high parameter flow cytometry analysis software offered by the FCC for the analysis of CyTOF data. The HIMSR will continue to innovate and improve analysis solutions for MIBI data, including development of tools for spatial analysis, scoring, and tissue region comparisons.

The Human Immune Monitoring Shared Resource Team



Multiple Ion Beam Imaging (MIBI) imaging of immune cells detected by antibodies specific for Foxp3 (Regulatory T Cells), CD4 (CD4 T Cells), CD8 (CD8 T Cells), CD68 (Macrophages) and CD20 (B Cells) infiltrating a metastases of metastatic breast cancer detected by Cytokeratin antibodies (specific for epithelial tumor cells).

HISTOLOGY (MORPHOLOGY AND PHENOTYPING) CORE

The Histology Core is now operated under new leadership with Igor Kogut, Ph.D., serving as director and a certified technician, Laura Hoaglin, as core manager. The core provides a full set of histology services including the following:

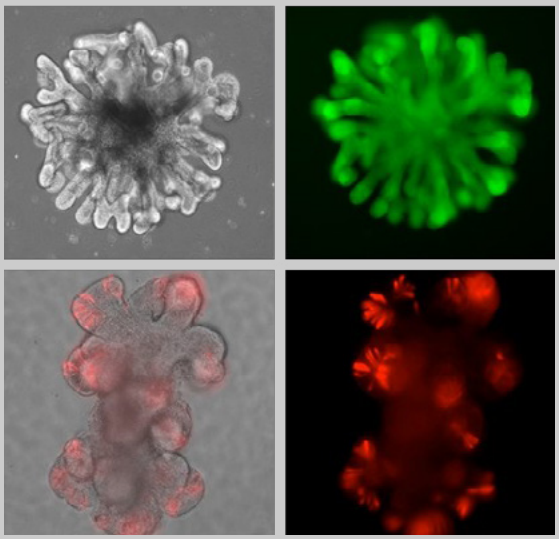
- Paraffin and OCT embedding
- Sectioning of frozen and paraffin blocks
- Routine (H&E) and special staining for all types of tissues
- Consultation to optimize tissue isolation and fixation procedures

In 2020, the Histology Core updated its automated equipment, which greatly improved the turnaround time and quality of provided services. Due to high demand, the core will enhance its service portfolio in 2021 by including immunohistochemistry staining.

Laura Hoaglin operating the microtome in the Histology (Morphology and Phenotyping) Core. (Photo courtesy of Nicole Diette)

ORGANOID CORE

Organoid and Tissue Modeling Shared Resource (OTMSR) is directed by Dr. Peter Dempsey and Dr. Bruce Appel from the Section of Developmental Biology in the Department of Pediatrics on the Anschutz Medical campus. The newly established OTMSR core facilities are located in research space on the third floor of the Barbara Davis Center for Diabetes, and is anticipated to be fully operational by late spring 2021. OTMSR looks forward to providing Gates Center members with discounted access to a variety of organoid technologies and to synergize with other core facilities and services provided by the Gates Center. The Organoid Core will provide the following: 1) access and training in current and emerging organoid technologies for in vitro disease modeling; 2) access, training and implementation of genome editing technology and gene expression systems; 3) critical key quality control and assurance measures to assure the validation and authenticity of core-derived resources to rigorously meet and exceed emerging NIH guidelines; and 4) data sharing of all Organoid Core-related resources, protocols and technologies to Gates Center members and the Anschutz Medical Campus community. The overall mission of the Organoid Core is to facilitate access, generation and usage of novel mouse and human organoid in vitro models to promote innovative basic and translational research. In January 2021, Sean McGrath, Ph.D., was recruited as the new OTMSR Lab Manager, and he is joined by PRAs Monica Brown and Claire Levitt, who are responsible for day-to-day operations.



Intestinal Organoids Generated in the Organoid Core

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., associate 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 patients' 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 a low cost. The core can reprogram multiple cell types, including dermal fibroblasts, urine-derived epithelial cells, freshly isolated and previously frozen peripheral blood mononuclear cells, etc. 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 by the introduction of gene-specific fluorescent reporters
- 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 for national and international external clients. Additionally, the core works on several projects that have been initiated and generously underwritten by community benefactors. These include using iPSCs to determine the underlying causes and specific treatments of neurogenetic diseases such as epilepsy funded by Rick and Janie Stoddard, as well as using iPSCs and gene editing approaches to identify novel mutations that cause Ehlers-Danlos Syndrome funded by support from The Sprout Foundation, a Denver-area foundation funded by Suzanne and Bob Fanch, and Annalee and Wag Schorr.

Shennea McGarvey feeds induced pluripotent stem cells in the Stem Cell Biobank and Disease Modeling Core. (Photo courtesy of Nicole Diette)

GATES BIOMANUFACTURING FACILITY

SUCCEEDS BOUND BY SHARED GOALS

> *We've come a long way from a concrete slab and some equipment in 2015. A few entrepreneurial scientists were willing to jump in and build a facility, technology platforms, and a Phase I clinical trial Quality system that can launch clinical trials. This accomplishment is not trivial – biotech companies are hesitant to be the first customers in a new facility. Our ability to attract and retain clients is a tribute to the technical aptitude, hard work, and customer service our employees provide. Both the protein and cell therapy groups had multiple 4 a.m. mornings safely getting the therapies out of the door in those early days. It's great to see that we are now producing four-to-six products monthly with a fully trained staff of 50. The Gates Biomanufacturing Facility (GBF) staff deserve a tremendous amount of credit for all this and for achieving its five-year vision of translating life-saving University of Colorado technologies into clinical trials – all during a world-wide pandemic.*
> *~Gates Biomanufacturing Facility Executive Director Matt Seefeldt, Ph.D.*

Determination is in the filtered air at the GBF. Also, the smell of pride and sterile Isopropanol are noticeable everywhere.

Over the past year, the GBF team continued its life-saving work despite many challenges brought on by the COVID-19 pandemic. In January 2020, there wasn't a conference room available anywhere in the building – nor an idle moment. The GBF was supporting manufacturing for ongoing Phase I clinical trials and developing new processes rapidly. Straight ahead was the direction, and full throttle was the speed. As the pandemic took hold in March, however, many project plans were upended and any sense of normalcy disrupted. Driven by duty, the urgency of the need, and scientific curiosity, GBF team members pressed forward and progress didn't miss a beat. Deemed essential workers, the GBF team continued to work on-site with proactive leadership and the finest HVAC system around, refusing to cede hard-won momentum to the virus.

It was a year of growth and change for the GBF, as the facility significantly expanded its footprint from 14,000 to 20,000 square feet in Bioscience 1 across the street from campus. The facility also expanded its headcount to 50 members despite a difficult hiring environment, and these new professionals provided fresh perspectives and abundant talent. In 2020, the GBF was further reorganized to move under the direction of the CU Anschutz Chancellor rather than the School of Medicine. This change in direction was important in providing more operational flexibility and greater coordination between the GBF and partner organizations on the CU Anschutz campus. Additionally, Matt Seefeldt, Ph.D., who joined the GBF management team in 2014 prior to the facility's opening in 2015, was elevated to Executive Director, and Charles Hickey MBA, was brought on as the new Director of Finance and Administration ***(see page 62)***.

Despite unprecedented pandemic challenges throughout the year, GBF leadership was able to grow the influence of the organization in multiple dimensions (and keep everyone

Former Gates Center CFO Tim Gardner (on left) helps direct Colorado Academy students during their educational visit to the Gates Biomanufacturing Facility in January 2020. We said farewell to Tim Gardner and want to thank him for his many contributions since 2013 to the growth of the Center and Gates Biomanufacturing Facility.

Felicia Mast and Graciela Gamez take steps to harvest the first UCD19 patient's cells for a University of Colorado clinical trial on July 30, 2020. A milestone day!

> *Dear Gates Center and Gates Biomanufacturing team, I feel like I've been held in a state of awe and wonder following the announcement of the first cell-based therapy, UCD19 CAR-T cells, produced at the Charles C. Gates Center for Regenerative Medicine. It is thrilling and slightly hysterical to think back on those early days, just over five years ago, as we huddled around Joy Mathew's living room framing a business plan on oversized post-it notes; when we gathered in obscure conference rooms with engineers and regulatory experts trying to sort through a maelstrom of safety protocols (many of which were still being formulated by the self-proclaimed expert regulators in ivory towers) as we hunted around campus for a suitable building to renovate, or a plot of land to claim and build; and when we sat in quiet wonder as Dr. Roop and his colleagues across the Anschutz Medical Campus...and around the world!...sketched out a vision for cures in our lifetime! As a lay person who had the honor of playing a very minor role in communicating our collective vision with influencers who could help bring it to fruition, my heart always ached with hope for early results, but a prudent mind governed those expectations toward an unforeseeable future. Witnessing the transference of the benchtop vision to bedside cure is nothing short of miraculous. Tutti Bravissimi to the giants, visionaries and courageous patients involved in making this dream come true. Here's to years of miracles in the making! ~With deep gratitude and fondness, Former Gates Center Executive Director Patrick Gaines*

testing negative). GBF management faced supply chain disruptions and increased uncertainty. In response, GBF teams immediately retooled and adapted. Whether working on-site or at their kitchen tables, team members supported the delivery of protein-based and cell-based therapies without interruption, including the successful launch of the UCD19 trial that has resulted in patients seeing complete remission for difficult-to-treat B-cell based malignancies. The GBF made this switch with zero lag-time, already poised to embrace the model of remote work. Such agility was made possible by a diverse team of individuals, pooling their collective drives to succeed, passions for helping people, and boundless scientific talents.

Here's a quick tour of GBF teams, what makes them great, and how they complement each other:

Protein and Biologic Chemistry (PRO):

Headed by Associate Director Gana Batt, Ph.D., the Protein Chemistry group boasts keen eyes, sharp wits, strong backs, and many advanced degrees. Undaunted, they face fresh challenges regularly in the scale-up and optimization of processes, as well as in the scratch development of new processes as needed. During Phase I manufacturing, clients may not fully appreciate the challenges of scale-up and process development, but Dr. Batt certainly does.

Currently PRO is developing several novel therapies in conjunction with University of Colorado under Good Laboratory Practices (GLP): the first for the treatment of Epidermolysis bullosa (EB), a life- threatening genetic skin condition; the second to ameliorate oral mucositis, a painful and nutrition-compromising side effect of head and neck radiation used for cancer treatment; and the third, a unique treatment paradigm using stem cells and gene therapy strategies to promote healing and tissue regeneration in multiple tissues.

Cellular Therapy (CT):

Cellular Therapy is a high-pressure environment. The demands are great in time, space and materials. Formally under the interim direction of Matt Seefeldt Ph.D., CT and the complex processes involved require great dedication. Such processes may begin with the blood of a patient/donor and then undergo genetic modification to recognize and fight cancers once considered uncurable. Each process is a unique endeavor – and a beacon of hope for patients who have exhausted all other therapies. Whereas PRO starts with something dirty (bacterially expressed proteins) and ends with something clean (drug substance), CT starts with something clean (a patient's own blood) and ends with something clean (final product for infusion). In 2020, CT manufactured cell therapies for the University of Colorado's UCD19 CAR-T trial for adult patients with relapsed and refractory B cell lymphomas, and was well underway planning for a second UCD19 CAR-T trial for children and young adults with resistant acute lymphoblastic leukemia in early 2021. The team was also working on a third trial scheduled to open in mid-2021 – a CD19x22 bicistronic CAR-T therapy that recognizes two separate targets on the malignant B lymphocytes of patients with relapsed/refractory leukemias and lymphomas.

As an emerging leader of CT, Felicia Mast M.S., sums it up this way: "The most critical aspect of our work is ensuring we manufacture a consistent, safe, and high-quality product for every single patient. The starting material for our manufacturing process comes directly from the patient's blood, and just as each individual is unique, each patient's cells are unique and can behave in unpredictable ways. The CT team must keep up with this unpredictable behavior because the cells do not take a break – once manufacturing has begun, it is a continuous process until we can get them back to the patient or in the storage freezer. In addition to accounting for unpredictable scheduling and cell growth, it is imperative that the cells are maintained in a sterile environment free from any contamination because they will be infused back into cancer patients with delicate immune systems. The CT operators must be highly skilled and trained not only on how to culture the patient's cells so they are better able to recognize and kill cancer, but also to prevent contamination of the patient's growing cells through the use of aseptic technique, gowning, and cleaning. Every step of the manufacturing process is carried out with dedication and care for each patient."

GBF Executive Director Matt Seefeldt shares the complex processes involved with cellular therapy with Colorado Academy students.

> *Matt Seefeldt, the GBF's new Executive Director, is a priceless asset. Matt is among the best industrial biochemists I've ever worked with and has proven his ability to translate mouse models into cell therapies. There are only a couple of places where people can go with early-stage regenerative medicine discoveries and produce drugs from them that work, and thanks to Matt, the Gates Biomanufacturing Facility is one of them.*
> *~Kyle Lefkoff, Founder and General Partner of Boulder Ventures Ltd.*

Quality Control (QC) and Quality Assurance (QA):

The QC team may be the over-thinkers of the bunch, keeping a laser focus on product safety. Team QA provides oversight and supports regulatory compliance. QC/QA act in close collaboration with the other departments to test and release products, as well as to conduct internal investigations and scientific studies relevant to clinical manufacturing. Led by Associate Director of Quality Assurance, Chandresh Undhad M.S., the Quality team has decades of combined experience testing and releasing manufactured products for human use, in both commercial pharmaceutical and investigational settings.

Supply Chain and Project Management (SCPM):

Headed by Director Terri Foote, this department has revolutionized both the flow of materials through the GBF and the flow of people and activities on a daily basis. Implementation of the Great Plains supply chain management system across the GBF for materials ordering and inventory tracking was a momentous achievement and removed major stumbling blocks and obstacles to growth. Additionally, project management tools were applied directly to all the GBF operations, enabling improved efficiency, dynamic forward-looking scheduling, and better relationship management with clients. Project Manager Jordan Krause, M.S., describes the pathway to sustainability for the GBF: "The success of our cell therapy and protein chemistry campaigns at the GBF relies not only on sharp technical skill and quality oversight, but also in efficient and adaptable facility-wide systems that keep projects on track and resources flowing. When the GBF operations began in 2015, we were a small group of scientists focused on developing our technical platforms, with clinical manufacturing merely an aspiration for the future. We have since grown in both staff size and vision. Today at the GBF, with full development and manufacturing schedules, SCPM is a dynamic team that drives routine activities and reacts quickly and effectively to unforeseen issues, keeping our facility focused on treating patients through translational research and manufacturing."

GBF's Supply Chain Planner, Denise Feasel, explains to Middle School student visitors, the importance of supplying high quality materials in a clean and timely manner to be used in producing and testing our products.

Proactive leadership is a big part of what makes GBF successful. Not top-down leadership, but more a distributed system based on shared goals and a sense of discovery among colleagues. Even with the challenges of 2020 and turnover at the director level, team members kept all projects moving forward. All stakeholders, including the Anschutz Medical Campus, valued hospital partners, external clients, and GBF staff, benefit from this collaborative environment, where subject matter experts are always consulted, and valuable information is shared broadly. With the great diversity of backgrounds of GBF staff, expertise and ideas have currency at the GBF. The long list of clinical ailments begging for solutions provides future challenges driving the GBF mission today and fuels staff pride and satisfaction. Unaccustomed to failure, GBF teams and leadership made 2020 one of the most productive years yet, through a collaborative work environment and sheer determination. Due to the promise and prominence of their work, GBF team members will be instrumental to the translation of life-saving therapies at the AMC, from the benchtop to the bedside, for many years to come. With the whole campus cheering them on, the GBF is a strategic asset in the delivery of 21st century cures. The sense of pride and smell of sterile Isopropanol are still noticeable throughout the facility.

GATES FRONTIERS FUND uchealth Children's Hospital Colorado School of Medicine UNIVERSITY OF COLORADO ANSCHUTZ MEDICAL CAMPUS University of Colorado Anschutz Medical Campus

EDUCATION

ACCELERATING EDUCATION WITH A FOCUS ON THE NEXT GENERATION

THE GATES SUMMER INTERNSHIP PROGRAM REINVENTED ITSELF AND CHARTED ITS IMPACT IN 2020

2020 was to be a brand-new chapter for the Gates Summer Internship Program (GSIP). Longtime GSIP mentor and Associate Professor in the Department of Ophthalmology Joseph Brzezinski, Ph.D. and Director of Marketing and External Relations Jill Cowperthwaite had been named co-directors of the GSIP program effective January 1, 2020. Along with Program Coordinator Jessica Taylor Heard and volunteer fellow Jane Rech, Ph.D., they looked forward to accepting another group of outstanding interns from around the country and beyond and planning a summer that could inspire and launch them into careers in biomedical research and regenerative medicine.

Joseph Brzezinski, Ph.D., and Jill Cowperthwaite became co-directors of the Gates Summer Internship Program on January 1, 2020.

What we did instead was develop new promotional materials, market the program, receive a record 376 applications by mid-February, navigate the selection of a stellar class of 22 with the help of a dedicated selection committee, recruit Gates Center mentors in early March, and reluctantly move to cancel the planned on-campus program at the end of April.

THE VIRTUAL SUMMER OF 2020

Imagining the disappointment of our interns had the program been entirely cancelled and their summer plans entirely dashed, the GSIP team revamped. After substantial negotiation and communication, all 22 members of the Class of 2020 (four of whom were the first in their families to attend college) participated in a highly interactive, weekly Gates Summer Virtual Webinar series from June through August. Further, we worked to arrange virtual internships for two seniors with GSIP mentors. Although a Zoom format did not hold a candle to an on-campus program, the Class of 2020 seemed to appreciate what our GSIP team worked hard to deliver.

> *I found the research extremely interesting and being able to interact with my fellow interns was really nice, especially given the fact that we weren't able to spend the summer with each other. It added a sense of normalcy to my summer, which was a lot more valuable than I realized.*
> *~Response from the anonymous GSIP Class of 2020 Exit Survey"*

> *I was originally pretty committed to just a Ph.D. Because of the GSIP, I was introduced to the possibility of an M.D./Ph.D. This was the first time I started to consider this option and see its potential. I'm now committed to pursuing an M.D./Ph.D., in part to the exposure that GSIP provided.*
> *~Griffin Hampton ('2019), Mentor: Kristin Artinger, Ph.D.*

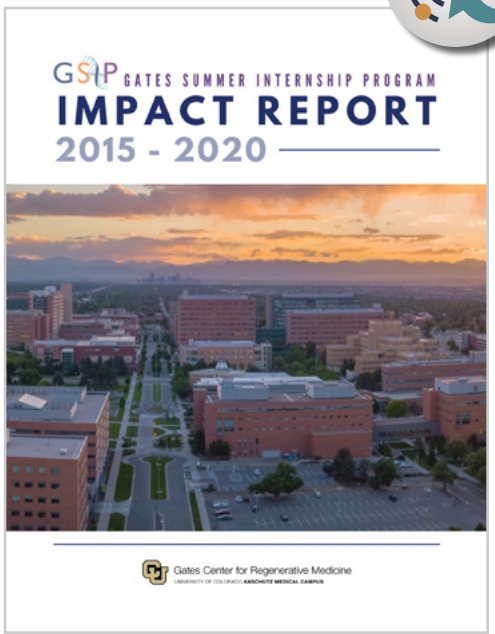
INTERN	COLLEGE/UNIVERSITY	INTERN	COLLEGE/UNIVERSITY
Joseph Adjei	Rochester Institute of Technology	Meet Patel	University of North Alabama
Gabriella Annest	University of California, Berkeley	Amrita Purkayastha	University of Colorado Boulder
Aleezah Balolia	University of Colorado Denver	Arteen Rasti	Purdue University
Chiara Dart	University of Colorado Boulder	Melia Schaefer	The University of Oklahoma
Evan Fedorov	Middlebury College	Karina Sharma	Middlebury College
Richard Granger	Davidson College	Natalie Shelden	The University of Colorado Boulder
Dustin Grossman	Georgia State University	Elyse Smiley	Regis University
Roksana Korbi	Caldwell University	Brooke Smith	High Point University
Maureen McNamara	University of Colorado Boulder	Jimmy Tangchittsumran	University of Colorado
Parth Mody	The University of Pennsylvania	Emily Thomas	The University of Oklahoma
Nupur Pandya	Virginia Commonwealth University	Raechel Tittor	Missouri Western State University

The Gates program was a major turning point in my undergraduate career, because not only did I receive a lot of career mentoring and help with my medical school applications from the lectures that we went to as GSIP interns, but the opportunity to work as a student in a cancer research lab in a major academic medical center was a fantastic experience for me to build my laboratory skills, problem-solving abilities, gain knowledge, and build lasting friendships along the way.
~Kaleb Todd ('2019), Mentor: Yiqun Shellman, Ph.D.

ASSESSING GSIP'S IMPACT

Fortuitously, the vicissitudes of 2020 allowed the GSIP team to focus on a project that had long been near and dear to the Gates Advisory Board's heart. Over the first five years of the program, we had only anecdotal information regarding a small number of GSIP alumni's post-college plans and accomplishments and ever-increasing numbers of applications with which to demonstrate the program's success. This project's goal was to augment that information with actuarial data. We wanted to enhance GSIP's ability to follow our interns' progress and successes, market, fundraise, submit grants and to maintain ties with the future physicians, scientists and professionals whose careers our program has helped launch.

We thank the GSIP team's Jessica Taylor Heard and Jane Rech and the GSIP alumni and mentors who generously shared a vast amount of information and comments throughout the summer and fall via surveys and countless emails. That data was compiled and included in the Gates Summer Internship Program Impact Report 2015-2020. This ambitious project enabled us to achieve several crucial outcomes. Happily, we reconnected with 66% of our 116 former interns and are committed both to strengthening those ties and cultivating others in the future. We now know much more about their demographics, the undergraduate institutions from which they have come, the graduate and medical institutions and programs they now attend, the number of publications



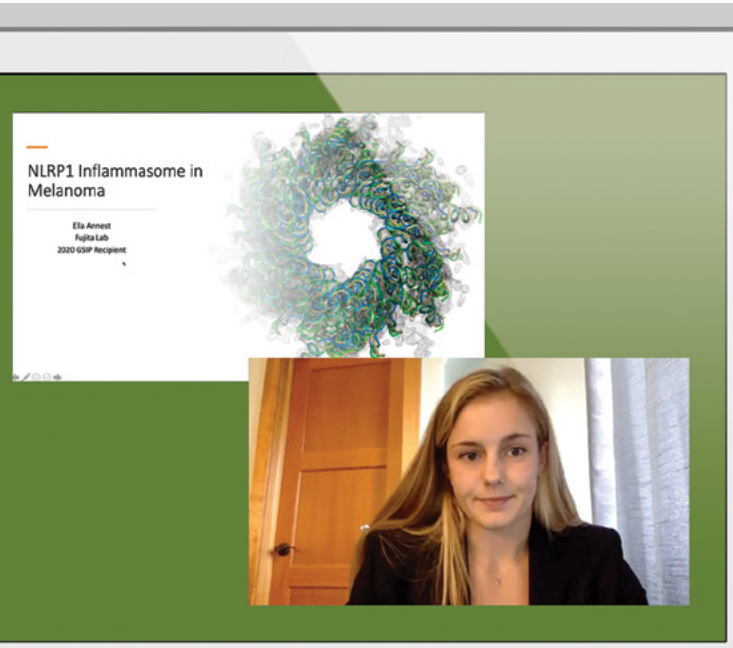
Report Highlights Impact of Gates Summer Internship Program's First Six Years

Middlebury College has had the great privilege and pleasure to send undergraduate students for a transformative summer internship at the Gates Center for Regenerative Medicine. Our students reflect on the experience in glowing terms, and describe the research opportunities as world class, the mentoring to be remarkable, and their fellow interns to crackle with energy, innovation and promise. We have been told time and again how helpful the experience was for students looking to gain admission into top medical and graduate school programs, and we highly value the GSIP opportunity for our young scientists.
~Hannah B. Benz, M.D., Associate Director, Health Professions and STEM Advising

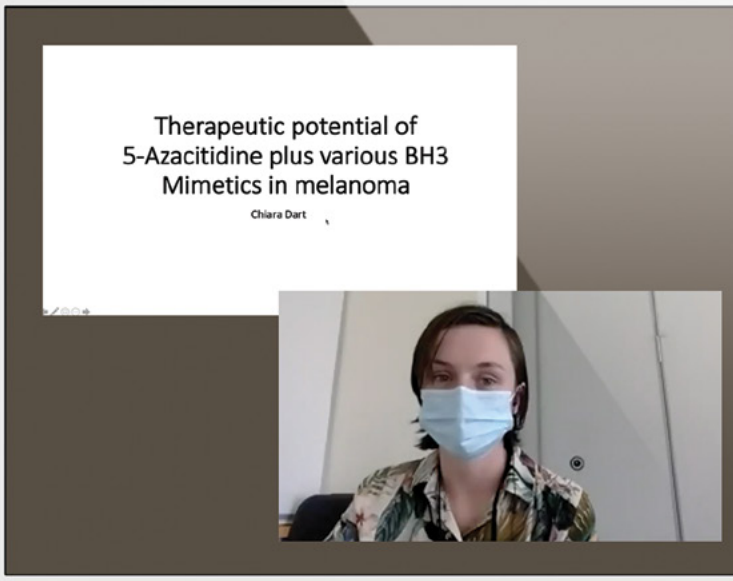
they have written (41!) and the 87 impressive awards and scholarships they have won. We have also shown that GSIP is helping recruit students to the Anschutz Medical Campus to work or pursue advanced degrees.

Out of the 13 former interns now on campus, we have included profiles in this section of three of those alums as well as an article on the CSD graduate program supported by the Gates Center two of them now attend. Most importantly, we have demonstrated that GSIP has become a premier, nationally-recognized program that is making a tremendous difference in the aspirations and lives of young people, some of whom stand to make a significant impact on the future of biomedical research and regenerative medicine.

As of the end of 2020, we had begun planning for next summer with high hopes of welcoming students to campus. We were particularly looking forward to REALLY meeting the majority of our Class of 2020 who had already indicated their desire to be a part of the Class of 2021, as well.



Ella Annest presented her virtual summer research project working with Dr. Fujita's Lab.



Chiara Dart presented her virtual summer research project working with Dr. Shellman's Lab.

I just wanted to say thank you again for GSIP. The program was truly incredible and looking back I realize how much I learned from the program. I used skills from the research and an increased understanding of the scientific process beyond the program. The seminars were so helpful in widening my awareness of many research fields and helping me work on my further study choices and applications to medical school. I am now living back in England. I started the Graduate Entry/ Accelerated Medical Degree at University of Oxford Medical School this past September. I am loving the challenge and the course so far. I hope to integrate research into my studies, inspired greatly by GSIP.
~Isabella Martus ('2019), Mentor: Mark Petrash, Ph.D.

ODE TO PETER GRANT, WHOSE FOCUS ON THE NEXT GENERATION KNEW NO BOUNDS

On December 12, 2020, the Gates Center lost an extraordinary friend in Peter Grant, whose interest in the Center and particularly in the Gates Summer Internship Program, seemed to know no bounds. Notably, Peter and his wife Rhondda were the first recipients of the Gates Center's "Charlie's Angels Award" in 2017. The Grants spent years enthusiastically helping the Gates Center advance the work of some of its seasoned clinicians and researchers, introducing new talent to groups of their friends over lunch, and purchasing state-of-the-art equipment for the Gates Biomanufacturing Facility. Peter and Rhondda were captivated by the Gates Center's plan to initiate an internship program focused on encouraging outstanding college undergraduates to pursue careers in stem cell biology and regenerative medicine and provided the2014 gift that enabled the launch of the Gates Summer Internship Program in the summer of 2015. Their ongoing encouragement and generous support along with that of the Glendorn Foundation, Penelope Lewis, Monty and Frank Kugeler, the Walter S. Rosenberry III Charitable Trust, members of the Gates Center Advisory Board and others has helped sustain the program ever since.

GSIP champions Peter and Rhondda Grant at the 2019 Final Day Program

> ***We have treasured being part of the development and growth of this program. We are thrilled about the impact it has had on its participants who have gone on to pursue a variety of educational career paths.***
> ***~Peter and Rhondda Grant***

Over the years, Peter and Rhondda followed GSIP's progress attentively and never missed the program's final day speaker and ceremony in August, at which interns shared posters highlighting their summer's research. Last summer and fall, they were delighted to hear regular reports on the data from former interns being collected and compiled to show the impressive impact of the program over the years. Sadly, the resulting ***2015-2020 GSIP Impact Report*** was not quite ready in time to share with Peter, but we were pleased to have secured permission from him and Rhondda to include their photo and the following quote on the report's back cover:

"We have treasured being part of the development and growth of this program. We are thrilled about the impact it has had on its participants who have gone on to pursue a variety of educational career paths."

Peter Grant and GSIP Co-director Jill Cowperthwaite

In turn, the Gates Center has treasured having a champion such as Peter. As GSIP co-director Jill Cowperthwaite wrote, "I will miss the sparkle in his eye, his wonderful sense of humor, his cheery and optimistic nature and all the encouragement and support he spread to me and many others. He and Rhondda were the Gates Center's first Charlie's Angels, but Peter was mine, as well."

THEY CAME FIRST TO THE ANSCHUTZ MEDICAL CAMPUS FOR GSIP, THEY SAW AND THEY RETURNED

The Gates Summer Internship Program (GSIP) has an ambitious charge to recruit top undergraduates from across the country, connect them with brilliant scientific mentors and talented laboratory staff, and immerse them in leading-edge research in stem cell biology and regenerative medicine. These summer internships create lasting impressions, forge professional relationships and inspire students to return to the Anschutz campus for advanced study.

Madison Rogers, Emily Paton, and Chris Schaaf are three alumni from over 116 undergraduates who have participated in the GSIP program since its inception in 2015. They are also among 13 GSIP alumni pursuing advanced degrees or employed in research laboratories on the University of Colorado Anschutz Medical Campus.

Madison Rogers, GSIP 2015, grew up in Evergreen, Colorado, skiing, hiking, playing tennis and running cross country. For as long as she could remember, her family volunteered for The Ability Experience, a philanthropic organization directed at reducing societal labels and empowering people with disabilities. Madison's involvement with this organization influenced her early interest in science and specifically developmental biology and oncology. At a welcome party for Colorado students accepted to Duke University, Madison met CU Anschutz oncologist Dr. David Rabin who suggested she apply to GSIP.

Emily Paton, GSIP 2015, also grew up in Colorado and likes to ski and hike. She enjoys visual arts and plays several instruments: piano, cello and recently guitar. Emily has always been interested in science. She recalled a poignant childhood memory in which her late grandfather, Bruce Paton, M.D., one-time Chief of Cardiothoracic Surgery and acting Dean of the CU Medical School, showed her an artificial heart valve similar to those he used in the operating room. Emily was also fortunate to have an inspiring high school biology teacher, Becky Mann, who "motivated her to consider science." As a promising undergraduate at Santa Clara University, Emily was encouraged to apply to GSIP by Jill Cowperthwaite, a friend of her grandfather's and now co-director of GSIP.

Madison Rogers, GSIP 2015 and a current graduate student in the CSD program, was feted after passing her Comprehensive Exam in September 2019.

Chris Schaaf, GSIP 2019, spent most of his childhood in Portland, Oregon. At 19, his interest in outdoor activities and hiking attracted him to Moab, Utah, where he spent "a few years figuring things out." A construction job opening led him to Colorado, where he "jumped at" an opportunity to return to college. While pursuing his Associate of Arts from Colorado Mountain College, he grew increasingly interested in his science classes. He found that chemistry and biology in particular, provided insights into Type 1 Diabetes, a disease affecting at least three generations of his family. With this growing interest, he transferred to Colorado Mesa University (CMU) to pursue a Bachelor of Science degree. Zeynep Ozsoy, CMU Professor of Genetics, provided him with a wonderful experience working in her lab and encouraged him to apply to GSIP. In 2019, Chris was the first CMU student to enter the Gates Center program.

INTERNSHIP EXPERIENCES

GSIP provided an unparalleled and challenging opportunity for all three interns with high-level lab work, regular seminar attendance and frequent social interactions with their fellow interns. Madison, Emily, and Chris gained valuable time-management skills balancing lab obligations and experiments with seminar attendance, developed leading-edge laboratory skills and formed close bonds with their cohorts and lab colleagues. Madison's college science classes at Duke had not provided her with lab experience, and she was particularly impressed with the stem cell biology aspect of her work to which she had not been introduced previously. She learned that "in science, a lot goes wrong" and that it requires "perseverance to figure it out and move forward through the difficult times." For Emily, GSIP was likewise a first opportunity for wet-lab research. She felt that she had "enough information and resources to be successful," but acknowledged that she had to master a "steep learning curve with research, terminology and lab techniques." Finally, Chris, though involved in genetics research at CMU, realized on his first day at the GSIP orientation and in the lab that the level of research, techniques and tools were "so far beyond what I even knew was happening." His first impression was that he was "in over my head" but he soon realized, it would be an incredibly valuable experience that he would never have gotten at CMU.

Madison's GSIP mentor was Yiqun Shellman, Ph.D. She recalled needing "a lot of training," which Shellman's lab staff generously provided. She also recounted how fun it was getting to know people in her GSIP class from all over—some of whom she still keeps in touch. Returning to Duke, Madison studied Bioinformatics, but realized how much she missed lab work. So, she decided to return to bench research and apply

Emily Paton, GSIP 2015 and CU School of Medicine Class of 2022, with Dr. Kjell Lindgren, M.D., CU School of Medicine Class of 2002, who journeyed to the International Space Station for 141 days

to graduate programs. Madison explained that GSIP exposed her to CU Anschutz and to its remarkably collaborative environment in which "lab spaces are set up so people interact and talk to one another" and she emphasized, "the campus just adds to this." Although she was accepted into other programs, they felt more closed and far less collaborative than those at CU Anschutz. In the end it was her relationship with Dr. Shellman and her increasing interest in cancer and development that led her to choose the Cell Biology, Stem Cells, and Development Program (CSD). Madison was unsure about her research focus and valued the interdisciplinary training across different subjects that CSD offered. She credits her introduction to bench research and cell culturing she received through Dr. Shellman and GSIP for her decision to pursue her Ph.D. at CU Anschutz.

Current CSD graduate student Chris Schaff, GSIP 2019, showed off his poster at the 2019 GSIP Final Day Program.

Emily interned with Antonio Jimeno, M.D., Ph.D., whose lab was both welcoming and very well-organized. Both Dr. Jimeno and Dr. Jason Morton (in the Jimeno lab) were great mentors who gave her early independence to work on her research project. She enjoyed the experience so much that upon college graduation, she returned to work as a clinical research assistant in the lab. Emily had been unsure whether to pursue a Ph.D. or an M.D. The position in the Jimeno lab gave her "good insight" into clinical research, and she soon discovered that she "wanted a career where she could work directly with patients, but still be able to pursue research." An M.D. provided the flexibility she desired. Emily applied to medical schools across the country and explored several different campuses, but the University of Colorado School of Medicine became her first choice. From the GSIP internship and other personal relationships, she knew people on the CU Anschutz campus and like Madison, found the community supportive and collaborative. Her summer internship and the additional year in the Jimeno lab gave her "more career direction and more career exposure" and was "a motivating factor in her decision to pursue medicine" at the University of Colorado School of Medicine.

Chris' mentor was Joseph Brzezinski, Ph.D., who now serves as GSIP co-director in addition to managing his laboratory in the Department of Ophthalmology. The Brzezinski lab was "really positive and supportive," and the Ophthalmology Department was collegial and welcoming. Chris immediately felt part of this group. He "got lucky having Joe as a mentor … He was there if I needed him and would provide all the guidance I wanted, but he could also let me do my thing." Chris relied on others in the lab, like CSD graduate student Michael Kaufman, who helped him with day-to-day questions and general guidance. For Chris, the impact of GSIP was "preparing me for what to expect in graduate school." As a GSIP intern, he would attend "weekly seminars, regularly read scientific papers, run a week's worth of experiments in a day and do it again the next day," all the while evaluating his progress and next steps. Working in the Brzezinski lab, Chris learned about the CSD graduate program, and also encountered the Barbara Davis Center for Diabetes (BDC). "The stars aligned" for Chris, realizing that the BDC was an "entire building" dedicated to all aspects of Diabetes research. Additionally, Chris was "enthralled" by Diabetes researcher Dr. Holger Russ's GSIP seminar, having waited all summer to see it (he says he still feels this way when he attends Holger's presentations). Chris completed his internship, received an award for his summer research and developed a plan for his future studies. He said, "GSIP was my first real exposure to what life in graduate school would be like. I was so positively influenced by my experience that I chose to apply to graduate school at CU Anschutz and am now attending the program in which my Gates mentor is a part. The exposure and my experience were very strong factors in my choice not only to attend graduate school but to apply to CU."

RETURNING TO THE ANSCHUTZ MEDICAL CAMPUS DURING THE PANDEMIC

Like everyone in the rest of the world, the COVID-19 pandemic has required these three students to accept modifications and adapt to their academic programs. Consistently, each of them feels lucky to be on the CU Anschutz campus during this time. In the initial stages of the outbreak, Madison, now a prestigious NIH NRSA Fellow, was abroad, attending a Gordon Research Conference in Italy. It was "very scary," and after her group left the conference, she was required to be in quarantine for two weeks, only to learn that the campus was shutting down as she was in the final days of her isolation. Having returned to campus, she feels fortunate to be at a point in her studies where her "research is up and running, and she can make good progress" despite the limitations. The pandemic also provided her with an opportunity to participate in a CU Dental Medicine promotional video, and to read and write more frequently. She and several CSD graduate students have launched an Advanced Writing Workshop to provide their peers in all departments with writing help, which is critical and often unavailable in the later stages of graduate school. She has enjoyed these experiences so much that she is now considering medical and scientific writing as a career.

Emily, too, feels lucky to be in her third year of medical school during the pandemic. Between her first and second pre-clinical years, she conducted research in Dr. Isabel Schlaepfer's laboratory. She has now completed most of her clinical rotations, sees lots of patients and different medical problems, and is not just learning about COVID. Reflecting on one of her family health clinical rotations, she said she has been impressed at how telehealth can improve efficiency in clinics. She described a COVID adaptation in which obstetric patients were given portable Doppler ultrasounds capable of detecting fetal heartbeats. Patients could report the Doppler results they obtained and reduce unnecessary in-person visits.

Despite some limitations imposed by the pandemic, Chris is enjoying his first year in the CSD program. He is currently participating in three-month laboratory rotations to gain exposure to the diverse research areas of focus for scientists in the CSD program. Initially, he missed the presence of senior lab members and the camaraderie in a fully-populated laboratory. Nevertheless, his rotations have been very smooth, each lab has adapted well to the COVID guidelines and Chris does not feel that his work has been affected. He particularly appreciates the labs' efforts to efficiently allow access to equipment so students can continue their research in a safe environment. He has loved his first two rotations with Dr. Olivia Rissland and Dr. Richard Benninger and is embarking on his third lab rotation with CSD professor and Barbara Davis Center for Diabetes Research Director Lori Sussel.

GRATITUDE FOR GSIP

Madison, Emily, and Chris are remarkably talented individuals, and they are thriving in their respective programs. They greatly appreciate the Gates Center and its commitment to the GSIP program and the many supporters who make it possible. Madison described GSIP as a "special experience to be exposed to cutting-edge research" and offered a big thank you to everyone involved "for their commitment to moving science forward and training the next generation." Emily echoed her gratitude for the opportunity to pursue research. Chris, too, is thankful that he was "given an opportunity despite his non-traditional background." For Chris, GSIP took him "from I think I want to do science to this is where I belong. This is what I am supposed to be doing!"

GATES CENTER HELPS STRENGTHEN PIPELINE AND OUTREACH FOR THE CELL BIOLOGY, STEM CELLS, AND DEVELOPMENT GRADUATE PROGRAM (CSD)

Since 2016, the Gates Center has supported the Cell Biology, Stem Cells, and Development Graduate Program (CSD), which helps attract and train talented candidates in the regenerative medicine field. The multidisciplinary program is based on the premise that scientists must pursue fundamental discoveries as to how cells function and form the different tissues of the body, which will ultimately enable the medical use of stem cells to treat human diseases and birth defects.

This past year has made one thing clear -- the world needs independent and creative biomedical researchers who are prepared to take on major challenges. As our campus and communities made an abrupt change to going remote last March, the (CSD) Program had to quickly reconfigure the ways we learn, work, and interact. This was especially difficult for our first year Ph.D. students, who were in the midst of coursework and their third rotations. I am incredibly proud of how this group dealt with these challenges and kept moving forward. The directors of our courses transitioned their syllabi to a virtual format in a matter of a few days, without diminishing the objectives of their courses. The students in these courses were resilient and helped work through this transition. We all learned what 'Zoom' was. Lab work also went remote for a time, and the students and mentors found new ways to advance their projects by diving deeper into the literature and learning new methods of data analysis. Overall, our students supported each other and kept on track toward their goals. This year three of our senior students successfully defended their theses and have now moved onto the next stages in their careers; two in the biotech industry and one as an officer in the U.S. Army Medical Department. As a program, we navigated the year with the same goals of training independent and creative scientists who will be the future leaders in biomedical research. In fact, the challenges of the past year have only increased our resolve.

Support from the Gates Center since 2016 has been a major factor driving the growth of CSD, and during the past year it helped us take on bigger challenges. In August we welcomed a new class of seven students; one of our largest and strongest yet. This continued growth is thanks to support from the Gates Center, which allowed a 50% increase in the size of our incoming class and enables beneficial interactions with the Gates Summer Internship Program. One of our incoming students this year is GSIP alumnus Chris Schaaf. Chris learned about CSD during his time as a GSIP intern in the lab of CSD faculty member Dr. Joe Brzezinski. Going forward, we plan to facilitate more interactions between CSD and the GSIP, and ultimately attract more GSIP alumni to apply to our program. In addition, we are developing a new mentoring program, the Developing Scholars Program, to expand access to training in biomedical research to undergraduate students in the Denver region, and create a pipeline to bring these students into the CSD program to pursue advanced degrees. With support from the National Science Foundation, the Department of Pediatrics and the Gates Center, we will launch the program in Summer 2021 and bring five students from historically excluded backgrounds onto the Anschutz Medical Campus for an immersive research education experience. This is part of our plan to overcome barriers so that more students from a greater diversity of backgrounds know about CSD and apply to join us for Ph.D. training. Our resilience and new initiatives have allowed us to emerge from this year with renewed focus and energy for the future.

Jeff Moore, Ph.D. is the director of the Graduate Program in Cell Biology, Stem Cells and Development (CSD).

OUTREACH

EXTENDING OUR CONNECTIONS

Lab Manager Charlie Wall helped orchestrate our most ambitious, but only tour of 2020.

2020 began audaciously as the Gates Center and Gates Biomanufacturing Facility staff teamed up to host a late January field trip for close to 100 Colorado Academy's seventh graders, teachers, and parents. Following a request from Gates Center Advisory Board member Kevin Reidy, whose daughter's teacher expressed interest in a campus visit, former Gates Center Lab Manager Charlie Wall choreographed a half-day involving bus arrivals and parking, presentations, lab tours, and even a police car barricade to guarantee our guests' safety as they crossed the street to tour the Gates Biomanufacturing Facility. Kevin Reidy followed up with thanks to the more than 25 staff who made the day possible:

"I am extremely grateful for all the efforts made by you and the various team members at Gates and GBF to put on what was an amazing demonstration of the advanced stem cell research, manufacturing and clinical delivery that is occurring on the CU Anschutz Medical Campus. There is no doubt that you changed the path of a least one student yesterday, and I hope you enjoyed the exposure to our young students as well. Undoubtedly, there will be an M.D. or Ph.D. that will come out of this pool of students someday!"

Over the years, the Gates Center has focused tremendous time and effort on expanding its reach. We have enjoyed welcoming guests to campus as well as reaching out within the community and beyond to introduce ourselves and share our operations and research with interested individuals and groups, fellow researchers, elected officials and students. How strange it was to have these sorts of opportunities curtailed in March with only photos to remind us of the spirited youngsters who crowded and invigorated our halls and labs in January.

Summer soon arrived, campus COVID-19 checkpoints were established, and researchers worked to schedule and accommodate the small percentage of Gates Center staff allowed in the labs at one time. Long in planning, Research Administrative Manager Carmen Garcia, now retired Lab Manager Charlie Wall and others also focused on and orchestrated the Gates Center's complex physical move from its home of thirteen years on the eighth floor of Research Complex 1 North to a new space on the fourth floor of Research Complex 2. Housing Gates Center administrative offices as well as the Morphology and Phenotyping and Stem Cell Biobank and Disease Modeling Cores, it is a space we look forward to sharing in the future with colleagues and guests, alike.

Although the pandemic cut Gates Center physical ties, we worked hard to maintain them virtually. As described in our Education section, we designed a weekly Gates Center Summer Virtual Webinar Series for our Gates Summer Internship Program's Class of 2020, covering a host of topics, all of which is recorded and available on our Gates Center website. Similarly, we planned for our Gates Center Seminar Series to begin in the fall featuring new Gates Center members, Gates Grubstake Fund awardees and guest speakers, recordings of which could be accessed from our website, as well.

Finally, we ruminated over how best to handle an event that has become near and dear to our hearts. The festive Gates Center's Charlie's Picnic has enabled us an annual opportunity to assemble our Gates Center members, Gates

Center Advisory Board, campus partners, volunteers, donors and friends to celebrate the successes their involvement has made possible. Since 2017, the party has also served to honor new recipients of the "Charlie's Angel" award given to special individuals who play unusual and often quiet roles helping the Gates Center thrive, practicing what Charlie Gates loved, which was stepping out, being bold, taking risks…and caring about making the world a better place.

While event cancellations in 2020 were rampant and wouldn't have been unexpected, Gates Center benefactor and champion Susan Bonsall Rosenberry brazenly maintained that people would be delighted to hear from the Gates Center and encouraged us to host a virtual celebration. Arms twisted, a planning group set its sights on such a creation. While there was no budget whatsoever given strictly imposed COVID-19-related campus financial restrictions, we were able to rely upon a wealth of talent and enthusiasm in video production veteran and Colorado native Lucy Garrity of Lucid Narratives. Lucy had naively volunteered to produce a short video for the occasion but ended up amassing a 20-minute video showcasing and honoring not just one "Charlie's Angel," but what Diane Wallach termed "a veritable herd of angels" composed of everyday heroes amongst our Gates Center members, Gates Center and Gates Biomanufacturing Facility staff, one of our patients and Gates Summer Internship Program students. The event attracted well over 150 viewers. These included participants located on both coasts and long-distance award winner Gates Center member Rob Plenter from Down Under, whose quote "When you're a part of the Gates Center family, you're never too far away," warmed our hearts. The virtual but spirited evening was capped off by Gates Center Director Dennis Roop's singing "It's a Wonderful World," along with toasts from University of Colorado President Mark Kennedy and his wife Debbie, Chancellor Don Elliman, and former Charlie's Angel awardees Peter and Rhondda Grant, board members Will Hiatt, M.D., and Wag Schorr, M.D. We are pleased to share screenshots and access to the video from that evening at the end of this report as they will always remind us of those who joined us to share our dedication to the Gates Center in the midst of extraordinarily challenging times. They will also provide us with cherished memories of Charlie's Angels Will Hiatt and Peter Grant whom we lost to real angelhood when they passed away in December 2020.

Our day at the Gates Center was full of vivid activities and speeches about stem cells, and how such a tiny organism could change our lives in such a huge way. The trip first began by being greeted by the Gates Center and Gates Biomanufacturing Facility's extremely kind staff members. Following that, we were taken into a large auditorium where we then learned about what kinds of research they do there related to stem cells. In one of the presentations, we learned how the process of making a medicine was almost like baking a cake. In another presentation we learned that if (for instance) a person were to have a chemical burn on their eye but still had some stem cells that were not burned, a doctor could transfer it into the burned side of the eye. After hearing all the presentations, we were lucky enough to be split into two groups where one toured the labs, and the other went on to see the kitchen (the Gates Biomanufacturing Facility!). Overall, I think our day at the Gates Center was full of learning as well as gratitude for being selected to be the only grade to see this place of magic. ~Colorado Academy 7th grader

Colorado Academy students gather for Gates Center lab and Gates Biomanufacturing Facility tours.

All in all, the temporary grounding of some of our Gates Center projects and outreach may have been manna from heaven, as no one could ever have imagined being quite so busy each and every day relatively isolated in labs or in front of computer screens on Zoom. Looking back, we are amazed and grateful at the dedication, creativity and good humor that helped assuage the hardships and make 2020 as productive and successful as it was.

NEW FACES AT THE GATES CENTER

Charles Hickey: Charles "Chuck" Hickey joined the Gates Center's affiliated Gates Biomanufacturing Facility (GBF)'s team in September of 2021 as director of finance and administration – bringing close to 20 years of financial experience, with over 15 years specifically in the manufacturing industry.

Charles was born in Southern Illinois, spent most of his life in the Midwest and moved to Colorado in 2012.

Auspiciously, Charles learned about the Gates Biomanufacturing Facility from a close mentor who had been affiliated with the original Gates Rubber Company years ago.

Most recently, Charles was the CFO for a mid-sized Colorado Springs biomanufacturing company, growing the business to over 200 employees. Prior to his role as CFO, Charles was senior financial controller for Evoqua Water Technologies, a division of Siemens Industry that spun off and relisted on the NASDAQ in Jan 2016 (AUQUA). Mr. Hickey was also the cost accounting manager for Ingersoll Rand's - Climate Control Division in St. Louis, where he led cost accounting for a multi-million-dollar manufacture of specialty refrigeration equipment (Hussmann). Previously, Mr. Hickey was the financial manager for GE Aviation's MRO & FBO business providing a variety of specialization in cost accounting, inventory control and financial reporting. Mr. Hickey started his career working for the City of St. Louis where he reached the level of chief fiscal officer for the City of St. Louis Department of Health and Hospitals. Other roles included fiscal manager for the City of St. Louis Office of Budget and Management responsible for Public Safety funding in the City of St. Louis.

Charles received a Bachelor of Science in Finance and Business Economics from Southern Illinois University, and a Master's in Finance from the University of Missouri.

What most intrigued him about the GBF was reading about the lifesaving therapies being developed, manufactured, and delivered to patients all on the same campus – a milestone that was achieved in 2020. He was further intrigued by the mission-based goals of the organization and its partners.

Charles says, “GBF’s culture is inspiring and drives a cooperative family atmosphere in which everyone is involved. The entire team meets every morning to address the day’s tasks and ensure that open communication across the facility’s departments is promoted.” He finds a lot of enjoyment working with the GBF team and partners, all of whom are constantly leveraging the amazing talent and skills of the group to produce lifesaving therapies.

Charles and his “wonderful wife Sydney” have two boys Talon (5) and Connor (9) and greatly enjoy traveling and spending time with their family. They especially love living in the great state of Colorado with all that it offers and can be found in the high country on most weekends.

Jane Rech: Jane Rech joined the Gates Center as a volunteer in January 2020 and will remain on the Gates Center staff going forward.

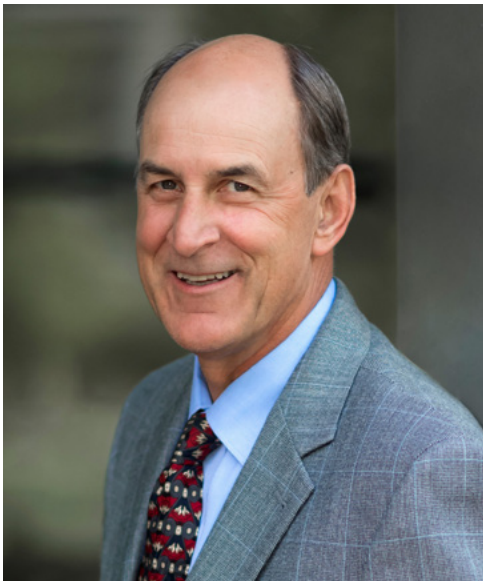
Jane grew up Philadelphia as the eighth child in a blended family of nine children in which both her father and grandfather were chemists. In the days before OSHA, her father owned a small chemical company that he literally operated from home, and Jane’s earliest laboratory experiences began in her family’s basement. Throughout high school, she worked at The Fox Chase Cancer Center with Drs. Manfred and Margret Bayer in their virology laboratory. She went on to attend Williams College, in Massachusetts, where she both obtained a B.A. with a double major in Chemistry and English and met her husband, Chris Toll, a native Coloradan.

Jane’s first job with the investment bank of Dillon, Read and Company in New York was truncated by the sudden death of her father and a move home to help her brother manage and eventually sell her father’s chemical company. Her continued interest in science led her back to research. She returned to Fox Chase to work while she considered, applied for, and was accepted to graduate school at Vanderbilt University where she received a doctorate in Molecular Biology.

Soon thereafter, Jane and her husband Chris, with his degree from Vanderbilt law school, headed west to Denver. Jane intended to take a year off to care for their first child, then decided to remain at home as their family eventually grew to three children. Over the years raising her family, Jane was a consummate volunteer serving on parent boards and in a development capacity for St. Anne’s Episcopal School, Kent Denver and Williams College. She completed her ninth and final year as a trustee for St. Anne’s Episcopal School, where she co-chaired and then chaired the Committee on Trustees, charged with organizing, selecting, training, and evaluating the board and school leadership.

Since arriving as a volunteer a year ago, Jane’s passion for science has been reignited, as has her love of working with others to advocate for and in support of individuals and educational institutions. Her exacting, gracious and thoughtful contributions toward enabling the Gates Center to best serve its members, interns and programs have likewise fueled our collective enthusiasm at having her join the center officially.

GATES CENTER FAREWELLS



Tim Gardner: We refused to say goodbye to Tim Gardner upon his retirement from the Anschutz Medical Campus in August 2020, where he had served since December 2013 as CFO of both the Gates Center for Regenerative Medicine and the Gates Biomanufacturing Facility. We much preferred to say, see you soon!

Tim arrived at the Gates Center with a wide array of experience leading innovative companies focused on growth and profitability. His financial acumen coupled with his business development, strategic planning and negotiation skills, and tremendous creativity made him an ideal candidate to serve in a number of roles, helping drive the development and growth of the Gates Center and Gates Biomanufacturing Facility during a crucially formative time.

Since moving to Denver in 1985, Tim has also been involved with a number of non-profit organizations, and it is no accident that he has consistently moved into the ranks of these entities' volunteer leadership. His willingness to simply roll up his sleeves to support those around him, help address challenging situations, and work constructively to promote and move organizations forward is readily apparent to those with whom he works closely. Professionally and as a volunteer, Tim inherently embraces and personifies Charlie Gates' focus on innovation and collaboration along with his adage that "No one does their best work alone."

Upon George H.W. Bush's death in 2018, Tim reached out to share the text of a letter President Bush had written to a friend with the following advice to young people:

1. Don't get down when your life takes a bad turn. Out of adversity comes challenge and often success.
2. Don't blame others for your setbacks.
3. When things go well, always give credit to others.
4. Don't talk all the time. Listen to your friends and mentors and learn from them.
5. Don't brag about yourself. Let others point out your virtues, your strong points.
6. Give someone else a hand. When a friend is hurting, show that friend you care.
7. Nobody likes an overbearing big shot.
8. As you succeed, be kind to people. Thank those who help you along the way.
9. Don't be afraid to shed a tear when your heart is broken because a friend is hurting.
10. Say your prayers!!

Tim Gardner is one who embodies these tenets, and his dedicated and selfless contributions to the Gates Center, the Gates Biomanufacturing Facility and the Anschutz Medical Campus will long be cherished and remembered.

Charles Wall: As 2020 drew to an end, so did the varied and interesting career of one of the Gates Center's loyal employees as he headed toward retirement in January 2021. Having arrived to fill the position of lab manager for the Gates Center in September 2014, Charlie Wall brought 26 years of experience working in academic or private science and a broad array of life experience to share. Born on an Air Force base in Kansas, Charlie joined the Navy at age 17, worked as an underground hard rock miner at the Henderson Mine in Empire, Colorado, and then landed at the University of Colorado Boulder once he decided to pursue his education. With a great interest in biology, nature, and the outdoors, Charlie graduated with a bachelor's degree in Molecular, Cellular and Developmental Biology -a program that was new, high tech, competitive, and very promising.

After several years working in biotech in Los Angeles, Charlie returned to Denver and moved professionally back and forth between National Jewish and the University of Colorado Health Sciences Center. At National Jewish he was first exposed to mouse embryonic stem cells and hematopoiesis and felt as if he had gotten in on the ground floor of stem cell research!

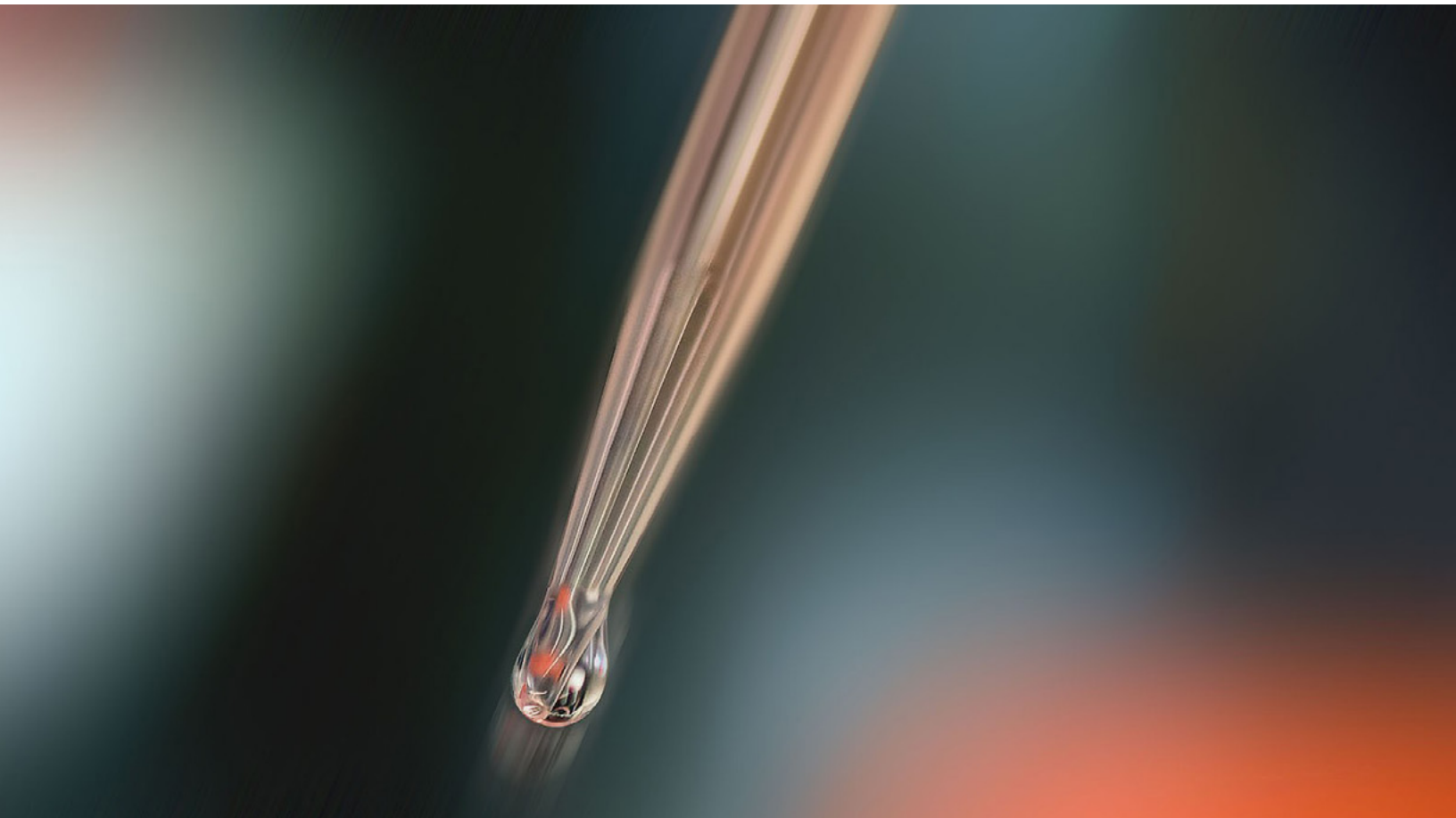
Over the years, Charlie has been thrilled to be in the position to support the science going on in the Gates Center labs and to see all that is being done to translate this work into human therapies. Like others, he sees tremendous potential for stem cell research in changing medicine as we know it. He has particularly reveled in planning and leading tours for school groups and in the promise of all the interns and young people with whom he's worked, who now stand to move the field of regenerative medicine ahead.

Leading up to and throughout the 2020 year, it was Charlie who planned, orchestrated and oversaw the lion's share of the renovation necessary to outfit a new space into which the Gates Center offices and labs moved during the summer of 2020. We look forward to thanking him in person for all his many efforts on our collective behalf and to hearing of the wide array of outside interests and adventures he and his wife Shelley (who was a longtime employee in the Dean's office) will be pursuing, shed of their campus responsibilities.

FINANCIAL OVERVIEW

The following financial statement reflects the operations of the Gates Center for Regenerative Medicine, which has been the grateful 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 Children's Hospital Colorado and UCHealth University of Colorado Hospital, 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, in 2020 the Gates Center supported three core laboratory facilities (Flow Cytometry, Morphology and Phenotyping, 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.



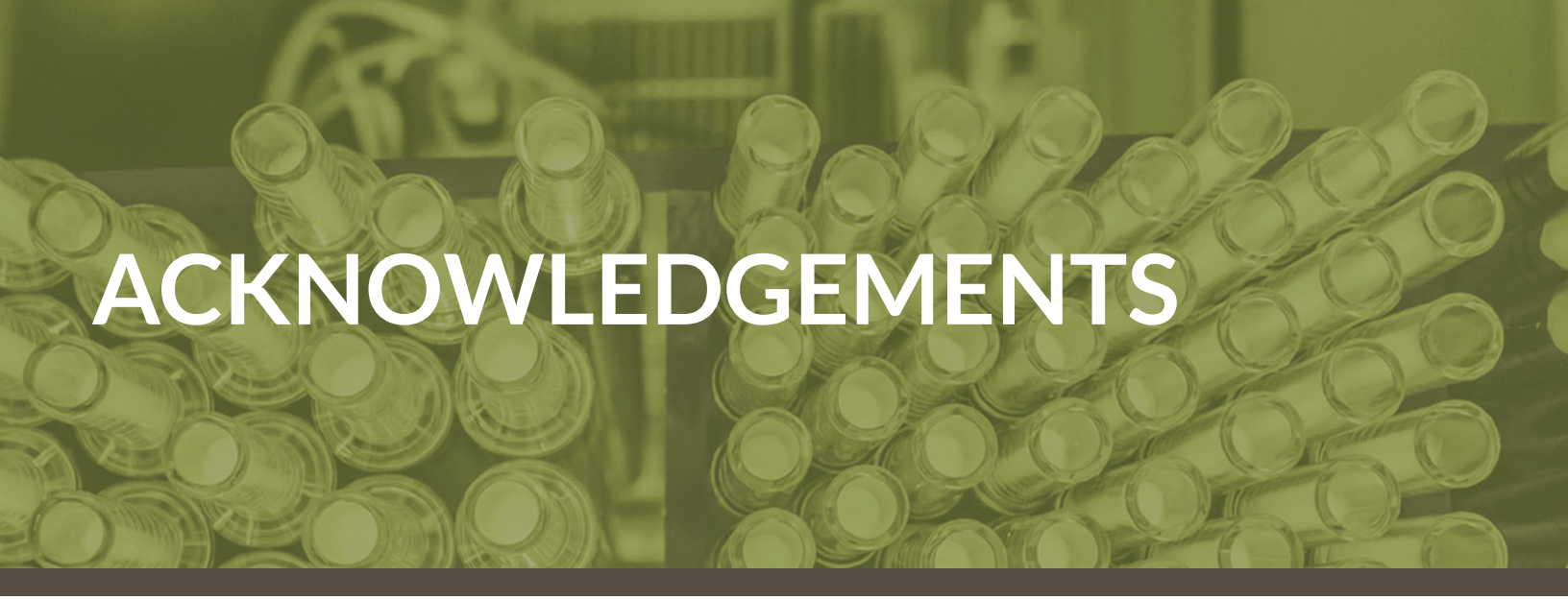
GATES CENTER OPERATIONS

Fiscal Year 2020 was the fifth 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. In 2020, a subsequent five-year agreement was finalized between the Gates Frontiers Fund, the Chancellor's Office and the School of Medicine in support of Gates Center operations and research through 2025. Additionally, the Gates Center was a critical partner in garnering support from new philanthropic support for key initiatives described in more detail on throughout this report.

Consistent with our mission and past priorities, center research program support of $583,003 was the largest expense category, totaling 29% of all spending for 2020. This amount was below our five-year average of $816,801 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 $294,726 (15% of expenses) in 2020, which was lower given pandemic-related challenges. The balance of our expenses was for marketing and development, totaling $547,913 (27% of expenses), center enrichment, educational activities and commercialization support totaling $299,297(15% of expenses), and center administration totaling $272,772 (14% of expenses).

The Gates Center net of sources of income less expenditures was ($76,508) at the end of the calendar year 2020. A delayed allocation from the CU Foundation posted after the closing of the CY 2020 will resolve the 2020 deficit.

	2016	2017	2018	2019	2020
Infrastructure and Operations Grants					
Gates Frontiers Fund	$1,200,000	$1,200,000	$1,200,000	$1,200,000	$1,200,000
University of Colorado Foundation	$600,000	$600,000	$600,000	$600,000	$7,100
University of Colorado Presidents Office	$600,000	$600,000	$600,000	$600,000	$600,000
Philanthropy	$147,617	$200,000	$327,585	$159,669	$114,103
Infrastructure and Operations Grants	**$2,547,617**	**$2,600,000**	**$2,727,585**	**$2,559,669**	**$1,921,203**
Gates Center Expenditures					
Center Research Program Support	$976,914	$721,053	$1,072,416	$730,619	$583,003
Lab Operations and Core Facilities	$494,696	$594,723	$580,161	$575,931	$294,726
Marketing and Development	$336,937	$530,526	$554,373	$562,529	$547,913
Center Admin/Maint/Supplies	$376,593	$389,380	$474,671	$235,213	$272,772
Center Enrichment, Education and Commercialization	$255,649	$285,939	$257,238	$374,986	$299,297
Total Expenditures	**$2,440,789**	**$2,521,621**	**$2,938,859**	**$2,479,278**	**$1,997,712**
Center Sources - Expenditures	**$106,828**	**$78,379**	**($211,274)**	**$80,391**	**($76,508)**



ACKNOWLEDGEMENTS

The Gates Center gratefully acknowledges the following individuals, foundations and organizations for supporting our research and mission during the 2020 year through gifts toward the Director's Innovation Fund, the Gates Summer Internship Fund, The iPSC Discovery Platform Fund, the Startup Toolbox Fund and other funds:

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Christina and Willis Wright, Jr.

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

As in years past, we would like to thank photographer and Denver native Edward DeCroce. He has provided a number of photographs within this report, and we would be hard-pressed to tell our Gates Center story without his talent and good humor. In addition, a number of Gates Center members contributed "scientific art" for this year's report demonstrating both their scientific and artistic talents.

The Gates Center would also like to express its profound appreciation to the enthusiastic and creative committee that planned the unique August 26, 2020 virtual Charlie's Picnic described on ***page 70*** and portrayed at the end of this report:

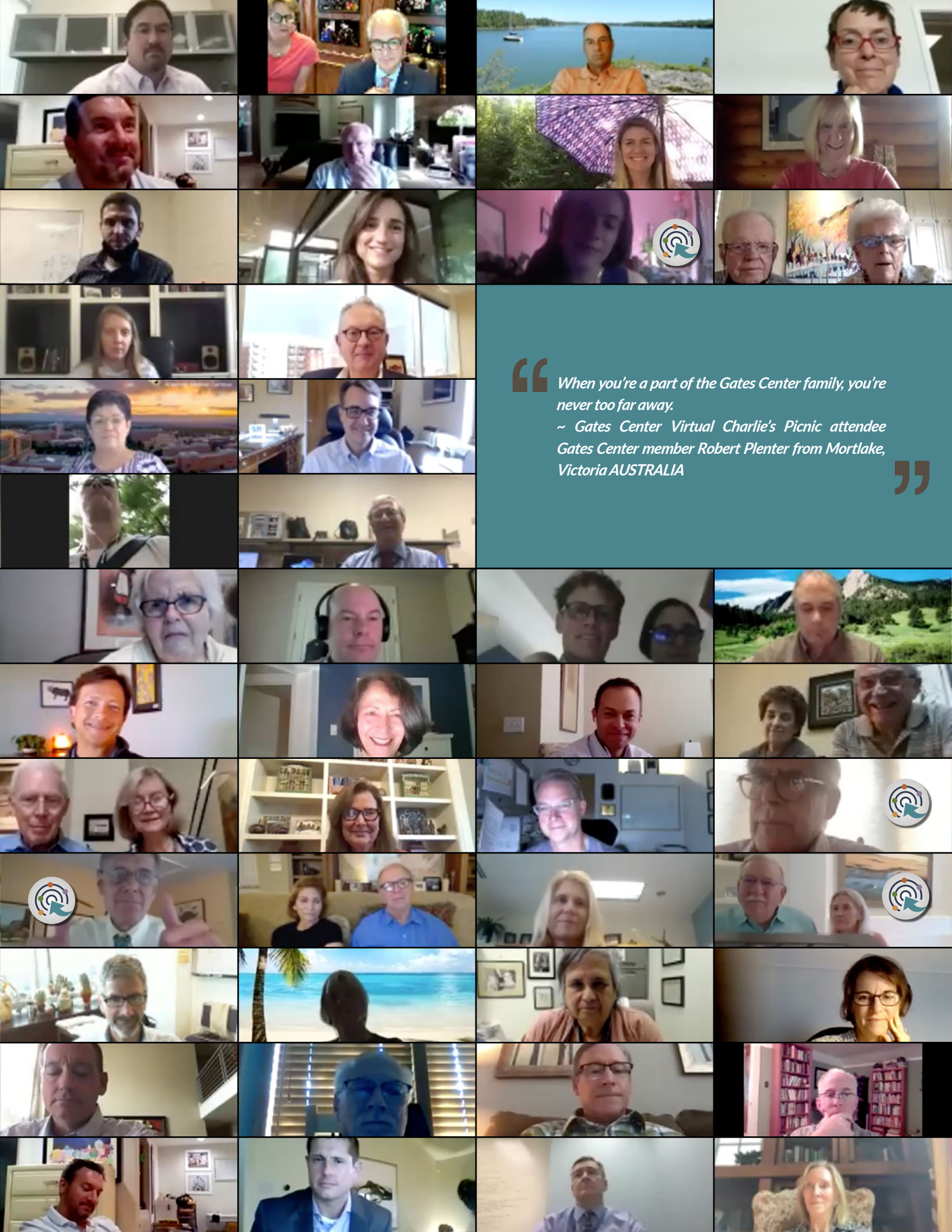
Janelle Blessing
Jill Cowperthwaite
Yvette Pita Frampton
Chris Garbe
Lucy Garrity and Lucid Narratives
Jessica Taylor Heard
Jane Rech, Ph.D.
Susan Bonsall Rosenberry
Michael Tortoro
Diane Gates Wallach
Calla Winchell

Michael Ferreyros retrieves specimens from the Isothermal Liquid Nitrogen Freezer at the Gates Center. (Photo courtesy of Nicole Diette)

2020 VIRTUAL CHARLIE'S PICNIC

On Wednesday, August 26, 2020, in lieu of gathering together at a bona fide 2020 Charlie's Picnic, we celebrated a herd of angels that made 2020 a memorable year. There were opening remarks, a video showcasing our front-line angels and a final Gates Center toast! Please click on our small icons to hear a few memorable video snippets from the evening or on the larger one to see the entire video.

I love working with you and your team. I love the communication, humor, intelligence, and friendship. I loved trying to capture The Gates Center family, interdependence, community. It has been amazing to be part of such humanly-driven and motivated brilliance. It felt good to be a part of The Gates Center family for a few moments! ~ Lucy Garrity, Lucid Narratives Video Production, creator of 2020 Charlie's Picnic video



When you're a part of the Gates Center family, you're never too far away.
~ Gates Center Virtual Charlie's Picnic attendee Gates Center member Robert Plenter from Mortlake, Victoria AUSTRALIA

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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 Matthew Seefeldt.

Members of the Gates Summer Internship Program's Class of 2020 gathered on one last Zoom to thank all those whose efforts, attitude, generosity and dedication enabled them to benefit from a highly interactive weekly Gates Summer Virtual Webinar experience and better focus on the future to come.