OPENING DOORS

2021 ANNUAL REPORT

Gates Center for Regenerative Medicine

UNIVERSITY OF COLORADO **ANSCHUTZ MEDICAL CAMPUS**

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.

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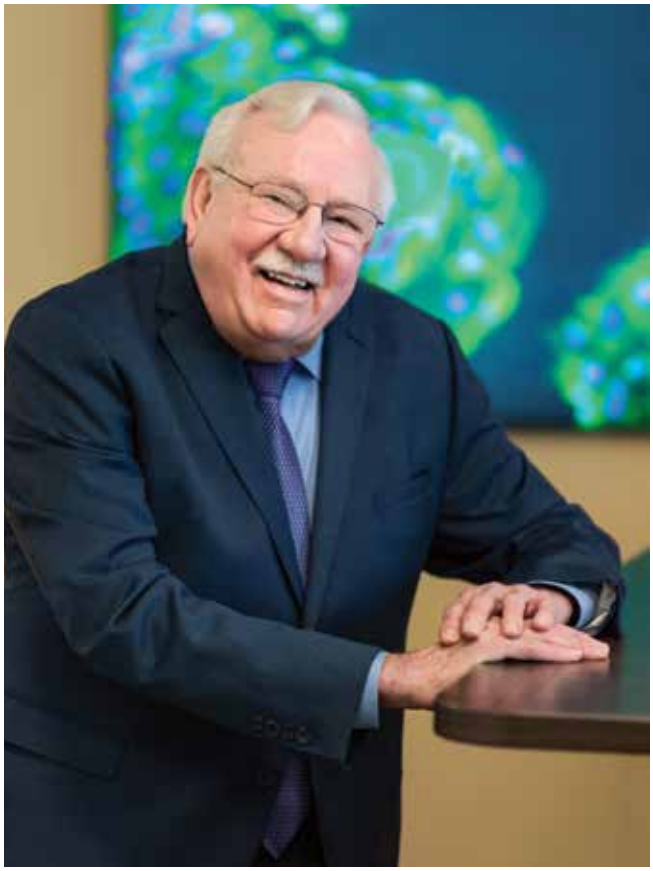
COVER, BACK COVER: *Opening Doors*, Christopher Weed, 2005

Letter from

DIRECTOR DENNIS ROOP, PhD



My Dear Friends & Colleagues,

Compiling this report is an annual ritual for the Gates Center, which enables us to reflect on and chronicle the year past and sometimes to look back even further—from where we have come. Now that it has been fifteen years since my arrival on the Anschutz Medical Campus to build the foundation for a program focused on stem cell biology and regenerative medicine, it seems timely and significant to look at the 2021 year in the context of this first decade and a half of accomplishment.

Not all organizations have the great fortune to have a heritage such as ours. Charles Gates' vision of 'opening doors' to the potential of stem cell biology and regenerative medicine to treat and cure patients through innovation and collaboration has been a constant beacon inspiring our work and our progress. We have been further blessed to have his daughter, Diane Gates Wallach, and son, John Gates, as our perennial champions.

In 2005, the Anschutz Medical Campus installed the formidable sculpture you see on the cover of this report. Three giant doors standing against the backdrop of our research buildings were conceived by celebrated artist Christopher Weed to symbolize the doors opened by the challenge and promise of science on the largest new biomedical and clinical campus in the United States.

In 2006, I accepted the offer from the University of Colorado and agreed to leave the Baylor College of Medicine in Houston, where I had worked for 18 years. I told Diane Wallach at the time that "my wife Betty and I grew up in the mountains of Southwest Virginia and to have a chance to live some place higher than 35 feet above sea level would be a dream come true." Little did I imagine that the doors opened by the Gates Center in partnership with the campus and our friends would exceed my expectations and all my dreams.

In this 2021 Gates Center Annual Report, our feature articles include a rather extraordinary story starring one of our very own. A beloved colleague, Tim Gardner, spent seven years as CFO of the Gates Center playing a significant role in its development and growth, as well as that of our affiliated and thriving Gates Biomanufacturing Facility that opened in 2015. Tim retired in late 2020, but unbelievably went on to benefit a year later from a novel CAR-T cell therapy, which is one of many treatments now being manufactured in our own Gates Biomanufacturing Facility (see page 44). Tim's journey was a cliffhanger for all of us, and it really brought home the significance of having the manufacturing capability and campus infrastructure Tim helped us build to benefit patients such as himself who end up with no other viable therapeutic options.

Another feature contributor to the report is Madison Rogers, an impressive member of our first Gates Summer Internship Program Class of 2015. Madison is now a 5th year PhD candidate in the Cell Biology, Stem Cells and Development graduate program the Gates Center helped create and continues to support. Madison, whom we profiled in our 2020 report, credits our internship program for introducing her to bench research, cell culturing and the remarkably collaborative environment at CU Anschutz. The pandemic provided a formative time in her studies during which she had the time to both read and to write, which she greatly enjoyed. She maintains in her article that scientific progress going forward is increasingly dependent upon crafting effective communication that even her non-science-oriented family can understand—and she even shows us how in some self-produced videos. Madison is, not surprisingly, considering medical and scientific writing as a career.

Our 2021 scientific updates hone in on two rare diseases that are among the primary areas of Gates Center research focus. They include a video introducing the devoted clinicians who care for patients suffering from the devastating blistering skin disease Epidermolysis Bullosa and the researchers who are moving toward a clinical trial, determined to find a cure. Additionally, Calla Winchell writes about her struggle as a patient diagnosed at age 19 with the confounding genetic disorder affecting the elasticity of her connective tissue—Ehlers-Danlos Syndrome. She happily reports that the ongoing treatment and research made possible by the Ehlers-Danlos Center of Excellence at CU Anschutz established in 2019 by several private benefactors, as well as Children's Hospital Colorado, the Gates Center and the Dean of the School of Medicine John R. Reilly, Jr., MD, is finally providing her and others with both relief and hope.

Much of this 2021 annual report centers on promoting our 124 multi-institutional members the Gates Center works to serve and the various benefits we help provide, including core facilities with expensive equipment and talented personnel, the Gates Biomanufacturing Facility and educational programming. Coming from the Anschutz Medical Campus, CU Boulder, CU Denver, Colorado School of Mines and National Jewish as well as private industry, our membership constitutes a diverse community rife with potential, collaborative opportunities. We are pleased to list them, to introduce our new members and to celebrate numerous publications, honors and grants they have amassed during 2021.

As in the past, the Center has worked to foster our members' promising research toward commercialization through the Gates Grubstake Fund awards (see page 33). These awards have been made possible since 2014 through the Gates Frontiers Fund, along with a brand-new grant this year inspired by the great progress 23 awardees to date are making toward the development of new regenerative therapies. The Gates Center's commercialization program is augmented by the Startup Toolbox program focused on providing regulatory support, market analysis and business planning, which is not typically funded by academic funding programs.

The 2021 year was one during which video production enabled us to delve behind the scenes and in some cases gain new insight into our research and programs. Such was the case with the video on Epidermolysis Bullosa (see page 30) and the Gates Summer Internship Program Reflections video (see page 57), which shows the benefit of GSIP and its diversity not just for the 141 student interns but also for the on-campus laboratories in which they have worked. Finally, we have shared the video (see page 67) highlighting our 2021 Charlie's Picnic at which our entire Gates Center community was able to gather and honor our former colleague Tim Gardner as he received the "Charlie's Angel" award.

In thanking benefactors who helped make our summer internship program possible, at least two students referred to the doors opened by the program. Their characterization led to this year's theme and our emphasis on the power of vision to open doors and make dreams come true.

We are grateful to Charlie Gates and his family, to our superb Gates Center Advisory Board, to our talented and hardworking staff at the Gates Center and the Gates Biomanufacturing Facility and to those individuals, foundations and organizations—all of whom have supported and advanced our mission.

Having grown up on a farm in the mountains of Virginia, this journey of progress has been beyond my wildest dreams.

With great appreciation,

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

Dennis & Betty Roop, Charlie's Picnic 2021

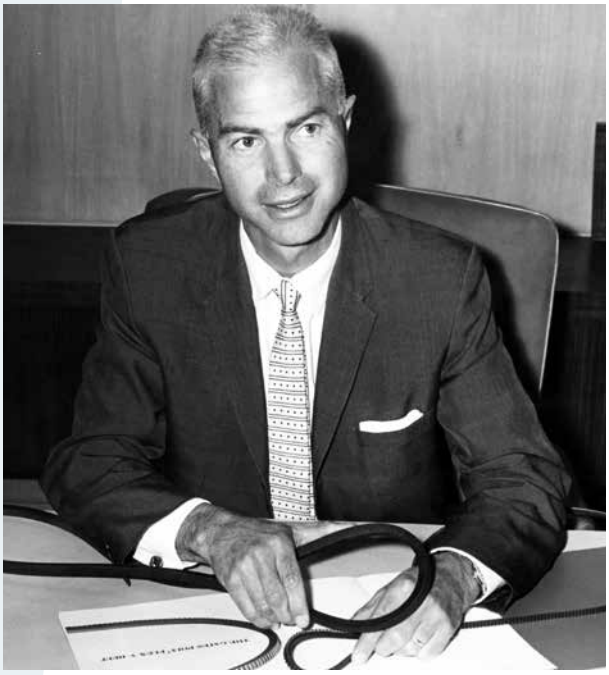
ABOUT US

OUR VISION

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 about the hope and benefit stem cell research promised for so many people in the world.

Suffering from age-related 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, family friend and former Gates Center Advisory Board member, the late Will Hiatt, MD. "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. The legacy of Charles Gates and his vision lives on in our mission and inspires our work.



TOP RIGHT: Charles Gates shown with V-belts invented in the early 1900's by his family's company, which revolutionized power transmission

RIGHT: Charlie was bullish on regenerative medicine!

15 YEARS—REALLY??

This photo of me at Charlie's Picnic (below right) *was taken at one of our early gatherings when I was reflecting on one of Dad's favorite sayings: "You only really need three things in life to be happy—someone to love; something productive to do; and something to look forward to… The Gates Center covers all three."*

A passion is something to love, and the Gates Center is about a passion to find cures. Research and discovery are productive, inspiring and rewarding ways to spend your career. Lastly, finding cures and making a difference are things you can look forward to.

My sister Diane, my wife Juls and I want to congratulate Dennis Roop and everyone on the team for 15 years of commitment and progress. Dad would be thrilled to see how far this has come and would be quick to add another plug to cure age-related macular degeneration—his original hope behind the creation of a center for regenerative medicine. We are cheering you on for the next 15 and are even more excited about the future.

John Gates
March 25, 2022

ABOVE: Diane Wallach stands next to portrait of her father that hangs in the Gates Biomanufacturing Facility, November 2019.

RIGHT: John Gates addresses Charlie's Picnic attendees on August 24, 2016.

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.

BASIC SCIENCE

▼

REGULATORY & COMMERCIALIZATION AID

▼

FUNDING

▼

CLINICAL TRIALS

▼

PATIENT BENEFIT

OUR VALUES

INNOVATION

Fostering research with an entrepreneurial spirit espoused by Charles Gates: balancing risks, opportunities and resources to overcome barriers to success.

TALENT

Pursuing, retaining and developing accomplished, passionate, and innovative change agents in both research and clinical settings.

COLLABORATION

Serving as an indispensable resource, connector, and shepherd of groundbreaking ideas and solid science, and coordinating and optimizing outcomes for all of our partners and customers. Charles C. Gates said: *No one does their best work alone.*

PATIENT OUTCOMES

Accelerating discoveries from the lab through clinical trials that lead to effective therapies and cures for those most in need of scientific breakthroughs.

RIGHT: GBF Liquid Nitrogen Storage Area, where critical reagents and cell therapy and biologic compounds produced in the GMP clean rooms are stored prior to patient administration

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 patients.

EHLERS-DANLOS SYNDROME (EDS)

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., MD. 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 (EB)

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 iPS entry 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 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.

Opening Doors, Chris Weed, 2005. Photo: Chris Weed

OUR HISTORY

2005 Installation of the sculpture "Opening Doors" on the University of Colorado Anschutz Medical Campus. Created by artist Christopher Weed, the giant, individual doors symbolize the doors opened by the challenge and promise of science on the largest new biomedical and clinical campus in the United States.


Photo: Chris Weed

2007 Dennis Roop accepted his appointment from the University of Colorado, arriving in January 2007 as Founding Director to establish the foundation necessary for the Gates Program (now the Gates Center) to be a vibrant component of CU Anschutz and a leader in accelerating discoveries using stem cells and related technologies through clinical trials to benefit patients.


Press Conference with Diane Gates Wallach, August 23, 2006: Dennis Roop, PhD, accepting the offer from the University of Colorado

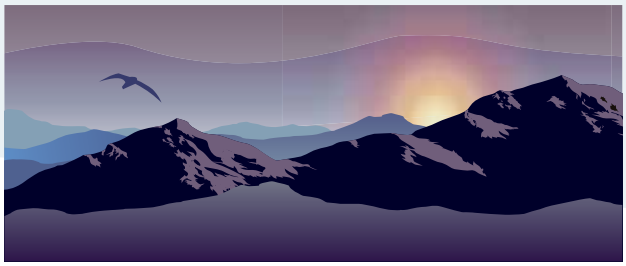
2015 Grand Opening for the Gates Biomanufacturing Facility (GBF), a state-of-the-art Good Manufacturing Practices (GMP) facility, which develops and manufactures investigational cell therapy and biologic products to support FDA-approved early phase clinical trials (see page 44).


The Grand Opening of the Gates Biomanufacturing Facility held on Tuesday, April 6, 2015. Attendees included (left to right): Gates Center Director Dennis Roop, PhD; Chancellor Don Elliman; CU President Bruce Benson; Diane Gates Wallach; U.S. Senator Michael Bennet; School of Medicine Dean John Reilly, Jr., MD; and Congressman Mike Coffman.

2015 Creation of the Gates Summer Internship Program in regenerative medicine (GSIP) for college undergraduates.


FIRST GSIP CLASS OF 2015
BACK ROW L-R: Abigail Luman, Weston Ryan, Frances Richardson, Emily Paton, Madison Rogers, Benjamin Rudeen
FRONT ROW L-R: Paige Ostwald, Nicholas Sarai, McKennah Repasky, Kaitlin Sweeney, Maria Anastasiadou

2015 Launch of the Gates Grubstake Fund to finance promising research discoveries of 23 investigators to date (see page 33).



GATES **GRUBSTAKE** FUND

2016 Partnership with the Department of Ophthalmology and benefactors to establish the CellSight program to investigate the promise of stems cells for patients with age-related macular degeneration and launch the international recruitment of Valeria Canto-Soler, PhD, as director.

Valeria Canto-Soler, PhD

2017 Establishment of "Startup Toolbox" in partnership with benefactor Ann Sperling and others 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).

Gates Center Advisory Board member Ann Sperling

2019 Establishment of the Ehlers-Danlos Center of Excellence in partnership with Children's Hospital Colorado and the Dean of the School of Medicine (see page 31).

Ehlers-Danlos Syndrome patient Calla Winchell

2020 Launch of 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 (CU) Anschutz Medical Campus.

2021

15 years of progress at the Gates Center supporting brilliant researchers and clinicians to accelerate their lab discoveries toward clinical trials to therapies and cures for patients.

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.

3D/BIOPRINTING • ANIMAL MODELS

BASIC SCIENCE • BIOENGINEERING • BIOMANUFACTURING

BIOMATERIAL SCIENCE • CARDIOLOGY • CELL THERAPIES

DERMATOLOGY • DEVELOPMENTAL/STEM CELL BIOLOGY

EXOSOMES • GENE THERAPY • IMMUNOLOGY • IPSC

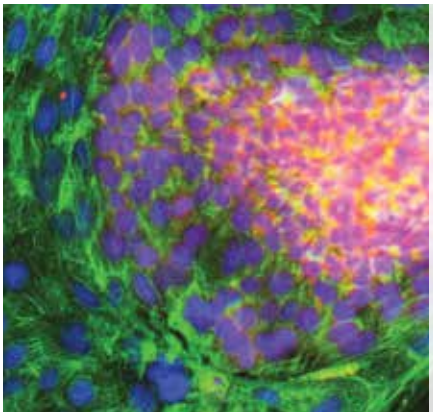
MEDICAL DEVICE • NEUROSCIENCE • OBSTETRICS • ONCOLOGY

OPHTHALMOLOGY • ORGANOIDS • ORTHOPEDICS

OTOLARYNGOLOGY • PROTEIN THERAPIES • PULMONARY

SMALL MOLECULE THERAPEUTICS • TISSUE TRANSPLANTATION

TRANSPLANTATION • WOUND HEALING



GENERATING SKIN STEM CELLS
Courtesy of Anya Bilousova, PhD and Dennis Roop, PhD

Human induced Pluripotent Stem (iPS) cells (pink) can be differentiated into ectodermal cells (green) which subsequently differentiate into skin stem cells. Nuclei are stained blue. This approach is being used to develop novel therapeutic strategies for inherited skin blistering diseases where patient-specific iPS cells are generated, genetically corrected and differentiated into normal skin stem cells which are then returned to the same patient as an autograft.

University of Colorado Anschutz Medical Campus

Boulder

Denver CU IN THE CITY

Colorado State University

uchealth

National Jewish Health

School of Mines 1874 Colorado

Children's Hospital Colorado

VA

PRIVATE INDUSTRY

GATES CENTER BENEFITS

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:

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 & 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. The Gates Center Seminar Series and community outreach highlight advances in stem cell biology and regenerative medicine.

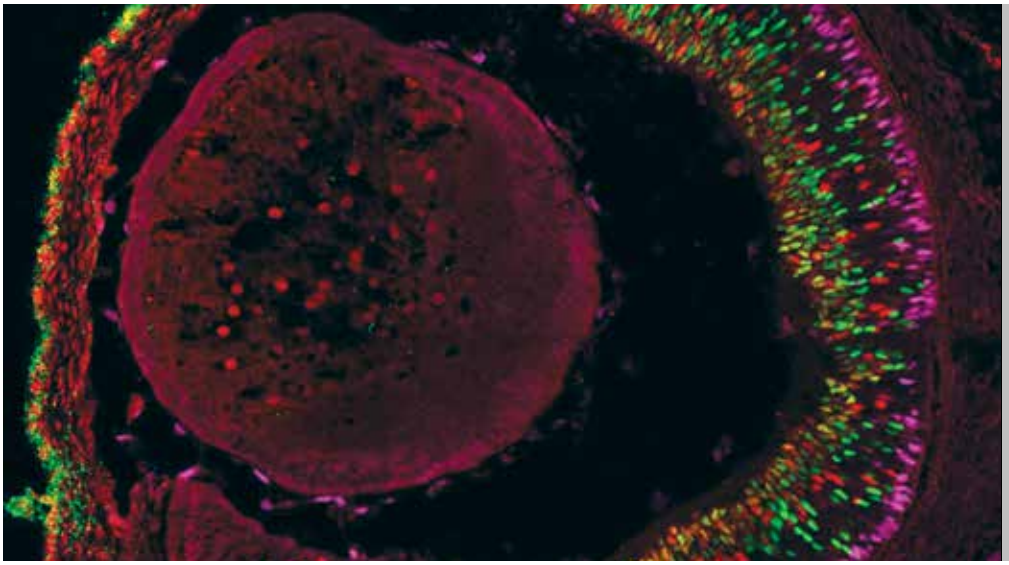
BUSINESS DEVELOPMENT, REGULATORY, COMMERCIALIZATION SUPPORT include the Gates Grubstake Fund and Startup Toolbox that provide crucial funding to bring promising regenerative discoveries to the clinic, and to give innovators access to regulatory and business formation support.

RESEARCH FUNDING provides financing at critical stages for projects/teams affiliated with the Gates Center through direct grants and endowment distributions.

NAME/*NEW MEMBERS IN 2021	POSITION	ACADEMIC INSTITUTION/ AFFILIATIONS	PRIMARY (& SECONDARY) APPOINTMENT(S)
BRUCE APPEL, PhD	Professor, Diane G. Wallach Chair in Pediatric Stem Cell Biology	University of Colorado Anschutz Medical Campus	Pediatrics, Cell and Developmental Biology
KRISTIN ARTINGER, PhD	Professor	University of Colorado Anschutz Medical Campus	School of Dental Medicine, Craniofacial Biology
REED AYERS, PhD	Assistant Research Professor	University of Colorado Anschutz Medical Campus	Orthopedics
SUSAN BAILEY, PhD	Professor	Colorado State University	Environmental and Radiological Health Sciences
CHRISTOPHER BAKER, MD	Associate Professor	University of Colorado Anschutz Medical Campus	Pediatrics
JAMES BAMBURG, PhD	Professor	Colorado State University	Biochemistry and Molecular Biology
LINDA BARLOW, PhD	Professor	University of Colorado Anschutz Medical Campus	Cell and Developmental Biology
JAIME BELKIND-GERSON, MD, MSc	Associate Professor	University of Colorado Anschutz Medical Campus	Pediatrics, Digestive Health Institute
GANNA BILOUSOVA, PhD	Associate Professor	University of Colorado Anschutz Medical Campus	Dermatology

NAME/*NEW MEMBERS IN 2021	POSITION	ACADEMIC INSTITUTION/ AFFILIATIONS	PRIMARY (& SECONDARY) APPOINTMENT(S)
STANCA BIRLEA, MD, PhD	Associate Professor	University of Colorado Anschutz Medical Campus	Dermatology
PETTER BJORNSTAD, MD	Assistant Professor	University of Colorado Anschutz Medical Campus Children's Hospital Colorado	Pediatric Endocrinology and Nephrology
NEIL BOX, PhD	Associate Professor	University of Colorado Anschutz Medical Campus	Dermatology
KRISTEN BOYLE, PhD	Associate Professor	University of Colorado Anschutz Medical Campus National Jewish Health	Pediatrics
ANNA BRUCKNER, MD, MSCS	Associate Professor	University of Colorado Anschutz Medical Campus Children's Hospital Colorado	Dermatology, Pediatrics
JUSTIN BRUMBAUGH, PhD*	Assistant Professor	University of Colorado Boulder	Molecular, Cellular and Developmental Biology
JOSEPH BRZEZINSKI, PhD	Associate Professor	University of Colorado Anschutz Medical Campus Children's Hospital Colorado	Ophthalmology
ELLEN BURNHAM, MD, MS	Associate Professor	University of Colorado Anschutz Medical Campus	Pulmonary Sciences and Critical Care
VALERIA CANTO-SOLER, PhD	Associate Professor, Doni Solich Family Chair in Ocular Stem Cell Research	University of Colorado Anschutz Medical Campus	Ophthalmology
WALLACE CHICK, PhD	Assistant Professor	University of Colorado Anschutz Medical Campus	Cell and Developmental Biology
RYAN CRISMAN, PhD	Co-Founder and Chief Technical Officer	Umoja Biopharma	
ANGELO D'ALESSANDRO, PhD	Associate Professor	University of Colorado Anschutz Medical Campus	Biochemistry and Molecular Genetics, Division of Hematology
JAMES DEGREGORI, PhD	Professor, Courtenay C. and Lucy Patten Davis Endowed Chair in Lung Cancer Research	University of Colorado Anschutz Medical Campus VA Medical Center	Biochemistry and Molecular Genetics
PETER DEMPSEY, PhD	Associate Professor	University of Colorado Anschutz Medical Campus	Pediatrics
STEVEN DOW, DVM, PhD	Professor	Colorado State University	Clinical Sciences
JASON DRAGOO, MD	Professor and Vice Chair of Academic Affairs, Endowed Chair of Regenerative Medicine, Head Team Physician Denver Nuggets, Director UCHealth Steadman Hawkins Clinic	University of Colorado Anschutz Medical Campus	Orthopedics

NAME/*NEW MEMBERS IN 2021	POSITION	ACADEMIC INSTITUTION/ AFFILIATIONS	PRIMARY (& SECONDARY) APPOINTMENT(S)
NICOLE EHRHART, VMD, MS, Diplomate ACVS	Professor	Colorado State University	Clinical Sciences, School of Biomedical Engineering
PATRICIA ERNST, PhD	Professor, Postle Family Chair in Pediatric Cancer and Blood Disorders	University of Colorado Anschutz Medical Campus	Pediatrics
XIYING FAN, PhD	Research Instructor	University of Colorado Anschutz Medical Campus	Dermatology
TERRI FOOTE, MBA	Director, Program Management and Supply Chain	University of Colorado Anschutz Medical Campus	Gates Biomanufacturing Facility
HEIDE FORD, PhD	Professor, David F. and Margaret Turley Grohne Chair in Translational Cancer Research	University of Colorado Anschutz Medical Campus	Pharmacology
SANTOS FRANCO, PhD	Assistant Professor	University of Colorado Anschutz Medical Campus	Pediatrics, Developmental Biology
BRIAN FREED, PhD	Professor	University of Colorado Anschutz Medical Campus	Allergy and Clinical Immunology
CURT FREED, MD	Professor,Leopold Korn and Michael Korn Chair in Parkinson's Disease	University of Colorado Anschutz Medical Campus	Clinical Pharmacology and Toxicology
JED FRIEDMAN, PhD	Professor	University of Colorado Anschutz Medical Campus	Pediatrics
TERRY FRY, MD	Professor, Robert J. and Kathleen A. Clark Endowed Chair for Pediatric Cancer Therapies	University of Colorado Anschutz Medical Campus	Pediatrics, Hematology and Immunology



THE DEVELOPING MOUSE EYE
Courtesy of Tatiana Eliseeva, BS and Joe Brzezinski, PhD

Retinal stem cells (green) produce photoreceptors (purple). Photoreceptors die in diseases like age-related macular degeneration. Photoreceptors derived from patient-specific induced Pluripotent Stem (iPS) cells could be used to treat macular degeneration.

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MAYUMI FUJITA, MD, PhD	Professor	University of Colorado Anschutz Medical Campus VA Medical Center	Dermatology, Immunology and Microbiology
CHRISTOPHER GARBE, MBA	Senior Director, CMC and Allogeneic Cell Therapy Program	Umoja Biopharma	
KATHLEEN GAVIN, PhD	Assistant Professor	University of Colorado Anschutz Medical Campus	Division of Geriatric Medicine
MOUMITA GHOSH, PhD	Assistant Professor	National Jewish Health	Division of Pulmonary, Critical Care and Sleep Medicine
LAURIE GOODRICH, DVM, MS, PhD	Associate Professor	Colorado State University	College of Veterinary Medicine
LIA GORE, MD	Professor, Ergen Family Endowed Chair in Pediatric Oncology	University of Colorado Anschutz Medical Campus	Pediatrics, Hematology/Oncology and Bone Marrow Transplantation
SAMUEL GUBBELS, MD	Associate Professor	University of Colorado Anschutz Medical Campus	Otolaryngology
JAMES HAGMAN, PhD	Professor	National Jewish Health University of Colorado Anschutz Medical Campus	Immunology and Genomic Medicine, Immunology and Microbiology, Program in Molecular Biology
KIRK HANSEN, PhD	Associate Professor, Doni Solich Family Chair in Ocular Stem Cell Research	University of Colorado Anschutz Medical Campus	Biochemistry and Molecular Genetics
PACO HERSON, PhD	Associate Professor, Vice Chair of Research, Director of the Neuronal Injury & Plasticity (NIP) program	University of Colorado Anschutz Medical Campus	Anesthesiology, Neuronal Injury Program
HUA HUANG, MD, PhD	Professor	National Jewish Health	Integrated Department of Immunology
SRIVIDHYA IYER, PhD	Assistant Professor	University of Colorado Anschutz Medical Campus	Orthopedics
NICHOLAS JACOBSON, MDes*	Research Faculty	University of Colorado Anschutz Medical Campus	Inworks Innovation Initiative
JEFFREY JACOT, PhD	Associate Professor	University of Colorado Anschutz Medical Campus	Bioengineering
SUJATHA JAGANNATHAN, PhD	Assistant Professor	University of Colorado Anschutz Medical Campus	Biochemistry and Molecular Genetics
WILLIAM JANSSEN, MD	Associate Professor	National Jewish Health	Division of Pulmonary, Critical Care and Sleep Medicine
ANTONIO JIMENO, MD, PhD	Professor, Daniel and Janet Mordecai Chair in Cancer Stem Cell Biology	University of Colorado Anschutz Medical Campus	Medical Oncology
MALIK KAHOOK, MD	Professor, Slater Family Endowed Chair in Ophthalmology	University of Colorado Anschutz Medical Campus	Ophthalmology

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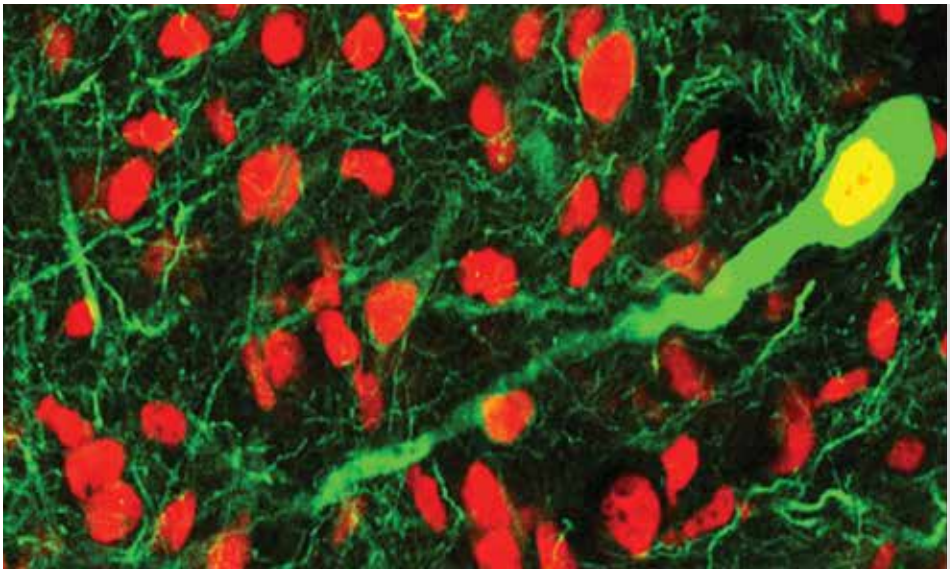
DWIGHT KLEMM, PhD	Professor	University of Colorado Anschutz Medical Campus	Pulmonary Sciences
IGOR KOGUT, PhD	Assistant Professor	University of Colorado Anschutz Medical Campus	Dermatology
MELISSA KREBS, PhD	Assistant Professor	Colorado School of Mines	Chemical and Biological Engineering
T. RAJENDRA KUMAR, PhD	Professor, Edgar L. and Patricia M. Makowski Family Endowed Chair	University of Colorado Anschutz Medical Campus	Obstetrics and Gynecology
KENNETH LIECHTY, MD	Professor, The Sandy Wolf Chair in Maternal Fetal Surgery	University of Colorado Anschutz Medical Campus	Surgery, Pediatric Surgery
CARLIN LONG, MD	Professor	University of Colorado Anschutz Medical Campus	Cardiology
SHI-LONG LU, MD, PhD	Associate Professor	University of Colorado Anschutz Medical Campus	Otolaryngology
TRACI LYONS, PhD	Associate Professor	University of Colorado Anschutz Medical Campus	Medical Oncology
CHELSEA MAGIN, PhD	Assistant Professor	University of Colorado Denver Anschutz Medical Campus	Bioengineering, Pediatrics
SUSAN MAJKA, PhD	Professor	National Jewish Health University of Colorado Anschutz Medical Campus	Medicine
NARESH MANDAVA, MD	Professor, Sue Anschutz-Rodgers Endowed Chair in Retinal Diseases	University of Colorado Anschutz Medical Campus	Ophthalmology



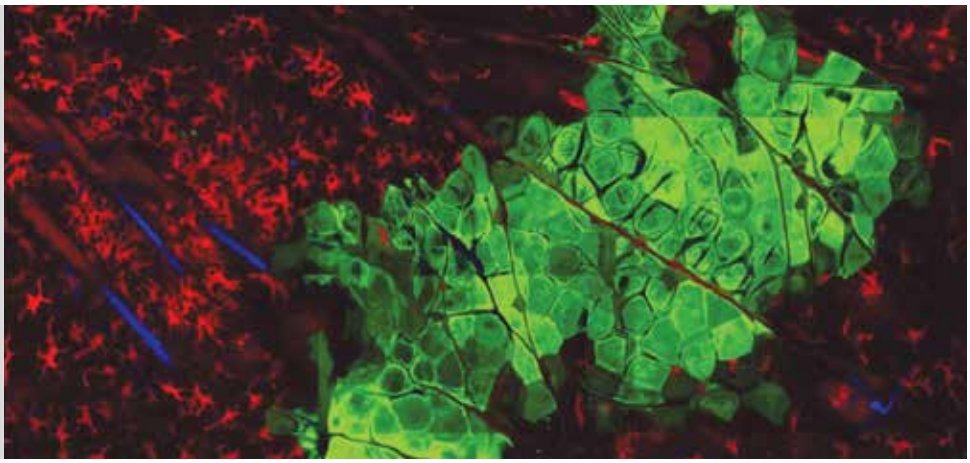
GENERATING DOPAMINE SECRETING NEURONS
Courtesy of Wenbo Zhou, PhD and Curt Freed, MD

Human induced Pluripotent Stem (iPS) cells can be differentiated into human neuronal cells (red nuclei), some of which are dopamine secreting neurons (green cells with yellow nuclei). Following implantation into a rat model of Parkinson's disease these human cells survive long term. The green fibers are connections of the human dopamine neurons to the rat brain cells. This approach may eventually be used to treat patients with Parkinson's disease.

NAME/*NEW MEMBERS IN 2021	POSITION	ACADEMIC INSTITUTION/ AFFILIATIONS	PRIMARY (& SECONDARY) APPOINTMENT(S)
JOANNE MASTERSON, PhD	Assistant Professor	University of Colorado Anschutz Medical Campus	Pediatrics
XIANZHONG MENG, MD, PhD	Professor	University of Colorado Anschutz Medical Campus	Cardiology
CHRISTIAN MOSIMANN, PhD*	Associate Professor, The Helen and Arthur E. Johnson Chair for Cardiac Research Director	University of Colorado Anschutz Medical Campus	Pediatrics, Section of Developmental Biology
RAM NAGARAJ, PhD	Professor	University of Colorado Anschutz Medical Campus	Ophthalmology, School of Pharmacy
DEVATHA NAIR, PhD	Assistant Professor	University of Colorado Anschutz Medical Campus University of Colorado Boulder	School of Dental Medicine
COREY NEU, PhD	Associate Professor, Donnelly Family Endowed Professor	University of Colorado Boulder	Mechanical Engineering
LEE NISWANDER, PhD	Professor	University of Colorado Boulder	Molecular, Cellular and Developmental Biology
DAVID NORRIS, MD	Professor	University of Colorado Anschutz Medical Campus	Dermatology
JEFFREY OLSON, MD	Associate Professor	University of Colorado Anschutz Medical Campus	Ophthalmology
BRADLEY OLWIN, PhD	Professor	University of Colorado Boulder	Molecular, Cellular and Developmental Biology
DaVID RYAN ORMOND, MD, PhD	Assistant Professor	University of Colorado Anschutz Medical Campus VA Medical Center	Neurosurgery, Translational Clinical Research
VIKAS PATEL, MD	Professor, Endowed Chair in Orthopedic Spinal Innovation	University of Colorado Anschutz Medical Campus	Orthopedics

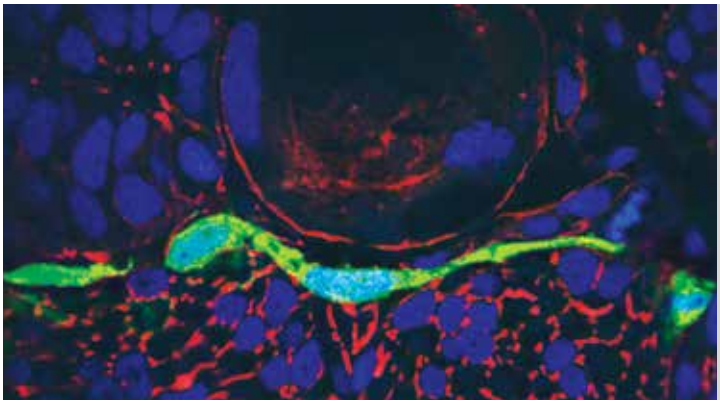
CANCER STEM CELLS EVADE IMMUNE DETECTION
Courtesy of Brad Kubick, BS and Dennis Roop, PhD

Live imaging of cancer stem cells (green evading immune cells (red) in a genetically engineered mouse model of skin cancer. In this model, skin cancers initiate around hair follicles (blue). This model may reveal how cancer stem cells avoid immune detection and suggest new therapeutic strategies to reverse this process.



NAME/*NEW MEMBERS IN 2021	POSITION	ACADEMIC INSTITUTION/ AFFILIATIONS	PRIMARY (& SECONDARY) APPOINTMENT(S)
KARIN PAYNE, PhD	Associate Professor	University of Colorado Anschutz Medical Campus	Orthopedics
MARK PETRASH, PhD	Professor, Associate Director	University of Colorado Anschutz Medical Campus	Ophthalmology, School of Pharmacy and Phamaceutical Science
CHRISTOPHER PHIEL, PhD	Associate Professor	University of Colorado Denver	Integrative Biology, Pharmacology
ERIC PIETRAS, PhD	Assistant Professor, Cleo Meador and George Ryland Scott Endowed Chair in Hematology	University of Colorado Anschutz Medical Campus	Hematology
ROBERT PLENTER	Senior Professional Research Assistant	University of Colorado Anschutz Medical Campus	Division of Pulmonary Sciences
CHRISTOPHER PORTER, MD	Associate Professor	University of Colorado Anschutz Medical Campus VA Medical Center	Pediatrics, Hematology/Oncology and Bone Marrow Transplantation
HUNTINGTON POTTER, PhD	Professor, Director CU Alzheimer's and Cognition Center	University of Colorado Anschutz Medical Campus	Neurology
CHAITANYA PURANIK, BDS, MS, MDent Sci, PhD*	Assistant Professor	University of Colorado Anschutz Medical Campus Children's Hospital Colorado	School of Dental Medicine Children's Hospital Colorado
NIDIA QUILLINAN, PhD	Associate Professor	University of Colorado Anschutz Medical Campus	Anesthesiology
YOSEF REFAELI, PhD	Associate Professor	University of Colorado Anschutz Medical Campus	Dermatology
MARY REYLAND, PhD	Professor	University of Colorado Anschutz Medical Campus	Craniofacial Biology, Cell Developmental Biology, Pathology
JENNIFER RICHER, PhD	Professor	University of Colorado Anschutz Medical Campus	Pathology
JAMES ROEDE, PhD	Associate Professor	University of Colorado Anschutz Medical Campus	Pharmaceutical Sciences
DENNIS ROOP, PhD	Professor, Charles C. Gates Endowed Chair in Regenerative Medicine and Stem Cell Biology	University of Colorado Anschutz Medical Campus	Dermatology
PAUL ROZANCE, MD	Professor	University of Colorado Anschutz Medical Campus	Pediatrics and Integrative Physiology
ANDRII ROZHOK, PhD	Research Instructor	University of Colorado Anschutz Medical Campus	Dermatology
HOLGER ANDREAS RUSS, PhD	Assistant Professor	University of Colorado Anschutz Medical Campus	Barbara Davis Center for Diabetes, Microbiology and Immunology Department

NAME/*NEW MEMBERS IN 2021	POSITION	ACADEMIC INSTITUTION/ AFFILIATIONS	PRIMARY (& SECONDARY) APPOINTMENT(S)
BRANDEN SALINAS, PhD	Senior Director, Manufacturing Science and Technology	Umoja Biopharma	
CAROL SARTORIUS, PhD	Associate Professor	University of Colorado Anschutz Medical Campus	Pathology
MATTHEW SEEFELDT, PhD	Executive Director	University of Colorado Anschutz Medical Campus	Gates Biomanufacturing Facility
KARINA SERBAN, MD	Assistant Professor	National Jewish Health	Division of Pulmonary and Critical Care Medicine
KARTIK SHANKAR, PhD*	Professor	University of Colorado Anschutz Medical Campus	Pediatrics, Section of Nutrition
YIQUN SHELLMAN, PhD	Associate Professor	University of Colorado Anschutz Medical Campus	Dermatology
DANIEL SHERBENOU, MD, PhD*	Associate Professor	University of Colorado Anschutz Medical Campus	Medicine-Hematology
VANESSA SHERK, PhD	Instructor	University of Colorado Anschutz Medical Campus	Endocrinology
KUNHUA SONG, PhD	Associate Professor	University of Colorado Anschutz Medical Campus	Cardiology
DANIELLE SORANNO, MD	Assistant Professor	University of Colorado Anschutz Medical Campus	Pediatrics
BALAJI SRIDHAR, MD, PhD*	Resident	University of Colorado Anschutz Medical Campus University of Colorado Boulder	
KURT STENMARK, MD	Professor, La Cache Endowed Chair in Pediatric Critical Care	University of Colorado Anschutz Medical Campus	Pediatrics, Critical Care
LORI SUSSEL, PhD	Professor, Sissel and Findlow Family Chair	University of Colorado Anschutz Medical Campus	Barbara Davis Center for Diabetes, Pediatrics, Cell and Developmental Biology



MIGRATING NEURAL CREST CELL IN ZEBRAFISH
Courtesy of Kristin Artinger, PhD

An elongated neural crest cell (green) migrating past the notochord (upper dark circle) and somite (red). Nuclei are stained blue. Neural crest cells are multipotent stem cells, giving rise to diverse cell lineages including peripheral neurons, glia, pigment cells (melanocytes) and craniofacial cartilage which forms the face. Understanding how neural crest cells differentiate into these different cell lineages may provide insight into the repair and treatment of birth defects such as cleft-lip and other craniofacial syndromes, as well as migration of cancer cells in melanoma.

NAME/*NEW MEMBERS IN 2021	POSITION	ACADEMIC INSTITUTION/ AFFILIATIONS	PRIMARY (& SECONDARY) APPOINTMENT(S)
TAMARA TERZIAN, PhD	Assistant Professor	University of Colorado Anschutz Medical Campus	Dermatology
DOUGLAS THAMM, VMD	Assistant Professor	Colorado State University	Clinical Sciences
ENRIQUE TORCHIA, PhD	Assistant Professor	University of Colorado Anschutz Medical Campus	Dermatology
RONALD VAGNOZZI, PhD	Assistant Professor	University of Colorado Anschutz Medical Campus	Cardiology, Consortium for Fibrosis Research and Translation (CFReT)
MARIA NATALIA VERGARA, PhD	Assistant Professor	University of Colorado Anschutz Medical Campus	Ophthalmology
MICHAEL VERNERIS, MD	Professor, The Barton Endowed Chair of Pediatric Bone Marrow Transplant	University of Colorado Anschutz Medical Campus	Pediatrics,Hematology/Oncology and Bone Marrow Transplantation
ESZTER VLADAR, PhD	Assistant Professor	University of Colorado Anschutz Medical Campus	Cell and Developmental Biology, Division of Pulmonary Sciences
DAVID WAGNER, PhD	Associate Professor	University of Colorado Anschutz Medical Campus	Neurology
LORI WALKER, PhD	Associate Professor	University of Colorado Anschutz Medical Campus	Cardiology
XIAO-JING WANG, MD, PhD	Professor, John S. Gates Endowed Chair in Stem Cell Biology	University of Colorado Anschutz Medical Campus VA Medical Center	Pathology, Dermatology
ZHIJIE WANG, PhD	Assistant Professor	Colorado State University	Mechanical Engineering
TREVOR WILLIAMS, PhD	Professor, Timpte/Brownie Endowed Chair in Craniofacial/Molecular Biology	University of Colorado Anschutz Medical Campus	School of Dental Medicine, Craniofacial Biology, Cell and Developmental Biology
CAROL WILUSZ, PhD	Professor	Colorado State University	Microbiology, Immunology and Pathology
JEFF WILUSZ, PhD	Professor	Colorado State University	Microbiology,Immunology and Pathology
RUI YI, PhD	Associate Professor	University of Colorado Boulder	Molecular, Cellular and Developmental Biology
MARTIN ZAMORA, MD	Professor	University of Colorado Anschutz Medical Campus	Division of Pulmonary, Critical Care Medicine
MICHAEL ZARETSKY, MD	Associate Professor, Medical Director Colorado Fetal Care Center	University of Colorado Anschutz Medical Campus Children's Hospital Colorado	Obstetrics and Gynecology, Maternal Fetal Medicine
WENBO ZHOU, PhD	Associate Professor	University of Colorado Anschutz Medical Campus	Clinical Pharmacology and Toxicology

WELCOME NEW MEMBERS

NICHOLAS JACOBSON, MDes

Nicholas Jacobson, trained as an architect and computational designer, is a translational research faculty member for Inworks Innovation Initiative. He has been working on the Anschutz Medical Campus for five years. Nicholas is also the founder of Mix Surgical Technology. He is interested in the development of patient-specific heart valves for pulmonary and aortic valve replacement. Nicholas joined the Gates Center to be part of its community of innovators in regenerative medicine. He is a 2021 Gates Grubstake Fund awardee.

CHRISTIAN MOSIMANN, PhD

Dr. Mosimann is an Associate Professor in the Department of Pediatrics. He has had a laboratory at CU Anschutz since 2019, where he studies the mechanisms of mesodermal cell fate determination in development, disease, and regeneration. His interest in being part of and contributing to the Gates Center stems from his long-standing work and collaborations on developmental mechanisms that contribute to the regeneration and generation of regenerative cell types.

MOSIMANN PANDEMIC LAB
FRONT ROW L–R: Harrison Wells (BSP Rotation); Abbigayl Burtis (MOLB Rotation); Robert Lalonde, PhD; Agnese Kocere; Jelena Kresoja-Rakic, PhD

BACK ROW L–R: Cassie I. Kemmler; Hannah Moran; Christian Mosimann, PhD; Alexa Burger, PhD

CHAITANYA P. PURANIK, BDS, MS, MDentSci, PhD

Dr. Puranik has been an Assistant Professor and Director of Predoctoral Education in the Department of Pediatric Dentistry at the University of Colorado's School of Dental Medicine since August 2018. His research interests focus on dental materials, caries biology, and pulp regeneration. In 2021, his research received first place, among 386 funded projects at the Proof-of-Concept Network (POCN) Innovator Showcase at the National Institutes of Health Small Business Education and Entrepreneurial Development (NIH-SEED). He is currently working on restorative dental materials that prevent dental plaque and caries while regenerating dental pulp. Dr. Puranik is a 2021 Gates Grubstake Fund awardee.

Dr. Chaitanya Puranik (far right) at the American Board of Pediatric Dentistry award ceremony

KARTIK SHANKAR, PhD

Dr. Kartik Shankar is a Professor in the Department of Pediatrics, Section of Nutrition. He has been a faculty member at the University of Colorado Anschutz Medical Campus since August 2019. His group focuses on fundamentally understanding the role of maternal and early-life nutrition and environmental factors in the development of obesity and its metabolic co-morbidities. In this context, his group conducts broad translational-research studying developmental programming in the placenta, embryo, stems cells,and early-life epigenetic mechanisms. He joined the Gates Center for Regenerative Medicine because of its exceptional intellectual and core research resources, world-class researchers in stem cell biology, and collaborative environment.

THE SHANKAR LAB,L–R: Kartik Shankar, PhD; Stephanie Gilley, MD, PhD; Meghan Ruebel, PhD; Auna Yazza; Puujee Jambal, MS

DAN SHERBENOU, MD, PhD

Dr. Sherbenou is a physician-scientist and Associate Professor in the Hematology Division, devoted to patient care and research on multiple myeloma. He has been at the University of Colorado for seven years after completing an oncology fellowship. His lab research focuses on drug and personalized medicine assay development, using samples donated by patients. His interest in the Gates Center stems from a desire to be involved with a group of like-minded individuals knowledgeable about the development of cell-based therapies and clinical diagnostics.

THE SHERBENOU LAB on a hiking outing. Daniel Sherbenou, MD, PhD (far right)

BALAJI SRIDHAR, MD, PhD

Dr. Sridhar has been active at CU Anschutz intermittently since 2009 for medical school, a research fellowship, and residency. He is interested in modifying biomaterials to enhance the properties of stem cells, especially for immunomodulating their environment. He became a Gates Center member because he is fascinated by the potential regenerative medicine holds, particularly in treating orthopedic conditions.

SELECT MEMBER PUBLICATIONS

JAMES DEGREGORI, PhD, Professor, Department of Biochemistry and Molecular Genetics • ERIC PIETRAS, PhD, Assistant Professor, Department of Medicine/Hematology

In this manuscript, Drs. DeGregori and Pietras describe how chronic inflammation can promote selection for an oncogenic event in hematopoietic stem and progenitor cells, which is relevant for understanding the increased leukemia incidence in the elderly (Higa et al., J Exp Med., 2021).

MAYUMI FUJITA, MD, PhD, Professor, Department of Dermatology • JAMES DEGREGORI, PhD, Professor, Department of Biochemistry and Molecular Genetics • ERIC PIETRAS, PhD, Assistant Professor, Department of Medicine/Hematology

In this manuscript, Drs. Fujita, DeGregori and Pietras describe the role of melanoma-derived NLRP3 in expanding immunosuppressive myeloid-derived suppressor cells and contributing to tumor progression (Tengesdal, etal., Proc Natl Acad Sci, 2021). They provide evidence that NLRP3 could be a target for immunotherapy resistance in melanoma.

TRACI LYONS, PhD, Associate Professor, Department of Medicine • JENNIFER RICHER, PhD, Professor, Department of Pathology

Drs. Lyons and Richer report that semaphorin 7A (SEMA7A) confers significantly decreased patient survival rates in ER+ breast cancer. They demonstrate that SEMA7A confers primary tumor resistance to the estrogen receptor antagonist, fulvestrant, by promoting pro-survival signaling. They propose that targeting this pathway with inhibitors of survival signaling such as venetoclax may prove efficacious for treating SEMA7A+ tumors.

SUSAN M. MAJKA, PhD, Professor, Department of Medicine, National Jewish Health • MOUMITA GHOSH, PhD, Assistant Professor, Division of Pulmonary

Drs. Majka and Ghosh report that the well-described Wnt inhibitor Dickkopf-1 (DKK1) plays a role in angiogenesis as well as regulation of growth factor signaling cascades in pulmonary remodeling associated with chronic lung diseases including emphysema and fibrosis (Summers et al., Am J. Physiol Cell Physiol, 2021). Prior to this study, the specific mechanism by which DKK1 influenced mesenchymal vascular progenitor (MVPC), endothelial and smooth muscle cells within the microvascular niche was not known. In this study, they demonstrate that DKK1 expression is necessary to maintain the microvascular niche.

ROBERT PLENTER, BS, Senior Professional Assistant, Department of Medicine

In this publication, Robert Plenter and his collaborators describe the results of using TLR4 knockout donor kidneys in wild-type recipients. Acute kidney injury after transplantation of human deceased donor kidneys is associated with upregulation of tubular TLR4. While immediate functional benefit was not demonstrated, histological markers were improved and results suggest that TLR4 deletion decreases apoptosis via inhibition of the death receptor pathway and decreases tubular injury and cast formation (Jain et al., Sci Rep, 2021).

DENNIS ROOP, PhD, Professor • GANNA BILOUSOVA, PhD, Associate Professor • ANNA BRUCKNER, MD, Professor • IGOR KOGUT, PhD, Assistant Professor • DAVID NORRIS, MD, Professor, Department of Dermatology

Drs. Roop, Bilousova, Bruckner, Kogut and Norris and their collaborators investigated 32 recessive dystrophic epidermolysis bullosa (RDEB) patient samples from the Southwestern United States, Mexico, Chile, and Colombia carrying common mutations in the COL7A1 gene to determine the origins of these mutations and the extent to which shared ancestry contributes to disease prevalence. The results demonstrate both shared European and American origins of RDEB mutations in distinct populations in the Americas and suggest the influence of Sephardic ancestry in at least some RDEB mutations of European origins (Warshauer et al., Am J Med Genet, 2021). Gene-editing treatments for RDEB patients using guide RNAs specific to pathogenic mutations are anticipated in the near future. As regulatory agencies may consider each guide RNA as a separate drug, separate clinical trials for each RNA would be required. Patient populations who share the same founder mutations therefore represent an increasingly important resource to facilitate early clinical trials and advance novel treatments.

Click or Scan
FOR RDEB VIDEO

XIAO-JING WANG, MD, PhD, Professor, Department of Pathology • ANTONIO JIMENO, MD, PhD, Professor, Division of Medical Oncology

In this paper, Drs. Wang and Jimeno and their collaborators examined spatial patterns of PD-L1+ cells in mouse and human SCCs that overexpress transforming growth factor beta (TGFβ) and found that PD-L1 was primarily expressed on infiltrating leukocytes. Cancer clinical trials using combined TGFβ inhibition and PD-L1 blockade are currently in progress, however there are no predictive markers for therapeutic responders. To address this, they used both a small molecule TGFβ inhibitor in combination with anti-PD-L1 and a bifunctional fusion protein, bintrafusp alpha, targeting both TGFβ and PD-L1 to treat mouse SCCs and found that TGFβ inhibition enhanced PD-L1 blockade-induced tumor eradication in multiple tumor models. They identified distinct cell populations of responders and non-responders to bintrafusp alfa, with responders showing a shift toward a more immune-permissive microenvironment (Strait et al., Commun Biol, 2021). The identification of cellular and molecular signatures of responders versus non-responders to combined TGFβ and PD-L1 blockade provide important insights into future personalized immunotherapy in SCC.

HONORS

BRUCE APPEL, PhD
Professor, Department of Pediatrics, received a National Institute of Neurological Disorders and Stroke (NINDS) R35 Outstanding Investigator Award (see grant awards section). The long-term goal of Dr. Appel's project is to understand how oligodendrocytes, which are glial cells of the central nervous system, form specific amounts of myelin on select axons during development. Completion of this research will substantially extend understanding of the cellular and molecular mechanisms by which myelin membrane is produced and modified by brain activity. This will provide important new insights to the developmental basis of learning, memory, psychiatric disease and a foundation for designing therapeutic strategies to promote myelination of brains damaged by disease or injury.

JUSTIN BRUMBAUGH, PhD
Assistant Professor, Molecular, Cellular and Developmental Biology, was named an International Society for Stem Cell Research Goldstein Policy Fellow.

IGOR KOGUT, PhD
Assistant Professor, Dermatology, became a member of the Cell Biology, Stem Cells and Developmental Graduate (CSD), Molecular Biology (MOLB) and Bioengineering programs.

T. RAJENDRA KUMAR, PhD
Professor, Obstetrics and Gynecology, was guest lecturer at the October 2021 Center for Reproductive Sciences' Neena B. Schwartz Memorial Lectureship at Northwestern University in Chicago, IL. He was also the keynote speaker for the Janice Bahr Lecture at the 2021 Illinois Symposium on Reproductive Sciences.

KENNETH LIECHTY, MD
Professor, Department of Surgery, and his company Ceria Therapeutics received a 2021 Advanced Industries Accelerator Grant from Colorado's Office of Economic Development and International Trade (OEDIT).

CHELSEA MAGIN, PhD
Assistant Professor, Bioengineering/Pediatrics, was named a 2021 *40 Gators Under 40* by her alma mater the University of Florida, which honors outstanding young alumni whose achievements make a positive impact on the world around them.

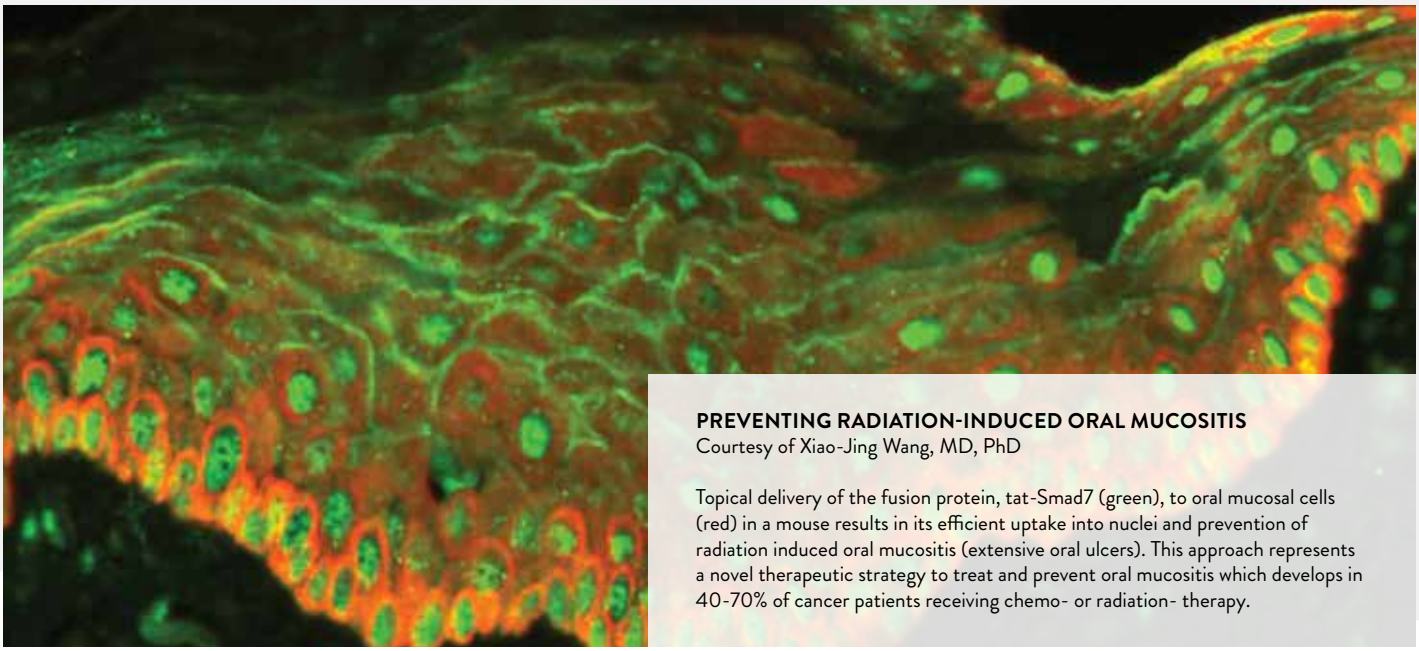
SUSAN MAJKA, PhD
Professor, Department of Medicine, CU Anschutz and National Jewish Health; a Gates Flagship Member, was elected to chair the 2025 Gordon Research Conference in Lung Development, Injury and Repair, with Darrell Kotton, MD, Director of Center for Regenerative Medicine at Boston University. She also received the Established Outstanding Investigator Award (R35) from the National Heart, Lung, and Blood Institute entitled "Mesenchymal Vascular Progenitor Depletion Promotes Lung Aging and Susceptibility to Emphysema" to develop a program in Pulmonary Vascular Regenerative Medicine.

CHRISTIAN MOSIMANN, PhD
Associate Professor, Pediatrics, Section of Developmental Biology, was elected to the Board of Directors of the International Zebrafish Society (IZFS).

NATALIA VERGARA, PhD
Assistant Professor, Ophthalmology, was awarded a 3D ROC prize by the National Eye Institute (NEI) for her research team's work to create better models to accelerate the development of new therapies for retinal diseases. This prize competition was established by the NEI to promote research on creating improved three-dimensional retinas in vitro, known as retinal organoids, derived from human stem cells, that can help researchers across the country with their work.

Click or Scan FOR MORE INFORMATION

DAVID WAGNER, PhD
Associate Professor, Cell and Developmental Biology, and his company, Op-T received a 2021 Advanced Industries Accelerator Grant from Colorado's Office of Economic Development and International Trade (OEDIT).



PREVENTING RADIATION-INDUCED ORAL MUCOSITIS
Courtesy of Xiao-Jing Wang, MD, PhD

Topical delivery of the fusion protein, tat-Smad7 (green), to oral mucosal cells (red) in a mouse results in its efficient uptake into nuclei and prevention of radiation induced oral mucositis (extensive oral ulcers). This approach represents a novel therapeutic strategy to treat and prevent oral mucositis which develops in 40-70% of cancer patients receiving chemo- or radiation- therapy.

GRANT AWARDS

APPEL, BRUCE
National Institute of Neurological Disorders and Stroke: $7,286,129
Mechanisms of Developmental Myelination
05/15/21 - 04/30/29

ARTINGER, KRISTIN
National Institutes of Health (NIH): $416,525
The Role of Epigenetic Modifiers in Regulating the Developmental Plasticity of Cranial Neural Crest Cells
06/01/21 - 05/31/23

BILOUSOVA, GANNA
DEBRA International: $330,000
Optimizing Gene Editing Strategies for Recessive Dystrophic Epidermolysis Bullosa
02/01/21 - 01/31/24

BOYLE KRISTEN
BROUSSARD, JOSIANE
CCTSI Translational Methods Pilot Grant Award: $60,000
Impact of Weight Loss on the Intrinsic Circadian Clock in Human Skeletal Muscle
05/01/21 - 04/30/22

BRUMBAUGH, JUSTIN
National Institutes of Health (NIH) $250,000
Defining Regulatory Roles for Histone H3 Methylation In Development
07/15/21 - 07/14/26

DeGREGORI, JAMES
National Institutes of Health (NIH) and National Cancer Institute (NCI): $1,250,000
Autophagy Regulation of Apoptosis and Necroptosis Within Cell Populations
05/01/21 - 04/30/25

FUJITA, MAYUMI
VA Merit Award: $165,000
Autoinflammation in Human Melanoma
10/01/21 - 9/30/22

FUJITA, MAYUMI
National Institutes of Health (NIH) and National Cancer Institute (NCI): $345,034
Modulation of Inflammasome-Mediated Cytokine Activation by EGCG in Human Melanoma
03/01/21 - 02/28/22

FUJITA, MAYUMI
National Institutes of Health (NIH) and National Institute of Allergy and Infectious Diseases: $2,969,880
The Role of IL-37 in Human Regulatory T Cells
07/06/21 - 06/30/26

FUJITA, MAYUMI
National Institutes of Health (NIH) and National Institute of Alcohol Abuse and Alcoholism: $408,187
Ethanol-Induced Skin Changes
09/01/21 - 07/31/23

FUJITA, MAYUMI
YAMAUCHI, TAKESHI
Cancer League of Colorado: $30,000
Non-UV Risk Factors of Melanoma
07/01/21 - 06/30/22

KOGUT, IGOR
National Institutes of Health (NIH) and National Institute of Arthritis and Musculoskeletal and Skin Diseases: $2,379,883
Developing a Platform for Human Somatic Cell Rejuvenation, Expansion and Genetic Engineering Using Synthetic RNA Molecules
05/01/21 - 04/30/26

KUMAR, T. RAJENDRA
National Institutes of Health (NIH) and Eunice Kennedy Shriver National Institute of Child Health and Human Development: $2,850,257
SH Glycoforms and Ovarian Signaling Pathways
04/01/21 - 03/31/26

LYONS, TRACI
SPARK/REACH: $200,000
A Novel Diagnostic and Companion Therapy for Breast Cancer
04/01/21 - 03/31/23

LYONS, TRACI
UCCC Aging and Cancer Pilot Grant: $50,000
Semaphorin 7a in Age/Parity Induced Breast Cancer Lung Metastasis
01/01/21 - 06/31/22

MAJKA, SUSAN
REINHARDT, LEE
MOORE, CAMILLE
RICHMOND, BRADLEY
SCOTT-BROWNE, JAMES
ROJAS, MAURICIO
ORTIZ, LUIS
ROOP, DENNIS
FRIEDMAN, RACHEL GERAGHTY
PAT NOZIK, EVA
KLEMM, DWIGHT
National Institutes of Health (NIH): $6,888,000
Mesenchymal Vascular Progenitor Depletion Promotes Lung Aging and Susceptibility to Emphysema
12/30/21 - 12/30/28

MAJKA, SUSAN
REINHARDT, LEE
National Institutes of Health (NIH): $335,918
Loss Of Progenitor Function Accelerates Lung Aging
07/01/21 - 06/30/26

PAYNE, KARIN
BRYANT, STEPHANIE
MCLEOD, ROBERT
VERNEREY, FRANCK
ZUSCIK, MICHAEL
National Science Foundation (NSF) $1,499,999
RECODE: Organoid Model of Growth Plate Development
12/01/21 - 11/30/25

PAYNE, KARIN
KREBS, MELISSA
Children's Hospital Colorado – University of Colorado/Colorado School of Mines Collaboration Pilot Award Program: $20,000
Targeting Angiogenesis for the Treatment of Growth Plate Injuries
06/01/21 - 06/30/22

ROOP, DENNIS
BILOUSOVA, GANNA
DEBRA International: $600,000
Translating Stem Cell Therapies for EBS into the Clinic
02/01/21 - 01/31/24

ROOP, DENNIS
NORRIS, DAVID
National Institutes of Health (NIH) and National Institute of Arthritis and Musculoskeletal and Skin Diseases: $1,892,776
Training in Translational Research of Skin Diseases
09/20/21 - 06/30/26

VERGARA, NATALIA
RENNA, JORDAN
BRZEZINSKI, JOSEPH
National Institutes of Health (NIH) and National Eye Institute (NEI): $387,000
Novel Tools for Screening Retinal Function Using Improved Human Retinal Organoid Models
09/01/21 - 08/31/23

WANG, XIAO-JING
JIMENO, ANTONIO
Cancer Institute: $15,000,000
Colorado Head and Neck Cancer SPORE
09/01/21 - 08/31/26

TOTAL AWARDS
$45,614,588

FEATURE ARTICLES

THE 'MAGICAL IRONY' OF TIM GARDNER'S LONG VOYAGE

Mark Stevens

Shortly before Christmas in 2020, Tim Gardner grew concerned about swelling in his stomach.

Fit, trim, and an active father and husband who worked and played hard, Gardner had enjoyed a healthy and stimulating life. Skiing. Golfing. Fly-fishing. Flying. And sailing. Originally from the Philadelphia suburbs, Gardner took to the Colorado lifestyle like a duck to water.

The sickness came out of the blue.

The pain increased to the point that Gardner checked himself in to the emergency room at the University of Colorado Hospital. The ER doctors and nurses ran tests and sent Gardner home. "They thought the pain would calm down," he recalls.

It didn't.

The holiday season meant gastroenterologists were on vacation. Gardner eventually found a specialist who agreed to an online appointment. "My stomach was getting really distended," he says. The doctor took a look at Gardner's stomach via Zoom and told Gardner to get back to the ER – pronto. It was New Year's Day, 2021.

"On the second trip, they really took the time to figure out what the hell was going on," says Gardner. The analysis took 10 days. Gardner had lymphoma. Specifically, large B-cell lymphoma, an aggressive non-Hodgkin lymphoma. He had the "triple hit" variety—dangerous rearrangements involving three specific genes that drive the lymphoma to grow rapidly while simultaneously reducing the ability of the lymphoma to die.

Treatment began immediately. The first round of chemo pushed Gardner's kidneys, heart and lungs close to failure. He was put on a respirator. "I was on death watch for about a week and then it took three or four weeks to get back to anything that was sort of stable and throughout most of that I was either asleep, delirious, or drugged," recalls Gardner. "I remembered some nightmares but that's about it."

> The voyage/adventure was more than I even dreamed it would be . . . For the rest of my life it has given me confidence to do things with unknown outcomes.

LEFT: Tim Gardner spent seven years building the infrastructure necessary to manufacture cutting-edge therapies at CU Anschutz.

In fact, Tim's wife Deb, his brother David and Tim's two sons Ben and Gus were left to huddle with the medical team and make critical decisions for Tim's care. When he came back to consciousness in late January, Gardner had to learn how to sit up. And walk. The chemo treatments—seven more rounds—would continue until June. "It was a very anxiety-prone, scary time. I was getting familiar with the idea that I had cancer and might not actually live," he recalled. In June of 2021, the chemo was complete.

"And we got the results that it didn't work."

Tim Gardner was at a critical crossroads. It wasn't his first big challenge in life, but clearly the one that carried dire consequences. Several options for treatment emerged. One involved a cutting-edge technology that Gardner knew on an up-close, intimate basis.

He'd spent the last seven years actively involved in helping make it happen.

Tim Gardner is the third of four boys. Gardner's father commuted daily from Philadelphia to New York City for his job in the paper business. Later, he worked in hospitals and restaurants closer to home. Gardner went from a "demanding and rigid" private school to the Deerfield Academy boarding school in western Massachusetts.

After prep school, Gardner knew he wanted to escape his east coast roots. Also, "I didn't want to go to a small school where people knew who I was and what I was doing." In 1977, he graduated from CU Boulder with a BS in political science.

Career? It could wait.

"I had a friend in college, Will Cowen, who was an adventurer like me. We were having a beer one afternoon and we discovered that we each had the same dream, and so we just shook hands and said we were going to do it," says Gardner.

That dream? Sailing across the Atlantic Ocean. The pair made crossings both ways in a 50-foot wooden sloop. The voyage took place before the availability of electronic navigation, so the pair relied on a clock and sextant to keep them on track—10,000 miles from Massachusetts to Nova Scotia, on to the Azores, Portugal, the Straits of Gibraltar and as far into the Mediterranean Sea as the island of Sardinia. The return trip stopped at the Canary Islands, West Indies, Bermuda, and back to Massachusetts. Friends joined them on various legs for four to six weeks at a time.

"The voyage/adventure was more than I even dreamed it would be," says Gardner. "For the rest of my life it has given me confidence to do things with unknown outcomes."

Back on shore, in 1979, Gardner had no plan. He met with advisers who steered him toward banking. "So then when I started talking to the banks, it was amazing. The HR people would either say, 'what the hell were you doing, playing around for a year on a sailboat? We don't want anybody like that.' Or they would say, 'Wait a minute. You did this? We want you to come work for us like now.' I could tell five minutes into the interview which way it was going to go."

Captain Tim's management of mini-emergencies proved his ability at sea and on shore.

Gardner opted for a job offer with a bank in Chicago. In the training program, he met Deb Froeb. They were married in 1981. Gardner worked on his MBA at night through the Kellogg School of Management at Northwestern University.

Froeb's keen pursuit of outdoor activities and their joint desire to live in a somewhat smaller city led them to Denver. Gardner worked first for a boutique investment banking company—William Blair & Co. Next he worked with a manufacturing company that made kitchen cabinets and, with his MBA in his back pocket, Gardner focused on marketing. "I interviewed with the treasurer, and he said, 'you know, you're a smart guy but you sound more like a marketing guy than a finance guy so you should go talk to our president.' They hired me."

In fact, throughout his career Gardner has blended marketing and finance. "You know, you think of the marketing guy being all hype and sales and the finance guy being the disciplined thinker, paying attention to the rules. I was sort of an odd hybrid. It's served me well."

He worked for five years for the kitchen cabinet company, and another 18 months after it was sold to Fortune 500 company Whirlpool Corporation. Tim then opted to lend his expertise to a series of start-ups.

"He was a sort of serial entrepreneur," says longtime family friend Ann Sperling. Ann first met Tim's wife Deb in the commercial real estate business before Deb switched out for a long career at The Nature Conservancy. "Tim handled a variety of roles, really—financing, new business development, marketing, or sales for early-stage or turnaround companies."

The Sperling/Archibald family often camped, sailed, and traveled together with the Gardner/Froeb family. On a sailing trip with six adults in The Grenadines, Sperling was impressed with Gardner's ability to tackle a variety of technical and weather-related challenges. "Watching him manage those mini emergencies reinforced in my mind his ability to step in as captain and completely muster leadership when the circumstances required."

Raising two sons led Gardner to an 11-year stint on the board of St. Anne's Episcopal School, including years as president and leading a search for a new head of school.

"What I really needed as the new head of school at St. Anne's was a board chair with wisdom and insight," reflects Alan Smiley, who would serve in that role from 2006 to 2019. "Somebody who conveys trust, loyalty, and confidence. Somebody who knows when to listen and when to offer advice. Somebody who is calm and thoughtful in times of tension. Somebody who has a sense of humor. Tim provided all of those things to me and more at that critical point in my career and I will be forever grateful to him for it."
When Gardner's friend Ann Sperling accepted an invitation to serve on the Gates Center Advisory Board, she soon realized that Gardner might have the perfect business and marketing skills that the Gates Center for Regenerative Medicine needed at the time. Sperling introduced Gardner to Diane Wallach, the board's co-chair. Wallach is the daughter of the former longtime Denver businessman Charles C. Gates, who long before his death in 2005 saw the potential for stem cell research and who established the center with a generous gift.

Gardner strengthened the Center's role within the university setting and helped drive the launch and build-out of the Gates Biomanufacturing Facility. If the GBF worked, patients at CU Anschutz would have ready access to the new therapies and treatments being developed under the broad banner of regenerative medicine.

"It was very challenging to prove-up an organization like that and get it compliant with FDA manufacturing requirements," says Wallach. "It was really quite daunting. To navigate that and bring the right people together and to make it happen, was truly remarkable."

One key for Gardner was hiring an executive director for the GBF—and in 2017 he landed Ryan Crisman, who had manufacturing experience at Juno Therapeutics, a cancer immunotherapy company that developed a CD19 directed chimeric antigen receptor T cell (CAR-T).

"I had always had in the back of my mind, 'could we make Colorado a cell and gene therapy hub?' And the more I talked with Tim, the more I realized this is the kind of guy who could make that happen," recalls Crisman.

When he joined GBF in 2017, Crisman took one look around and realized the design and build phase was well done but the facility needed time to transition to best-in-class drug manufacturing. "It was just lack of experience," says Crisman. "Starting up a facility, especially something as novel as cell and gene therapies, takes some unique experience. Having started up a facility like this before, I was able to identify some missing pieces and work with Tim to fill those gaps within the organization."

Next was "building trust with the university," says Crisman, and ensuring that the institution knew they would soon see a return on their investment. "Without Tim," says Crisman, "There is no GBF."

In May of 2017, the GBF reached a critical milestone when it manufactured its first clinical trial-grade product for direct infusion into patients. That first product involved treating multiple myeloma. CU Anschutz and the Gates Center's growing reputations had attracted one of the nation's leading cancer researchers, Dr. Terry J. Fry, who had investigated the potential of applying CAR-T therapy to many types of cancer. In the CAR-T process, a patient's own T-cells are isolated and genetically modified to fight cancer and then infused back into the patient's body.

"I will be forever grateful to the Gates Center's Director Dr.

Dennis Roop for giving me the opportunity to be the CFO of the Gates Center and to the GBF for allowing me the latitude to make the day-to-day operating decisions to help transform the GBF from start-up to operating manufacturing facility," says Gardner. Gardner retired from the Gates Center in early 2020 but didn't do a very good job of retiring. He began consulting with Crisman's new firm, assisting with the leadership transition at GBF into the capable hands of its current CEO Matt Seefeldt, and contributing as a board member with several non-profits. It was just before Christmas when the lymphoma started rearing its ugly head.

Tim Gardner finished his last of six rounds of chemotherapy on May 12, 2020, and two rounds of what's called CNS (Central Nervous System) prophylaxis on June 11. He also went through resynchronization therapy of his heart, improving the timing of how his ventricles pumped. The work on his heart allowed him to receive a full-strength dose of chemotherapy during his last couple cycles.

Gardner's doctor, Steven Bair, says that "getting lymphomas to respond to treatment is not the main challenge with double- and triple-hit lymphomas, it's getting them to go away and stay away for good. You're always thinking, 'what is the next step going to be?' In the majority of cases with this type of aggressive lymphoma, they tend to reach the end of treatment and still have persistent disease."

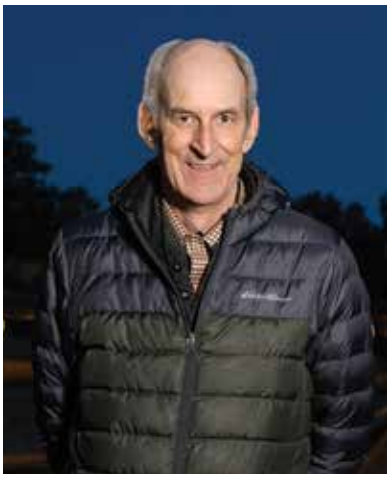
On June 24, a PET scan revealed exactly that Gardner's lymphoma was still hanging around.

"It was devastating," says Gardner's friend Alan Smiley, the former St. Anne's head of school. "You feel so helpless as a friend who loves this guy and yet you don't know what to say. You feel as if there's nothing you can do. It was so unfair. And yet your emotions and your feelings are a fraction of what he and his family are feeling. We all knew that."

"Tim was always focused on 'this is not going to fail.' He was always optimistic," says Bair.

One option was a second line of intensive chemotherapy followed by higher-dose chemotherapy and a stem cell transplant with his own stem cells—standard treatment for patients in Tim's situation. The second option, one that was demonstrating increasingly better outcomes, was CAR-T cell therapy.

"There were a lot of nuanced discussions," recalls Dr. Bair. "About what made the most sense." With GBF focused on products for clinical trials, Dr. Bair prescribed a product known as Breyanzi, manufactured by Juno Therapeutics in Seattle and the precise drug Dr. Crisman had co-developed before coming to GBF. Breyanzi had only been approved by the FDA two months prior to when Gardner needed it—and its clinical trials included patients at CU Anschutz. "I didn't know what CAR-T cell therapy was like from a patient's perspective, but I certainly knew how it was made," says Gardner. The next step was apheresis. Gardner's blood was circulated through a machine that filtered out T-cells. About six million of Gardner's cells were flown to Seattle. Over weeks, the T-cells were activated, multiplied, and transfected with a virus that gives the cells the genetic instructions to make the CAR (chimeric antigen receptor) and to express the CAR on the surface of the T-cell.



Tim attended the 2021 Charlie's Picnic at which he received the "Charlie's Angel Award."

Some two billion cells were flown back to Denver. Two injections put the CAR-T cells into Gardner's body in a process called infusion. The idea is that the CAR-T cells circulate throughout the body and identify the lymphoma cells because they recognize a protein expressed on the surface of these cells. The CAR-T cells then kill the cancer cells. Gardner was infused with CAR-T cells in August 2021. Except for a few days of a major fever, something his doctors anticipated, Gardner started to feel a little bit better every day. In December, a follow-up PET scan showed Gardner to be in complete remission.

"To have someone like Tim who was very involved in helping with the buildout of the Center and who helped make the GBF become so successful, and who was very involved with bringing CAR-T cell therapies to the facility, and for him to turn around and actually need that and to watch that journey and be the cheerleader on the side, it was very emotional for everyone," says Dr. Dennis Roop, the director of Gates Center for Regenerative Medicine.

"The irony of this whole journey," says Smiley. "It's a magical irony—he was so integral in creating the resources to make this kind of treatment possible and then to be the beneficiary of the treatment. It's something out of a storybook."

Gardner doesn't disagree.

"Either you can call it a coincidence, or you can call it a divine intervention," he says. "I tend to think of it as both."

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CHARLIE'S
PICNIC 2021
VIDEO

THE STEPPING STONES OF SCIENTIFIC COMMUNICATION

Madison Rogers

Communication is the foundation of scientific progress. The greatest advancements made in scientific endeavors occur when scientists are consistently and accurately communicating research findings across multiple levels of complexity.

As scientists, many of us spent our very early scientific careers studying examples of previous scientific communication in our textbooks. We may have analyzed the early cladograms investigating evolutionary relationships initiated by Will Henning, studied the first drawing of a cell with a cell wall by Robert Hooke, or read Charles Darwin's musings on evolution and adaptation.

At the surface level, these assignments seemed like a way to learn and appreciate how far science has progressed. They may have even left us bewildered by how little society once knew about the world around us compared to the depth of knowledge the scientific community possess now. However, digging a little deeper, these examples are an intricate study on communication—communication of the discovering, hypothesizing, experimentation, and analyses of many scientists that came before us.

This then allows us to investigate commonly asked questions about the way we as scientists discuss our research with the public: How do we best explain our results and our future directions? Who is privy to knowing and understanding scientific advancement? Is it only our scientific peers who have the privilege of learning, or do we have a responsibility to make science broadly understandable? These questions are asked time and again and, thus, require an analysis on how science is communicated today.

Let's start at the level of the scientist. To bolster scientific expertise, the traditional scientific route is to gain an advanced degree in a particular field of interest. The route to a PhD, in particular, has designated checkpoints along the way to determine a student's level of success. For a PhD student at the University of Colorado Anschutz Medical Campus, these steps include a preliminary exam in the first year, a comprehensive exam in the third year, and a doctoral dissertation to complete the degree with numerous, smaller points at which we are required to share our research progress. Each of these hurdles requires us to discuss our science on both a technical and analytical level, but they are primarily focused on effective writing, presenting, and communicating scientific knowledge, critical thinking, and future directions.

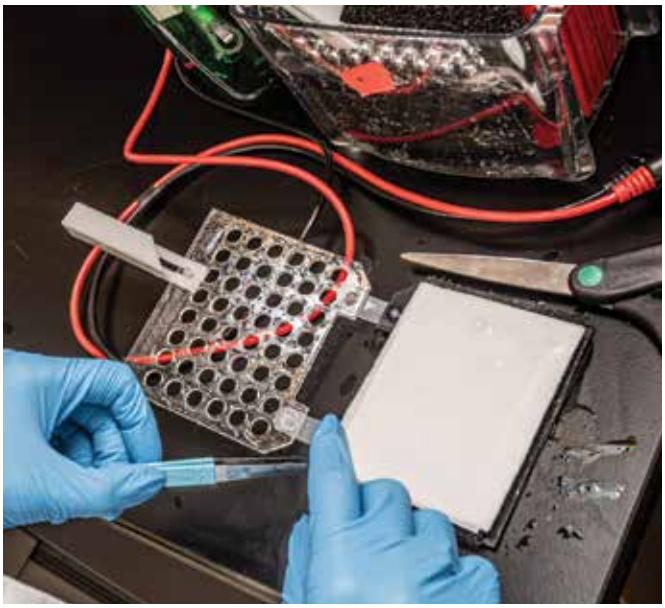
The requirement to successfully and accurately communicate ideas and results is arguably more important than scientific skill or the ability to perform a given experiment. These checkpoints are where we, as students, gain the most experience and expertise in our journey to a PhD!

Madison Rogers was a member of the first cohort of the Gates Summer Internship Program in 2015 and is currently a 5th year PhD candidate in the Cell Biology, Stem Cells and Development program. She has focused her studies on how biological specificity is introduced downstream of receptor tyrosine kinase signaling to allow a cell to respond to its environment. Madison aspires to work in science communication following her graduation from the University of Colorado Anschutz Medical Campus.

In fact, PhD students do not work to become doctors of cell biology, stem cells, or cancer biology. Rather, we strive to become Doctors of Philosophy (hence the PhD), which translates to quite literally mean "love of wisdom." It isn't the speed at which we pipette, the number of assays we know how to perform, or the significance of our data that defines us as a scientist. Instead, scientists are defined by the love of wisdom that propels us to continuously learn more, including learning how to communicate scientific advances to diverse audiences. Writing, presenting, sharing—these are the pillars of scientific success in an academic community. This is how we inform other scientists about our studies and allow them both to understand and become interested in our work.

Now let's move beyond the academic scientific community. First, we as scientists must learn to communicate to people outside of traditional academic or even industry-based environments who strive to gain scientific knowledge. They want to be in the know—did scientists find water on Mars? Was there a new species discovered in the depths of the oceans? What can jellyfish neurons tell us about human memories?

Today, there is a massive push in the scientific community to explain research to lay audiences. There are initiatives like "Gong Shows" where we explain our research in layman's terms and are "gonged" with a cow bell if we use any scientific jargon. There are outreach efforts to explain scientific research to high school students so that they understand it at a young age and get excited about furthering their own scientific knowledge. Additionally, there are competitions where we must explain our research in three minutes or less, so it must be concise and instantly captivating for the audience. The challenge behind each of these forms of communication is to balance engagement with accuracy. Preparation garnered from PhD-level training, as described above, ensures that we as scientists value this accuracy and don't lose sight of it as we expand our communication outwards.



But the question remains, how do we as scientists expand science communication in our immediate communities? Conveying scientific findings to family and friends is immensely challenging, yet incredibly rewarding. Science communication is putting an end to saying "It's too complicated to explain" when asked about a given research topic. It is delving into the PhD-level communication training to pull out the most important points in the most common terms.

> I love explaining my research to my non-science-oriented family because it is so rewarding when I can see the "light bulb" moment. This moment shows me that I have succeeded in communicating my scientific knowledge in terms that non-scientists understand.

It doesn't have to be a full-length presentation, but a few short phrases that get at the "why" behind my research and expand upon where my research is going. Further, when people ask my family what I research, I want them to be able to answer accurately so that the knowledge they have is circulated to their friends and loved ones. From there, the breadth of science communication is endless!

Bringing each of these components together, it is critical that we as scientists recognize our role beyond that of the lab bench or the computer screen—we are science communicators! Let's use our love of wisdom that we so carefully fostered to spread our data and analyses beyond the confines of our lab space and institutions. We as scientists must continue to develop innovative ways to describe our work and implement dissemination of knowledge. By doing so, our impact on the world around us will be tremendous.

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MADISON'S VIDEO
FOR LAYMEN

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FORMAL VIDEO

SCIENTIFIC UPDATES

EPIDERMOLYSIS BULLOSA

DETECTIVES AT WORK

Scientists from the Gates Center focus on Epidermolysis Bullosa (EB) and strive to make real progress treating this rare and debilitating skin disease. Scan the QR code below to meet some of the determined clinicians caring for these heartbreakingly afflicted patients and the devoted scientists searching for a cure.

L-R: Dennis Roop, PhD, Anna Bruckner, MD, and Steve Berman, MD

A SINGLE MUTATION CAN CHANGE YOUR LIFE

A Single Mutation in the Collagen 7 Gene Causes RDEB

CCCTGGGGCTCCTGAGTGCCACCTAGGGCGACCCCTTTC **Mutant Sequence**

CCCTGGGGCTCCTGAGTGCCACCCAGGGCGACCCCTTTC **Normal Sequence**

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FOR MORE INFO

CURES FOR THE UNEXPLORED REGIONS OF EHLERS-DANLOS SYNDROME

Calla Winchell

Calla visited the Gates Center lab that works toward a cure for her rare disease.

When you have a rare disease, you quickly learn that doctors who understand you are nearly as rare. Since my diagnosis at age nineteen, I've had physicians blatantly look up Ehlers-Danlos Syndrome (EDS) in front of me. When they misspelled it, it didn't exactly inspire confidence.

While getting a diagnosis had been difficult, that struggle didn't end once I had an answer for why my body seemingly worked differently than others. In the post-diagnosis years, I realized the painful lesson that there was no one who could or would manage my health, other than me. And in the first years, there was no guidance at all. Rheumatologists in Chicago, where I attended graduate school, would flat out refuse to see EDS patients at all, citing our complexity (a complexity I was even less qualified to manage). Unbelievably, it was up to me to research and pore over scientific publications I could barely understand and to try to get my head around the implications of this condition.

In addition to lacking treatments, EDS also struggles to be pigeonholed into a single medical discipline, leaving it mostly to be managed and coordinated by the patients themselves. Collagen is one of the underlying building blocks of soft tissue, so when your body cannot produce it correctly you end up with structurally weak tissue. That is what makes EDS so tricky: it straddles many different bodily symptoms and can express itself in a stunningly wide array of symptoms from constant nausea, easy and often joint dislocation, nerve pain, dizziness, poor vision, headaches, on and on. No two patients will present the same, in severity or symptom. You send the cancer patient to the oncologist, the multiple sclerosis patient to the neurologist. But where do you send us? There is no single specialist. For that reason, EDS is best managed in a collaborative model, with specialists coordinating care.

> The opening of Dr. Ellen Elias's Special Care Clinic at Children's Hospital Colorado addressed this lack of home for us and took the burden of management off me.

Before I even met the physicians, there were forms to fill out that asked specific questions about the condition that I'd never been asked before. They asked the right questions out of the gate and my experience only got better. I left the first appointment with the strangest feeling: what if my time as an ignorant expert on my own condition was finished? What if actual experts would guide me, better and more efficiently than my own bumbling?

Over the coming months, that question was answered. Yes, there were people there that knew more than me. What a relief! Accessing appropriate medical care had been difficult for me in Illinois and with my condition devolving, I needed more support than ever, not less. So, I moved to Denver from Chicago because I was so sick. The home I have found at CU Anschutz and the Children's Hospital's Special Care Clinic has turned things around for me.

I'm feeling better than I did half a decade ago, thanks to a combination of many things: adequate pain management, treatment of underlying comorbidities, the right medication for my dysfunctional stomach, and an EDS-aware physical therapist.

Symptomatic treatment of EDS has also improved, with more understanding of the constellation of comorbidities that can appear in an EDS patient; it turns out, many of us are Venn diagrams of several different, overlapping conditions, and that treating them all can significantly alleviate symptoms.

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NEW FRONTIER OF REGENERATIVE MEDICINE ARTICLE

To me, creations of centers like the Special Care Clinic are a testament to the progress made in recognizing and managing EDS. The concept is simple: all your specialists in one place, on one day. If I'm having an increase in stomach pain, my pain management doctor might pull one of the GI docs in to consult on which medication might be preferable. This clinical model is what I credit with the progress I've made with the condition; the team of experts there, headed up by Dr. Elias, make a compelling case for this collaborative organization of clinics to be applied to the management of EDS generally.

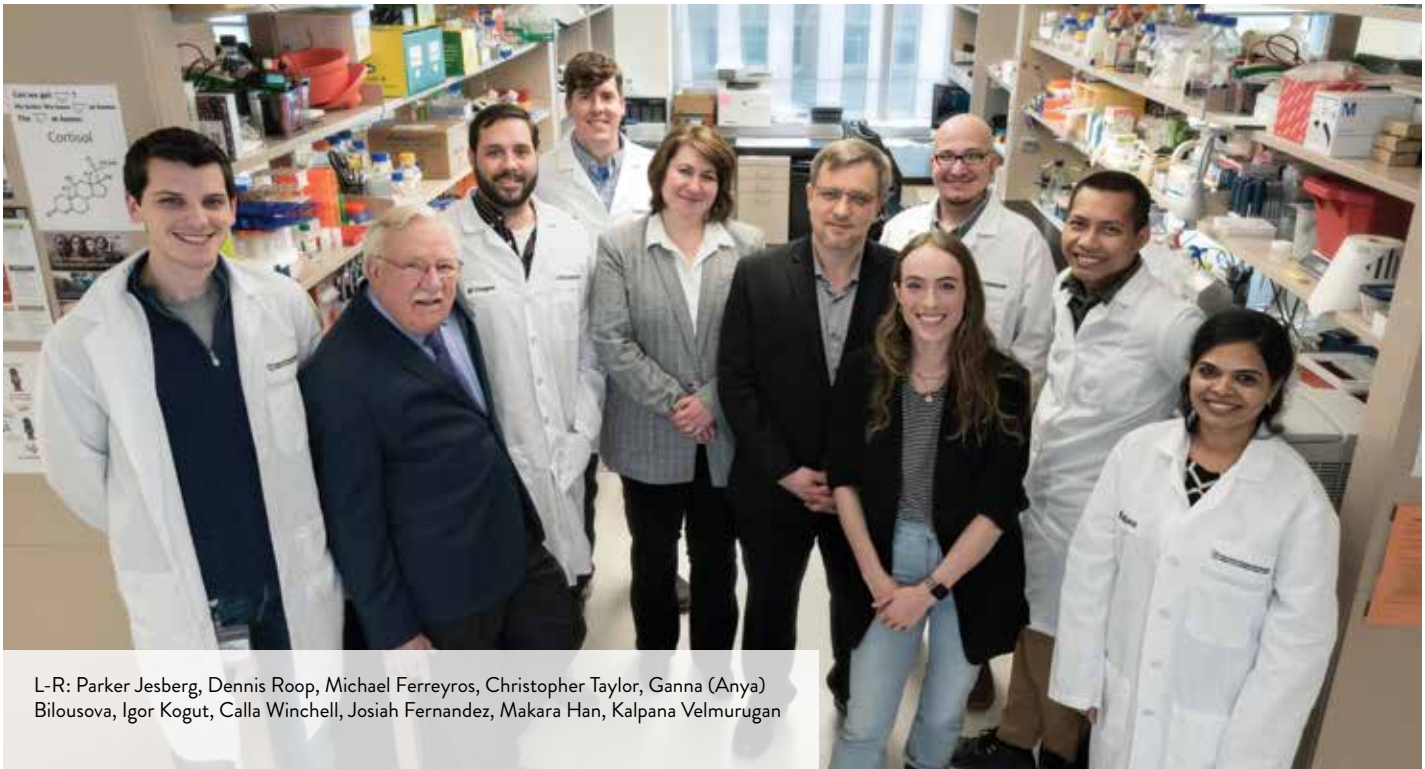
Meanwhile, a parallel team of experts have been working beyond symptom management at the Gates Center for Regenerative Medicine. EDS has no true therapies; this group, headed up by Drs. Dennis Roop and Ganna Bilousova, Co-directors of the Ehlers-Danlos Syndrome Center of Excellence Research Program, aims to change that. Then, after therapy, the much desired, much contested "c" word looms: cure. For a nineteen-year-old girl who, post-diagnosis, envisioned her life as slow but inexorable degeneration, that word stirs wild hope and trepidation. Being able to see that research take off, to actually meet the bright minds at work on this problem, has been healing for me, in a less literal and more emotional way.

There is much promise in the future treatment of EDS, as I learn in every research update. There are new methods of discovery to try or a new class of drugs which might slow degeneration of collagen. As a result, the sense of boundary expansion is exciting.

There are many unknowns. It reminds me of a map of Antarctica I bought from an antique store that was old enough that there were huge swathes of white, unexplored and unmapped regions. I was charmed by that representation of the unknown. The area of research with EDS that we are working on feels similar: it is deeply inspiring and exciting, but a lot feels unmapped and unexplored.

I've been privileged to be involved in the research. There's been a certain trend there: what had seemed simple invariably revealed itself to be complex the more an aspect of EDS was looked into. For example, the initial excitement of gene editing. Laypeople (read: me) envision a tiny scissor snipping out the bad gene and replacing it with a good one and while simplistic, that isn't necessarily wrong. Of course, the "scissors" will likely be a lab-created version of Cas9, the enzyme that cuts DNA to enable gene editing, taking advantage of the astonishing ability that viruses have to modify genetic codes. However, EDS is not caused by a single bad gene, or even two. It is heterogenous, meaning multiple genes are involved in its expression. What's more, not all of these genes have even been properly identified at all. So, it would be difficult for our proverbial scissors to cut out and replace what still remains unidentified. At least for now.

Having been sick for a decade now and having dealt with iterations of EDS problems my whole life, I have had little choice but to live up to my occupational title of patient. In 2024, it will be a decade since my own diagnosis. Predictably, my condition has progressed in those years and for many years I struggled even to get good symptomatic management of the condition. I felt trapped as I felt worse and worse, new systems of the body showing dysfunction, new dislocations of joints that had previously been okay. Yet in recent years, I am pleased to see a change, a shift, in the awareness and treatment of EDS. I've not had a physician need to look the illness up and even non-specialists, like ER doctors, have at least a jolt of recognition of the name. For all these reasons, all these steps forward, I feel a sense of optimism for the next decade of my illness that I could never have predicted. In the next ten years, I can only hope that every EDS patient (and truly, every patient with any underrecognized condition) is able to feel that same hope and to benefit from the advancement being done, in the clinic and the laboratory.



L-R: Parker Jesberg, Dennis Roop, Michael Ferreyros, Christopher Taylor, Ganna (Anya) Bilousova, Igor Kogut, Calla Winchell, Josiah Fernandez, Makara Han, Kalpana Velmurugan

COMMERCIALIZATION

THE GATES GRUBSTAKE FUND

Supporting the best ideas in regenerative medicine, and the talented researchers behind those ideas, is at the very core of the Gates Center's mission. One of the ways the Gates Center fosters promising research is through the Gates Grubstake program. The program, supported by private philanthropic contributions, makes annual awards to help teams of researchers speed their discoveries from the lab to the patient bedside.

One recent recipient of Grubstake funding is Traci Lyons, PhD. Dr. Lyons is a homegrown talent. She began her journey with the University of Colorado as an undergraduate at CU Boulder. She then went on to graduate studies in the Department of Pathology towards a doctorate in Biophysics and Genetics. Following her early career training at CU, Dr. Lyons served as a postdoctoral fellow in the lab of CU Cancer Center member Virginia Borges, MD, researching breast cancer. Dr. Lyons has dedicated her career to researching postpartum breast cancer, a subset of breast cancers typically diagnosed in young women after pregnancy. Postpartum breast cancer is all too common—with 150,000 to 350,000 worldwide diagnoses per year—and has a relatively low five-year survival rate. Because postpartum breast cancer affects young mothers, the disease has a tragic effect on thousands of families.

In late 2021, Dr. Lyons received a Gates Grubstake Award for her work on a new therapeutic approach to postpartum breast cancer. Postpartum breast cancers are more likely to become metastatic, spreading to other parts of the body. Dr. Lyons, along with her longtime collaborator Dr. Borges, is developing a monoclonal antibody therapy. They hope that the therapy will prove effective at killing cancer stem cells, the small subpopulation of cells that give rise to a tumor and allow the cancer to persist. Dr. Lyons and her team are testing the antibody therapy in mice in order to prove their concept.

"The Grubstake funding will aid in our development of a novel treatment for breast cancer patients that targets therapy resistant cancer stem cells," says Dr. Lyons. She hopes to take to this work to clinical trials within two years.

Dr. Lyons' work has garnered the enthusiasm of colleagues and collaborators at the Anschutz Medical Campus and beyond.

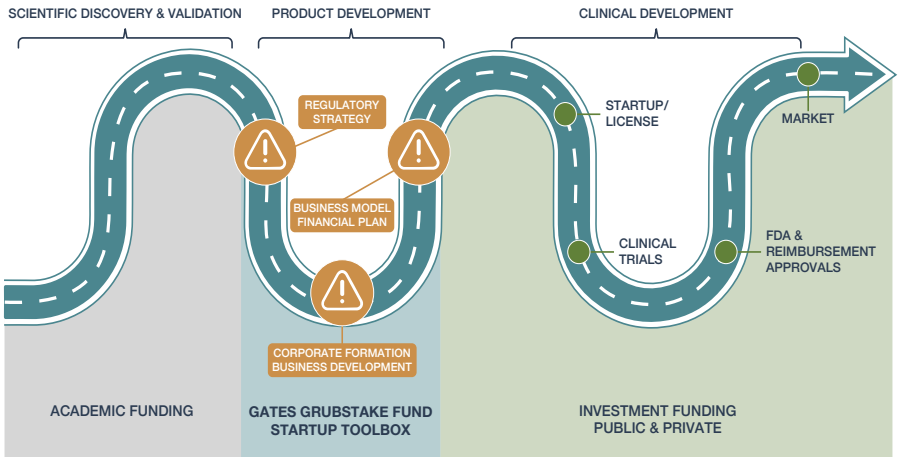
Heather Callahan, Director of Licensing at CU Innovations, works closely with Grubstake awardees. Heather is encouraged by Dr. Lyons' progress.

"Dr. Lyons and Dr. Borges are a fantastic team combining expertise in oncology research and medicine driving toward new therapies for breast cancer," says Heather. "They have partnered with an experienced business and research development team to found Perla Therapeutics and bring their new biologic to patients."

Dr. Lyons is just one of many talented researchers to have received a Grubstake award since the program's inception in 2014. The 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. The program uses a competitive grant

Traci Lyons, PhD, and her husband John at Charlie's Picnic 2019

THE PATH TO COMMERCIALIZATION



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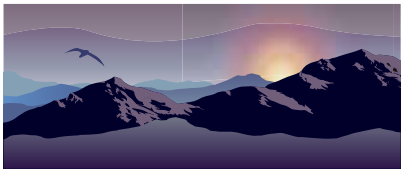
SCIENTIFIC INVESTMENT ADVISORY COMMITTEE BIOGRAPHIES

making process, managed by the Scientific Investment Advisory Committee, a group of volunteers with professional backgrounds in biosciences. The Committee meets each year to review applications from a pool of worthy contenders, and then receives presentations from a selection of applicants. Following the presentations, the committee members draw upon their experience in medicine and biotechnology startups to choose the year's awardees.

Dr. Lyons' Grubstake Award was generously funded by a group of Gates Center donors. These donors created the ABN Ohana Grubstake Award—the initials ABN refer to Atherton, Brooks and Newell families, and "ohana" is Hawaiian for family, a nod to their roots on the islands. Frank and Margie Newell say that the families "were inspired to support the program after learning of the great progress researchers have made towards taking the next steps in developing new regenerative medicine therapies."

The Grubstake program is a testament to the collaborative nature of the Gates Center: it is made possible through private philanthropy and facilitated by a committee of talented volunteers, and awardees aspire to partner with the Gates Biomanufacturing Facility to produce therapeutic products for clinical trials. The program has been a major success, providing hope that through research, philanthropy and teamwork, regenerative medicine will provide effective treatments for the most challenging diseases affecting patients today.

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 2nd Tranche funding to achieve a significant inflection point.



GATES **GRUBSTAKE** FUND

2021 GATES GRUBSTAKES AWARDEES

NICHOLAS JACOBSON, MDes
Voxel Printed Microstructures with Cells for Patient Specific Coronary Stents

Nicholas Jacobson is a research faculty member affiliated with the Inworks Innovation Initiative within the School of Engineering, Computation, and Design at the University of Colorado Denver and Anschutz Medical Campus. Nick and his team, which includes Dr. Mitchel Vedepo, a post-doctoral fellow in the Department of Bioengineering, and Dr. Gareth Morgan, the Director of Interventional Cardiology at Children's Hospital, received a Grubstake Award to design and test a 3D printed patient-specific heart valve with cellular ingrowth. The unique 3D printing technology was invented at Inworks and is currently being tested in numerous clinical studies for surgical planning. Building on this technology with biocompatible materials to focus on congenital heart disease will allow for over 800,000 patients to receive a heart valve replacement. This funding will accelerate development toward a working prototype for large animal testing.

TRACI LYONS, PhD
A Novel Therapeutic for Breast Cancer

Dr. Traci Lyons is an Associate Professor in the Department of Medicine at the University of Colorado Anschutz Medical Campus. Dr. Lyons received a Gates Grubstake Award to perform animal testing of monoclonal antibody based therapeutic in-mouse models of breast cancer stem cells and postpartum breast cancers (PPBCs), which are defined as breast cancers diagnosed within 10 years of recent childbirth. PPBCs appear to be enriched for therapy-resistant cancer stem cells, which may account for the high rates of metastasis observed in these patients. The therapeutic antibody has already proven efficacious in multiple mouse models of breast cancer, and exploration of its role in killing breast cancer stem cells will be evaluated. Thus far, the antibody appears to have minimal toxicities in mice. Worldwide estimates of PPBC range from ~150,000 to 350,000 cases annually, based on global breast cancer and/or childbirth rates, respectively. Since PPBC five-year survival rates of PPBCs are low, PPBC puts thousands of children at risk to grow up without their mothers. If successful, this therapeutic may result in life-extending or life-saving improvements by eliminating the effects, in part, of therapeutic resistance driven by cancer stem cell populations.

CHAITANYA PURANIK BDS, MS, MDENT.SCI, PhD
Dental Filling for Regeneration of Dental Pulp

Dr. Puranik is an Assistant Professor and Director of Predoctoral Dental Education in the Department of Pediatric Dentistry at the School of Dental Medicine and Children's Hospital Colorado, University of Colorado Anschutz Medical Campus. Dr. Puranik and his co-PIs, Drs. Devatha Nair and Michael Schurr, received a Gates Grubstake Award to develop a dental coating for dental pulp regeneration. Dental pulp is the living part of a tooth with blood vessels, nerves, and connective tissue. Unlike the outer covering of the teeth, pulp houses numerous stem cells which are capable of regenerative response after an insult, such as deep dental caries. Damage to dental pulp can cause patients to need root canals or even suffer the loss of their teeth. The annual estimated health care expense for management of dental caries in children alone is $5.2 billion. This funding will help complete studies for pre-IND filing with the FDA.

MICHAEL VERNERIS, MD
Therapeutic Development of Innate Lymphoid Cells

Dr. Michael Verneris, the Barton Endowed Chair of Pediatric Bone Marrow Transplant, received a Gates Grubstake Award to perform studies using stem cell-derived innate lymphoid cells. These tissue resident lymphocytes play a critical role in ameliorating intestinal inflammation and thus have promise in the treatment of intestinal inflammatory disorders, such as Crohn's disease (occurring in ~1% of the population). Crohn's disease is a devastating and life-threatening disorder that causes considerable physical, financial and societal burden. Dr. Verneris's laboratory has pioneered techniques to differentiate hematopoietic stem cells into Innate lymphoid cells, paving the way for clinical trials of cellular therapy for patients with Crohn's disease. Grubstake funding will be used to establish the activity of these cells in animal models, to scale these techniques to levels necessary to treat humans and to transfer this technology to the Gates Biomanufacturing Facility.

2021 2nd TRANCHE GRUBSTAKE FUNDING RECIPIENTS

JEFFREY OLSON, MD
Intraocular Device to Potentiate Retinal Stem Cell Transplantation in Macular Degeneration

Dr. Jeffrey Olson, Associate Professor of Ophthalmology at the Sue Anschutz-Rodgers Eye Center, used the first round of Grubstake funding to develop and test a prototype device for reducing intraocular inflammatory proteins associated with blinding conditions such as age-related macular degeneration (AMD) and diabetic retinopathy (DR). This preclinical pilot data catalyzed the formation of a startup company, AmpVision, which is actively pursuing NIH and NSF grants as well as private funding. The second tranche of Grubstake funding will help to move this technology into the FDA approval process with the goal of conducting First-in-Man studies.

2021 2nd TRANCHE GRUBSTAKE FUNDING RECIPIENTS

HOLGER RUSS, PhD
Generation of Functional, Patient Specific Thymi for Cell Therapy

Dr. Holger Russ is an Assistant Professor, Pediatrics in the Barbara Davis Center at the University of Colorado Anschutz Medical Campus. With the support of Grubstake funds, Dr. Russ has developed approaches to generate a functional patient-specific thymus from stem cells that has garnered considerable interest from business partners. Second tranche funding will allow Dr. Russ to conduct critical proof of principle experiments, using preclinical animal models. These efforts are geared towards transitioning histechnology into an industry setting with the goal to conduct clinical trials in the near future.

DAVID WAGNER, PhD
A 15-Amino Acid Peptide to Potentially Stop Demyelination and Restore Myelin Production 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 has successfully conducted a Phase 1a clinical trial for the treatment of autoimmune inflammation using a therapeutic peptide, OPT101, developed in part using the original Grubstake Award. In conjunction with the Colorado State University Veterinary Teaching Hospital in Fort Collins, CO, and partially supported by Grubstake Second Tranche funding, the efficacy of a canine version of OPT101 (OPT501) was tested in diabetic dogs and showed remarkable improvements in dog health with owners commenting on increased activity and general wellbeing. This year's Grubstake Second Tranche funding will continue to support studies in Type 1 diabetes and well as developing OPT601 for multiple sclerosis.

GATES GRUBSTAKE AWARDEES 2014-2021

AWARDEE		PROJECT		YEAR
In Vitro		NICHOLAS JACOBSON	ProjVoxel Printed Microstructures with Cells for Patient Specific Coronary Stents	2021
In Vivo	**Rodent**	TRACI LYONS, PhD	A Novel Therapeutic for Breast Cancer	2021
		CHAITANYA PURANIK, BDS, MS, MDent.Sci, PhD	Dental Filling for Regeneration of Dental Pulp	2021
		MICHAEL VERNERIS, MD	Therapeutic Development of Innate Lymphoid Cells	2021
		MICHAEL ZUSCIK, PhD	Abaloparatide as the First Chondroregenerative Therapy for Osteoarthritis	2020
		EDUARDO DAVILA, PhD	Tumor Infiltrating Lymphocyte Therapy	2020
		HOLGER RUSS, PhD	Generation of Functional Patient Specific Thymii for Cell Therapy	2019
		RAJ KUMAR, PhD	Production of Efficacious Recombinant Hypoglycosylated FSH Glycoform	2019
		MICHAEL VERNERIS, MD	Engraftable Hematopoietic Stem Cells from iPSCs	2018
		KUNHUA SONG, PhD	Genetic Conversion in Situ of Non-myocytes to Cardiomyocytes	2018
		ANTONIO JIMENO, MD, PhD	Exact Mice for Cancer Therapy Evaluation and Screening	2014
	Non-Rodent	ULLI BAYER, PhD	Pharmacological Restoration of Ischemic Spinal Cord Injury	2020
		VALERIA CANTO-SOLER, PhD	Stem cell-derived Retinal Transplant to Treat dry-AMD	2017
		KARIN PAYNE, PhD	Bioresorbable 3-D Printed Implant Pediatric Growth Plate Injuries	2017
Pre-Clinical	**Pre-IND**	RAM NAGARAJ, PhD	Therapeutic Peptide for Protection in Acute Closed Angle Glaucoma	2019
		MARTY ZAMORA, PhD	Autologous CD117+ Cell Therapy for Solid Organ Transplantation	2017
		STEVE DOW, PhD	Activated MSCs for Chronic Antibiotic Resistant Wounds	2015
		GANNA BILOSOUVA, PhD & IGOR KOGUT, PhD	High Efficiency & Quality Method for Producing iPSCs from Adult Cells	2015
		XIAO-JING WANG, MD, PhD	Smad7 for the Treatment of Wound Healing	2014
	IND/IDE	KEN LIECHTY, MD	Inhaled Nanoceria Conjugate that Prevents & Treats Pulmonary Fibrosis	2018
		"	Conjugated Nanoceria to Treat Inflammatory Disorders	2016
		JEFF OLSON, MD	Intraocular Device for Macular Degeneration	2016
		XIAO-JING WANG, MD, PhD	Smad7 for the Treatment of Oral Mucositis	2014
Clinical Trials	**Phase I/II**	TERRY FRY, MD	Optimized Manufacturing of CD19XCD22 Car Expressing T Cells for Clinic	2018
		DAVID WAGNER, PhD	Therapeutic for Protection/Regeneration in Type I Diabetes	2016

STARTUP TOOLBOX

The path from the "Eureka!" moment when a discovery is made to its use in patient care is like a long and arduous journey on a pot-holed road filled with twists and turns and occasional rockslides, in a car running on empty and in danger of getting lost. This is especially true when the discovery is made by a university researcher, as the skills needed to continue the journey are very different from the research that led to the discovery, and the future costs of development are orders of magnitude greater than the costs of the prior years of research. In industry, in addition to greater access to funding, researchers have teams of people who specialize in product development to prepare for clinical trials, other teams whose focus is to shepherd the new therapeutic through clinical trials, and yet other teams to commercialize the product for use in patients. Despite this, academia is the engine driving new discoveries for patient benefit. Fortunately, for entrepreneurs at the Gates Center for Regenerative Medicine, there are resources available to help bridge the gap between discovery and commercialization.

Startup Toolbox is Ann Sperling's brainchild. Ann, a member of the Gates Advisory Board and the Grubstake Scientific Investment Advisory Committee, recognized the need in 2017 after hearing pitch presentations from applicants for Gates Grubstake funding, which is generally used for continued product development. In contrast, Startup Toolbox provides microgrants to pay for regulatory support, market analysis, and business planning that is not typically available through standard academic funding programs. Startup Toolbox brings together a network of advisors and consultants to work with the scientists to guide them down the path of product development, clinical trial planning, financial planning, and commercialization. Startup Toolbox and the Gates Grubstake Fund work together to keep academic scientists driving down the road and to accelerate the commercial development of regenerative medicine innovations.

Startup Toolbox is jointly managed by the Gates Center and its partners at CU Innovations, which allows for synergies with similar programs managed by the venture team that includes Spark/REACH and the Chancellor's Discovery and Innovation Fund. Startup Toolbox currently has funding available for five to 10 microgrants, and the application form can be found online or scan the QR Code at right.

Ken Liechty, MD, a Gates Center member and Grubstake awardee, took advantage of Startup Toolbox resources to help with startup formation and the regulatory process. Dr. Liechty says that the program was "instrumental in connecting with regulatory consultants to start down the path to filing pre-IND packages with the FDA," which is a critical step toward approval for starting clinical trials. Likewise, Steve Dow, DVM, PhD, another Gates Center member and Grubstake award recipient, says that Startup Toolbox provided essential support in developing a business plan, generating pre-IND documentation and identifying regulatory consultants.

Ken Liechty, MD, Heather Callahan, PhD, JD, EMBA

With the success of their research, and help from Startup Toolbox, both Dr. Liechty and Dr. Dow have launched companies to take their discoveries to clinical trials.

CU Innovations Executive Director Kim Muller says that the success of Startup Toolbox "shows how we can support the very best ideas on their path towards clinical application." As an additional testament to the program's success, CU Innovations has launched a campus-wide program, modeled off Startup Toolbox, to support projects outside of regenerative medicine. The hope is that a campus-wide program will lower barriers to commercialization and allow faculty to focus more of their time in the lab developing the science. This new program received funding from the Colorado Office of Economic Development and International Trade in 2021 and will be up and running by mid-2022.

The Gates Center's Startup Toolbox program was made possible through private philanthropic support. The program demonstrates how Gates Center benefactors play an important part in not only supporting research, but also helping to ensure that the research makes its way to the clinics to benefit patients.

If you are a Gates Center member and interested in learning more about how Startup Toolbox resources can benefit your project, please contact Heather Callahan.

Click or Scan
STARTUP
TOOLBOX

CORE FACILITIES

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

CORE FACILITIES	CORE DIRECTORS	CORE LAB MANAGERS
FLOW CYTOMETRY	Eric Clambey, PhD	Christine Childs
GENOMICS	Bifeng Gao, PhD, MBA	Nicole Manning
HUMAN IMMUNE MONITORING	Jill Slansky, PhD Kim Jordan, PhD	N/A
HISTOLOGY (MORPHOLOGY & PHENOTYPING)	Igor Kogut, PhD	Laura Hoaglin
ORGANOID	Peter Dempsey, PhD Bruce Appel, PhD	Sean McGrath, PhD
STEM CELL BIOBANK & DISEASE MODELING	Ganna Bilousova, PhD Igor Kogut, PhD	Michael Ferreyros

FLOW CYTOMETRY CORE

The Flow Cytometry Shared Resource (FCSR) is committed to providing quality state-of-the-art cytometry-based research services through standard and cutting-edge equipment and continued education in cytometry-based research. The staff of the FCSR has more than 60 years of combined experience in all aspects of flow cytometry and cell sorting. They specialize in high-end equipment that performs sophisticated multiple parameter analysis and sorting in addition to standard assays.

The FCSR has a long-standing relationship with the Gates Center for Regenerative Medicine, supporting more than 25 Gates Center-associated investigators in the past year alone. FCSR services have supported research ranging from stem cell biology to oncology, spanning multiple areas of research focus for the Gates Center. Leveraging the established collaboration between the FCSR and the Gates Center, the FCSR has been able to acquire cutting-edge equipment to enable new scientific discoveries. These acquisitions have included the Agilent Novocyte Penteon flow cytometer, which provides researchers the opportunity to use a five-laser, 30 fluorescent channel instrument with a wide 7-log dynamic range for better signal collection. In addition to traditional fluorescent-based cytometry, the Fluidigm Helios Mass Cytometer allows our researchers to measure more than 40 different metal tagged markers in a single assay, to achieve comprehensive profiling of cellular states. The FCSR has also established a Mass Cytometry Antibody Bank, allowing researchers the opportunity to use this powerful technology with low up-front cost. An example of Dr. Xiao-Jing Wang's data generated with the Fluidigm Helios Mass Cytometer is shown in Fig. 1 (facing, top).

As a full-service facility, the FCSR staff provides flow cytometry education, assistance in experimental design, instrument and software training, troubleshooting, and the creation of figures and analyzing data for publication. Through its ongoing collaboration with the Gates Center, the FCSR seeks to empower new scientific discoveries and transform regenerative medicine.

Click or Scan FLOW CYTOMETRY

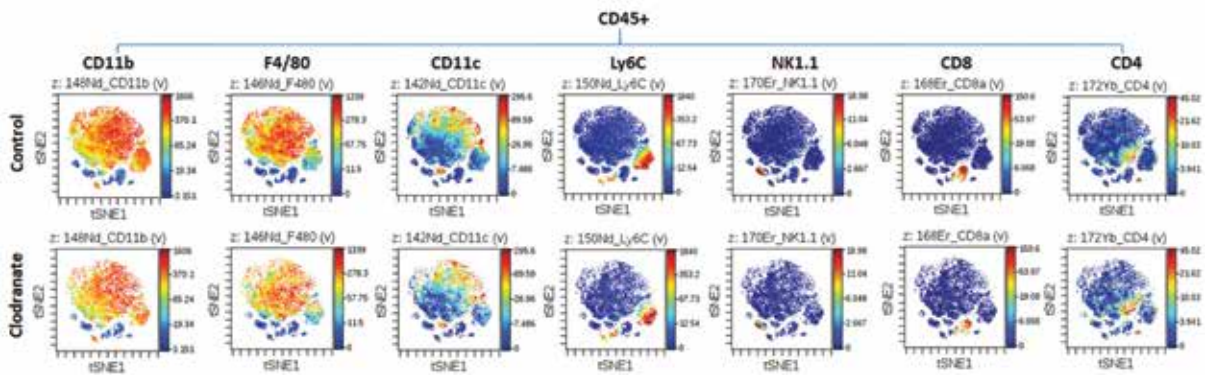


Fig. 1: Mass cytometry analyses of leukocytes in SCCs of control and clodronate-treated mice presented in t-SNE maps

GENOMICS CORE

The "omics" technologies and data have revolutionized regenerative medicine research and are increasingly being deployed to guide clinicians in diagnosis and treatment decision-making. The Genomics Core (GC) provides Gates Center members rapid and affordable access to cutting-edge Illumina next generation sequencing (NGS), 10X Genomics Chromium single cell and Visium spatial multi-omics, as well as NanoString GeoMx spatial transcriptomics, technologies for stem cell biology and regenerative medicine research. Members are further empowered with tools to interpret the genomic, transcriptomic, and epigenomic landscapes of individual tissues and cells as well as specific disease types and subtypes. In 2021, the GC supported 33 Gates Center investigators and made significant contributions toward their research. As an example, the GC supported Moumita Ghosh, PhD, in her research geared toward understanding the role of airway stem/progenitor cells during lung health and disease. Progenitor cells have important characteristics allowing them to return injured tissue to normal structure and function. This is critical for diseases that lack the ability to return organs to normal structure and function, such as chronic obstructive pulmonary disease (COPD) and lung cancer that may have defects in progenitor function. The GC has been instrumental for her research and helped her generate preliminary data to form the basis of multiple RO1, DOD grants and manuscript (Fig. 2 below).

COVID restrictions slowed down our ability to introduce new technologies and platforms to Gates Center members and other University investigators in 2021. Prior to the COVID closure we were in the middle of testing/training for the 10X Genomics Visium Spatial Transcriptomics. This project had been on hold primarily due to the inability to access needed equipment in three different buildings, as well as coordinate technician schedules. However, prior to placing this technology on hold, the GC was able to use the 10X Genomics Visium Spatial Transcriptomics platform to perform a pilot study for Drs. Xiying Fan and Dennis Roop. This pilot study generated beautiful spatial transcriptomics data comparing "equilibrium" vs. "escape lesions" that developed in their novel mouse model. This allowed, for the first time, observation of all three phases of immunoediting: elimination, equilibrium, and escape, in live mice. This novel model also revealed a role for innate immune

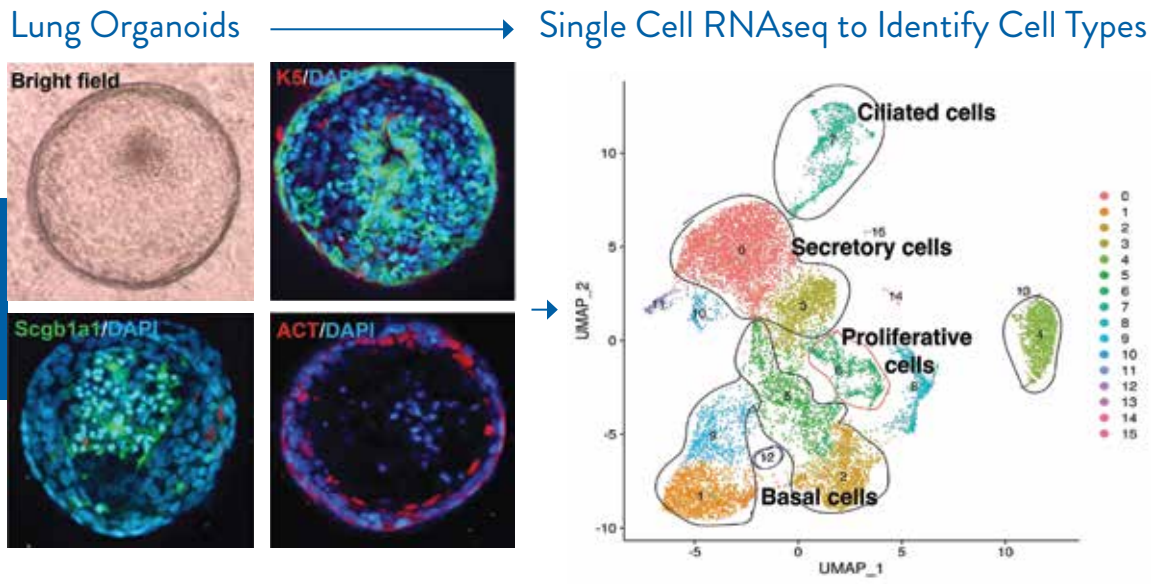
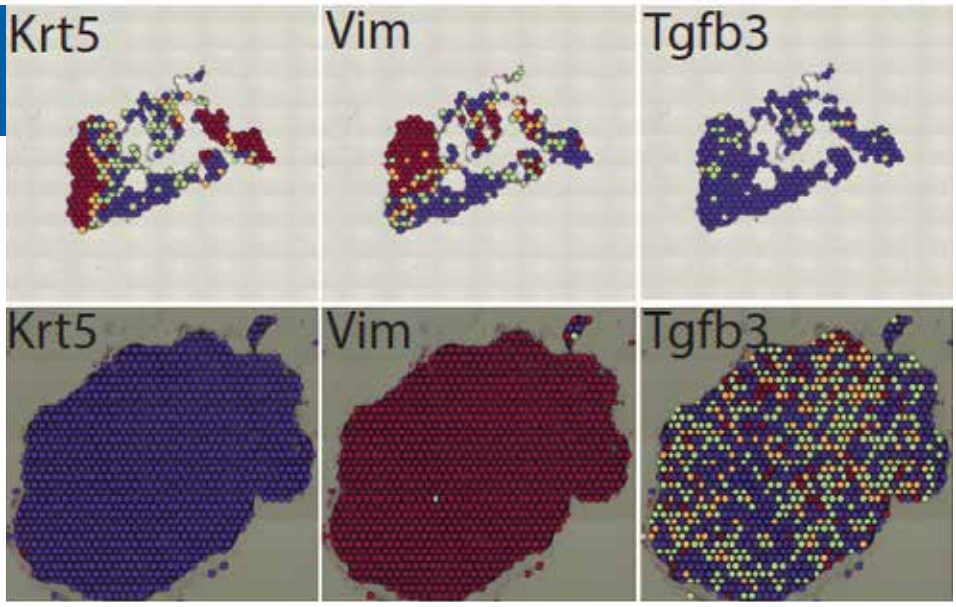


Fig. 2: Single cell RNAseq analysis to identify different cell types in lung organoids (generated for Moumita Ghosh)

Fig. 3: Spatial transcriptomics analysis



cells in the early stages of immune surveillance of skin cancer and in the maintenance of the equilibrium phase. The spatial transcriptomics data (Fig. 3, right) are in complete agreement with RNAseq data also generated by the GC (data not shown). These new preliminary data allowed these investigators to recently receive a fundable score on their revised NIH R01 application and document the value of the GC and other core facilities to Gates Center members. In 2021, the GC purchased the necessary equipment to conduct spatial transcriptomics analysis within the GC. The GC also acquired the NanoString GeoMx digital spatial profiler technology to strengthen our capability in supporting spatial biology research.

Click or Scan GENOMICS

Although COVID has disrupted our daily routines, the GC has made every effort to ensure that Gates Center members have access to NGS, single cell, and spatial genomics services and that their research remains robust. The GC is currently running at full capacity with a steady stream of NGS, single cell, and spatial genomics projects from Gates Center investigators. We fully expect this trend to continue.

HUMAN IMMUNE MONITORING CORE

The Gates Center offers 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, PhD, and Assistant Director Kim Jordan, PhD. The HIMSR offers state-of-the-art multiplex tissue imaging using high-parameter instrumentation.

- **MIBI:** The HIMSR leveraged resources from across campus to obtain one of only six Multiple Ion Beam Imaging (MIBI) instruments (IonPath) in operation in North America. The MIBI allows single cell analysis in situ using antibodies tagged with isotopically pure metal reporters to image up to 39 target proteins with a five-log dynamic range, and 250 nanometer cellular resolution. We have partnered with Dennis Roop, PhD, to develop a panel of antibodies suitable for the analysis of murine skin tissue and are excited to offer this panel to Gates Center members upon its completion (targeted for Spring 2022). The HIMSR also offers a standardized panel of 32 antibody targets for human tissue, with seven metal channels available for customization for Gates Center members.

- **Vectra Polaris:** This enables us to visualize and quantify tissue microenvironments in human, humanized mouse, and mouse model tissues on the Vectra Polaris multispectral fluorescence imaging system. We have worked with many Gates Center members to develop customized seven- and nine-color panels on this platform. An example of a multispectral image generated for Dr. Xiao-Jing Wang is shown in Fig. 4 (facing, top). 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.

- **Nanostring GeoMX:** The HIMSR has partnered with the Gates Center Genomics Core to offer members access to the "new" Nanostring GeoMX for spatial transcriptomics, which allows for whole transcriptome analysis of selective tissue regions without the need for microdissection. Building on our extensive multiplex IHC experience, HIMSR prepares tissue slides with standardized or customized protein targets and RNA probes for analysis in the Genomics Core.

Click or Scan IMMUNE MONITORING

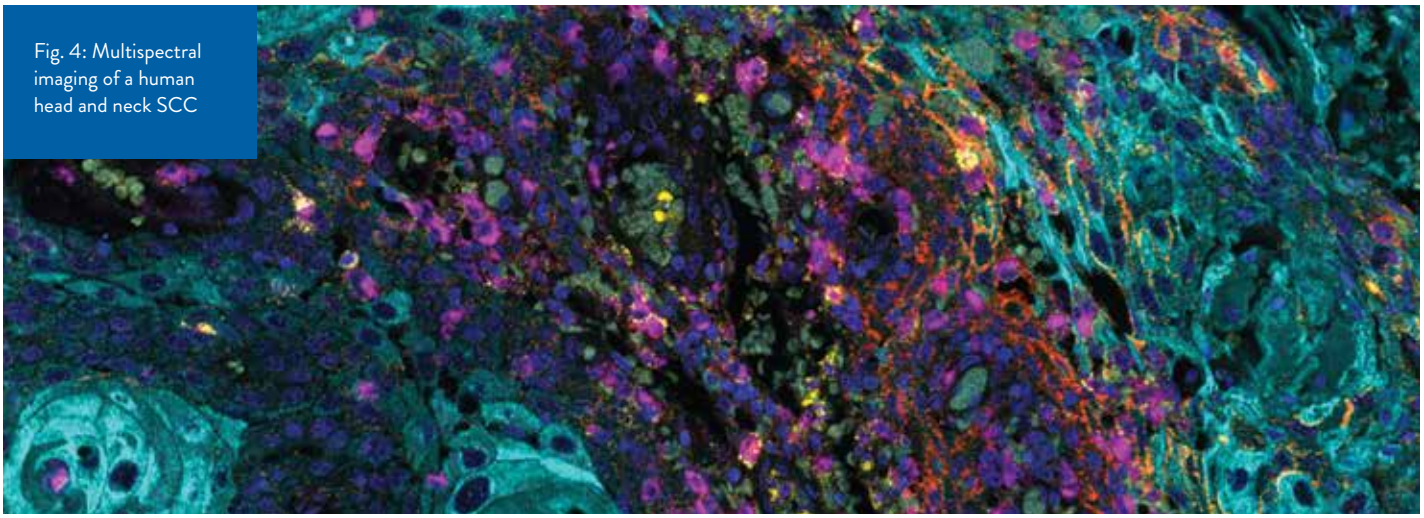


Fig. 4: Multispectral imaging of a human head and neck SCC

HISTOLOGY (MORPHOLOGY & PHENOTYPING) CORE

The Histology (Morphology and Phenotyping) Core has been part of the Gates Center for 14 years and is directed by Igor Kogut, PhD, and managed by Laura Hoaglin, HT (ASCP). Laura brings 28 years of Histology expertise to the core and was the founding manager of this core back in 2008. Over the years, the core has grown from eight PI core users to over 90 PI users, from CU Anschutz, CU Boulder, Children's Hospital, National Jewish Medical Center, and the Denver VA.

The goal of the Histology Core is to produce diagnostic quality blocks and slides to aid researchers in obtaining the very best data possible. The technicians are able to accommodate any special request and can help each researcher come to creative conclusions for the best histologic outcomes.

Services include:

- Paraffin and OCT embedding
- Sectioning of frozen and paraffin blocks
- Routine (H&E) and special staining (Trichrome, PAS, Fontana Masson, etc.) for all types of tissue samples (Fig. 5, right)
- Consultation services to optimize tissue isolation, fixation and technical customization

The core has invested in a top-of-the line Immuno-histochemistry and Immunofluorescence automated staining instrument that has the capability of staining up to 36 slides with up to 15 antibodies on each run. Each staining run will be completed in less than eight hours which will maximize turnaround time.

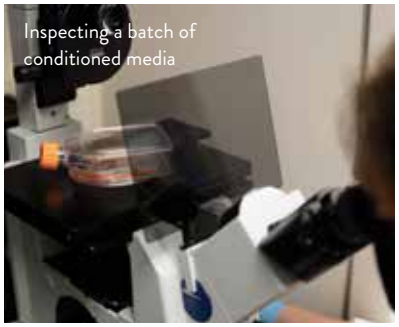
Click or Scan HISTOLOGY

Fig. 5: H+E stain of an 85-day old iPS Cell-Derived Skin Organoid. Note the presence of hair follicles as well as a fully differentiated epidermis. Skin organoid grown by Shennea McGarvey, histological section cut and stained by Laura Hoaglin.

ORGANOID CORE

The Organoid and Tissue Modeling Shared Resource (OTMSR), directed by Peter Dempsey, PhD, and Bruce Appel, PhD, from the Section of Developmental Biology in the Department of Pediatrics on the Anschutz Medical campus, became fully operational in July 2021 following its move into the Barbara Davis Center for Diabetes. 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 (Fig. 6, below). To support these activities, the OTMSR provides Gates Center members with discounted access to a variety of organoid technologies and services:

- Expertise and training in current and emerging organoid technologies for in vitro disease modeling
- Banked organoid and pluripotent stem cell (PSC) lines, which are fully characterized to meet and exceed emerging NIH guidelines
- Ready-to-use growth factors, 3D matrices, and fully validated conditioned medias to support organoid cultures
- Consultation, training, and implementation of genome editing technologies and gene expression systems in organoid models
- Data sharing of all Organoid Core-related resources, protocols, and technologies to Gates Center members and the Anschutz Medical Campus community

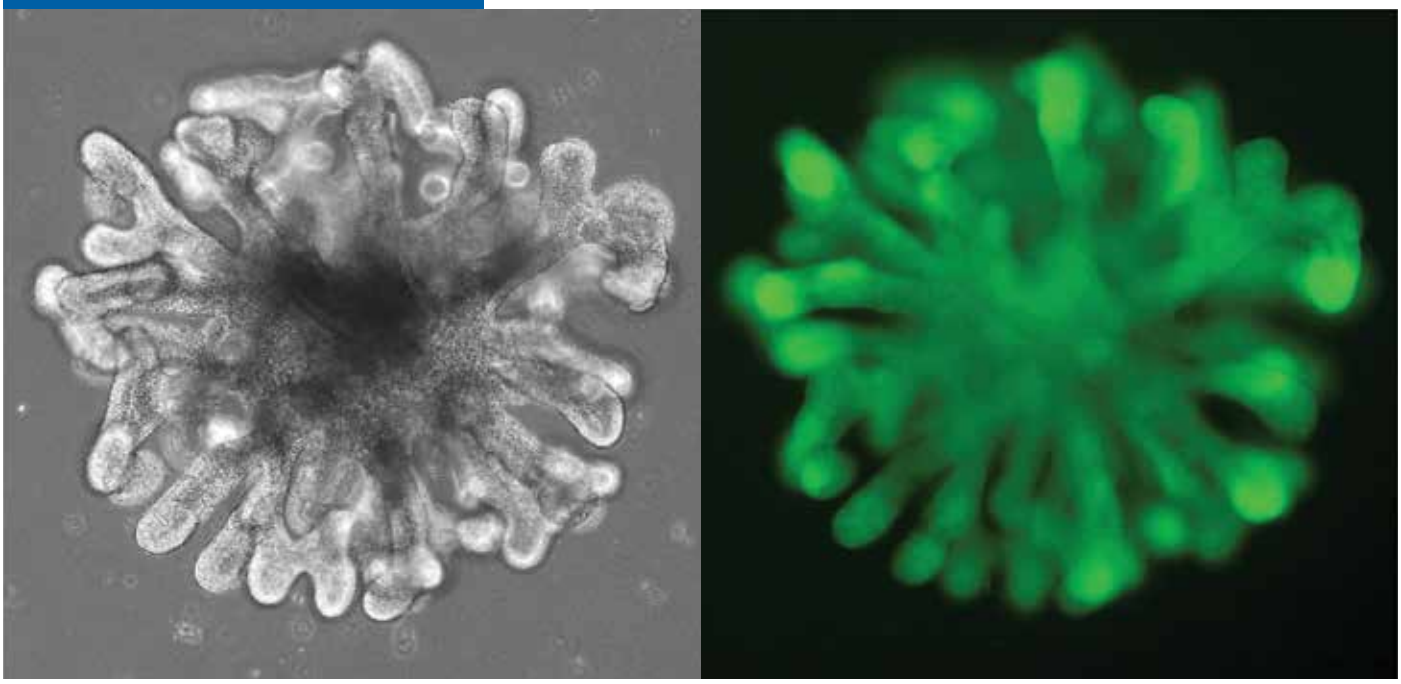


Inspecting a batch of conditioned media

Click or Scan
ORGANOID CORE

The OTMSR (managed by Sean McGrath, PhD, and operated by two research assistants Brandon Goldstein and Cole Skeffington), had a very busy and successful inaugural year, servicing many Gates Center members both at the Anschutz Medical Campus and CU Boulder. Holger Russ, PhD, (2020 Gates Grubstake awardee) Lori Sussel, PhD, and Joseph Brzezinski, PhD, utilized the OTMSR to develop a variety of genetically modified human PSC lines for their in vitro studies. Conditioned medias and cell culture reagents provided by the OTMSR have enabled organoid studies for many investigators, such as the development of novel lingual organoids developed by Linda Barlow, PhD. Intestinal organoids generated by the OTMSR have even made their way to Justin Brumbaugh, PhD, at CU Boulder, which he uses to study the epigenetics of intestinal cellular development and function. The OTMSR continues to innovate and provide the latest in 3D organoid technologies and looks forward to continued and expanded utilization by the Gates Center research community.

Fig. 6: Phase contrast and GFP images of Lgr5-EGFP intestinal organoids grown under stem cell conditions (phase contrast – left image; GFP –right image)



STEM CELL BIOBANK & 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 including Ganna Bilousova, PhD, associate professor of dermatology, Igor Kogut, PhD, assistant professor of dermatology, and Gates Center Director Dennis Roop, PhD. The process, which was described in a paper published in Nature Communications in February 2018, reports a clinically safe approach that consistently reprograms healthy and disease-associated patient's skin cells into induced pluripotent stem cells (iPSCs) with an unprecedented efficiency.

This core is co-directed by Drs. Bilousova and Kogut and offers complete services related to the production of high-quality human iPSCs from patient-derived somatic cells at a low cost, (Fig. 7, below). 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 and ongoing projects on the Anschutz Medical Campus and at CU Boulder, as well as for national and international external clients. In collaboration with Sara Sawyer, PhD, the core is generating a biobank of iPSCs from non-human primates and has successfully reprogrammed cells from a chimpanzee. The generation of iPSCs from non-human primates provides a valuable model for late preclinical development of regenerative medicine therapy products, such as iPSC-based therapies.

Additionally, the core continues working on projects initiated and generously underwritten by community benefactors. These include using iPSCs to determine the underlying causes and specific treatments of neurogenesis diseases such as epilepsy (this work is funded by Rick and Janie Stoddard) as well as using iPSCs and gene editing approaches to identify novel mutations that cause Ehlers-Danlos Syndrome (this work is funded through support from the Sprout Foundation, a Denver-area foundation funded by Suzanne and Bob Fanch, and Annalee and Wag Schorr).

Click or Scan
STEM CELL
BIOBANK
& DISEASE
MODELING

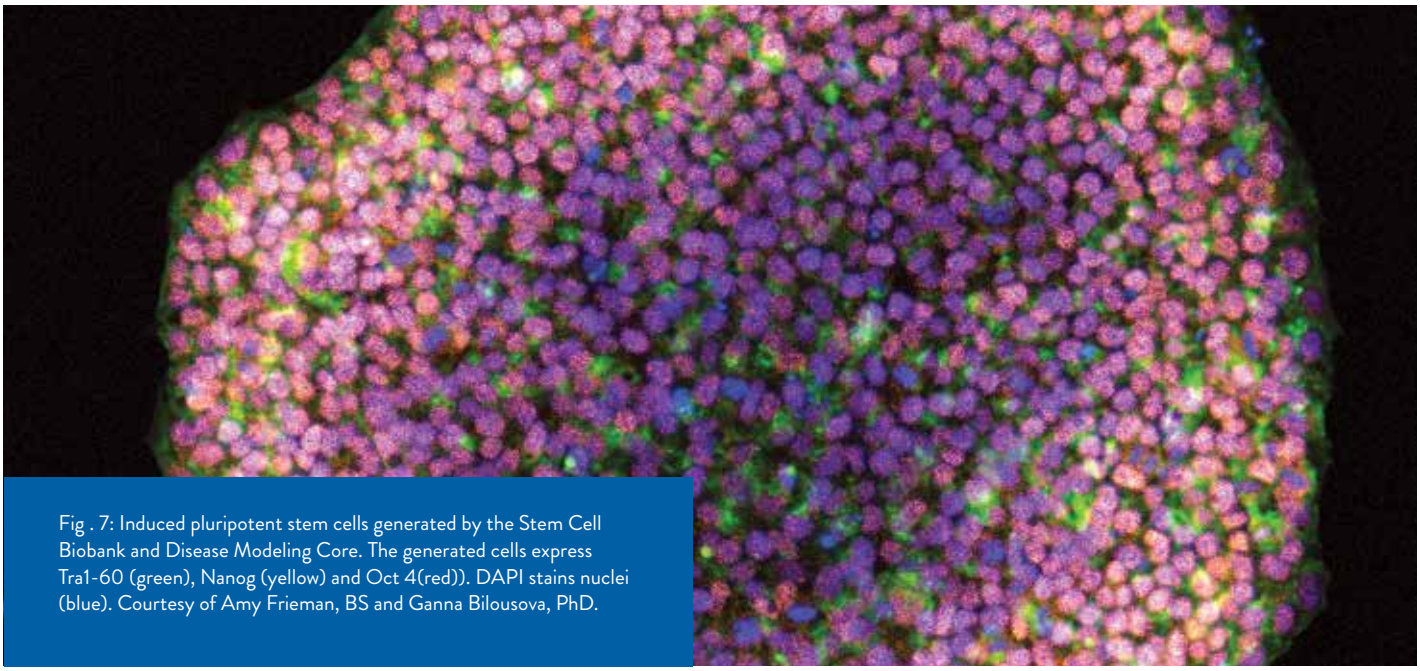


Fig . 7: Induced pluripotent stem cells generated by the Stem Cell Biobank and Disease Modeling Core. The generated cells express Tra1-60 (green), Nanog (yellow) and Oct 4(red)). DAPI stains nuclei (blue). Courtesy of Amy Frieman, BS and Ganna Bilousova, PhD.

GATES BIOMANUFACTURING FACILITY

PRODUCING HOPE, OPENING DOORS AND CREATING NEW THERAPIES—TODAY AND INTO THE FUTURE

GBF MISSION

Accelerate translation of scientific discoveries from academic and industry partners into human clinical trials as safely, efficiently, and cost effectively as possible according to high quality standards.

The Gates Biomanufacturing Facility (GBF) is coming of age and opening doors for innovative translational scientists both on and off the Anschutz Medical campus. Established in 2015, several years of intensive start-up followed. Labs were built out for technology transfer and process development to allow the GBF staff to take discoveries from basic science lab researchers and translate them into products to be tested in people with serious medical conditions.

This translation from a lab discovery to the manufacture of a treatment, for which the GBF was designed to facilitate, is highly complex. The GBF needed to prepare for all the components involved with defining methods for manufacturing the new treatment and developing analytic tests to assure absolute quality of the product. All this information, along with data on preclinical testing in test tube and animal models, is what needs to be submitted to the Food and Drug Administration (FDA) for an Investigational New Drug (IND) permit to begin clinical testing.

In parallel to these other start-up activities that were accomplished over the first few years, the detailed procedures for "Good Manufacturing Practice" (GMP) production of investigational agents for patient testing were put in place. The GMP clean room suites for cell therapy and protein and other biologic compound manufacturing were equipped and tested.

The nuts and bolts are now in place, but at its heart, GBF operations is about its people— passionate staff intent on developing new therapies for unmet medical needs such as cancer, wound healing, lethal genetic diseases and others. The staff at GBF come from diverse backgrounds and have varied training and expertise. However, they all share a number of key qualities that make the facility tick including high skill levels, inquisitive minds and team spirit. This blend creates an environment where solving problems of clinical relevance drive a spirit of innovation.

Beyond the facility and its staff, in order to successfully move forward with early phase, first-in-human research, GBF also had to effectively integrate itself into the complex matrix of stakeholders in the CU-Anschutz clinical investigation programs. This process began by building close alliances with the campus Regulatory Affairs office. Their team assures ethical and properly monitored conduct of research through the Institutional Review Board/ Human Subjects Committee and optimizes the safety of patients receiving these investigational products as well as safety of staff manufacturing and administering the agents through the Institutional Biosafety Committee. The Investigational New Drug applications generated by campus faculty working with the GBF also are managed through the Regulatory Affairs office to assure compliance with FDA guidance.The next essential elements to bring into the matrix were the adult and pediatric clinical research teams at the University of Colorado Hospital (UCH) and Children's Hospital Colorado (CHCO), respectively. Here, GBF leaders and project managers have worked closely with physician scientists and their research staffs at the two hospitals to develop detailed protocols that guide the various clinical trials. These protocols spell out which patients are eligible and once on study, how they are cared for and monitored for effectiveness and safety. Because the studies involve testing products never before used in human patients, there is often a "dose finding" or "dose escalation" component to the trials. These components aim to identify a safe and effective number of cells or milligrams of drug required to achieve the desired benefit. Project managers at GBF, research nurses and cell processing labs at the hospitals work through the logistics of getting the right treatment to the correct patient at the proper time.

To unify the on-campus efforts and translate discoveries by University of Colorado School of Medicine faculty, the Cell Therapy Operations Program (CTOP) was created under the auspices of the Vice Chancellor for Research, Thomas Flaig, MD. CTOP has proven highly effective at fostering productive, synergistic communication between the various groups.

At its heart and central to its mission, the GBF was developed to foster early phase clinical research based on new, innovative ideas created on the Anschutz Medical Campus. In addition, the GBF also offers its services to researchers at other academic institutions and in the biotechnology industry who share similar goals of creating new medical therapies.

To pursue its goals, GBF has organized itself around eight core teams and a central leadership group:

EXECUTIVE DIRECTOR **Matt Seefeldt, PhD**

PROJECT MANAGEMENT & SUPPLY CHAIN
Terri Foote, Director

CELL THERAPY GMP **Felicia Mast, MS, GMP Manager**

CELL THERAPY PROCESS DEVELOPMENT
Russell Marians, PhD, Associate Director

PROTEIN AND BIOLOGIC COMPOUNDS (BIO)
Gana Batt, PhD, Director

QUALITY ASSURANCE
Chandresh Undad, MS, Associate Director

QUALITY CONTROL **Chris Freedman, Manager**

FINANCE, FACILITIES AND ADMINISTRATION
Chuck Hickey, MBA, Director

CLINICAL LIAISON **Roger Giller, MD, Medical Director**

DOORS OPENED & ENTERED — WHERE WE'VE BEEN

The dictum "if they build it, they will come" has held very true for the GBF. GBF now enjoys a full stable of internal Anschutz Medical Campus and external national clients with whom they collaborate to bring novel products to the clinic for early phase investigation. The initial products manufactured under GMP rolled out to their respective clinical trials sites in 2018. Since that time, GBF has accomplished more than 70 GMP runs, delivering potentially lifesaving new therapies to patients. The model of serving both internal Anschutz and external clients has allowed GBF to serve more patients, expand its technical capabilities, gain increasing national exposure and move its balance sheet toward its goal of financial independence.

PAST AND ONGOING PROJECTS AT GBF INCLUDE:

■ ***Chimeric Antigen Receptor (CAR)-T Lymphocyte Therapy***
Patient lymphocyte blood cells are genetically modified by inserting a gene coding for a tumor protein receptor. The inserted CAR directs the modified lymphocytes to attack cancer cells that have resisted other more conventional treatments such as surgery, radiation and chemotherapy.

Diseases Targeted: Multiple Myeloma, Leukemia, Non-Hodgkin Lymphoma

Results to Date: Clinical studies are ongoing. Early preliminary results of the various phase 1 trials have shown feasibility of clinical scale manufacturing, acceptable toxicity profiles and signals of clinical activity with anti-cancer responses. Of note, interim results of the UCD19 trial of CAR-T cells for adult non-Hodgkin lymphoma have been accepted for presentation at the 2022 Annual Meeting of the American Association for Cancer Research (AACR).

■ **Natural Killer (NK) Lymphocyte Therapy**
NK lymphocytes are another type of cell with inherent anti-cancer potential. However, as with the CAR-T cells approach, enhancement of their numbers and function seem key to making them an effective therapeutic tool. Hence, GBF has engaged in projects involving co-culture of NK cells with a stimulating protein prior to administration and another involving insertion of gene for a growth factor capable of enhancing NK number and function. Approaches using both autologous (the patient's own) and allogeneic (donor) NK cells are under investigation. The latter allogeneic approach, if successful, would offer an "off the shelf" cell therapy product for cancer treatment, and reduce "time to treatment," logistical and cost concerns that exist with the more boutique autologous products.
Diseases Targeted: Melanoma skin cancer, Leukemia

Continued growth of GBF activities has led to recruitment of additional scientific, technical, facilities management and administrative staff, which now totals 60 FTE's. In addition, growth in the number of projects onboarded resulted in a need for additional process development, materials intake and storage and office and conferencing space. Hence, an additional 6000 sq. ft. of space in the Biosciences 1 building was acquired and renovated. This expansion brought the GBF total footprint in BSC-1 to 20,000 sq. ft.

PROGRESS AT GBF

It has been gratifying to see the GBF go from concept to reality over the past five years. It has been particularly exciting over the last few years to see an increasing number of promising new products move forward into clinical trials aimed at benefitting patients impacted by serious illnesses. The coming years look to be bright and productive at GBF.

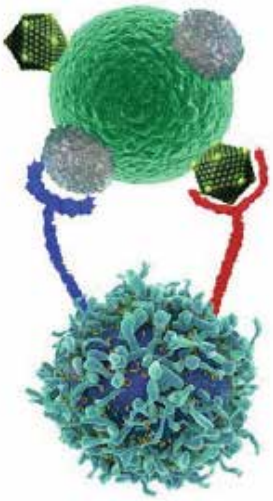
Matt Seefeldt, PhD, Executive Director

PRODUCING HOPE – INTO THE FUTURE

The pipeline of new projects at GBF remains robust. Some are ready to launch their clinical trials in 2022 and others in the technology transfer and process development phases are aiming for clinical trial openings in 2023 and beyond. These new initiatives include:

■ A New Kind of CAR-T Cell

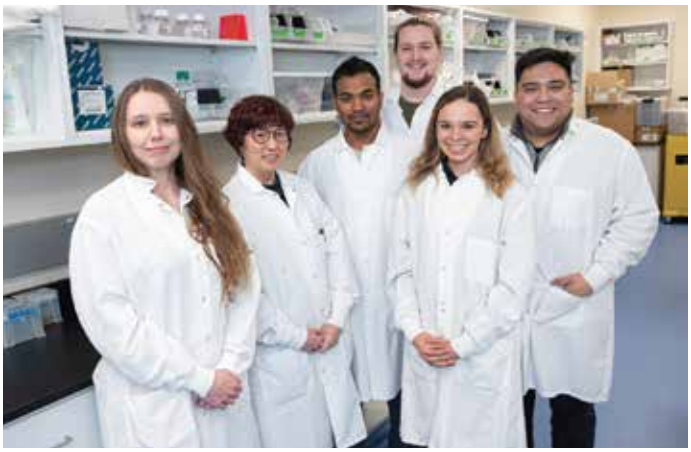
Current CAR-T cell therapies targeting the CD19 protein antigen have shown an impressive ability to cure some patients with heretofore intractable pediatric acute lymphoblastic leukemia and adult non-Hodgkin's lymphoma. This appears to be the case with the UCD19 product conceived by Terry Fry, MD, and manufactured at the GBF since 2020 for UC Heath/University of Colorado Hospital (UCH) and Children's Hospital Colorado clinical studies. While gratifying, other patients continue to have disease that resists CD19 targeting. In many of the cases, failure of the CD19 CAR-T cells is due to loss of CD19 on the cancer cell, implying that the cancer has evolved a clone that has selectively lost that protein antigen from the cell surface. The UCD19x22 CAR-T cell product has been developed in the Fry lab to target not one, but two protein antigens on the leukemia or lymphoma cell surface. This strategy hopes to overcome this important CAR-T cell resistance mechanism. The preclinical process development and GMP preparation work for the project has been accomplished over the past two years, and an IND has been secured. The UCD19x22 phase 1 clinical trial for non-Hodgkin's lymphoma was scheduled to treat its first patient at UCH in the first quarter of 2022. It is expected that pediatric leukemia/lymphoma trials with this new CAR will follow in later 2022.



Bicistronic CAR T Cell

■ New Applications of Existing CAR-T Cell Technology

The UCD19 CAR-T product has shown encouraging early results with respect to both tolerability/toxicity and cancer response in pediatric leukemia and adult lymphoma. We now have the opportunity to leverage these lessons learned and apply UCD19 to another unmet medical need, adult acute lymphoblastic leukemia (ALL). Adult ALL tends to have a poorer prognosis than pediatric ALL, in part due to biologic differences and in part because adults often cannot tolerate the aggressive chemotherapy regimens given to children and adolescents. Allogeneic bone marrow transplant is more often resorted to in adult ALL and that too presents tolerability issues. Hence, a new adult ALL trial is being developed at UCH to begin testing the hypothesis that CAR-T cell therapy may represent a more effective and less toxic alternative to intensive chemotherapy and bone marrow transplant in some patients. Investigations of this type also represent a paradigm shift in thinking about initial leukemia and lymphoma treatment, potentially moving cell therapy into the frontline.



Gana Batt, PhD (2nd from left), Associate Director of BIO, leads the GBF team responsible for synthesizing protein and other biologic compounds, such as messenger RNA for eventual phase 1 clinical trials.

■ Tumor Infiltrating Lymphocyte Therapy

Effective cell therapies for malignant solid tumors have proved more challenging to develop than those for blood cancers. This problem appears to relate to the barriers to immune cell entry and function in the solid tumor microenvironment. Dr. Eduardo Davila, a PhD scientist in Medical Oncology at CU Anschutz, is investigating extraction of patient lymphocytes from their tumors, expanding their numbers in culture and introducing genes that overcome tumor microenvironment resistance mechanisms. Dr. Davila is currently collaborating with the GBF to transfer this technology from his research lab to the GMP setting and do the necessary preclinical process development work to prepare an IND. Initial clinical trials are likely to focus on melanoma skin cancers and head and neck tumors.

■ Gene Therapy for Epidermolysis Bullosa (EB)

EB is a devastating genetic skin disease whose severe variants result in blistering and loss of skin with minimal contact, painful infection of the raw areas left by skin loss and premature development of aggressive skin cancers. Quality of life is severely impacted in affected children and their families, and an early death occurs by young adulthood, if not sooner. The most severe forms of EB are caused by genetically determined defects in production of Collagen VII, a protein that holds the various layers of the skin together. Dennis Roop, PhD, founding director of the Gates Center for Regenerative Medicine, has dedicated his career to finding treatment that addresses the underlying etiology of EB. He and his long-term collaborators, Drs. Ganna Bilousova and Igor Kogut have developed a method to genetically correct the Collagen VII gene in a patient's cultured skin stem cells, which can then be grown into a reparative

skin graft to cover the wounds these patients develop. Drs. Roop, Bilousova and Kogut and their team are currently collaborating with GBF scientists to transfer this technology from their research labs to the GMP setting and do the necessary preclinical process development work to prepare an IND. It is hoped that the first patients can be treated in 2023.

■ Alzheimer Vaccine Therapy

The vaccine compound will be synthesized by the BIO team for an outside biotechnology company, IMM. Alzheimer's Disease (AD) is a complex and multifactorial disease involving various genetic and environmental risk factors that together lead to the development of two hallmark pathologies: β-amyloid (Aβ) oligomers/fibrils/plaques and tau aggregates/tangles followed by inflammation and severe neurodegeneration. A recent report on anti-Aβ monoclonal antibodies (mAb) treatment suggests that high doses of these antibodies significantly reduce and/or clear pathological amyloid in the brains of vaccinated mild/moderate AD patients without providing substantial clinical benefits. These results support IMM's long-standing tenet that immunizations of cognitively unimpaired people with a dual vaccine, simultaneously targeting pathological Aβ and tau molecules, might be optimal for preventing or delaying the onset of AD. Based on this goal within the scope of the IMM and NIH cooperative AG060965 program, Gates Biomanufacturing Facility is manufacturing two recombinant proteins, AV-1980R and AV-1959. These drug substances, based on the universal MultiTEP technology, will be used for three different Phase I vaccine clinical trials.

■ New Inflammatory Disease Therapies

Life-altering and life-threatening inflammatory processes exacerbate a variety of common conditions, including acute lung infections, ulcerative colitis and diabetic wounds, and can impair recovery and even survival of affected patients. Ceria Therapeutics, Inc., a Colorado-based preclinical biotechnology company founded in 2019 by Ken Liechty, MD, a pediatric surgeon at Children's Hospital Colorado, is working on a novel solution to damaging forms of tissue inflammation. Their technology involves microRNA/nanoparticle conjugates that target inflammation and oxidative stress. Ceria is partnering with the BIO group at GBF to develop Good Laboratory Process (GLP) versions of the product for preclinical testing and GMP production methods for eventual human clinical trials of their novel drug product.

It's been a highly productive year at GBF. Despite the challenges presented by the COVID pandemic, GBF has persevered, grown and reached new heights—more projects, more INDs, more patients treated, greater financial stability—MORE DOORS OPENED WIDE!

Chandresh Undad, MS, Associate Director of Quality, leading a team meeting. The Quality Assurance Team reviews the production details and final testing results of all products manufactured in the GMP facility prior to their release for patient administration.

THE LONG PERSPECTIVE

Through the course of my career, I've had the privilege to witness and play a role in the arc of human cellular therapy as it's been developed over the past fifty-plus years. What began as more rudimentary bone marrow transplant to treat cancer, blood disorders and genetic conditions is now evolving to genetically modified cell products manufactured to precisely target cancer cells and correct life-threatening hereditary diseases like sickle cell anemia, immunodeficiencies and epidermolysis bullosa. GBF has become a growing part of that story.

Roger Giller, MD

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EDUCATION

THE GATES SUMMER INTERNSHIP PROGRAM 2021

On May 24, 2021, we joyfully welcomed the lion's share of the 25 Gates Summer Internship Program (GSIP) interns who were invited to join our Class of 2021 on the Anschutz Medical Campus. Composed of 14 students from the Class of 2020 eager to experience an actual on-campus internship and an additional 11 chosen through another enormously competitive selection process, interns arrived on campus on a variety of dates to accommodate their personal circumstances during what had proved to be another challenging year dealing with pandemic-related challenges.

Our Gates Summer Internship Program (GSIP) team began the 2021 year with a difficult assignment. This was due to planning for both a normal on-campus program along with contingency plans for a wide range of restrictions that might be implemented due to COVID. Mapping out where prospective interns might be located in mentors' labs on campus to maintain social distancing, ensuring students' vaccination status, and requiring out-of-town students to stay in downtown UC Denver housing were just a sampling of the myriad hoops our program jumped through to comply with COVID precautions and requirements instituted to keep our Anschutz Medical Campus safe.

The Class of 2021 was another extraordinary class able to take advantage of assignments in individual Gates Center members' labs, regular seminars covering an array of scientific, clinical, and professional development topics, and various social events in and out of the metropolitan area. Among this group of interns were three who ended up being prominently portrayed in a video included in this report entitled "Reflections from the Summer of 2021." Aleezah Balolia was due to begin her studies on campus in the Gates Center-supported Cell Biology, Stem Cells and Development (CSD) PhD program following her GSIP experience and could not have been a more enthusiastic booster for the virtues of the CU Anschutz campus. Jimmy Tangchittsumran,

2021 GSIP TEAM L-R: Jessica Taylor Heard, Jill Cowperthwaite, Jane Rech and Joe Brzezinski

who was assigned to the Gates Biomanufacturing Facility, was another member of the Class of 2021, but from a particularly non-traditional background. Jimmy had started out working as an apprentice under two well regarded Manhattan chefs but enlisted in the US Air Force after high school. Selected for the 48th Operations Group Airman of the Year, he received an early promotion to the rank of Senior Airman and served in the UK, Kyrgyzstan in support of Operation Enduring Freedom, and South Korea. Before being honorably discharged, Jimmy was awarded the Air Force Commendation Medal, Air Force Achievement Medal with two oak leaf clusters, Meritorious Unit Award, and Air Force Outstanding Unit Award with two oak leaf clusters. He later moved to Denver with his family, became an undergraduate research lab assistant at the Community College of Denver and applied to GSIP. Finally, our program included a very special deaf student from Ghana, Joseph Adjei, whose needs presented us with an enormous, but instructive opportunity to make our program more accessible to

our increasingly diverse intern population. Happily, we found a wonderful mentor for Joseph, and we provided American Sign Language interpreters for each seminar, event and staff meeting of which Joseph was a part. His mentor described him as one of the most brilliant students with whom he had ever worked, and we hope the gorgeous smile we often saw on Joseph's face is indicative of the positive nature of his GSIP experience. In short, the enthusiasm, intelligence, potential, and appreciation we saw in this Class of 2021 sustained and inspired us through yet another demanding year.

The Gates Center for Regenerative Medicine considers the Gates Summer Internship Program to be one of its most important offerings. Having the opportunity to inspire the next generation of investigators and clinicians is an enormous but gratifying responsibility, and we appreciate the many people who have banded together over the first seven years of the program to help us make a profound impact on 141 young people's lives. As we will never forget, our beloved, late Peter Grant and his wife Rhondda enabled the Gates Center to establish the GSIP program and see it grow by way of their encouragement, promotion, and generosity. Peter's wonderful bequest to the GSIP program in 2021 was a significant reminder of all he and Rhondda have done to help us and of his hope that the program might thrive through the support of others who might likewise treasure being a part of a program, which could have such a profound impact on talented, aspiring young people dedicated to science.

Following a summer of hard work in Gates Center members' labs, regular seminars covering an array of scientific, clinical, and professional development topics and various social events, we prepared for our Final Day Ceremony. Our interns each created a poster to describe their summer projects, and we gathered with mentors, family, friends, donors and the campus community on Wednesday, August 4, to celebrate the conclusion of the program. We were particularly pleased to inaugurate the Grant Family Distinguished Lectureship with the President and CEO of Washington D.C.-based Alliance for Regenerative Medicine Janet Lambert as our virtual speaker. Janet kindly met with the entire GSIP class and campus leadership before presenting a compelling picture of the public policy realm she inhabits as well as the regenerative medicine landscape and the many potential opportunities therein. The interns then shared their summer projects at a poster session and campus reception topped off by a celebratory dinner with their mentors and donors hosted by Gates Center Director Dennis Roop and his wife Betty.

FIRST DAY! GSIP CLASS OF 2021

STUDENTS & MENTORS

The GSIP Program has hosted 141 interns from 2015-2021

- The Class of 2021 was the largest ever with 25 students
- 32 mentors have participated in the program since its inception

JOSEPH ADJEI
Rochester Institute of Technology
Mentor: Ronald Vagnozzi, PhD
Poster Title: *The Effect of TLR7-Mediated Viral RNA Stress on Macrophages and Fibroblasts*

GABRIELLA ANNEST
University of California, Berkeley
Mentor: Mary Reyland, PhD
Poster Title: *Conditioned Media from PKCδ Knock Down Cells is Sufficient to Transfer Radioprotection*

ALEEZAH BALOLIA
The University of Colorado Denver
Mentor: Santos Franco, PhD
Poster title: *Ascl1 Cooperates with Shh to Promote Oligodendrocyte Fate*

ELIZABETH BELCHER
North Carolina State University
Mentor: Kristin Artinger, PhD
Poster Title: *Prdm3 Controls Neural Crest Cell Fate During Craniofacial Development*

CHIARA DART
The University of Colorado, Boulder
Mentor: Yiqun Shellman, PhD
Poster Title: *A Novel Regimen for Treating Melanoma: MCL1 Inhibitors and Azacitidine*

PHOEBE DILLON
University of Denver
Mentor: Kunhua Song, PhD
Poster Title: *Investigation into Alternative Modeling and Treatment of Hypertrophic Cardiomyopathy*

EVAN FEDOROV
Middlebury College
Mentor: Holger Russ, PhD
Poster Title: *Investigating the Functional Roles of NKX 6.1 and NKX 2.2 in Human Beta Cell Development*

STAUNTON GOLDING
Vanderbilt University
Mentor: Jeffrey Jacot, PhD
Poster Title: *Improved Capillary Like Network Formation in High Salt Fibrin Hydrogels*

DUSTIN GROSSMAN
Georgia State University
Mentor: Lori Walker, PhD
Poster Title: *The Molecular Basis of Cardiomyocyte Dedifferentiation*

SABRINA HAFEEZ
The University of Colorado Boulder
Mentor: Jennifer Richer, PhD, MS
Poster Title: Modulation of Heme Oxygenase-1 by Androgen Receptor to Enhance Survival and Stemness Properties During Breast Cancer Metastasis

CHARLES HENRY
Clemson University
Mentor: Joseph Brzezinski, PhD, MS
Poster Title: *Determining the Role of Enhancers in Otx2 Regulation in the Mouse Retina*

HELEN LI
Cornell University
Mentor: Maria Natalia Vergara, PhD
Poster Title: *Development of a Novel Stem-Cell Derived Organoid Model of Retinal Alzheimer's Histopathology*

DAYLE MATHENY
Ball State University
Mentor: Eric Pietras, PhD
Poster Title: *Itaconate and IL-1 Increase the Clonogenic Activity of Hematopoietic Stem Cells*

PARTH MODY
The University of Pennsylvania
Mentor: Curt Freed, MD
Mentor: Jeffrey Jacot, PhD
Poster Title: *Screening Drugs for Neuroprotective Effects in a Novel Parkinson's Disease Cell Model*

NUPUR PANDYA
Virginia Commonwealth University
Mentor: Linda Barlow, PhD
Poster Title: *An Examination of Retinoic Acid Signaling in Taste Cell Differentiation*

MEET PATEL
University of North Alabama
Mentor: Stanca Birlea, MD, PhD
Poster Title: *Understanding Cellular and Molecular Changes in Vitiligo Lesions That Do Not Respond to Treatment*

AMRITA PURKAYASTHA
University of Colorado Boulder
Mentor: Michael Verneris, MD
Poster Title: Lentivirus Transduction Into HSCs Results in Increased NK Cell Differentiation

NOAH RANIER
Colorado School of Mines
Mentor: Russell Marians, PhD
Poster Title: *Development of Potency Assay for CAR T Cell Therapy by Monitoring Cytokine Production*

ARTEEN RASTI
Purdue University
Mentor: Traci Lyons, PhD
Poster Title: *Semaphorin 7A Influences Survival Factors In Macrophages and Human Dermal Lymphatic Endothelial Cells*

KARINA SHARMA
Middlebury College
Mentor: Peter Dempsey, PhD
Poster Title: *Generating SOX2 and E-Cadherin Fluorescent Reporters in iPSC's*

NATALIE SHELDEN
The University of Colorado Boulder
Mentor: Ganna Bilousova, PhD
Poster Title: *Developing an In Vitro 3D Model of Ehlers-Danlos Syndrome*

CATHY SHI
Carnegie Mellon University
Mentor: Karin Payne, PhD
Poster Title: *Differentiation Potential of Implanted Mesenchymal Stromal Cells in a Cartilage-Mimetic Hydrogel for Growth Plate Injuries*

ELYSE SMILEY
Regis University
Mentor: Patricia Ernst, PhD
Poster Title: *Pre-Clinical Development of MLL2 Specific Inhibitors for Leukemia*

JIMMY TANGCHITTSUMRAN
University of Colorado
Mentor: Gana Batt, PhD
Poster Title: *Biologics Development and Manufacturing: Research Cell Bank*

RAECHEL TITTOR
Missouri Western State University
Mentor: Nidia Quillinan, PhD
Poster Title: *Cerebellar Stroke Causes Increased Activation of the Deep Cerebellar Nuclei*

GSIP SEMINARS 2021

TUESDAY, JUNE 8
NATALIA VERGARA, PhD
Assistant Professor, Department of Ophthalmology
Using Stem Cell-Derived Retinal Organoids for Therapeutic Development

THURSDAY, JUNE 10
JEFFREY JACOT, PhD
Associate Professor
Department of Bioengineering
Director of the Graduate Program
Laboratory-Grown Heart Tissue to *Understand and Treat Heart Defects*

THURSDAY, JUNE 17
WAGNER SCHORR, MD
University of Colorado School of Medicine Graduate, Transplant Pioneer, Gates Center Advisory Board Member, University of Colorado Medical School Admissions Committee

EMILY PATON
GSIP 2015 Alumna
University of Colorado School of Medicine
Fourth Year Medical Student,
Class of 2022
Medical Careers: Choices & Strategies

TUESDAY, JUNE 22
LINDA BARLOW, PhD
Professor, Department of Cell and Developmental Biology
The Sense of Taste: Development, Regeneration, and Dysfunction

THURSDAY, JUNE 24
NIDIA QUILLINAN, PhD
Associate Professor, Department of Anesthesiology
Ischemic Brain Injury – Beyond Acute Cell Death

THURSDAY, JULY 1
SANTOS FRANCO, PhD
Associate Professor, Department of Pediatrics
Control of Neural Stem Cell Fate in the Developing Brain

THURSDAY, JULY 8
KRISTINE SIKORA, PhD
Assistant Dean,
Director, Graduate School
Pathways to Translational Research and Medicine

THURSDAY, JULY 8
CELL BIOLOGY, STEM CELLS AND DEVELOPMENT, (CSD) PhD Program
Career Paths in Biomedicine Panel Discussion

THURSDAY, JULY 15
RONALD VAGNOZZI, PhD
Assistant Professor, Department of Cardiology
Translational Cardiovascular Research and the Dream of Heart Regeneration

FRIDAY, JULY 16
GATES BIOMANUFACTURING FACILITY
Introduction to GMP Manufacturing for Biologic and Cell Therapy Clinical Trials

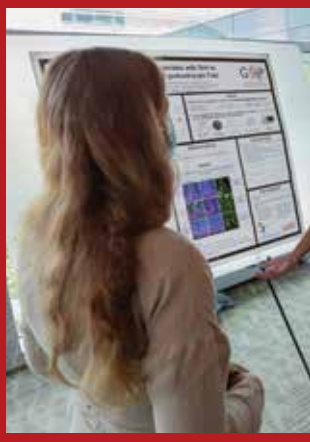
TUESDAY, JULY 20
ERIN GOLDEN, PhD
Director, CU Denver Office of Undergraduate Research and Creative Activities
Perfecting Your Pitch: Tips and Tricks for Effective Science Communication

THURSDAY, JULY 22
JEFF MOORE, PhD
Director, Graduate Program in Cell Biology, Stem Cells and Development (CSD) and CSD Admissions Committee Members
Applying to Graduate School

Ron Vagnozzi, PhD, hears about GSIP intern Elizabeth Belcher's summer project at GSIP's Final Day poster session.

I can honestly say that the Gates Summer Internship Program has given me my favorite research experience yet. I have met so many great people, learned so many new things, and seen more of the beautiful state of Colorado than ever before. I would sincerely like to say thank you for all of the support that you have provided to the program. Without it, I would not have had the experience I did this summer. Thank you again for your support of the GSIP program. It will continue to inspire young scientists in their journey of changing the world.

Charles Henry, GSIP 2021



FINAL DAY! GSIP CLASS OF 2021

FRONT ROW L-R: Dayle Matheny, Evan Fedorov, Raechel Tittor, Karina Sharma, Staunton "Hank" Golding
BACK ROW L-R: Gabriella "Ella" Annest , Cathy Shi, Phoebe Dillon, Charles Henry, Amrita Purkayastha, Meet Patel, Aleezah Balolia

Thank you so much for your kind support and guidance as we navigated the COVID-19 pandemic and everything that came along with it. Despite some setbacks, the two summers I spent as a GSIP intern were invaluable as I was provided an outlet for my scientific passions, allowed to grow as a scientist, and able to pursue cutting-edge research projects. I am honored to have been selected to participate in this wonderful, door-opening program, and hope that this opportunity is available to young students for years to come.

Aleezah Balolia,
GSIP 2020 & 2021

FRONT ROW L-R: Natalie Shelden, Parth Mody, Elizabeth "Lizzie" Belcher, Arteen Rasti, Helen Li
BACK ROW L-R: Nupur Pandya, Joseph Adjei, Sabrina Hafeez, Elyse Smiley, Noah Rainer, Jimmy Tangchittsumran

CAPTURING GSIP ON FILM: DIVERSITY OPENS DOORS

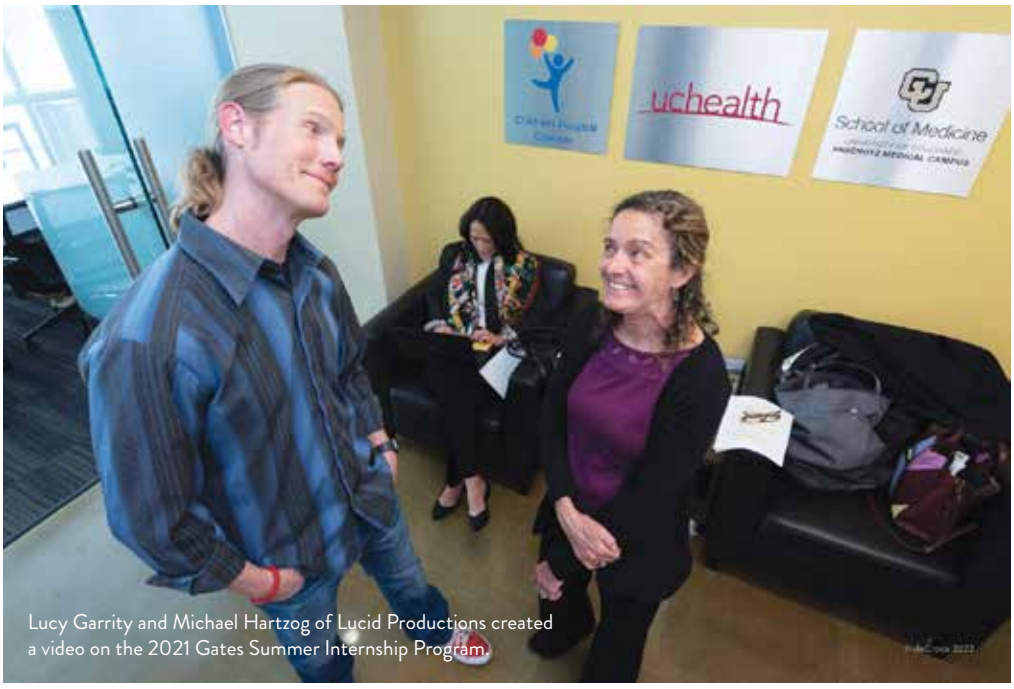
Lucy Garrity

Last summer, Lucid Narratives was invited to create a video story about the Gates Summer Internship Program (GSIP) for the Gates Center. As part of this process, we met with many of the students in the Class of 2021, and several of their mentors. We visited a number of labs where interns were working and were able to witness first-hand how GSIP (and other internship programs) serves as a powerful mechanism for connecting experts and practitioners with students who are aspiring professionals.

GSIP unites diverse groups of people around a shared purpose or mission. Mentors are world-class scientists and professors who represent a wide variety of backgrounds and sciences. They speak a plethora of languages and work in a multitude of research specialties. GSIP mentors are well-respected in their fields and often internationally renowned. Understandably, this heterogeneity among scientists and practitioners enhances scientific problem-solving and ultimately research discoveries and cures. GSIP students are also a diverse group, hailing from around the country as well as the world and bringing with them a broad range of university and training experiences. Program leaders report that as GSIP has become more established, and word of it has spread, the application pool has grown and the opportunity to include even more diverse students continues to expand.

AN UNPARALLELED EXPERIENCE

At a basic level, GSIP helps students determine whether they wish to pursue research or medical school (or both) for their advanced studies. Being on the Anschutz Medical Campus offers interns a full continuum, from world-class research through biomanufacturing to direct medical care. Researchers are working with minute biological particles and processes that the average (or above-average) person can neither understand nor pronounce. Partnering hospitals and hospital staff are recognized internationally for the care, compassion, and hope they offer patients. At the on-campus Gates Biomanufacturing Facility, moving lab discoveries toward clinical trials, the potential for alleviating suffering explodes exponentially, and students can experience both the technology and the hope involved. Participating in an internship program on a campus like CU Anschutz gives students intimate contact with a spectrum of activities, which can help them explore where their passions and skills might be applied most effectively.



Lucy Garrity and Michael Hartzog of Lucid Productions created a video on the 2021 Gates Summer Internship Program.

Researchers and practitioners are all motivated to develop cures for devastating diseases and ultimately create a future in which human suffering from disease is dramatically diminished. The robust nature of this vision implies overcoming intensely complex scientific and medical challenges that are ongoing and likely to be multigenerational. GSIP builds for the future of this system.

> GSIP mentors participate in the program for a variety of reasons. One mentor is motivated to encourage girls and young women in the sciences. Another mentor never had a lot of research opportunities as an undergraduate student and wants to help make opportunities available to undergraduates. Some mentors had great mentors themselves and want to "pay it forward."

The scientists are passionate and love to talk about their research, and some GSIP participants shared that having interns helps mentors learn how to communicate about their research more effectively. With interns, mentors learn and practice explaining their research to someone who is both knowledgeable and curious. A mentor helps an intern learn about options in research and medicine, and an intern helps a mentor learn and improve communication with other scientists, family and friends, and potential funders.

MAKING STRONG MATCHES

Ron Vagnozzi, PhD (he allows me to call him "Ron") is a mentor because he loves to share his passion and is deeply grateful to his own mentors. Ron grew up in Philadelphia and fell in love with science in middle school. In science he discovered a whole other world that he found fascinating, baffling and exciting. Later, when he studied biology, he was captivated by the idea that "all these different cells are talking to each other." Although he was intrigued by biological processes, it wasn't until college that he came to appreciate what a career in this area would look like.

A biology major, Ron did a lab rotation in college, which inspired him to get a job working in a lab and he fell in love. As he recalls, he particularly enjoyed learning about living organisms. He was captivated by the science of trying to understand how they communicate, what they are saying, and certainly what they are doing in response. He loved defining questions and then doing experiments to try to find answers. Trying to understand this world, teeming with different players, conversations, inputs and responses, became his passion. Ron met his first mentor by chance when he was in graduate school, and this set him solidly on a path in cardiology research and teaching.

Ron's 2021 GSIP intern, Joseph Adjei, shares his endless fascination with science. Joseph freely admits that he wants to learn about and understand everything. Joseph was born and grew up in the Republic of Ghana (Ghana), a country on the west coast of sub-Saharan Africa. While Ghana is approximately the same geographic size as Colorado, the population is much denser (31 million versus Colorado's population of 5.8 million - in 2020). English is the official language, plus there are over 50 indigenous languages. Joseph's family lives in Tema, which is a city of around 161,000 people (a little smaller than Fort Collins) and located near Ghana's capital city of Accra.

In some ways, life in Ghana is similar to life in Colorado. Mornings start with preparations for school and work, and evenings are for family and social times. Most people work in small business settings, and this includes young people. Family life includes cooking and eating at home and church on Sunday mornings. Joseph's life in Ghana was a little different from his family's, in that he is deaf. On Sunday afternoons, Joseph was part of a community gathering of local deaf and hard-of-hearing people who share information and connect. This group swaps news about job openings, significant events, important announcements, and other information that hearing relatives do not offer.

In Ghana, Joseph was drawn to science but there were no science labs for students, and studying science was a difficult task. Joseph also felt the subject was inaccessible to him because "it was for the highly intelligent," which he did not consider himself to be.

Despite that mentality, he loved whatever he could learn and shared what he learned with his classmates. His scientific understanding was decidedly auto-didactic (self-taught) through his primary and into his high school years. While his passion and interest were clear, advanced education in science was a tough path for him to follow. Scientific studies in Ghana were underdeveloped, especially for a deaf person like Joseph. In addition, he "was never in a viable financial position to study in any tertiary institution."

Throughout his youth in Ghana, Joseph had multiple experiences where deaf people had trouble receiving proper medical care because of communication challenges (sometimes with devastating consequences). He says the U.S. is better but admits there is great room for improvement. Generally speaking, quality communication is critical in medical (and other) environments and because of his personal experiences, Joseph is extremely motivated to "lead the way" in helping medicine better serve deaf people. As fortune would have it, a friend who was a few years ahead of him in school became a Rochester Institute of Technology (RIT) student. This friend helped Joseph understand the international student application process; he applied to RIT and was accepted. At RIT, said Joseph, "the access services offered are boundless!" Similar to Ron, Joseph's life took a meaningful turn when he encountered a science lab during his orientation week at RIT. He is now committed to science and medicine. Joseph took particular interest in GSIP because it was offered in a medical school environment and (he) found the research fields where interns got the opportunity to work unique and interesting.

WORKING IN HARMONY

Ron's cardiology lab conducts research related to heart function, cardiovascular disease, and cardio-immunology. One research angle involves the impact of viruses on the heart. In my best understanding, one impact of cardiovascular diseases is that they stimulate the cells holding the heart cells together (the body's natural defense system) to overproduce. This, in turn, produces "scarring," which at a certain point becomes counter-productive and inhibits healthy heart functioning. The lab's question was: Do certain types of viruses have a similar impact, in effect making them another potential form of heart disease? When Joseph came into the lab, he already had a vision (as Ron puts it)—he wanted to "study a particular component of the immune response of the heart"—so Ron and Joseph designed a project around that.

The lab team is relatively small, and Joseph worked closely with Ilaria Ferrari, Ron's research assistant. Ilaria is currently applying to MD/PhD programs and has worked as an EMT and in the ER. During these experiences, she found that protocols that were given were somewhat limited, and she is committed to improving these for patients and practitioners. Thinking about protocols, which are essentially communication guides for activities, Ilaria was well-equipped to work with Joseph's unique communication needs. According to Ilaria, Joseph "showed (her) how to communicate with him." For example, Illaria and Ron learned to always carry a whiteboard, which they used to share ideas and information and to ask questions of Joseph.

One of the first things that Joseph learned from Ron was to take information that is known (through a published research study or even unpublished results), then step back to assess, analyze and question what comes next or what's missing? Joseph is guided by these questions as he passionately pursues studies to enable him to improve medical care for people with hearing challenges in Ghana, and perhaps even in the United States although jobs and visas are a constant source of stress for international students.

Ron, Ilaria, and Joseph are each dedicated to advancing medicine through science and each is motivated by something much larger than him or herself. Ron describes it as a "great partnership."

"Joseph stands out in a larger group as someone who has insights beyond his level of training. He has a sort of scientific instinct that is really hard to develop. It's hard to train in someone; it has to be a sort of intrinsic curiosity and passion and skill. It's a hard combination to get."

Ron, Ilaria and Joseph all said they grew and learned, greatly benefiting from the internship and the research they worked on together.

WHY IT WORKS

GSIP requires a meaningful investment—from mentors, lab staff, and interns, as well as program leaders and those who kindly support the program financially. Bringing an intern into lab work is a formidable task for mentors—people who already carry a full load. The mentors I spoke with are all designing, driving and monitoring lab experiments, while also collecting, analyzing and documenting data, publishing, submitting grants, teaching... The list goes on and doesn't even consider their personal responsibilities. An effective mentor must design a project for an intern that is based on the young person's interests, skill set and time parameters. An internship project must address the question: What is something that can be done in the time allowed that can give this young person growth in his/her area of interest, as well as ownership, and will at the same time be of benefit to the lab and ultimately research? Mentors commit to this additional work and time, as do their lab assistants. Interns also work hard, putting in lab hours on top of their scholarship and personal commitments. GSIP administrators, in addition to the obvious needs of running the program, found and hired sign language interpreters specifically trained in science and medicine to assist Joseph. They invested in interpreters for lab meetings, weekly Zoom seminars, social events (bowling, rafting and a baseball game), as well as for the Final Day Ceremony.

The returns on investment are significant and subtle. Joseph and other interns bring new energy and ideas into their labs, invigorating both mentors and research. Many mentors describe walking into the room with interns and feeling immediately rejuvenated. According to Ron, one fear that scientists face is that their ideas will grow stagnant because "you're thinking about things the same way for months or years. The only way to deal with this is to bring more fresh ideas into the mix."

Interns' developing scientific minds and inquiries can shake loose seemingly-fixed problems. While they learn what it takes to generate one figure in a research paper, they may question why that figure is being sought, or what it implies. Coming from a young scientist, these questions can be invaluable to the research itself.

Joseph Adjei

In short, interns have infectious curiosity, and they bring fresh perspectives—the more diversity the better.

As one mentor said: Bringing different backgrounds, training, science, and perspectives solves problems faster."

Finally, GSIP mentors find that working with GSIP students challenges them to think and communicate differently. Ideas grow as a result, stretching in new directions and potentially helping researchers to develop entirely new approaches to long-term problems that need solving. Ron says he got really lucky with Joseph and this sentiment is echoed by other mentors we met. It is clear that GSIP is an investment with great impact. As the program grows and continues, we are left with a modified application of Ron's research question: Who are we missing—because they are outside of our sphere and don't know about the program, or have different abilities or needs that make them hard to accommodate? Or as Ron succinctly puts it: "Who are we missing, as the next great scientist?"

Click or Scan
GSIP VIDEO REFLECTIONS
FROM SUMMER 2021

GATES CENTER SUPPORT BOLSTERS GROWTH & OPPORTUNITIES

Graduate Program in Cell Biology, Stem Cells and Development Program

Jeff Moore


Jeff Moore

In 2021, the Gates Center continued its support for the Graduate Program in Cell Biology, Stem Cells and Development (CSD). CSD is one of 12 PhD programs on the Anschutz campus, and is uniquely defined by its mission to equip students with a strong foundation of knowledge in cell function and tissue development and then enable them to apply that knowledge toward understanding and treating human diseases and birth defects.

CSD's student body and program quality has grown over the last six years thanks to support from the Gates Center. In that time, CSD enrollment increased 50%. Several of these students have been alumni of the Gates Summer Internship Program, including Madison Rogers '15 (see page 28) and Chris Schaaf '19. In the training program, CSD faculty tap experts from the Gates Center to build experiential learning modules into our courses, including a course in embryology taught by Gates Center members Dr. Linda Barlow and Dr. Kristin Artinger, and a course on organoid technology taught by Gates Center member Dr. Peter Dempsey. These training opportunities expose students to cutting-edge technologies and allow them to learn by doing hands-on experiments. In addition to training strong researchers at the bench, CSD emphasizes training in communications and leadership to prepare students to become the next generation of leaders in biomedical research and education. In 2021, CSD launched the Developing Scholars Program to create mentor training opportunities for current PhD students and research training opportunities for undergraduates from the Denver-Aurora metro area. For the PhD students, this program provides first-hand experience in project design, project management, candidate interviewing, and student training as they conduct the research. For the undergraduate, the program provides first-hand experience working in a research lab and professional development opportunities through a series of workshops. Developing Scholars focuses on training undergraduate students who come from backgrounds that are historically underrepresented in STEM, helping to eliminate barriers to their career goals and positioning them to successfully apply to graduate school. There are excellent opportunities for synergistic benefits between the Developing Scholars Program and the Gates Summer Internship Program, including joint professional development activities, joint research presentation sessions, and social events. These synergies help create a more vibrant undergraduate training environment on the Anschutz Medical Campus.

With this trajectory of program growth, outreach and curriculum innovation, CSD applied for and was awarded a prestigious T32 training grant from the National Institutes of Health in 2021. This five-year grant will support a new training focus within CSD on the Genetics of Development, Disease and Regeneration. In addition, the training grant will support student travel to courses and conferences at other institutions and create new professional development opportunities in which CSD students can network with researchers from the clinical and biotech sides of biomedical research. Support from the Gates Center has been key to the growth of CSD and the creation of these new opportunities.

CSD DEVELOPMENT SCHOLARS
L–R: Amy Briggs, Tina Piarowski, Hannah Jones, Jeff Moore, Kelsey Abrams, Morgan Nebbia, Trinity Jackiewicz, Zeke Thomas, Meghna Bagchi, Charles Griffin, Blossom Lee, Nicole Moss, Linnea Wethekam, Ian Stancil, David Villani

GATES CENTER 2021 SEMINAR SERIES

TUESDAY, JANUARY 12
MILICA RADISIC, PhD
Professor, University of Toronto Department of Biomedical Engineering
Instructive Biomaterials for Cardiac Healing and Regeneration

TUESDAY, JANUARY 26
KEN LIECHTY, MD
The Sandy Wolf Chair in Maternal Fetal Surgery Director
Professor, Pediatric Surgery Basic and Translational Research
Targeting Inflammation and Oxidative Stress in Disease

TUESDAY, FEBRUARY 9
MOUMITA GHOSH, PhD
Associate Professor, Department of Medicine
Airway Stem/Progenitor Cells in Lung Health and Diseases

ESZTER KATALIN VLADAR, PhD
Assistant Professor, Department of Medicine
Building and Maintaining a Functional Multiciliated Epithelium

TUESDAY, FEBRUARY 23
XIYING FAN, PhD
Research Instructor, Department of Dermatology
Defining the Role of Innate Immune Cells for Cancer Immunoediting in Epidermal Neoplasms Via Intravital Imaging

TUESDAY, MARCH 9
SUJATHA JAGANNATHAN, PhD
Assistant Professor, Department of Biochemistry and Molecular Genetics
Early Embryonic Transcription Factor DUX4 Rewires RNA Processing in Muscle Disease

TUESDAY, MARCH 23
NATALIA VERGARA, PhD
Assistant Professor, Department of Ophthalmology
Harnessing the Potential of Stem Cell-Derived Retinal Organoids for Therapeutic Development

TUESDAY, MAY 11
XIAO-JING WANG, MD, PhD
Professor, Department of Pathology
Smad7: From a Genetic Model to Drug Development

2021 CSD Program retreat in Breckenridge, Colorado. This was the first in-person program retreat since 2019.

FINANCIAL OVERVIEW

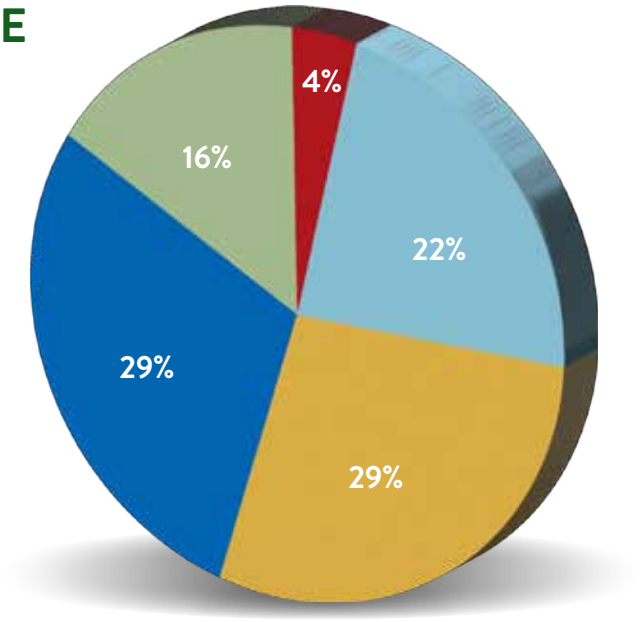
The following financial statement reflects the operations of the Gates Center for Regenerative Medicine, which has been the grateful recipient of funding from a number of sources including the Gates Frontiers Fund, the University of Colorado Foundation, the University of Colorado President's Office, the CU Anschutz Chancellor's Office, the School of Medicine and private donors. Notably, fiscal Year 2021 was the first year of operations under a new five-year funding agreement between the Gates Frontiers Fund, the Chancellor's Office and the School of Medicine in support of Gates Center operations and research through 2025. In addition to this generous funding from our partners, the Gates Center received wonderful philanthropic support for key initiatives described in more detail throughout this report.

We continue to collaborate with other centers, departments, and divisions on campus, as well as our hospital partners. 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 we have helped secure. 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 2021 the Gates Center supported six core laboratory facilities: Flow Cytometry, Genomics, Human Immune Monitoring, Histology (Morphology and Phenotyping), Organoid and Stem Cell Biobank & Disease Modeling. The Gates Center also provided laboratory infrastructure to members for work done outside of the core facilities. The Gates Center's affiliation with the Gates Biomanufacturing Facility is an increasingly 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 FOR REGENERATIVE MEDICINE EXPENSES 2021

- Center Research Program Support
  $754,511: 29%
- Lab Operations & Core Facilities
  $750,469: 29%
- Marketing & Development
  $589,693: 22%
- Center Enrichment, Education & Commercialization
  $426,873: 16%
- Center Admin/Maint/Supplies
  $107,209: 4%



INFRASTRUCTURE & OPERATIONS GRANTS

CALENDAR YEAR	2017	2018	2019	2020	2021
Gates Frontiers Fund	$1,200,000	$1,200,000	$1,200,000	$1,200,000	$1,500,000
University of Colorado Foundation	$600,000	$600,000	$600,000	$7,100	$600,000
UC - SOM Dean's & Chancellor's	$600,000	$600,000	$600,000	$600,000	$1,000,000
Philanthropy	$200,000	$327,585	$159,669	$114,103	$152,079
REVENUE: INFRASTRUCTURE & OPERATIONS GRANTS	**$2,600,000**	**$2,727,585**	**$2,559,669**	**$1,921,203**	**$3,252,079**

GATES CENTER EXPENDITURES

Center Research Program Support	$721,053	$1,072,416	$730,619	$583,003	$754,511
Lab Operations & Core Facilities	$594,723	$580,161	$575,931	$294,726	$750,469
Marketing & Development	$530,526	$554,373	$562,529	$547,913	$589,693
Center Admin/Maint/Supplies	$389,380	$474,671	$235,213	$272,772	$107,209
Center Enrichment, Education & Commercialization	$285,939	$257,238	$374,986	$299,297	$426,873
TOTAL EXPENDITURES	**$2,521,621**	**$2,938,859**	**$2,479,278**	**$1,997,712**	**$2,628,755**
CENTER SOURCES: EXPENDITURES	**$78,379**	**($211,274)**	**$80,391**	**($76,508)**	**$623,324**

ACKNOWLEDGMENTS

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BOARD BIOGRAPHIES

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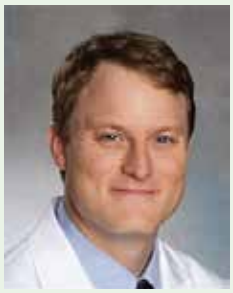
FRONT ROW L - R: Gates Center Director Dennis Roop, Dan Ritchie, Kevin Reidy, Ann Sperling, Diane Wallach
BACK ROW L - R: Don Elliman, Rick Stoddard, Geoff "Duffy" Solich, Marc Bonaca, Janelle Blessing, Yvette Frampton and Wag Schorr (not shown: Cathey Finlon)

WELCOME

The Gates Center was pleased to welcome Marc P. Bonaca, MD, MPH, as the newest member of our Gates Center Advisory Board in January 2021.



Marc is a cardiologist and vascular medicine specialist. He has served as the executive director of CPC Clinical Research and Community Health, as well as Director of Vascular Research and Professor of Medicine at CU Anschutz, since his arrival on campus in August 2018. Recruited by our late, beloved Gates Center Advisory Board member, Will Hiatt, MD, Marc is befittingly the inaugural holder of the William R. Hiatt Endowed Chair in Cardiovascular Research.

Born in Virginia and raised in Connecticut, Marc attended Bucknell College where he majored in economics & finance and minored in physics. Following a five-year stint working as a computer programmer for Price Waterhouse Coopers, Dr. Bonaca earned his medical degree from the University of Connecticut School of Medicine and his master's degree in Public Health at Harvard University. He completed his residency, cardiovascular fellowship and vascular medicine fellowship at Brigham and Women's Hospital and Harvard Medical School. He served as a cardiovascular research fellow with the TIMI (Thrombolysis in Myocardial Infarction) Study Group with the Cardiovascular Division of Brigham and Women's Hospital. Following his training, he joined the faculty at Brigham and Women's Hospital and Harvard Medical School and became an investigator at the TIMI Study Group. Clinically he was a core vascular medicine faculty and the Medical Director of The Aortic Center. He also continues to serve as center director and clinical project principal investigator of the Brigham and Women's Hospital and Dartmouth Hitchcock Center in the American Heart Association Strategically Focused Research Network in peripheral vascular disease.

Throughout Marc's recruitment to campus, Will Hiatt described CU Anschutz as a special place where big transformational projects can happen. Will cited the spirit and involvement of visionaries such as Diane Gates Wallach, whose willingness to take risks, practicality and generous support of the Gates Center have helped the campus to move ahead in the promising regenerative medicine space. Marc's broad expertise and experience in running large clinical trials will be most helpful as more and more campus researchers move their discoveries toward the clinic.

Marc's wife Lauren was convinced that moving to Colorado was the right decision for their family, and she seems to have been spot-on. Marc's family enjoys traveling to Italy in the summers to visit Marc's big family. Meanwhile, during the winter his two children, Luca (6) and Giulia (4), are respectively skiing double black diamonds and loving "going bump, bump, bump through the trees." We welcome Marc to the board as a clinician scientist eminently qualified to help us pursue and weather the storms of what he calls the "exquisite experiment" that is science.

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FRONT ROW L-R: Kalpana Velmurugan, Jocelyn Castillo Flores, Christa Gaskill, Amy Frieman, Igor Kogut, Ganna "Anya" Bilousova, Velmurugan Balaiya
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VADAKKAN, DEEPA
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The Gates Center gratefully acknowledges the following individuals, foundations and organizations for supporting our research and mission during the 2021 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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Mary & Bob Bearman
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The Berenice Gates Hopper Family Fund
Dori Biester, PhD, FAAN
Janelle & Buck Blessing
Lauren & Marc Bonaca, MD
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Kathy & Michael Chevalier
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TO LEARN MORE ABOUT HOW YOU CAN PLAY A ROLE
in accelerating research through philanthropic gifts contact Michael Tortoro at 303.724.7618, Michael.Tortoro@cuanschutz.edu or click/scan the QR Code.

CHARLIE'S PICNIC 2021

ENTREPRENEURS HAVE FUN

The Gates Center community joins together annually to savor food and camaraderie and reflect upon the year's progress and those who have made it possible. Enjoy this video recording of 2021's celebratory gathering.

Click or Scan CHARLIE'S PICNIC 2021

Wood-fired pizza by Mountain Crust Catering

L-R: Diane Wallach and Christy Honnen

L-R: Ella Annest, Jill Cowperthwaite and Emily Paton

Ted Parks, MD (far right) and the Busted Bones

Mary and George Sissel

L-R: 2021 Charlie's Angel Tim Gardner, Deb Froeb, Gus Gardner, John Fisher, Jann Freed and Steve Bair, MD

L-R: David Norris and Igor Kogut

Susan Majka and James Degregori

Yvette Frampton and Janelle Blessing

Brooks Stewart, Missy and John Warner

Brian Turner and Yosef Refaeli

Annette and Bill Peltzman

Charlie's Picnic 2021 from afar

L-R: Santos Franco, Aleeza Balolia and Luuli Tran

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2021 ANNUAL REPORT

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