

# 2017

## *Annual Report*

The Gates Center



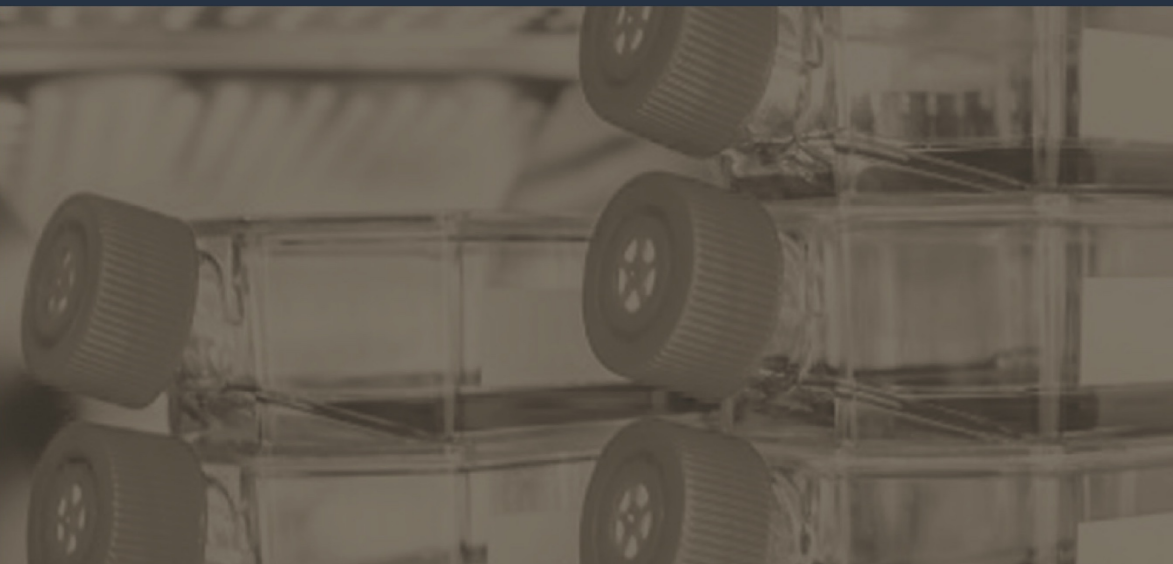
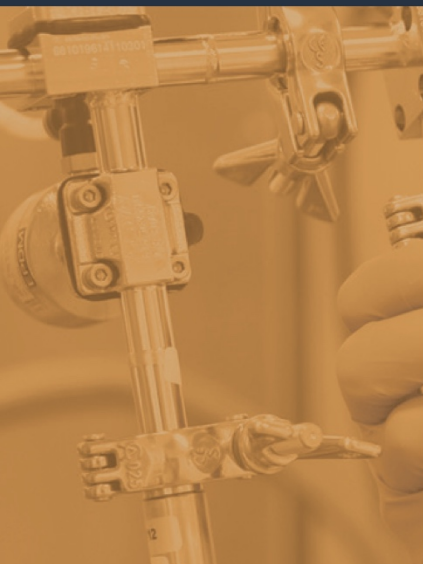
Gates Center for Regenerative Medicine  
UNIVERSITY OF COLORADO **ANSCHUTZ MEDICAL CAMPUS**







2017 Gates Summer Internship Program (BACK ROW, left to right) Andrew Parker, Bay Vagher, Nicholas Essek, Katherine Johnson, Matthew Ramsey, Jen Pakieser, Sarah Seiwald, Oscar Yip, Tricia Oyster, Nick Elder, Alisha Eskew, Alyssa Downey, Shannon McCallan, Roshni Kalkur, Elena Fulton, Jerry Chang, Alanna Horton, Michaela Berens, Joy Abraham, Zachary Feuer







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*\*Cover Photo: Gates Center for Regenerative Medicine Staff*





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



# THE VISION



When wagon trains headed west and came to a challenging creek, pioneers threw their hats to the other side. Since no one in their right mind would leave a hat behind, throwing it across committed them to ford the creek, retrieve it and carry on.

To entrepreneur and philanthropist Charles C. Gates, throwing the hat symbolized a commitment to take the risks necessary to keep moving toward a goal.

Toward the end of his life, he foresaw the future in regenerative medicine and exhorted his children, Diane Gates Wallach and John Gates, and others to bring it to fruition. We are grateful for the legacy of his vision that lives on at the Gates Center for Regenerative Medicine and within its Charles C. Gates Biomanufacturing Facility, which is dedicated to enabling the safe and expedited translation of discovery into human therapies for people worldwide.



# WHO WE ARE

Established in 2006 with a generous gift in Charles Gates' memory, the Gates Center for Regenerative Medicine is a world-class, multi-institutional center headquartered on the University of Colorado Anschutz Medical Campus, researching transformative human therapies using stem cells and other tools while shepherding clinical trials to bring them to patients as quickly as possible.

## We are:

- Inspired by Charlie Gates' vision of the future of regenerative medicine and guided by four strategic drivers that distinguish our approach:
  - **Frontier Spirit:** Do business in an entrepreneurial way, balancing risks, opportunities and resources while minimizing barriers to success.
  - **Talent:** Focus on the acquisition, development and retention of accomplished, passionate, innovative change agents, both clinicians and basic scientists.
  - **Collaboration:** Serve as an indispensable resource, supporting, coordinating and optimizing outcomes for all of our partners and customers – “No one does their best work alone.” – Charles Gates
  - **Patient Outcomes:** Accelerate discoveries from the lab through clinical trials leading to effective therapies and cures.
- Led by Professor Dennis Roop, Ph.D., who was recruited from the Baylor College of Medicine in January 2007, to establish a critical mass of faculty, clinicians, students, research staff and administrators to execute the center's mission.
- Supported by an extraordinary Gates Center Advisory Board (see photo on opposite page)
- Dedicated to bringing together outstanding medical researchers and clinicians and providing the following to accelerate discoveries into clinical practice as quickly as possible:
  - Grant and philanthropic funding
  - Four state-of-the-art core scientific facilities
  - The Gates Biomanufacturing Facility, in which future cellular therapies and protein-based biologics are being manufactured for human trials under the highest FDA standards—one of six combined cell therapy and protein manufacturing facilities in the United States and the only one of its kind within an 800-mile radius
  - Commercialization support
  - Education and outreach
- Comprised of 97 multi-institutional members from the University of Colorado Anschutz Medical Campus, CU Boulder, CU Denver, Colorado State University, Colorado School of Mines, National Jewish Health and private industry, investigating regenerative therapies and stem cell treatments in the areas of bioengineering, cardiology, dermatology, diabetes, immunology, neurology, oncology, ophthalmology, and orthopedics, among others specified on our list of members on page 9.
- Focused on adult stem cells, which can be reprogrammed into embryonic-like stem cells, referred to as induced Pluripotent Stem Cells (iPSCs), and then differentiated into virtually any cell type in the body. The long-term goal is to return genetically corrected iPSC-derived adult stem cells to the patient from which they were derived. In this way, the Gates Center's clinical pathway is leading toward a new paradigm of personalized medicine in which an individual's own cells can be used to cure a number of diseases and conditions.





2017 Gates Center Advisory Board: (BACK ROW, left to right) Kevin Reidy, Marilyn Coors, Ph.D., Geoff "Duffy" Solich, Yvette Pita Frampton, Ann Sperling, Will Hiatt, M.D., Rick Stoddard, Dori Biester, Ph.D., FAAN (FRONT ROW, left to right) Wag Schorr, M.D., Janelle Blessing, Dan Ritchie, Diane Gates Wallach, Dennis Roop, Ph.D., Don Elliman, Wayne Hutchens



## 2017 GATES CENTER ADVISORY BOARD

Diane Gates Wallach, *Co-Chair*  
Daniel Ritchie, *Co-Chair*  
Donald Elliman, *Co-Chair*  
Dori Biester, Ph.D., FAAN  
Janelle Blessing

Marilyn Coors, Ph.D.  
Yvette Pita Frampton  
William Hiatt, M.D.  
Wayne Hutchens  
Kevin Reidy

Dennis Roop, Ph.D.  
Wagner Schorr, M.D.  
Geoff "Duffy" Solich  
Ann Sperling  
Rick Stoddard



# WHAT WE DO

## MISSION

We conduct leading-edge research in stem cell biology and regenerative medicine, accelerating discoveries from the lab through clinical trials leading to effective cures and therapies for patients.

RECRUIT  
& RETAIN  
TOP TALENT

SECURE  
FUNDING

SUPPORT  
RESEARCH &  
INNOVATION

FACILITATE  
CLINICAL  
TRIALS

BENEFIT  
PATIENTS

97 CENTER MEDICAL  
RESEARCH AND CLINICIAN MEMBERS



University of Colorado  
Anschutz Medical Campus



Boulder



Colorado  
State  
University



Children's Hospital Colorado

uhealth



PRIVATE  
INDUSTRY

PROVIDE ACCESS TO GATES CENTER'S  
STATE-OF-THE-ART LABORATORY FACILITIES:

GATES  
BIOMANUFACTURING  
FACILITY

FLOW  
CYTOMETRY  
CORE

MORPHOLOGY  
AND PHENOTYPING  
CORE

BIOENGINEERING  
CORE

STEM CELL  
BIOBANKING  
AND DISEASE  
MODELING CORE

SUPPORT MEMBERS THROUGH THE GATES CENTER INFRASTRUCTURE:

MARKETING AND PHILANTHROPY

EDUCATION AND OUTREACH

COMMERCIALIZATION SUPPORT



# LIST OF MEMBERS

NAME	DEGREE(S)	POSITION	ACADEMIC INSTITUTION/AFFILIATES	PRIMARY (AND SECONDARY) APPOINTMENT(S)
Appel, Bruce	PhD	Professor Diane G. Wallach Chair in Pediatric Stem Cell Biology	University of Colorado Anschutz Medical Campus	Department of Pediatrics/ Developmental Biology
Artinger, Kristin	Ph.D.	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Craniofacial Biology, School of Dental Medicine
Bailey, Susan	Ph.D.	Professor	Colorado State University	Department of Environmental and Radiological Health Sciences
Baker, Christopher	M.D.	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Pediatrics/ Developmental Biology
Bamburg, James	Ph.D.	Professor	Colorado State University	Department of Biochemistry and Molecular Biology
Barlow, Linda	Ph.D.	Professor	University of Colorado Anschutz Medical Campus	Department of Cell and Developmental Biology
Battaglino, Ricardo*	Ph.D.	Visiting Associate Professor	University of Colorado Anschutz Medical Campus	Department of Physical Medicine and Rehabilitation
Bilousova, Ganna	Ph.D.	Assistant Professor	University of Colorado Anschutz Medical Campus	Department of Dermatology
Birlea, Stanca	M.D., Ph.D.	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Dermatology
Box, Neil	Ph.D.	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Dermatology
Boyle, Kristen	Ph.D.	Assistant Professor	University of Colorado Anschutz Medical Campus	Department of Pediatrics
Bruckner, Anna	M.D.	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Dermatology
Brzezinski, Joseph	Ph.D.	Assistant Professor	University of Colorado Anschutz Medical Campus	Department of Ophthalmology
Burnham, Ellen	M.D., M.S.	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Medicine/ Pulmonary Sciences and Critical Care
Canto-Soler, Valeria*	Ph.D.	Associate Professor Doni Solich Family Chair in Ocular Stem Cell Research	University of Colorado Anschutz Medical Campus	Department of Ophthalmology
Chan, Sanny	M.D., Ph.D.	Assistant Professor	National Jewish Health	Department of Pediatrics/ Division of Allergy and Immunology
Chick, Wallace	Ph.D.	Assistant Professor	University of Colorado Anschutz Medical Campus	Department of Cell and Developmental Biology
De Langhe, Stijn	Ph.D.	Associate Professor	National Jewish Health	Department of Pediatrics
DeGregori, James	Ph.D.	Professor Courtenay C. and Lucy Patten Davis Endowed Chair in Lung Cancer Research	University of Colorado Anschutz Medical Campus	Department of Biochemistry and Molecular Genetics
Dempsey, Peter	Ph.D.	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Pediatrics
Dow, Steven	DVM, Ph.D.	Professor	Colorado State University	Department of Clinical Sciences
Ehrhart, Nicole	VMD, Diplomate, ACVS	Professor	Colorado State University	Department of Surgical Oncology
Ford, Heide	Ph.D.	Professor	University of Colorado Anschutz Medical Campus	Department of Pharmacology
Franco, Santos	Ph.D.	Assistant Professor	University of Colorado Anschutz Medical Campus	Department of Pediatrics/ Developmental Biology
Freed, Brian	Ph.D.	Professor	University of Colorado Anschutz Medical Campus	Department of Medicine/ Allergy and Clinical Immunology
Freed, Curt	M.D.	Professor	University of Colorado Anschutz Medical Campus	Department of Medicine/ Clinical Pharmacology and Toxicology
Friedman, Jed	Ph.D.	Professor	University of Colorado Anschutz Medical Campus	Department of Pediatrics

\* New members in 2017



NAME	DEGREE(S)	POSITION	ACADEMIC INSTITUTION/AFFILIATES	PRIMARY (AND SECONDARY) APPOINTMENT(S)
Fujita, Mayumi	M.D., Ph.D.	Professor	University of Colorado Anschutz Medical Campus	Department of Dermatology
Gavin, Kathleen*	Ph.D.	Assistant Professor	University of Colorado Anschutz Medical Campus	Division of Geriatric Medicine
Goodrich, Laurie	DVM, M.S., Ph.D.	Associate Professor	Colorado State University	College of Veterinary Medicine
Gore, Lia	M.D.	Professor The Robert J. and Kathleen A. Clark and Ergen Family Endowed Chairs	University of Colorado Anschutz Medical Campus	Department of Pediatrics/Hematology, Oncology and Bone Marrow Transplantation
Gubbels, Samuel	M.D.	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Otolaryngology
Hagman, James	Ph.D.	Professor	National Jewish Health	Department of Immunology
Herson, Paco	Ph.D.	Principal Investigator	University of Colorado Anschutz Medical Campus	Department of Anesthesiology, Neuronal Injury Program
Hiatt, William	M.D.	Professor Novartis Endowed Chair in Cardiovascular Research	University of Colorado Denver Anschutz Medical Campus	Department of Medicine/Cardiology
Huang, Hua	M.D., Ph.D.	Professor	National Jewish Health	Integrated Department of Immunology
Jacot, Jeffrey	Ph.D.	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Bioengineering
Janssen, William	M.D.	Associate Professor	National Jewish Health	Division of Pulmonary, Critical Care and Sleep Medicine
Jimeno, Antonio	M.D., Ph.D.	Professor Daniel and Janet Mordecai Chair in Cancer Stem Cell Biology	University of Colorado Anschutz Medical Campus	Department of Medicine/Medical Oncology
Kahook, Malik	M.D.	Professor Slater Family Endowed Chair in Ophthalmology	University of Colorado Anschutz Medical Campus	Department of Ophthalmology
King, Karen	Ph.D.	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Orthopedics
Klemm, Dwight	Ph.D.	Professor	University of Colorado Denver Anschutz Medical Campus	Department of Medicine/Pulmonary Sciences
Koch, Peter	Ph.D.	Professor	University of Colorado Denver Anschutz Medical Campus	Department of Dermatology
Kogut, Igor	Ph.D.	Assistant Professor	University of Colorado Anschutz Medical Campus	Department of Dermatology
Königshoff, Melanie	M.D., Ph.D.	Professor	University of Colorado Anschutz Medical Campus	Division of Pulmonary, Critical Care Medicine
Koster, Maranke	Ph.D.	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Dermatology
Krebs, Melissa	Ph.D.	Assistant Professor	Colorado School of Mines	Chemical and Biological Engineering
Kumar, Raj	Ph.D.	Professor	University of Colorado Anschutz Medical Campus	Department of Obstetrics and Gynecology
Lee, Katherine	Ph.D.	Assistant Professor	University of Colorado Anschutz Medical Campus	Department of Pediatrics/Infectious Disease
Liechty, Kenneth	M.D.	Professor	University of Colorado Anschutz Medical Campus	Department of Surgery/Pediatric Surgery
Long, Carlin	M.D.	Professor	University of Colorado Anschutz Medical Campus	Department of Medicine/Cardiology
Lu, Shi-Long	M.D., Ph.D.	Assistant Professor	University of Colorado Anschutz Medical Campus	Department of Otolaryngology
Lyons, Traci	Ph.D.	Assistant Professor	University of Colorado Anschutz Medical Campus	Department of Medicine/Medical Oncology
Magin, Chelsea	Ph.D.	Assistant Professor	University of Colorado Anschutz Medical Campus	Division of Pulmonary/Department of Medicine
Mandava, Naresh	M.D.	Professor Sue Anschutz-Rodgers Endowed Chair in Retinal Diseases	University of Colorado Anschutz Medical Campus	Department of Ophthalmology
Masterson, Joanne	Ph.D.	Assistant Professor	University of Colorado Anschutz Medical Campus	Department of Pediatrics
McCurdy, Carrie	Ph.D.	Assistant Professor	University of Colorado Anschutz Medical Campus	Department of Pediatrics/Neonatology



NAME	DEGREE(S)	POSITION	ACADEMIC INSTITUTION/AFFILIATES	PRIMARY (AND SECONDARY) APPOINTMENT(S)
Meng, Xianzhong	M.D., Ph.D.	Professor	University of Colorado Anschutz Medical Campus	Department of Medicine/Cardiology
Morse, Leslie*	D.O.	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Physical Medicine and Rehabilitation
Neu, Corey*	Ph.D.	Associate Professor Donnelly Family Endowed Associate Professor	University of Colorado Boulder	Department of Mechanical Engineering
Niswander, Lee	Ph.D.	Professor	University of Colorado Boulder	Department of Molecular, Cellular, and Developmental Biology
Norris, David	M.D.	Professor	University of Colorado Anschutz Medical Campus	Department of Dermatology
Olson, Jeffrey*	M.D.	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Ophthalmology
Olwin, Bradley	Ph.D.	Professor	University of Colorado Boulder	Department of Molecular, Cellular and Developmental Biology
Ormond, David Ryan	Ph.D.	Assistant Professor	University of Colorado Anschutz Medical Campus	Department of Neurosurgery/ Translational Clinical Research
Patel, Vikas	M.D.	Professor	University of Colorado Anschutz Medical Campus	Department of Orthopedics
Payne, Karin	Ph.D.	Assistant Professor	University of Colorado Anschutz Medical Campus	Department of Orthopedics
Perraud, Anne-Laure	Ph.D.	Assistant Professor	National Jewish Health, University of Colorado Anschutz Medical Campus	Department of Biomedical Research/ Immunology and Microbiology
Petrash, Mark, J.	Ph.D.	Professor	University of Colorado Anschutz Medical Campus	Department of Ophthalmology
Phiel, Christopher	Ph.D.	Assistant Professor	University of Colorado Denver	Department of Integrative Biology
Pietras, Eric	Ph.D.	Assistant Professor	University of Colorado Anschutz Medical Campus	Department of Medicine/Hematology
Porter, Christopher	M.D.	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Pediatrics/Hematology, Oncology and Bone Marrow Transplantation
Purev, Enkhee	M.D., Ph.D.	Assistant Professor	University of Colorado Anschutz Medical Campus	Division of Hematology
Refaeli, Yosef	Ph.D.	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Dermatology
Ribera, Angeles	Ph.D.	Professor	University of Colorado Anschutz Medical Campus	Department of Physiology and Biophysics
Roop, Dennis	Ph.D.	Professor Charles C. Gates Endowed Chair in Regenerative Medicine and Stem Cell Biology	University of Colorado Anschutz Medical Campus	Department of Dermatology
Russ, Holger	Ph.D.	Assistant Professor	University of Colorado Anschutz Medical Campus	Barbara Davis Center for Childhood Diabetes
Sartorius, Carol	Ph.D.	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Pathology
Sclafani, Robert	Ph.D.	Professor	University of Colorado Anschutz Medical Campus	Department of Biochemistry and Molecular Genetics
Sherk, Vanessa	Ph.D.	Instructor	University of Colorado Anschutz Medical Campus	Department of Medicine/Endocrinology
Song, Kunhua	Ph.D.	Assistant Professor	University of Colorado Anschutz Medical Campus	Department of Medicine/Cardiology
Soranno, Danielle	M.D.	Assistant Professor	University of Colorado Anschutz Medical Campus	Department of Pediatrics
Stenmark, Kurt	M.D.	Professor	University of Colorado Anschutz Medical Campus	Department of Pediatrics/Critical Care
Terzian, Tamara	Ph.D.	Assistant Professor	University of Colorado Anschutz Medical Campus	Department of Dermatology
Thamm, Douglas	VMD	Assistant Professor	Colorado State University	Department of Clinical Sciences
Torchia, Enrique	Ph.D.	Assistant Professor	University of Colorado Anschutz Medical Campus	Department of Dermatology
Verneris, Michael*	M.D.	Professor The Barton Endowed Chair of Pediatric Bone Marrow Transplant	University of Colorado Anschutz Medical Campus	Department of Pediatrics/Hematology, Oncology and Bone Marrow Transplantation

\* New members in 2017



NAME	DEGREE(S)	POSITION	ACADEMIC INSTITUTION/AFFILIATES	PRIMARY (AND SECONDARY) APPOINTMENT(S)
Wagner, David	Ph.D.	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Neurology
Walker, Lori	Ph.D.	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Medicine/Cardiology
Wang, Xiao-Jing	M.D., Ph.D.	Professor John S. Gates Endowed Chair in Stem Cell Biology	University of Colorado Anschutz Medical Campus	Department of Pathology
Wang, Zhijie	Ph.D.	Assistant Professor	Colorado State University	Department of Mechanical Engineering
Williams, Trevor	Ph.D.	Professor	University of Colorado Anschutz Medical Campus	Department of Craniofacial Biology and Cell and Structural Biology, School of Dental Medicine
Wilusz, Carol	Ph.D.	Professor	Colorado State University	Department of Microbiology, Immunology and Pathology
Wilusz, Jeff	Ph.D.	Professor	Colorado State University	Department of Microbiology, Immunology and Pathology
Yi, Rui	Ph.D.	Associate Professor	University of Colorado Boulder	Department of Molecular, Cellular and Developmental Biology
Zamora, Martin*	M.D.	Professor	University of Colorado Anschutz Medical Campus	Division of Pulmonary, Critical Care Medicine
Zhou, Wenbo	Ph.D.	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Medicine/ Clinical Pharmacology and Toxicology

\* New members in 2017



Lab of Valeria Canto-Soler, Ph.D.





# Gates Center for Regenerative Medicine

UNIVERSITY OF COLORADO **ANSCHUTZ MEDICAL CAMPUS**

Charles C. Gates embodied the pioneer spirit, but he was also fond of saying that the most effective way toward progress in a venture was to find the best people and move forward together. At the Gates Center for Regenerative Medicine, 2017 was the year that spirit of collaboration greatly expanded our reach, our research, our talent and our support.

Gates Center Advisory Board Member Wag Schorr, M.D., is a superb example. Much like Charlie Gates, Wag has a vision for the future expansion of the center and the campus, as well as an indefatigable commitment to help drive and support our research to treat and potentially cure patients, such as his granddaughter, Calla (see page 15). We nominated Wag as the 2017 recipient of the Florence Rena Sabin Award, for his leadership and example in the kind of collaboration that is helping the center advance rapidly into the future.

Collaborative highlights of the year included welcoming Valeria Canto-Soler, Ph.D., to campus in July, whose recruitment was made possible through the center's collaboration with the Department of Ophthalmology and benefactors including the Gates Frontiers Fund. With great pride and appreciation, Valeria proceeded to set up her pristine lab to serve the campus, help acclimate her colleagues who followed her from Johns Hopkins, and plan for the future. In the fall, we made our own plans to co-host a unique two-day conference with Colorado State University's College of Veterinary Medicine in October 2018. Called Zoobiquity Colorado: Connecting Human and Animal Health through Regenerative Medicine, the conference will highlight the laboratory and clinical research of human and veterinary investigators, and foster ongoing and future collaborations amongst our participants. Lastly, our partnership with Stanford and Columbia, the Epidermolysis Bullosa (EB) iPSC Cell Consortium, formed to collectively fight the rare and debilitating genetic skin blistering disease, was rewarded with an additional funder and private and public funding, including one of the first of a very few grants awarded nationwide through the 21st Century Cures Act.



In the area of research, we established a new Stem Cell Biobank and Disease Modeling Core that is spurring research into a variety of new areas through philanthropic partnership. Utilizing Ganna Bilousova, Ph.D. and Igor Kogut, Ph.D.'s novel technology as a platform, this core uses iPSCs as tools to understand the underlying basis of diseases—particularly those that affect tissues that cannot be easily biopsied, such as the brain. We also celebrated Gates Center members who received grant awards from the National Institutes of Health and other sponsors, some of whom reminded us of the critical weight they gave to their collaborations and to early-stage support from the Gates Center, the Gates Grubstake Fund and private philanthropy. (see Grant Awards on page 26) In this report, we have listed a selection of members whose research has led to published articles or honors by way of awards, mention or membership (see Publications and Honors on page 21). We also have updates on those whose distinguished research has led to receipt of Gates Grubstake Awards over the last four years, and the establishment of the Startup Toolbox to help members through key steps in moving



discoveries into products and services that benefit patients (see Commercialization on page 30).

Auspiciously, abundant talent came through the door of the Gates Center during 2017. We recruited Mark Petrash, Ph.D., to augment his responsibilities as Professor and Director of Research in the Department of Ophthalmology by serving as Associate Director of the Gates Center. We also increased the size of the Gates Biomanufacturing Facility (GBF) staff to expand quality systems and put a trained team in place to deliver the first clinical-grade products by the end of 2017. The GBF expansion also accommodates the arrival of world-renowned cancer researcher Terry Fry, M.D., and other top researchers in 2018. Specifically, Ryan Chrisman, Ph.D., from Juno Therapeutics and Chris Garbe, M.S., M.B.A., from the Fred Hutchinson Cancer Research Center are two stellar recruits who now hold positions as interim Facility Director and Director of Quality respectively (see New Faces at the Gates Center on page 45). Additionally, the center focused on the development of younger talent, with the arrival of 20 students in June for the third year of the increasingly popular

Gates Summer Internship Program (GSIP), and its ongoing support of the Graduate Program in Cell Biology, Stem Cells and Development (CSD) (see Education on page 39).

Finally, the Gates Center is grateful for the wonderful and ongoing gifts of all sizes it receives from its board, employees and friends. It is a pleasure to list our donors in this report and to thank them each year at our annual Charlie's Picnic. Speaking of which, it was an absolute picnic to watch Diane Gates Wallach surprise and honor Rhondda and Peter Grant on that occasion in August 2017 as the first-ever recipients of the Gates Center "Charlie's Angels" award.

With great appreciation,



Dennis R. Roop, Ph.D.

Director, Gates Center for Regenerative Medicine

Charles C. Gates Endowed Chair in Regenerative Medicine and Stem Cell Biology





In collaboration with former University of Colorado School of Medicine Dean Richard Krugman, M.D., and the Office of Admissions, the Gates Center is delighted to have initiated the successful nomination of Wagner (Wag) J. Schorr, M.D., for the 2017 Florence Rena Sabin Award. Colorado native Dr. Sabin was a nationally renowned researcher in neuroanatomy who later in life made significant contributions in the area of public health. As one of the Gates Center's first informal but formative advisors, Wag Schorr was an absolute given when it came to populating the initial Gates Advisory Board in the spring of 2013. Wag is a graduate of the University of Colorado's School of Medicine, where he studied under transplant pioneer Thomas Starzl, M.D., Ph.D., who performed the world's first successful solid organ transplant in 1963. Wag likewise became a transplant pioneer, introducing kidney transplant within the United Kingdom prior to a long and successful professional career as Chief of Medicine at Presbyterian Medical Center, President of the Medical Advisory Board for the National Kidney Foundation and Clinical Professor of Medicine for the CU School of Medicine. Wag has gone on to passionately serve his alma mater as well as the citizens of Colorado through his leadership and contributions toward the health and welfare of the people in our state. We at the Gates Center were hard-pressed to

imagine another alumnus of the University of Colorado who would better emulate Florence Sabin's dedication to medicine and to her home state of Colorado.

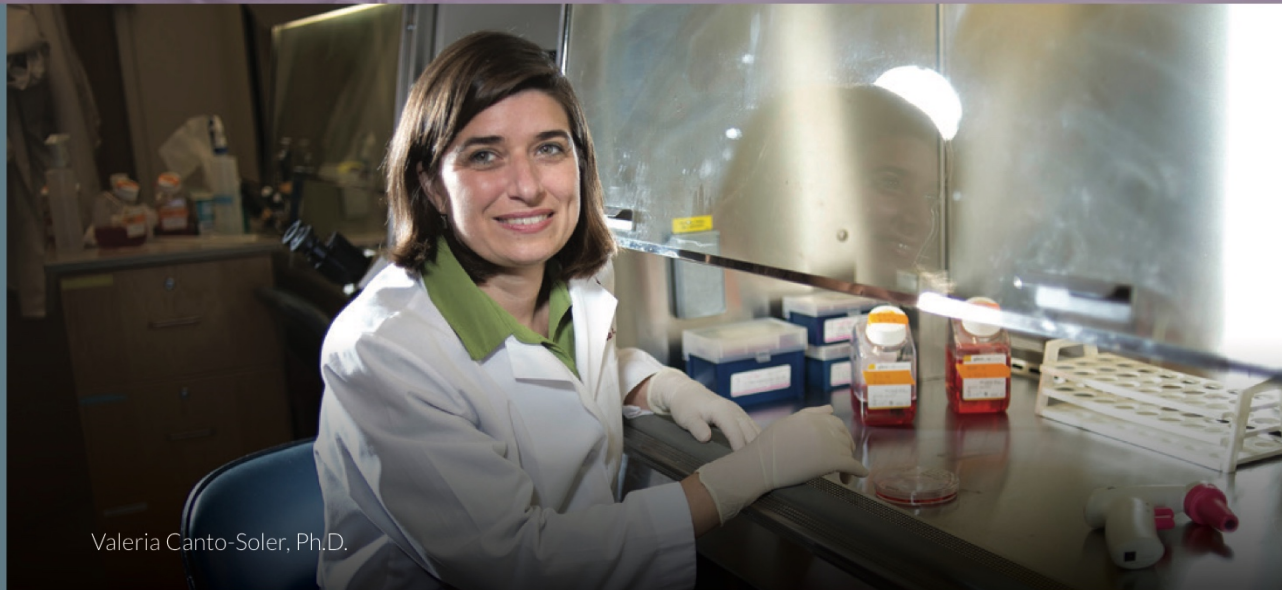
Apart from his myriad professional and leadership positions, "Wag," as we know him, has been one of the most extraordinary and generous friends a center such as ours could hope to have. His wisdom, experience and generosity of spirit have endeared him to the center's faculty, staff, volunteers and many others on the Anschutz Medical Campus, and throughout the Rocky Mountain Region. Aside from his position on the Gates Advisory Board, Wag has been one of our most popular Gates Summer Internship Program lecturers on the subject of pursuing a medical school education. Also a former President of the Medical Alumni Association and perennial admissions volunteer, Wag has never turned down a request to meet personally with any of the young people who come our way searching for career advice. Ultimately, his pride in the fast growing Anschutz Medical Campus inspires us to imagine that much as the University of Colorado was highlighted internationally for being the site of the first human liver transplants in the 1960s, we may be similarly touted in the future for our advances in the discovery of stem cell and regenerative therapies.



Left: Wagner "Wag" Schorr, M.D. receives the 2017 Florence Rena Sabin Award from Vice Chancellor Brenda J. Allen on May 26, 2017.  
Right: Wag sits to the left of Governor John Hickenlooper during Anschutz Medical Campus Spring Commencement.



# COLLABORATION EXPANDS OUR REACH



Valeria Canto-Soler, Ph.D.

## COLLABORATION ACROSS CAMPUS: *CellSight Program*

The recruitment of Valeria Canto-Soler, Ph.D., from Johns Hopkins University in July 2017 as the inaugural director of *CellSight* was made possible by a visionary collaboration conceived by Gates Center leaders Diane Gates Wallach and Dennis Roop, and Ophthalmology leaders Naresh Mandava and Mark Petrash. Canto-Soler's research first stirred excitement in 2014 when she was the first in the world to publish evidence showing how to induce stem cells in a culture dish to grow into miniature human retinas that sense light. Having grown up in Mendoza, Argentina, which is similar in climate and character to Colorado, and having brought along most of her team from Hopkins, Valeria feels very much at home on and off campus. A centerpiece of the *CellSight* program she oversees is a state-of-the-art stem cell culture facility (see photo on page 12), where *CellSight* researchers coax human iPS cells over a period of months to develop into light-responsive retinal tissue—material that may one day be transplanted to restore vision in patients with retinal degeneration. Designed with the intent to support a variety

of stem cell projects beyond those within the Department of Ophthalmology, the *CellSight* culture facility will bring together scientists from diverse areas to collaborate on cell-based strategies to treat diseases and degenerative conditions that are among today's biggest medical challenges.

Valeria creates miniature layers of the retina, which replicate the structure of the human eye and respond to light. The challenge is that these “organoids” require a nine-month gestation, which necessitated the construction of a “bomb-proof” culture facility. There are two labs where the organoids will grow under strict environmental control: a training area and a quarantine chamber. Moreover, the new culture facility is large enough to accommodate users from many disciplines on the Anschutz Medical Campus. The Department of Ophthalmology's Professor and Vice Chair of Research and Associate Director of the Gates Center Mark Petrash anticipates the culture facility's future use not only by the Department of Ophthalmology, but also by those working on growing organoids representing the brain, heart, GI tract, and more.



**COLLABORATION ACROSS THE STATE:  
Gates Center will co-host Zoobiquity Colorado:  
Connecting Human and Animal Health through  
Regenerative Medicine in October 2018**

In fall 2017, Dean Stetter of the College of Veterinary Medicine and Biomedical Sciences at Colorado State University approached the Gates Center for Regenerative Medicine regarding the intriguing possibility of co-hosting a Zoobiquity conference in October 2018. Researchers at CSU and CU Anschutz already have ongoing collaborations involving natural animal models that include clinical trials at the CSU's James L. Voss Veterinary Teaching Hospital and multiple studies in the CU Cancer Center and the Gates Center for Regenerative Medicine. Co-hosting a conference, suggested Dr. Stetter, would give us an opportunity to highlight the laboratory and clinical research of human and veterinary investigators and foster ongoing and future collaborations.

Coined by Dr. Barbara Natterson-Horowitz and Kathryn Bowers in their 2012 book, "Zoobiquity: The Astonishing Connection Between Human and Animal Health," zoobiquity comes from the Greek for "animal," zo, and the Latin for "everywhere," ubique.

Animals and humans share the planet, and they have many illnesses in common: cancer, arthritis, organ failure, injuries, and toxicities. In the past, the art and science of medicine

was practiced across species because human and domestic animals were so co-dependent. But as humans have lived farther from their livestock and food-source wildlife, a gulf opened between veterinary medicine and human medicine. Zoobiquity seeks to bridge that gulf. Founded in 2011, Zoobiquity Conferences are designed to bring together leading clinicians and scientists in human and veterinary medicine to discuss the same diseases in a wide spectrum of animal species and human beings. The intention of this cross-disciplinary conference is to create conversations and relationships between human and veterinary colleagues confronted with similar clinical challenges. By crossing disciplines in this way, we can significantly expand the perspective of clinicians, scientists and patients about these shared disorders and broader health concerns.

Zoobiquity Colorado, cohosted by the Gates Center and the veterinary college at CSU, is scheduled for Friday and Saturday, Oct. 5 and 6. It will feature a half day field trip to Fort Collins and a tour of the CSU Veterinary Teaching Hospital and research laboratories, followed by a full day of case presentations and panel discussions on the Anschutz Medical Campus in Denver. Busing between campuses, meals and receptions will be provided. For further information, please contact Jill Cowperthwaite at [jill.cowperthwaite@ucdenver.edu](mailto:jill.cowperthwaite@ucdenver.edu) or 303 724-6143. To register, consult the conference website at [www.Zoobiquity.colostate.edu](http://www.Zoobiquity.colostate.edu)

*Save the Date!*

**ZOOBIQUITY COLORADO:**  
Connecting Human and Animal Health  
through Regenerative Medicine

**OCTOBER 5-6, 2018**





## **COLLABORATION ACROSS THE COUNTRY AND WORLD: *Epidermolysis Bullosa (EB) iPS Cell Consortium progresses in 2017, acquiring a new funder and funding***

On New Year's Day 2017, Stanford University was able to reprogram cells using the one-step technology developed in the Gates Center laboratory of Ganna Bilousova, Ph.D., and Igor Kogut, Ph.D., commenting, "You've developed a very robust technology!" As a result, the unique Epidermolysis Bullosa (EB) iPS Cell Consortium—formed in 2016 to unite the University of Colorado, Stanford and Columbia Universities in search of a treatment for this rare and debilitating skin blistering disease—agreed to adopt Colorado's reprogramming approach described on page 35.

Additional highlights of 2017 for the Colorado team led by Dennis Roop, Ph.D., and their Consortium partners were the addition of a private funder and the award of significant public funding. Early in the year, the EB Research Partnership (founded by Alex and Jamie Silver, Heather and Ryan Fullmer, and Jill and Eddie Vedder of Pearl Jam) and the EB Medical Research Foundation (directed by Gary & Lynn Fechser Anderson and Paul and Andrea Joseph and family) were joined by the Sohana Research Fund from Great Britain (founded by Sharmila and James Collins). With the exception of the Vedders, all these dedicated and generous families have children who sadly have been afflicted by this disease. When the Consortium reported its achievement of year one milestones in only six months, these funders approved an additional award for research and one to establish the new iPS Biobanking Core also described on page 35.

Later in the spring, the funders moved to fund a non-federal match, enabling the Consortium to apply for highly restrictive Regenerative Medicine funding made available through the 21st Century Cures Act. Remarkably, the Consortium received one of the first and few National Institutes of

Health grants funded by the bill. The award was a wonderful affirmation of our significant advances in developing safer cell reprogramming and gene editing technologies here in Colorado. It additionally recognizes the potential of the Consortium with Stanford and Columbia Universities to develop and advance an induced pluripotent stem cell (iPSC)-based therapy toward a Phase I Clinical Trial to treat this devastating, inherited skin blistering disease.

2017 also uncovered some fascinating new findings relative to the descent of local Hispanic EB patients. An initial suggestion by Steve Berman, M.D., who founded the EB Clinic at Children's Hospital Colorado, led to working with a Dermatology resident, Emily Warshauer, to submit patient DNA samples for genetic testing. Preliminary results show that at least two of our local patients may be related to 100's of EB patients in Mexico who share the same founder mutation, and may well be descended from a group of families who fled the Spanish Inquisition 300 to 400 years ago. Finding sufficient patients for a clinical trial for an orphan disease such as EB is a real challenge, so this was an auspicious development toward identifying future potential participants.

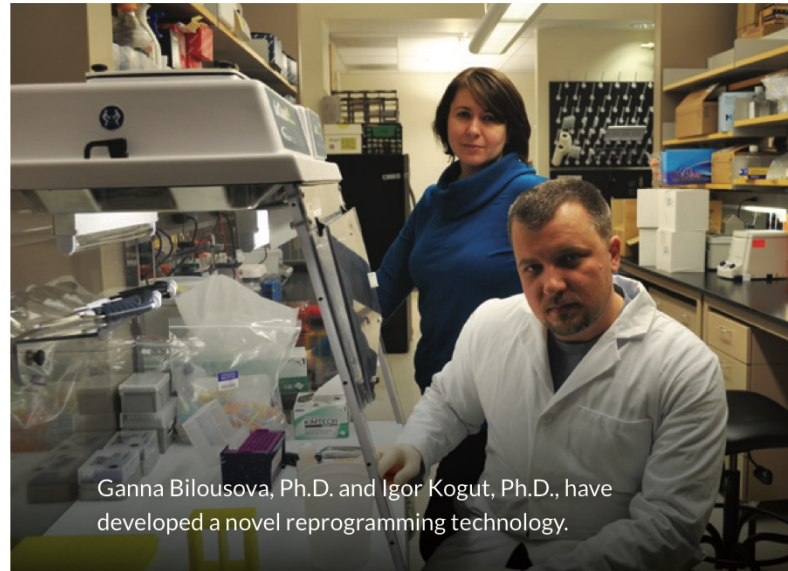
Finally, having the Consortium made up of three institutions collaborating toward a cure proved fruitful when it came to applying for funding from the California Institute of Regenerative Medicine (CIRM). Stanford had had a previous CIRM grant, the renewal of which was stifled due to concerns expressed in preliminary discussions with the FDA over their multi-step reprogramming process and use of viral vectors that have been shown to be cancer-producing. Fortunately, the data showing the safer cell reprogramming and gene editing technologies produced in Colorado addressed these concerns, and the application received the highest score of those submitted and an award of \$5.5 million over three years, moving the Consortium closer to clinical trials in 2017.



# NEW iPSC DISCOVERY PLATFORM SPURS RESEARCH AND CREATES OPPORTUNITIES FOR PHILANTHROPIC PARTNERSHIPS

In 2017, the Gates Center established a new Stem Cell Biobank and Disease Modeling Core (see page 35). This core generates banks of induced pluripotent stem cells (iPSCs) using Ganna Bilousova, Ph.D. and Igor Kogut, Ph.D.'s novel technology as a platform and the iPSCs as tools to understand the underlying basis of diseases that affect tissues that cannot be easily biopsied, such as the brain. This reprogramming technology has already helped fuel the success of federal and state grant applications submitted in 2017 by the Epidermolysis Bullosa (EB) iPS Cell Consortium described in the previous article. But it can also be used for many other applications—particularly those in which there is no readily-accessible, affected tissue. Gates Center's Associate Director Mark Petrash, Ph.D. pointed out the significance of this new approach saying, "Having this capability opens up a new research mechanism with tremendous opportunity." The following projects using this platform were initiated in 2017, thanks to generous contributions cited below.

- **Epidermolysis Bullosa (EB) iPS Cell Consortium:** Angela Christiano, Ph.D., Anthony Oro, M.D., Ph.D., and Dennis Roop, Ph.D. formed this consortium in 2016, which unites the University of Colorado with Stanford and Columbia Universities in the race to find a treatment for this rare and debilitating skin blistering disease. At the end of 2016, the Consortium agreed to adopt Colorado's reprogramming technology described above. Funded by the EB Research Partnership, the EB Medical Research Foundation and the Sohana Research Fund.



Ganna Bilousova, Ph.D. and Igor Kogut, Ph.D., have developed a novel reprogramming technology.

- **Ehlers-Danlos Syndrome (EDS) Project:** Ganna Bilousova, Ph.D., Igor Kogut, Ph.D., Karin Payne, Ph.D., Dennis Roop, Ph.D. and Ellen Elias, M.D. This project will address Ehlers-Danlos syndromes—a group of connective tissue disorders that can be inherited and are varied both in how they affect the body and in their genetic causes, characterized by joint hypermobility (joints that stretch further than normal), skin hyperextensibility (skin that can be stretched further than normal), and tissue fragility. This study examines biopsies from an EDS patient and family members in order to narrow down where to look for mutations. This has led to the creation of an in-vivo model with which to study the disease. This technique will become another new tool to accelerate innovative research into therapies for genetic diseases. Funded by Wagner and Annalee Schorr.



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*Ellen Elias, M.D., who is Professor of Pediatrics and Genetics and Director of the Special Care Clinic at Children's Hospital Colorado, and cares for all of the EDS patients at Children's Hospital Colorado sees about two new patients a week with the unfortunate diagnosis of Ehlers-Danlos Syndrome, a disease that affects our granddaughter, Calla. We feel this research holds the door to the promise of real change and the foundation for new treatments and a potential cure for this disease.*

*—Wag Schorr, M.D., Gates Center Advisory Board Member*

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- **iPSCs as a Tool for the Evaluation and Treatment of Specific Neurogenetic Disease:** Tim Benke, M.D., Ph.D., Scott Demarest, M.D., Jason Aoto, Ph.D., Katherine Smith, Ph.D., Tamim Shaikh, Ph.D., Dennis Roop, Ph.D., Igor Kogut, Ph.D., and Ganna Billousova, Ph.D. The goal of this project is to determine the underlying causes and specific treatments of neurogenetic diseases such as epilepsy. A neurogenetic disease is a brain or nervous system disorder that is thought to be caused—at least in part—by mutations or changes within genes in the patient's DNA. Funded by Rick and Janie Stoddard and the newly formed Gates Center Director's Innovation Fund.
- **Linda Crnic Institute for Down Syndrome:** The Linda Crnic Institute for Down Syndrome is interested in understanding why individuals with Down syndrome rarely develop solid tumors and yet are prone to Alzheimer's disease, congenital heart defects, autoimmune disorders, autism, and some forms of leukemia. To facilitate the research of the unique

characteristics of Down syndrome, the Institute has initiated the Human Trisomy Project that will generate a large biorepository of specimens from individuals affected by Down syndrome and normal controls. The generation of iPS cells constitutes a significant part of the Human Trisomy Project and is being accomplished by the Stem Cell Biobank and Disease Modeling Core. Since taking a skin biopsy, which is necessary to isolate appropriate skin cells for reprogramming, is an invasive approach, individuals with Down syndrome are less likely to consent to this procedure. Taking this into consideration, the Stem Cell Biobank and Disease Modeling Core now isolates live cells from urine specimens and successfully reprograms these urine-derived cells into iPS cells using the reprogramming technology developed by Drs. Bilousova and Kogut. The reprogramming of urine-derived cells provides a unique, non-invasive platform for the generation of integration-free iPS cells to model and better understand Down syndrome and potentially other developmental disorders.

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*Janie and I were very impressed when Tim Benke and his colleagues described their research plans to determine the underlying cause of epilepsy. Seizures are very hard to control in many children and medications often come with undesirable side effects. Then when we learned from Dr. Roop that this research might set the standard for understanding the cause of many different diseases, we were thrilled to be a part of it.*

*—Rick Stoddard, Gates Center Advisory Board Member*

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*The establishment of the new Biobanking and Disease Modeling Core has enabled the Linda Crnic Institute for Down Syndrome to embark on an ambitious project to generate a sizable panel of induced pluripotent stem cells (iPSCs) from people with and without trisomy 21, the genetic abnormality that causes Down syndrome. This iPSCs panel will catalyze myriad investigations to elucidate how trisomy 21 causes the diverse developmental and clinical impacts observed in the population with Down syndrome.*

*—Joaquin Espinosa, Ph.D., Executive Director, Linda Crnic Institute for Down Syndrome*

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# SELECT MEMBER PUBLICATIONS AND HONORS\*

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

In this original article, our team describes a new application that combines rapid immunostaining with laser capture microdissection followed by RNA-Sequencing (Goldstein et al., *J Invest Dermatol*, 2017). With this method, we isolate genetic material from skin cells (melanocyte and keratinocytes) located at specific sites (hair follicle bulge and epidermis), which enable us to provide an in-depth characterization of populations of melanocyte stem cells in the bulge (the repigmentation source), and to show how the gene signature of melanocyte precursors differ from that of the pigment cells in the regenerated vitiligo epidermis. We identified Wnt/ $\beta$ -Catenin canonical pathway and GLI1 as key-players in activation of the bulge melanocyte stem cells during vitiligo repigmentation.

**Kristen Boyle, Ph.D.,** *Assistant Professor, Department of Pediatrics,* and **Jed Friedman, Ph.D.,** *Professor, Department of Pediatrics*

In this study, we cultured mesenchymal stem cells from fresh umbilical cord tissue from human infants born to mothers with obesity or normal weight mothers (Boyle et al., *Molecular Metabolism*, 2017). Comparisons of stem cells between these groups of infants revealed excess fat content in the cells from infants born to mothers with obesity. This was attributable to lower fat metabolism and greater fat storage in the stem cells. We also observed epigenetic differences in genes regulating fat metabolism, which may be one mechanism for altered fat metabolism in these cells. Moreover, the metabolic and epigenetic differences correlated with the fat mass of the infants, measured shortly after birth. These findings reveal that intrauterine exposure to obesity may have long-term consequences for infant stem cell metabolism. As we continue to follow the children from which the stem cells were derived, we may be able to use these stem cells to answer the question of whether infant stem cell metabolism predicts future weight gain or the development of obesity in these children.





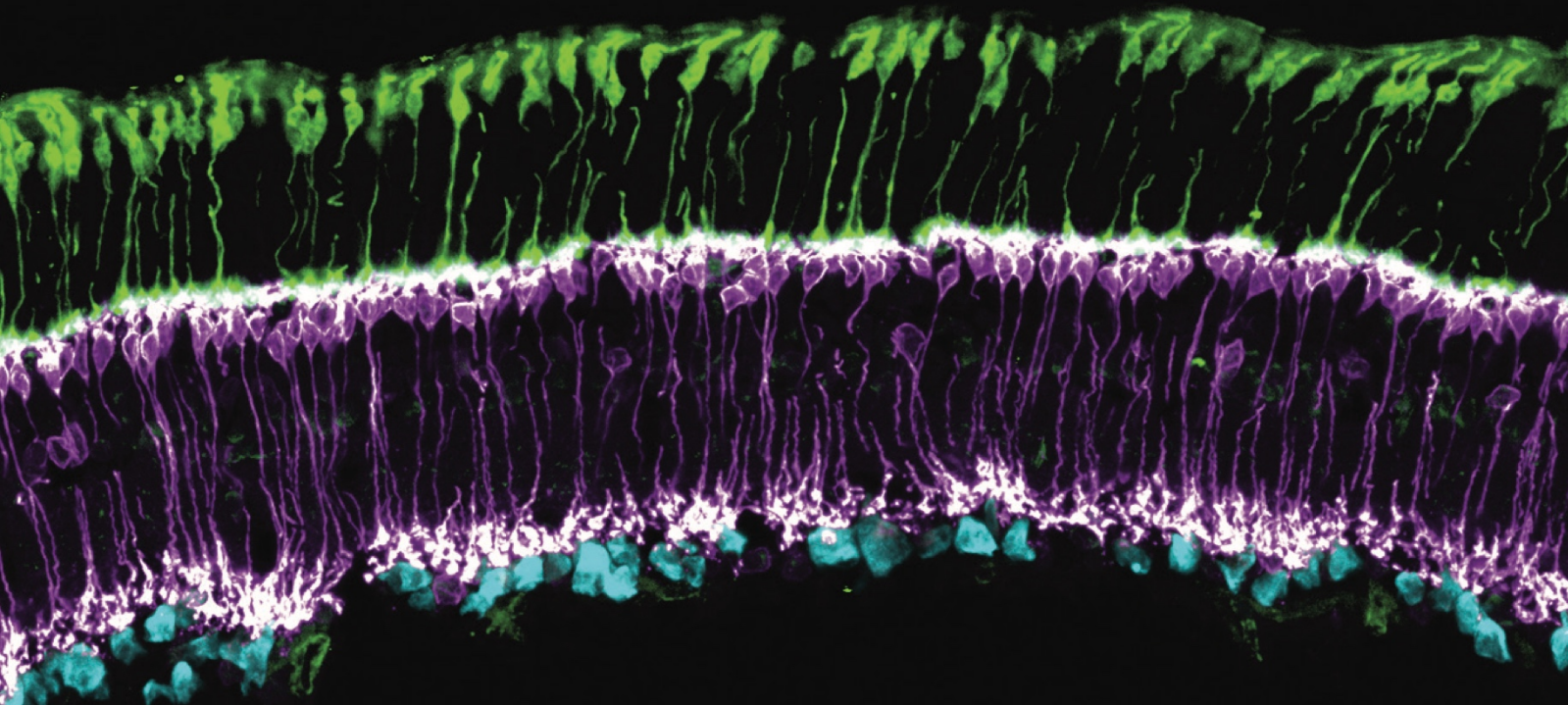


Image of the retina, showing cone photoreceptors in green, bipolar cell relay neurons in purple, and ganglion cell output neurons in cyan. These three neuronal types form a circuit to relay light stimuli to the brain. (Courtesy of Joseph Brzezinski, Ph.D.)

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

In this paper, we investigated how retinal stem cells decide whether to become rod and cone photoreceptors or a related retinal neuron called a bipolar cell (Park et al., *Invest Ophthalmol Vis Sci*, 2017). Using an informatic approach, we identified genes that distinguish early bipolar cells from photoreceptors. Several of these genes were unknown and we discovered that they specifically mark bipolar cells. Our findings are helping us identify what genes control retinal stem cell behavior and will be essential in our efforts to program stem cells for regenerative medicine applications.

**Valeria Canto-Soler, Ph.D.,** *Associate Professor, Department of Ophthalmology*

In collaboration with Dr. Vergara, Assistant Professor, Department of Ophthalmology, Dr. Canto-Soler published a paper describing the establishment of a platform that allows screening of complex stem cell-derived retinal tissue (Vergara et al., *Development*, 2017). This platform, termed 3D automated reporter quantification (3D-ARQ), will make possible the applicability of retinal organoid systems for translational purposes such as the discovery of new therapeutic drugs for retinal diseases.

**Kathleen Gavin, Ph.D.,** *Assistant Professor of Medicine, Division of Geriatric Medicine* and **Dwight Klemm, Ph.D.,** *Professor of Medicine, Division of Pulmonary and Critical Care Medicine*

In this paper, Drs. Gavin and Klemm described a new lineage for the development of fat cells in mice (Gavin et al., *Adipocyte*, 2017). They found that a population of immune cells that arise from the bone marrow and migrate to fat tissue (adipose tissue macrophage) are capable of undergoing a novel transition, ultimately becoming fat cells. Although it has been long recognized that immune cells localize to the fat tissue, particularly in obesity, these cells have not previously been considered as contributors to the generation of new fat cells. The paper also identified integrin  $\beta 1$ , which is involved in cell signaling, as a regulator of this process. More stringently identifying the progenitor/stem cell sources of new fat cells may lead to novel therapies aimed at controlling the cellular composition of fat tissue to decrease risk of obesity-related chronic diseases.



**Jim Hagman, Ph.D., Professor, National Jewish Medical Research Center, Department of Immunology**

Many types of genetic lesions contribute to pediatric B-acute lymphoblastic leukemia (B-ALL). One type with particularly poor prognosis is associated with the fusion of two genes with very different functions: the Early B-cell Factor 1 (EBF1) gene, which encodes a nuclear protein that directs stem cells to become antibody-producing white blood cells, fuses with the Platelet-Derived Growth Factor Receptor-Beta (PDGFRB) signaling gene to make EBF1-PDGFRB. In collaboration with researchers at St. Jude Children's Research Hospital (Memphis, TN), the Hagman laboratory demonstrated that, in the context of EBF1-PDGFRB, EBF1 is unable to turn genes on and off, while PDGFRB makes cancer cells divide in an uncontrolled manner. EBF1-PDGFRB is sufficient to cause stem cell-like leukemia, but is enhanced by other cancer-causing mutations (Welsh et al., *Leukemia*, 2017). The investigators are now exploring new ways to treat EBF1-PDGFRB+ malignancies, which may also be useful for improving outcomes in patients with other types of leukemia.

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

Heart defects are the most common fatal birth defect and are often repaired with Dacron or Gore-Tex patches that are inactive and become a large scar area in the heart. Our researchers have developed a novel, biodegradable patch composed of synthetic materials combined with proteins and other molecules isolated from pig hearts. These patches will recruit native heart cells after implantation and will slowly disappear as the patient's heart cells invade and mature, leaving native heart tissue. In this study, we implanted these patches as a replacement for a portion of the wall of the right ventricle in a rat heart (Pok et al., *Advanced Healthcare Materials*, 2017). We found that these patches are effective at patching the heart wall and maintaining mechanical stability as the materials degrade, that cells will invade and form blood vessels and muscle tissue as in the rest of the heart, and that this has the effect of increasing heart function significantly compared to a commercial patch.

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

Cataracts are a leading cause of vision loss worldwide. Although cataract surgery is very effective at restoring clear vision, 10-15% of patients develop a surgical complication that requires further treatment in the clinic. In this paper, we elucidated an important molecular signaling cascade that can be effectively targeted with small molecule inhibitors to reduce the chances cataract patients will need to undergo a follow up treatment (Chang et al., *Chemistry & Biology*, 2017).

**Michael Verneris, Professor, Department of Pediatrics/Hematology, Oncology and Bone Marrow Transplantation**

Myelodysplastic syndrome (MDS) is a life-threatening cancer of the blood and bone marrow that occurs throughout life (from birth to the 8th decade of life). The only curative therapy for MDS is bone marrow transplantation. At present, the causes of MDS are largely not known, but there are recurring genetic changes (mutations) described in the MDS cells. The purpose of this work was to genetically sequence ~1500 patient samples prior to transplantation and to determine whether these genetic changes were associated with bone marrow transplant outcomes. The findings of this study showed that genetic mutations in certain genes (i.e., TP53) were associated with inferior outcomes regardless of BMT approach (Lindsley et al., *New England Journal of Medicine*, 2017). In contrast, genetic mutations in another set of genes (i.e., RAS signaling pathway) showed inferior outcomes with some types of transplants (i.e., reduced intensity), but not other types (i.e., myeloablative). Lastly, we found that the genetic changes present in adults were almost exclusively absent in children and that the cause of pediatric MDS is largely unknown. Collectively, this is the largest and most focused analysis of patients with MDS undergoing bone marrow transplant. The results of this study will help us to decide the best therapy for adults based on genetic mutations. It also sheds light on the lack of knowledge of the genetic changes that underlie the pediatric form of this disease.



**Xiao-Jing Wang, M.D., Ph.D., Professor,** Department of Pathology and **Antonio Jimeno, M.D., Ph.D., Professor,** Department of Medicine/Medical Oncology

The midbody is a protein-rich structure that is formed during cell division. It is required for the final separation step of cell division, called mitosis, where two new daughter cells are generated. After mitosis, the midbody is mostly inherited by one of the daughter cells and often viewed as junky cell debris. Until recently, the midbody was thought to be degraded after cell division. In this study, the authors discovered that a protein is responsible for regulating the recycling of midbodies after cell division by generating a limiting membrane that surrounds the midbody (Dionne et al., Journal of Cell Science, 2017). They further showed that cancer stem cells have more accumulated post-mitotic midbodies than non-cancer stem cells. Interestingly, depleting the protein responsible for midbody degradation causes an increase in midbody accumulation in cancer stem cells and the ability of these cancer stem cells to grow and invade surrounding cells. Collectively, this study presents the first evidence that cancer invasiveness is a feature that can be modulated by the accumulation of midbodies in cancer stem cells.

## HONORS

**Kristen Boyle, Ph.D., Assistant Professor,** Department of Pediatrics, was invited and accepted as a member of the Perinatal Research Society.

**Valeria Canto-Soler, Ph.D., Associate Professor,** Department of Ophthalmology, had her research featured in a special interview published in the third edition of the Review of Ophthalmology in Spanish in July 2017, and in an August 2017 article in CU Anschutz Today.

**Jeffrey Jacot, Ph.D., Associate Professor,** Department of Bioengineering, and his team at Children's Hospital Colorado were highlighted in an October 2, 2017 video and article published in the National Science Foundation's online Science Nation, posted on the NSF YouTube site, the NSF Science360 News Service, as well as NSF social media platforms. Jacot and team's pioneering new techniques in regenerative medicine focus on creating a heart patch made of an infant's own tissue that would repair the defect and then grow right along with the baby. This research is supported by NSF's Early-concept Grants for Exploratory Research (EAGER) funding mechanism.

**Antonio Jimeno, M.D., Ph.D., Professor,** Department of Medicine/Medical Oncology, was one of three members of the University of Colorado School of Medicine elected to the American Society for Clinical Investigation (ASCI) in 2017. Founded in 1908, ASCI is one of the nation's oldest and most respected medical honor societies for physician-scientists. About 40 members of the School of Medicine faculty have been elected to the Society for their outstanding scholarly achievements in biomedical research.







Melissa Krebs, Ph.D., Assistant Professor, Colorado School of Mines, accepts the 2017 Colorado School of Mines Inventor of the Year Award.

**Melissa Krebs, Ph.D., Assistant Professor,** Chemical and Biological Engineering Department, Colorado School of Mines, received the 2017 Colorado School of Mines Inventor of the Year Award in recognition of the high number of patents she has put through CSM's tech transfer office, and the commercial interest that they have attracted. At the time of the award, Dr. Krebs had filed several patents in each of three new major areas for the school: glaucoma monitoring, regenerative bone and dental materials, and sustained drug delivery biomaterial systems. Accepting the award with her two young daughters, Krebs said "I'm incredibly honored, and it's been fun to bring more biomedical research to Colorado School of Mines." She credits her success to the undergraduate, graduate and postdoctoral fellows in her lab, as well as her collaborations with the University of Colorado School of Medicine. Krebs works closely with several CU Anschutz faculty including Assistant Professor Karin Payne, Ph.D., Department of Orthopedics, on developing hydrogels to block bone formation in growth plate injuries; Associate Professor Mina Pantcheva, M.D., Department of Ophthalmology, on biopolymer-cell constructs for better understanding the trabecular meshwork and for improved drug screening for glaucoma; and Professor Ken Liechty, M.D., Department of Surgery at Children's Hospital, on developing sustained drug-releasing hydrogels to enhance wound healing.

**Carol Sartorius, Ph.D., Associate Professor,** Department of Pathology, was a recipient of a Department of Pathology Educator Awards 2017 (Co-director CANB7680 & Director CANB7613).

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

# GRANT AWARDS

PRINCIPAL INVESTIGATOR(S)	SPONSOR	AMOUNT AWARDED	TITLE	FUNDING PERIOD
Bruckner, Anna	National Institutes of Health, National Institute of Arthritis and Musculoskeletal and Skin Diseases	\$90,000	Pediatric Dermatology Research Alliance (PeDRA) Annual Conference	08/01/17 - 07/31/21
Ford, Heide	Cancer League of Colorado	\$30,000	Role of Six2 in mediating late stage metastasis	07/01/17 - 06/30/18
Ford, Heide/Co-I Zhao, Rui	Colorado Cancer Translational Research Accelerator (CCTRA)	\$100,000	In vivo assessment of novel Six1/Eya inhibitors as anti-breast metastasis agents	07/01/17 - 06/30/19
Ford, Heide/Zhao, Rui	National Institutes of Health, National Cancer Institute	\$406,700	Role of Eya3 in regulating the immune microenvironment to promote breast tumor progression	08/01/17 - 07/31/22
Fujita, Mayumi	Veterans Affairs Merit Award Grant	\$200,000	Autoinflammation in human melanoma (to understand how autoinflammation from melanoma cells contributes to immune escape and tumor progression in tumor microenvironment)	10/01/17 - 09/30/21
Fujita, Mayumi	National Institutes of Health, National Cancer Institute	\$55,800	Modulation of inflammasome-mediated cytokine activation by EGCG in human melanoma (to enhance the training of Jenny Mac Samson—eligible for diversity supplement as a female Pacific Islander—who is enrolled in the Cancer Biology Ph.D. program at University of Colorado Anschutz Medical Campus)	09/01/17 - 06/30/22
Hagman, Jim	Gift of Life Bone Marrow Foundation-In Honor of Wendy Siegel	\$100,000	Molecular and biological studies of B-cell acute lymphoblastic leukemia	07/01/17 - 06/30/18
Hagman, Jim/Torres, Raul	Department of Immunology & Microbiology (UC Denver) 2017-18 Pilot	\$45,000	Regulation of humoral immunity by SR Protein Kinase 3	07/01/17 - 06/30/18
Jimeno, Antonio	National Institutes of Health, National Cancer Institute	\$2,336,426	Characterizing the regulation of PD-1 ligands in head and neck cancer stem cells using an autologous humanized model with T cell education capability	07/01/17 - 05/31/22
Jimeno, Antonio	National Institutes of Health, National Cancer Institute	\$1,742,377	Development of an autologous humanized model of melanoma exploring human thymic education capacity	08/01/17 - 07/31/20
Koch, Peter/Koster, Maranke	National Institutes of Health, National Cancer Institute	\$2,263,020	Mechanisms Underlying Tissue Fragility in Ectodermal Dysplasias	09/21/17 - 07/31/22
Krebs, Melissa	National Institutes of Health, National Eye Institute	\$419,700	Development of a 3D human trabecular meshwork cell culture system using natural biopolymer scaffolds	04/01/17 - 03/31/20
Lyons, Traci	National Institutes of Health, National Cancer Institute	\$1,142,500	Deciphering COX-2/SEMA7A dependent mechanisms of breast tumor progression	06/19/17 - 06/18/21
Lyons, Traci	American Cancer Society	\$165,000	Investigating the role(s) of SEMA7A in breast tumor progression	01/01/17 - 12/31/20
Lyons, Traci	Cancer League of Colorado	\$60,000	Evaluating the role of pro-lymphangiogenic factor SEMA7A in dampening anti-tumor immunity	07/01/17 - 06/30/18
Petrash, Mark	National Institutes of Health, National Eye Institute	\$1,943,750	Molecular signaling in cataracts	09/01/17 - 06/30/22
Payne, Karin/ Bryant, Stephanie/ Ferguson, Virginia/ Hadley-Miller, Nancy	National Institutes of Health, National Institute of Child Health and Human Development	\$416,796	Treatment of pediatric physeal injuries using a 3D printed biomimetic of growth plate cartilage	03/01/17 - 02/28/19



PRINCIPAL INVESTIGATOR(S)	SPONSOR	AMOUNT AWARDED	TITLE	FUNDING PERIOD
Payne, Karin/ Bryant,Stephanie	National Institutes of Health, National Institute of Child Health and Human Development	\$427,337	Physal cartilage tissue engineering using mesenchymal stem cells directed towards chondrogenesis	12/01/17 - 11/30/19
Pietras, Eric	Boettcher Foundation	\$235,000	Blood system dysfunction as an early driver of rheumatoid arthritis	06/01/17 - 06/01/20
Refaeli, Yosef	TAIGA Biotechnologies, Inc.	\$968,227	#5 In vivo Analysis of Protein expanded and /or virally transduced HSC/#6 Invitro expansion of antigen specific T-cells and in vivo Analysis of Effector functions	01/01/17 - 01/31/18
Roop, Dennis/ Bilousova, Ganna	EB Charities	\$293,616	Support the development of novel therapies for Epidermolysis Bullosa	04/29/17 - 04/28/18
Roop, Dennis/Bilousova, Ganna	EB Charities	\$83,790	Support for EB iPS Cell Biobank	07/01/17 - 06/30/18
Roop, Dennis/ Bilousova, Ganna	National Institutes of Health , National Institute of Arthritis and Musculoskeletal and Skin Diseases	\$428,909	Testing the Therapeutic Potential of iPS Cells for Inherited Skin Diseases	09/21/17 - 08/31/18
Roop, Dennis/ Bilousova, Ganna	EB Charities - Match	\$428,909	Support the development of novel therapies for Epidermolysis Bullosa	09/21/17 - 08/31/18
Sartorius, Carol	Breast Cancer Research Foundation 16-072	\$208,333	Molecular determinants of ER+ breast cancer metastasis	10/01/17 - 09/30/18
Sartorius, Carol / E. Wellberg)	Libations for Life – University of Colorado Cancer Center	\$30,000	Targeting obesity in women's cancers using a novel patient-host model	11/01/17 - 10/31/18
Song, Kunhua	University of Colorado Department of Medicine Outstanding Early Career Scholar Program	\$375,000	Translational research of human cardiomyopathy and heart failure	07/01/17 - 07/01/22
Walker, Lori	Colorado Department of Public Health and Environment	\$99,000	Cardiovascular effects of marijuana use in at risk patients	04/01/17 - 06/30/18
Walker, Lori/ Tompkins, Christine/ Kao, David	Colorado Clinical and Translational Sciences Institute (CCTSI); Team Science Award	\$100,000	Cardiovascular effects of marijuana: from single cells to big data	06/01/17 - 05/31/18
Wang, Xiao-Jing	2018 CO-Pilot CSU/CU Collaboration award	\$60,000	Therapeutic intervention of radiation-induced derematitis for canine cancers treated with radiation therapy	06/13/17 - 06/12/18
Total Awards =		\$15,255,190.00		



## **COLLABORATION AND EARLY FINANCIAL SUPPORT FROM THE GATES CENTER'S DIRECTOR'S INNOVATION FUND, WHICH IS MADE POSSIBLE THROUGH GENEROUS INDIVIDUAL GIFTS, LEADS TO GRANT SUPPORT**

To the Gates Center,

I wanted to share the news that we had another NIH grant funded December 1. It is an R21\* with my collaborator at CU Boulder, Associate Professor Stephanie Bryant, Ph.D., who was named Associate Director of the Materials Science and Engineering Program at CU Boulder in March 2017. The project title is: Physéal cartilage tissue engineering using mesenchymal stem cells directed towards chondrogenesis. It focuses on a cartilage biomimetic hydrogel with and without MSCs in a rat model of growth plate injury.

Melissa Krebs, Ph.D., from the Colorado School of Mines and I also have another R21 pending that was scored in the 2nd percentile. It looks at delivery of siRNA with Melissa's hydrogels to block bone formation in growth plate injuries. We are hoping the funding will soon come through as well. Thank you for all your support. The funding you provided to the lab was crucial in getting the preliminary data for these proposals.

—Karin Payne, Ph.D.

*\* "An R21 grant from the NIH supports the development of new research activities to encourage exploratory and developmental research projects by providing early and conceptual stages support."*

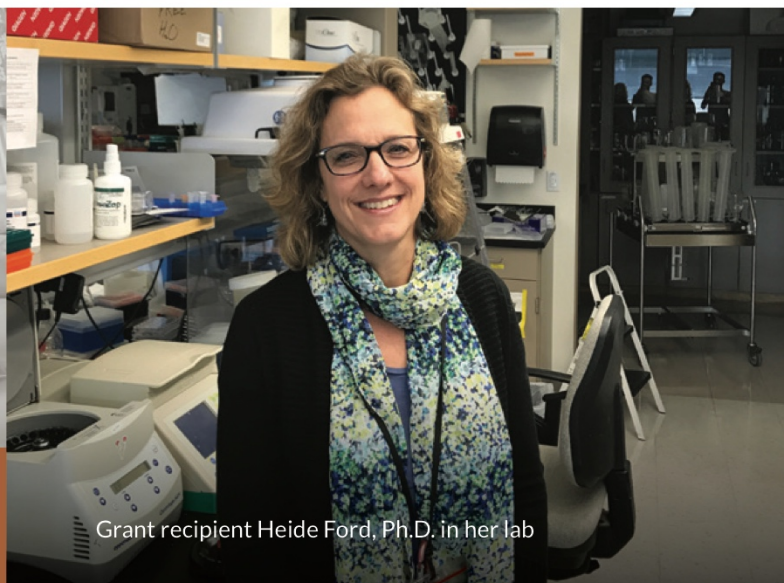
**Antonio Jimeno, MD, PhD, earns R01 grants\* to make new models testing cancer immunotherapies**

A September 11, 2017 article written by Garth Sundem in the Cancer Center Blogs includes the following:

As Harry Potter characters use an invisibility cloak to avoid detection in Hogwarts' forbidden areas, cancer cells make themselves invisible to the immune system to avoid destruction. The recent advent of immune-directed therapies that remove an "invisibility cloak" from the surface of cancer cells has opened up a new horizon of opportunity, but also a new set of challenges.


A key difficulty has been that previous animal models of cancer depend on wiping out a rodent's immune system so that it won't attack tumor cells it sees as foreign. But without an immune system, the models can't teach us how cancer evades immune surveillance, nor can they test immunotherapies, whose actions depend on the presence of an immune system.

Antonio Jimeno, M.D., Ph.D., has developed potential solutions to this problem. He recently renewed a 5-year NIH R01 grant with a new focus on studying how head and neck cancer stem cells trick the immune system.



Grant recipient Heide Ford, Ph.D. in her lab





Nearly simultaneously, Jimeno obtained another R01 grant to develop new animal models of melanoma that allow the study and testing of immunotherapies against cancer. Jimeno is director of the Head and Neck Cancer Clinical Research Program at the University of Colorado Cancer Center, a member of the Gates.

Center for Regenerative Medicine, and the Daniel and Janet Mordecai Endowed Chair for Cancer Stem Cell Research at the CU School of Medicine. Jimeno's team for these two grants includes co-investigators CU cancer immunologist Jing Wang, PhD, and Gates Center member and CU stem cell biologist Holger Russ, PhD, to model the cells to be implanted on mice. The second R01 award focusing on melanoma was a direct result of preliminary data generated thanks to the enthusiastic collaboration of melanoma specialists Drs. Rene Gonzalez, Karl Lewis, and William Robinson.

R01 grants are not approved on ideas alone. Investigators must complete early studies showing the promise of their line of research. For many researchers, this can prove to be a Catch-22 in which funding for their studies is only available after performing studies. In this case, funding for Jimeno's early explorations came in the form of seed monies provided by CU Cancer Center and the Department of Defense. In 2010, the Gates Center for Regenerative Medicine, in

partnership with the Gates Frontiers Fund, provided early support for Dr. Jimeno's research. Between 2011 and 2016, Dr. Jimeno also leveraged generous philanthropic gifts from the Daniel and Janet Mordecai Foundation, the Karsh family, and Peter and Rhondda Grant.

"This philanthropic support took us through the difficult times of chasing an idea that seemed novel and difficult to prove. Now these ideas are validated by these simultaneous awards. For us, philanthropy was a fire-starter," Jimeno says.

This fire-starter, accelerated by the creativity and hard work of Jimeno's team and collaborators, sparked grants now nearing a five-fold return on investment, and allows the multidisciplinary team led by Jimeno to continue pushing test models for immunotherapies in head and neck cancer and melanoma. Dennis Roop, Ph.D., Director of the Gates Center for Regenerative Medicine, commented that this is a wonderful example of how philanthropic support can be used to de-risk novel, cutting edge research to the point that it is eventually funded in today's risk-averse funding environment.

*\* "The Research Project Grant (R01) is the original and historically oldest grant mechanism used by NIH. The R01 provides support for health-related research and development based on the mission of the NIH."*

# COMMERCIALIZATION

“

*Getting great ideas out of the lab and off the shelf is critical to realizing future therapies. In a world of shrinking public funding, we need new solutions like venture philanthropy, forward-thinking business/investor partnerships, and competitive ‘valley of death’ funding to drive innovation and keep brilliant investigators in the game.*

*—Diane Gates Wallach, Co-Chair, Gates Center Advisory Board*

”

With new solutions in mind, the Gates Grubstake Fund was incorporated as a private 501(c)(3) foundation and a key component of the Gates Center for Regenerative Medicine’s commercialization strategy for projects and teams affiliated with the Gates Center. Overseen by the Gates Center with deep support from CU Innovations, Grubstake Fund investment decisions are made on a competitive basis by a Scientific Investment Advisory Committee (SIAC) comprised of subject matter experts and institutional investors with a focus on biotechnology:

- **William Hiatt, M.D.**, *Professor, Division of Cardiology, University of Colorado Anschutz Medical Campus; President, CPC Clinical Research*
- **Ryan Kirkpatrick**, *Partner, Colorado Impact Fund*
- **David L. Lacey M.D.**, *Biopharmaceutical Consultant, former SVP, head of research, Amgen*
- **Mark Lupa, Ph.D.**, *Principal, High Country Ventures*
- **Kimberly Muller, J.D.**, *Managing Director, CU Innovations, University of Colorado Anschutz Medical Campus*
- **Michael Perry, DVM, Ph.D., FACVPT**, *Chief Executive Officer, Avita Medical Ltd.; Managing Director, Bioscience Managers Pty Ltd*
- **Mark Petrash, Ph.D.**, *Professor and Vice Chair, Department of Ophthalmology, Associate Director, Gates Center for Regenerative Medicine, University of Colorado Anschutz Medical Campus*
- **Geoff “Duffy” Solich**, *Executive Vice President, E & P Resources LLC; member, Gates Center Advisory Board*
- **Ann Sperling**, *Senior Director, Trammell Crow Company; member, Gates Advisory Board*
- **Robert Traver, J.D.**, *Patent Attorney, Sheridan Ross*



# 2017 GATES GRUBSTAKE FUND UPDATE

2017 Gates Grubstake Award applicants included faculty from several institutions who are developing new therapies, such as pharmaceuticals, biologics, or medical devices, as well as those who are developing diagnostics and platform technologies, such as delivery scaffolds or bioreactors. In November 2017, the SIAC reviewed 12 Grubstake Fund applications and selected seven for oral presentations a month later. Following the committee's recommendations, each of the following individuals received awards of \$350,000.

## **Valeria Canto-Soler, Ph.D.**

Dr. Valeria Canto-Soler is the director of *CellSight*, the Ocular Stem Cell and Regenerative Research Program in partnership with the Gates Center and Department of Ophthalmology at CU Anschutz. Dr. Canto-Soler was awarded a Gates Grubstake Award for a stem cell-derived retinal transplant to treat dry, age-related macular degeneration. She hopes that one day her research will uncover the cure to blindness through transplanting retinal patches in patients' eyes.

## **Martin Zamora, M.D.**

Dr. Martin Zamora joined the Division of Pulmonary Sciences and Critical Care in 1990 and has served as directing pulmonologist for the Lung Transplant Program since it was founded in 1991. Dr. Zamora was awarded a Gates Grubstake Award for clinical development of autologous CD117+ progenitor cell therapy for solid organ transplantation. His research aims to improve outcomes and quality of life following organ transplantation.

## **Karin Payne, Ph.D.**

Dr. Karin Payne is an assistant professor within the CU Anschutz Department of Orthopedics and is also the lab director for the Payne Regenerative Orthopedics Laboratory. This lab focuses on the regenerative potential of stem cells for bone and articular cartilage tissue engineering to enhance bone fracture repair, improve spine function, and treat articular cartilage defects. Dr. Payne was awarded a Gates Grubstake Award for a bioresorbable 3-D printed personalized implant for cartilage regeneration in pediatric growth plate injuries.



Heather Callahan, Ph.D., J.D., EMBA, is the Gates Center Entrepreneur in Residence. As such, she helps manage the Gates Grubstake Fund and works closely with Gates Center members to help identify the resources needed to develop and protect intellectual property, translate scientific discoveries and commercialize regenerative medicine products.

# PROGRESS REPORTS FROM 2016 GRUBSTAKE FUND RECIPIENTS

- **Jeffrey Olsen, M.D.:** Intraocular Device to Potentiate Retinal Stem Cell Transplantation in Macular Degeneration
  - In vitro testing of implant completed; 40-fold improvement in trapped pathologic proteins.
  - Built and tested a working prototype ex vivo in an eye bank eye for surgical placement.
  - Created a smaller mouse-sized prototype for animal studies.
  - Additional ex vivo and animal studies underway.
  - Regulatory and manufacturing activities are ongoing.
- **Ken Liechty, M.D.:** Nanocerium for the Treatment of Diabetic Foot Ulcers
  - Validated preliminary data of improved wound healing in diabetic mice.
  - Generated positive preliminary data for wound healing in a porcine model of diabetes.
  - Working with regulatory consultants to prepare a pre-IND regulatory package.
  - Preliminary nonclinical and toxicology studies are almost complete.
- **David Wagner, Ph.D.:** A 15-amino acid Peptide to potentially Stop Demyelination and Restore Myelin Production in Multiple Sclerosis
  - Confirmed the pathological cell type in mouse models as Th40 cells.
  - Confirmed elevated levels of Th40 cells in the peripheral blood of MS patients.
  - Identified a lead candidate for drug development, KGY6, in a preventative mouse model.
  - Testing of lead candidate in treatment model of MS is ongoing.

## PAST GATES GRUBSTAKE FUND AWARDEES

### 2014

- **Xiao-Jing Wang, M.D., Ph.D.:** Human Smad7-based proteins combined with a cell permeable peptide called Tat. Tat-Smad7 and its derivatives can be used via topical application to treat at least four diseases: oral mucositis, psoriasis, chronic wounds, and fibrotic diseases.
- **Antonio Jimeno, M.D., Ph.D.:** Proprietary humanized mouse model to assess cancer treatments

### 2015

- **Ganna Bilousova, Ph.D., and Igor Kogut, Ph.D.:** Induced pluripotent stem cell services as a platform for clinical research
- **Steven Dow, DVM, Ph.D., and Mary Ann DeGroote, M.D.:** Antimicrobial stem cell therapy for infected diabetic foot ulcers
- **Karin Payne, Ph.D., and Vikas Patel, M.D.:** Structural living bone allografts to enhance bone formation in orthopedic surgery

### 2016

- **Jeffrey Olsen, M.D.:** Intraocular device to potentiate retinal stem cell transplantation in macular degeneration
- **Ken Liechty, M.D.:** A platform technology useful for treating a variety of diseases where inflammation and oxidative stress are pathognomonic in the progression of the disease; initial focus is treatment of diabetic ulcers, where compelling in vitro and animal model data exists showing that treatment results in closure rates of diabetic wounds equal to nondiabetic wounds
- **David Wagner, Ph.D.:** A 15-amino acid peptide to potentially stop demyelination and restore myelin production in multiple sclerosis



# GATES CENTER ADVISORY MEMBER ANN SPERLING ESTABLISHES “START-UP TOOLBOX”



Thanks to the creativity and thoughtful generosity of Gates Center Advisory Board member Ann Sperling, Gates Center members will have assistance in moving ideas from bench to bedside through Startup Toolbox. A partnership with CU Innovations, Startup Toolbox will provide Gates Center members with a novel platform containing the services and resources required to move discoveries from the lab into products and services that will impact patients. Resources will include corporate/legal, product development, regulatory, Small Business Innovation Resources (SBIR) consultants, as well as business plan and financial modeling support. As a member of the Gates Grubstake Fund’s Scientific Investment Advisory Committee, Ann has reviewed and recommended awards for promising regenerative medicine opportunities. Nonetheless, she also recognizes the need to help researchers when they need help outside of the science to build a business plan, or access IP, legal/regulatory help, pricing etc. In describing the novel platform, Ann said, “It attracts me because as a business person I see the need to get these great scientific ideas into action through financial and organizational transformation, too, and access to this platform of services addresses this essential, non-scientific part.” The goal of the program is to lower the barrier to commercialization in advancing more regenerative medicine opportunities, and to allow Gates Center members to focus more of their time in the lab developing the science.

Ann hopes that this platform will be evergreen and grow, attracting other donations as well as her ongoing support. “As the Gates Center grows,” she says, “this can, too.”



A close-up, slightly blurred image of a microscope's objective lenses and eyepiece, overlaid with a semi-transparent purple filter. The text 'CORE FACILITIES' is prominently displayed in white, bold, sans-serif capital letters across the middle of the image.

# CORE FACILITIES

Since January 2011, the Gates Center has established and operated three core facilities that provide members with access to expert advice and state-of-the-art equipment and technologies at discount rates. The three core facilities are the Flow Cytometry Core, Morphology and Phenotyping Core, and Bioengineering Core. These core facilities have been partially established and operated with funding from the Gates Frontiers Fund, Gates Frontiers Fund/CU Foundation matching funds, a Skin Diseases Research Core Center grant from the National Institute of Arthritis and Musculoskeletal and Skin Diseases awarded to Drs. David Norris and Dennis Roop, and Academic Enrichment Funds provided by the dean of the CU School of Medicine.

The success of these cores in providing quality service with a quick turnaround time is further illustrated by the fact that in addition to being utilized by Gates Center members, they are utilized by investigators in 15 different departments, divisions or centers within the School of Medicine and including the following: the schools of pharmacy and dentistry, National Jewish Health, CU Boulder and Colorado State University. In addition, the Bioengineering Core has users from outside Colorado that include the University of Alaska Fairbanks,

the University of Alabama at Birmingham, Thomas Jefferson University, the University of Lausanne (Switzerland) and Stony Brook University.

The five-year Skin Diseases Research Core Center grant to Drs. Norris and Roop, which was renewed in September 2014, provides \$400,000 per year in direct costs to support four research core facilities, three of which (the Flow Cytometry Core, Morphology and Phenotyping Core, and Bioengineering Core) are all located in the Gates Center. This grant provides partial salary support for the directors of these cores, and subsidizes the costs of the cores to keep usage fees low for Gates Center members. This grant also provides partial salary support for an administrative assistant, who additionally serves as the administrative assistant for the center.

In 2017, the Gates Center for Regenerative Medicine also invested in opening the new Stem Cell Biobank and Disease Modeling Core, which became operational in September 2017. The core utilizes cutting-edge RNA-based technologies to provide services related to human somatic cell reprogramming into induced pluripotent stem cells (iPSCs), the biobanking of human primary cell and iPSC lines,



as well as gene editing using the CRISPR/Cas9 system. The patent-pending RNA-based reprogramming technology used by the core facility has been developed by the co-directors of the core, Drs. Ganna Bilousova and Igor Kogut, together with Dr. Dennis Roop. This novel approach provides significant advantages over traditional cell reprogramming methods, such as lentiviral-, episomal-, and Sendai virus-based methods. The approach relies on the use of non-integrating, synthetic RNA to deliver reprogramming factors. The approach used in the core consistently reprograms human skin fibroblasts (including adult, disease-associated, and aged/senecent fibroblasts) with ultra-high efficiency (up to 800%) and produces high-quality iPSCs. The approach is reproducible (as reported by several independent groups) and cost-effective (significantly less expensive than alternative reprogramming protocols), which makes it well-suited for the generation of biorepositories of disease-associated iPSCs.

In addition to fibroblast reprogramming, the core reprograms renal epithelial cells (RECs) isolated from urine specimens using the RNA-based approach and can assist in establishing primary fibroblast and RECs lines from human specimens. The REC reprogramming protocol was optimized with generous support from the Linda Crnic Institute for Down Syndrome and a grant from the Gates Grubstake Fund awarded to the directors of the core in 2016.

The core also provides services related to the long-term storage and maintenance of generated iPSC lines and primary cell lines. The facility is equipped with top of the line Isothermal Liquid Nitrogen Freezers, a Controlled Rate Freezing System to provide uniform freezing, and utilizes specialized Freezerworks software to ensure the integrity of the cell line database.

Since its opening, the Stem Cell Biobank core has secured reprogramming and gene-editing projects for multiple investigators from the University of Colorado and universities across the United States. Investigators affiliated with the Linda Crnic Institute for Down Syndrome at the University of Colorado Anschutz Medical Campus, the EB iPS Cell Consortium, University of Colorado Boulder, Stanford University, Columbia University, and the Mayo Clinic Arizona are among the clients of the core.

Following is a brief description of our three original core facilities established in 2011 and graphic summaries illustrating their use by both Gates Center members and nonmembers.



# 1

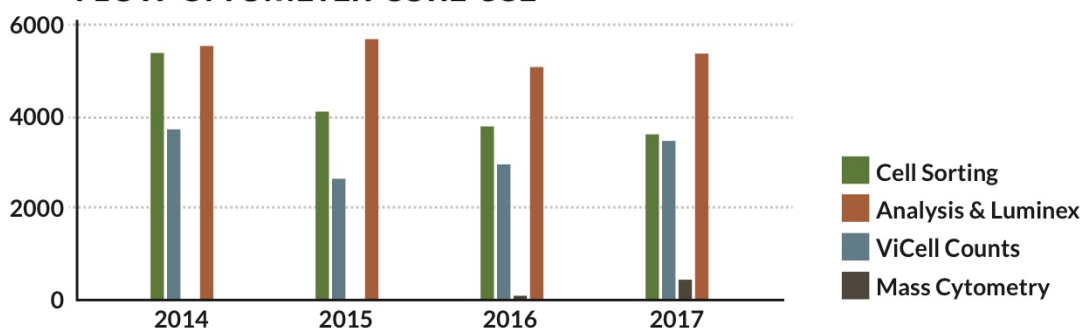
## FLOW CYTOMETRY CORE

Flow cytometry (FC) is an essential tool for stem cell research, allowing the examination of cells at the single-cell level by using cell surface, internal, and nuclear labels. We also have more specialized equipment that can rapidly isolate and collect unique types of cells.

Traditional flow cytometers use laser beams and fluorescent tags to identify the presence or absence of cell markers, however the number of easily identifiable labels is limited to 10 to 15 in conventional systems. Recently, with funding provided by the Gates Center and other campus sources, the core purchased a mass cytometer. This instrument uses rare-earth metal tags to easily identify up to 45 different markers on each cell.

The FC Core provides cutting-edge equipment at a cost-effective price, a highly enthusiastic and skilled staff, experiment design consultation, data analysis assistance, and instrument training services to Gates members.

### FLOW CYTOMETER CORE USE

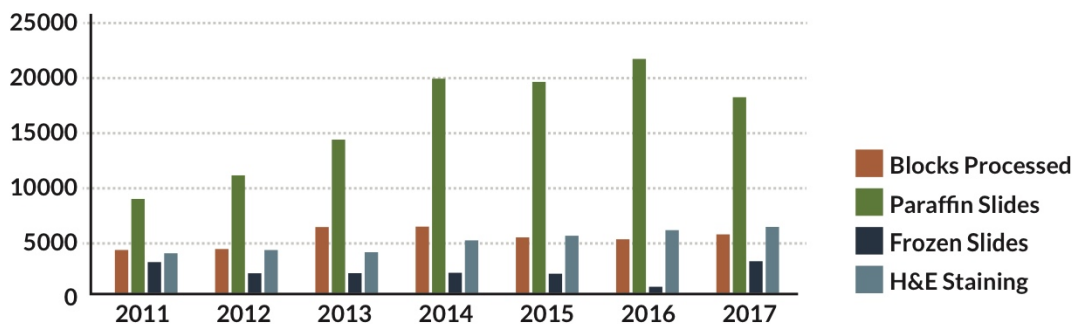


# 2

## MORPHOLOGY AND PHENOTYPING CORE

The ability of clinicians and scientists to analyze tissues at the microscopic level is essential for understanding disease mechanisms. To facilitate this, the Morphology and Phenotyping Core provides a full set of histology services. Upon consultation with the core's histotechnicians, users submit tissue specimens that are processed according to the investigator's needs. Tissue sections are prepared from the specimens to allow for a qualitative and quantitative analysis of the tissues. Analysis of these tissue sections using various staining procedures further contributes to understanding disease pathology.

### MORPHOLOGY AND PHENOTYPING CORE USE





# 3

## BIOENGINEERING CORE

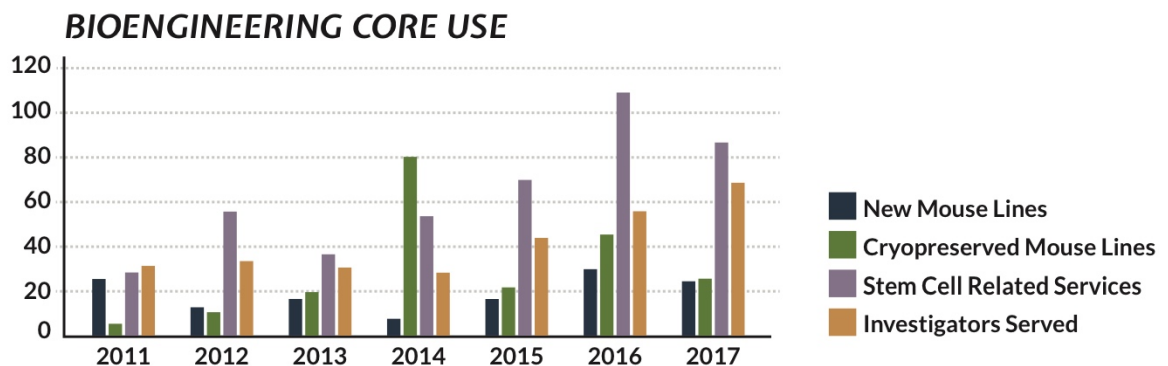
The generation of genetically modified animals is a powerful tool for understanding the role of genes and gene mutations in normal tissue and organ development, as well as in diseases. The Bioengineering Core provides pronuclear injections and embryo-electroporations to produce transgenic mice. We are also providing our customers with the option to generate mice via CRISPR/CAS-mediated genome editing. In addition, we conduct gene-targeting experiments in mouse embryonic stem cells, which enables us to generate mouse lines with custom-designed genes. Additional services include cryo-preservation of embryos and embryo re-derivation.

With the advent of induced iPSC technology, researchers can now reprogram adult tissue-derived cells into stem cells that can differentiate into any type of cell in the adult body. This approach has tremendous potential, not only for designing new therapies, but also for the understanding of complex human diseases. The Bioengineering Core generates iPSC from various species used in biomedical research (e.g., human, mouse, dog, horse) and conducts genome editing experiments in these cells using the CRISPR/CAS system. This approach enables researchers to specifically change gene sequences in these cells (e.g., create or eliminate disease-causing mutations).

In 2017, the Bioengineering Core supported the research projects of 69 investigators. Our services included the generation of 25 genetically engineered mouse lines, the cryo-preservation of 26 mouse lines, and 87 stem cell-related services (e.g., gene targeting in mouse embryonic stem cells, iPSC generation, iPSC differentiation into defined cell types and gene editing in iPSC).

The Bioengineering Core serves investigators from the Anschutz Medical Campus as well as investigators from other universities and institutions in the United States and abroad (e.g. UC Boulder, University of Wyoming, Colorado State University and the University of Australia).

Financial support of our facility is provided by grant funding from the NIH (SDRC, CCTSI), funding from the CU School of Medicine (dean's funding) to Dr. Peter J Koch and user fees. The Gates Center for Regenerative Medicine has provided space and equipment for our stem cell operations.



# GATES BIOMANUFACTURING FACILITY



Gates Biomanufacturing Facility Staff (left to right) Rebecca Vartuli, Kaela Siahpush, Russell Mariani, Sadhna Mehra, Deepa Vadakkan, Renee Jesser, Mitchell Fraller, Bailey Leadford, Sonja Giguere, Heather Clark, Tim Gardner, David Hahn, Frances Brostrom, Paul Lemaire, Jackie Nelson, Matt Seefeldt, Juan Mantalvo, Carter Sarah, Bertina Minjares, Graciela Gamez, Felicia Lanzarone, Christopher Freedman, Jaclyn Valentine, Debbie Keenan, Jessica Freeman, Sandra Jernberg, Tom Street



## Charles C. Gates Biomanufacturing Facility

UNIVERSITY OF COLORADO **ANSCHUTZ MEDICAL CAMPUS**

After providing process development services to both internal and external clients since opening in April 2015, the Gates Biomanufacturing Facility focused on having the quality systems and trained team in place to deliver its first clinical grade cell therapy products by the end of 2017.

With the recruitment of Terry J. Fry, M.D., one of the leading cancer researchers in the country, and the Investigational

New Drug (IND) filings of several of our commercial clients, the GBF needed to recruit some key directors to better position itself for GMP operations. In July 2017, we recruited Ryan Crisman, PhD., the former Associate Director – Head of Late Stage Process Development at Juno Therapeutics. At Juno, Ryan led a cross-functional team responsible for development of commercial autologous CAR-T cell therapies for adult Acute Lymphoblastic Leukemia (ALL), Non-Hodgkin's



Lymphoma (NHL), and Chronic Lymphocytic Leukemia (CLL). Ryan's experience in commercial scale-up of cell therapy products and thorough understanding of FDA regulations for cell therapies is an invaluable asset for the GBF. In December we hired Chris Garbe as the Director of Quality. Chris came to us from Fred Hutchinson Cancer Research Center where he was the Director, Quality Control/Analytical Development for Cellular Therapeutics. Chris' experience in setting up quality systems for an academic GMP facility that provides both process development services and GMP manufacturing for cell therapies and protein products is directly applicable to GBF operations. While we were strengthening our management team, Matt Seefeldt oversaw both protein and cell therapy projects to keep our pipeline of customers moving towards GMP production runs in 2018. Our team of experienced project managers, system operators and quality engineers grew from 20 at the beginning of 2017 to 33 at the end of the year.

In November of 2017, the GBF hired an outside consulting firm to perform an analysis of its GMP readiness, after having completed its equipment validations and drafted its

Facility Master File, Quality Manual and all of its Standard Operating Procedures. The consultant's report indicated that the GBF had designed and implemented a very robust quality management system and that an identified number of final tasks for GMP readiness could be completed in the first month of 2018. In preparation for delivering products for clinical trials in early 2018 the University put in place an Immunotherapy Advisory Committee to coordinate University sponsored clinical trials and advise University GMP production facilities on regulatory and compliance issues. The GBF appointed Ryan Crisman as Interim Facility Director and Roger Giller, M.D., as its Medical Director to add to its clinical trial capabilities and position it for long term Foundation for the Accreditation of Cell Therapy (FACT) accreditation.

Looking forward to 2018, the GBF has a healthy pipeline of both University and outside clients ready to do clinical trials, combined with an experienced staff and a strong quality system. This positions us well to fulfill our mission, which is "To help our clients accelerate the translation of their discoveries into human clinical trials as efficiently and cost effectively as possible."

GATES FRONTIERS FUND

uhealth



The Cell Therapy team's creative picture was one of the top three entries in Drexel University's work category photo contest.





# EDUCATION

## THE GATES SUMMER INTERNSHIP PROGRAM



Final day Gates Summer Internship Program (GSIP) poster session and reception

aspect of the program show that we are meeting our goal of encouraging outstanding undergraduates to consider careers in stem cell and regenerative medicine research by providing state-of-the-art training opportunities at the Gates Center. When asked how they would rate the program, 40% of the Class of 2017 called it “excellent,” and 60% deemed it “outstanding.” While we will institute an official survey in summer 2018 to gather follow-up information about our former

Thanks to a generous gift from the first “Charlie’s Angels” awardees, Rhondda and Peter Grant in December 2014 (see page 52), The Gates Center for Regenerative Medicine inaugurated what has become one of the center’s hallmarks: the Gates Summer Internship Program (GSIP). With the Grants’ ongoing support and additional help from others, the summer of 2017 marked the program’s third year, and by fall 2017, our three dedicated program directors and others were working hard to prepare for the summer of 2018.

This has become an increasingly competitive program, attracting undergraduates from colleges and universities across the country. We received 135 applications for 20 internship positions in the 2017 program—a 260% increase over the prior year, and there is likewise a growing waiting list for Gates Center members hoping to serve as mentors. Annual surveys of interns and mentors regarding every conceivable

interns’ subsequent academic and professional paths, we are heartened to hear through the grapevine that a number of program graduates are applying to or pursuing medical and graduate school paths. We were also encouraged to hear that an intern from our first class matriculated in the Anschutz Medical Campus’s Cell Biology, Stem Cells and Development Graduate (CSD) Program in the fall of 2017. Other testaments to the success of the program are the touching intern “thanks” we assembled into a booklet for donors who collectively contributed over \$100,000 toward our 2017 program. See one of these quotes on page 43 and the GSIP 2017 Summer Internship Program Thank You Booklet ([http://gatescenter.org/wp-content/uploads/2018/04/GSIP\\_ThankYouBooklet2017\\_FNL.pdf](http://gatescenter.org/wp-content/uploads/2018/04/GSIP_ThankYouBooklet2017_FNL.pdf)).

Class of 2017 interns were assigned to individual mentors’ labs during the 11-week program and attended bi-weekly



lectures that included various researchers, clinicians and career development planning, with support from the Anschutz Medical Campus Office of Inclusion and Outreach and the Clinical and Translational Science Institute (CCTSI). Interns also worked toward the creation and presentation of posters highlighting their summer research to share on the program's final day on August 11. This event featured guest speaker Director of Alzheimer's Disease Research Huntington Potter, PhD, the poster session, and a reception for interns, donors, families, friends and campus guests.

Last summer, the GSIP program initiated a pilot collaboration with the Colorado Leaders, Interns, Mentors in Business (CLIMB) program, which gave interns access to downtown housing and weekly educational and social events. While it was nice to provide both group housing and activities,

the interns' regular lab commitments and duties made getting back and forth to downtown Denver problematic. Going forward, the GSIP program will offer its own series of choreographed social events to augment the program. It will also continue to offer the two fully funded summer training positions added to the program's budget in 2017 that include stipends, lodging, transport, parking and food for highly qualified undergraduates from Colorado in financial need. Finally, we hope to grow the program by adding a few additional mentors to diversify the program's areas of focus within the field of regenerative medicine. In so doing, we would like to accommodate our growing list of Gates Center members seeking to become mentors--some of whom are exceptional new campus recruits attracted to the campus by our Gates Biomanufacturing Facility, and who work in bioengineering, diabetes and immunology among others.

INTERN	UNDERGRADUATE INSTITUTION	MENTOR	DEPARTMENT/FACILITY
Joy Abraham	Regis University	Joe Brzezinski, Ph.D.	Department of Ophthalmology
Michaela Grace Berens	Middlebury College	Enrique Torchia, Ph.D.	Department of Dermatology
Jerry Chang	Davidson College	Xiao-Jing Wang, M.D., Ph.D.	Department of Pathology
Alyssa Jeanette Downey	University of Texas at El Paso	Thomas Payne, Ph.D.	Gates Biomanufacturing Facility
Nicholas Howard Elder	Davidson College	Peter Dempsey, Ph.D.	Pediatrics-Gastroenterology/Hepatology and Nutrition
Alisha Grace Eskew	Colorado School of Mines	Curt Freed, M.D.	Department of Medicine/Clinical Pharmacology and Toxicology
Nicholas Lawrence Essek	University of Colorado	Shi-Long Lu, M.D., Ph.D.	Department of Otolaryngology
Zachary Feuer	Rensselaer Polytechnic Institute	Karin Payne, Ph.D.	Department of Orthopedics
Elena C. Fulton	University of Puget Sound	Ganna Bilousova, Ph.D.	Department of Dermatology
Alanna Richelle Horton	Davidson College	Tamara Terzian, Ph.D.	Department of Dermatology
Katherine Rose Johnson	Middlebury College	Heide Ford, Ph.D.	Department of Pharmacology
Roshni Kalkur	Rensselaer Polytechnic Institute	Lori Walker, Ph.D.	Department of Medicine/Cardiology
Shannon Alyson McCallan	Northeastern University	Mayumi Fujita, M.D., Ph.D.	Department of Dermatology
Tricia M. Oyster	Case Western Reserve University	Antonio Jimeno, M.D., Ph.D.	Department of Medicine/Medical Oncology
Jen Elizabeth Pakieser	Regis University	Stanca Birlea, M.D., Ph.D.	Department of Dermatology
Andrew Lawrence Parker	Amherst College	Neil Box, Ph.D.	Department of Dermatology
Matthew Robert Ramsey	St. Olaf College	Paco Herson, Ph.D.	Department of Pharmacology/Neuronal Injury Program
Sarah Nicole Seiwald	Regis University	Mark Petrash, Ph.D.	Department of Ophthalmology
Bay Lee Vagher	Fort Lewis College	Yiqun Shellman, Ph.D.	Department of Dermatology
Oscar Star Yip	Occidental College	Kristin Artinger, Ph.D.	Department of Oral & Craniofacial Biology

“ On behalf of the Gates Center, we want to thank the directors of our program, whose photo is on page 43 and especially our interns, for the sparkle, intellect, energy and countless hours they contributed toward their respective labs, individual research projects and to the Gates Center itself. These students, who were chosen from a nationwide pool of 130 applicants, represented us beautifully during the summer of 2017 and made us exceptionally proud!

—Dennis Roop, Ph.D., Gates Center Director

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“

Again, we have treasured being part of the development and growth of the Gates Summer Internship Program (GSIP), and other Gates Center friends have also enjoyed contributing gifts toward the program, individual interns' stipends, event fees or scholarships. Together with the Gates Center staff, we remain committed to the success and sustainability of this program in the future. We are thrilled about the progress that has been made by the fine team at the Gates Center and even more excited about the potential of this GSIP program to inspire young people to pursue educational and career opportunities in this promising field. We hope you might be interested in learning more!

—Rhondda and Peter Grant

”

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

Another ongoing educational initiative, which was spurred by our 2015 self-study reviewers' recommendation, is our collaboration with and support of the Graduate Program in Cell Biology, Stem Cells and Development (CSD), directed by Bruce Appel, Ph.D., Gates Center member and Diane G. Wallach Chair in Pediatric Stem Cell Biology. This combined program is based on the premise that although medical use of stem cells holds great promise for treatment of human diseases and birth defects, to advance the use of stem cells in the clinic scientists must continue to pursue fundamental discoveries as to how cells function and how cells in embryos form the different tissues of the body.

In the area of graduate recruitment, Gates Center support enabled CSD to recruit two first year graduate students in addition to the four student slots provided by the Graduate School. For the second year in a row, the program had seven students accept offers—one more than the total allotment of six students. The Graduate School provided funds to support the additional student. According to Dr. Appel, Gates Center support has helped propel CSD's student group to an all-time high of 33. As previously mentioned, one student who matriculated in 2017, Madison Rogers, was a Gates Center Summer Program intern. The Gates Center looks forward to incorporating Dr. Appel into its future programming to familiarize our summer interns with this superb program.

The Gates Center's support also enabled nine students to travel to scientific conferences in 2017. These meetings

included the Keystone Symposium on Mitochondria, Metabolism, and Heart, Santa Fe, NM; Keystone Symposium on Adult Neurogenesis, Squaw Creek, CA; IUBMB Focused Meeting on the Emerging Concepts of the Neuronal Cytoskeleton, Puerto Varas, Chile; Digestive Disease Week, Chicago; EMBO conference on Gene Regulatory Mechanisms in Neural Fate Decisions, Alicante, Spain; American Society of Cell Biology, Philadelphia; and Society for Neuroscience, Washington DC.

Finally, the Gates Center helped with program recruitment and course support. Center funds covered the costs for the CSD Admissions Committee Chair, Jeff Moore, to visit several small colleges in Missouri and Iowa, as well as for a CSD postdoc, Rwik Sen, to represent CSD at the Society for Advancement of Chicanos/Hispanics & Native Americans in Science (SACNAS) meeting, the largest diversity-in-STEM conference in the country. Gates Center support also paid for materials for our Stem Cell and Developmental Models graduate courses and underwrote a portion of two sessions of the program's summer Bootcamp, in which CSD graduate students provide introductory training for over 30 summer research interns.

We look forward to continuing to help support, grow and promote this superb program.





The Colorado Melanoma Foundation granted Nicholas Elder from Davidson College the "Colorado Melanoma Foundation Citizenship award" that was sponsored by the Wallaroo Hat Company.



CSD 2017 Retreat



GSIP Directors (left to right) Enrique Torchia, Ph.D., Tamara Terzian, Ph.D., Neil Box, Ph.D.

#### **A final comment from one of our 2017 GSIP interns:**

To the Donors of the Gates Summer Internship Program,

This past summer helped me solidify my career goals more than any other singular experience I have had. I worked independently in Dr. Dempsey's lab on a project, and in a field, no less, that had been completely new to me a few weeks earlier. Nearly everything I did in lab involved a new method that I had never had hands-on experience with before. I attended our bi-weekly lectures by Gates scientists from a range of fields and departments, and not once did I want those hour-long lectures to end. I gained some much-needed confidence in plans to apply to grad school. I experienced Colorado for the first time. I experienced snow in July for the first time. I somehow managed to wake up at 3:30 am to climb a 14er. And then I did it again.

This summer was more than just formative; it was an extremely positive and enjoyable experience that would not have been possible without your generous support of the GSIP program. I gained a new mentor and new friends, and I even intend to pursue stem cell research in grad school. Your continued support of GSIP will ensure that many more students like myself get a chance to have these impactful experiences.

Since I cannot be with you in person to shake your hand, I instead offer a humble Thank You for your desire to give meaningful opportunities to students interested in improving the lives of other through research and medicine.

Sincerely,

**Nicholas Elder**

Davidson College



# OUTREACH

Gates Center staff and others spent a significant amount of time in 2017 sharing our story with external and internal audiences. Among other efforts, we welcomed school groups and visitors to the Gates Center and the Gates Biomanufacturing Center, accepted invitations to address outside groups and worked with elected officials and others to further regenerative medicine initiatives.

Gates Center's Lab Manager Charlie Wall arranged presentations and lab tours at the Gates Center's headquarters on campus in Research Center 1 North for nearly 400 students and their teachers in 2017. Groups included long lines of young people hailing from the K-12 Aurora Public Schools' Aurora LIGHTS Biotechnology Academy, Colorado Early Colleges, the CU Science Discovery Program, the Denver Public Schools X Program, Graland Country Day School, Mountain Ridge Middle School, Rocky Mountain Lutheran High School, St. Mary's Academy and Valor High School.

Likewise, on-and-off campus visitors continued to stream in to hear about and see our Gates Biomanufacturing Facility across Montview Boulevard from campus. In particular, Gates Center Advisory Board member Rick Stoddard, past chair of the Children's Hospital Colorado Foundation, continued his crusade to assist us in expanding our reach, extending countless invitations to Children's Hospital Colorado clinicians and foundation members. Between his efforts and those of others, we hosted 40 tours to introduce over 170 people to our facility, where close to 40 employees now work to manufacture protein and cell-based therapies for human trials. In the meantime, Rotary groups continued to be particularly enthusiastic audiences for the Gates Center story. Gates

Center's Executive Director Patrick Gaines crisscrossed the metropolitan area and beyond, addressing Rotarians at the following array of clubs: Anschutz, Castle Rock, Erie, Evergreen, Franklin Frederick, Highlands Ranch, Lakewood, Littleton and Twin Peaks in Longmont.

For the second year, the Gates Center also participated in a summer interactive learning opportunity for high school girls interested in exploring healthcare and science careers, sponsored by the Center for Women's Health Research and UCHHealth. In this superb annual program, 60 young women spend a day on the Anschutz Medical Campus, during which they are introduced to a variety of facilities and health care professionals. During a morning session at the Gates



Tim Gardner describes the state-of-the-art CliniMACS Prodigy system to Gates Biomanufacturing Facility visitors.



Biomufacturing Facility, the group observed how lab discoveries are translated into cell-based therapies and visited with female facility employees who shared the oftentimes-circuitous paths that have led to their scientific careers.

Late summer featured the 2017 International Pigment Cell Conference for which Gates Center members David Norris, M.D. and Neil Box, Ph.D., were the conference co-director and program director respectively. Supported by the Gates Center, the conference drew 540 national and international pigment cell and melanoma researchers to Denver. As the co-founder of the Colorado Melanoma Foundation, Dr. Box is a perennial advocate for melanoma outreach and awareness in the local Colorado community, participating in local TV shows to promote sun safe habits, and along with his Gates Center colleagues and volunteers, hosting events to support the development of educational programs targeting Colorado children and the community at large. This year's summer events included the annual Mallets for Melanoma in partnership with the Denver Polo Club, and the Summit Melanoma at Cordillera charity golf tournament in Vail.

In the area of public policy, thanks to Kent Springfield in the University of Colorado's Office of Government Relations, the Gates Center staff interacted throughout the year with elected representatives and national associations Research!America and the Alliance for Regenerative Medicine to promote the regenerative medicine field. In February 2017, Congressman Mike Coffman and his Chief of Staff, Ben Stein, visited the Gates Biomufacturing Facility. This occasion allowed the Gates Center to thank them and their Legislative Director, Jeremy Lippert, for their indefatigable efforts to ensure the inclusion of regenerative medicine in the 21st Century Cures Act, which passed and was signed into law in December 2016. Significantly, the Epidermolysis Bullosa (EB) iPS Cell Consortium, which includes the University of Colorado's Gates Center team, received one of eight awards in the country resulting from this legislation—a wonderful affirmation of our significant advances in developing safer cell reprogramming and gene editing technologies here in Colorado.

Senator Michael Bennet and his staff were likewise most helpful in including Epidermolysis Bullosa in the FY 17 DOD Peer-reviewed Medical Research Program. While EB had been included on the list in the past due to its relevance to combat-related thermal wounds, it had evidently fallen off the list due to an advocacy gap. Redressing this was considered a long shot, but EB was returned to the list in the final FY 2017 omnibus appropriations bill, and its funding was increased.

Gates Center representatives also participated in an on-campus roundtable with Senator Bennet and incoming FDA Commissioner Gottlieb in August 2017, and in ongoing meetings coordinated by the Colorado Biomedical Association to develop regenerative medicine proposals. Finally, Gates Center Director Dennis Roop was invited to present and participate in a National Institutes of Health (NIH)/Food and Drug Administration (FDA) Workshop in December 2017, at which 400 attendees and several Gates Center representatives heard about the FDA's commitment to advancing regenerative medicine into the clinic. As Gates Center's Entrepreneur in Residence Heather Callahan said, "Everything is now ready. Science is ready, patients are desperate and the FDA doesn't want to be a roadblock. The FDA will help."

Finally, the Gates Center remains concerned about the proliferation of self-identified stem cell clinics in the United States and elsewhere in the world. We receive regular inquiries from individuals regarding these clinics and hope we can make a contribution in dispelling some of the misinformation that lures people to seek costly treatments for which there is no data to show efficacy based on carefully conducted clinical trials—only anecdotal evidence. We feel strongly that clinics need a better way to expand cells and determine biomarkers and standards, and that the website [clinicaltrials.gov](http://clinicaltrials.gov) needs to be more selective in listing legitimate clinical trials. We are heartened that the FDA has recently pledged to work with inventors early on so that they don't go down the path without the promise of safety and efficacy. We will continue to work toward ensuring that unscrupulous actors do not harm patients or jeopardize this promising field.

# NEW FACES AT THE GATES CENTER



**Ryan Crisman, Ph.D:** Effective August 2017, Ryan Crisman joined the Gates Center as the Gates Biomanufacturing Facility's new Director of Cell Processing and now serves as interim Facility Director. Prior to arriving on the Anschutz Medical Campus, Ryan was associate director—head of late stage process development and CMC lead of JCAR017 for Juno Therapeutics in Seattle, WA, which licensed in CAR-T cell technology developed by Terry J. Fry, M.D., one of the leading cancer researchers in the country and a new recruit to the Anschutz Medical Center.

Ryan grew up in the State of Washington in a small logging town outside Seattle and went on to receive his Ph.D. in Chemical and Biological Engineering at the University of Colorado Boulder. While there, he and Gates Biomanufacturing Center's Director of Protein Chemistry & Manufacturing Matt Seefeldt worked together under advisor Dr. Theodore Randolph, considered "a world leader in protein stabilization and supercritical fluid technology in processes for enzymatic catalysis, particle formation, and drug delivery."

A recipient of numerous honors and awards, Ryan likes the idea of being affiliated with a superb facility within an academic institution with great science and for-profit industry opportunities. He looks forward to getting back to his roots in cutting-edge research as well as staying close to the CAR-T area and working with Terry Fry to pave the way for other cell therapies to serve as-yet-unmet patient needs. In the meantime, we feel fortunate to have added Ryan's skills in GMP process manufacturing, FDA regulations and team building to those of our accomplished and growing Gates Biomanufacturing staff. It's great to have Ryan, his wife and labradoodle now with us in Colorado!



**Christopher Garbe, M.S., M.B.A:** Christopher Garbe joined the Gates Center as the Gates Biomanufacturing Facility's Director of Quality in the final days of 2017. Formerly the director of quality control/analytical development of cellular therapeutics and interim director of process development at the Fred Hutchinson Cancer Research Center in Seattle, WA, Christopher heard about the position from our Interim Facility Director Ryan Crisman, with whom he worked at Zymogenetics, Inc; a Bristol-Myers Squibb Company, also in Seattle.

Chris describes himself as a military brat, whose father was "tethered" to the Navy for 30 years. As such, he was born in Rota, Spain, and spent his formative years living up and down the East Coast from Florida to Rhode Island, as well as in Stuttgart, Germany, where he attended high school.



Chris graduated from the Rensselaer Polytechnic Institute (RPI) in Troy, NY, with a bachelor's degree in chemistry, received his Master of Science, Biochemistry and Molecular Biology from George Washington University in Washington, D.C., and his MBA from the University of Texas, in Austin. While living in the DC area, Chris first pursued "gigs" in the biotech arena for over a decade. Later he was recruited to Seattle to work for Zymogenetics, Inc., where he started the company's first GMP pilot facility and oversaw a quality laboratory to support the company's recombinant protein programs, working on pre-clinical through commercial projects. Since 2014, Chris has worked at the Fred Hutchinson Cancer Research Center, renowned as one of the most prolific biomedical research institutions in the area of company formation, based on center inventions.

Chris's former colleague Ryan Crisman is particularly delighted to have helped recruit such a fantastic and sharp individual to the Gates Biomanufacturing Facility, whose knowledge of quality and experience working in the CAR-T space in both academia and industry will help guide the entire team. In the meantime, Chris and his two canine and one feline "fur babies" are looking forward to living in Denver and to helping both the Gates Biomanufacturing Facility and the Gates Center build a tight network based on transparency and a shared sense of goals and mission. We enthusiastically welcome him to our midst!



**Ellen McGrath, B.S., M.S.:** Ellen McGrath began working as the Accounting Coordinator for the Gates Center in April 2017. She works with Carmen Garcia and provides purchasing, budget, and administrative support to both the Gates Center and the Gates Biomanufacturing Facility. Ellen received her B.S. in Agricultural Biotechnology from the University of Kentucky, and her M.S. in Accounting from the University of Connecticut. She has professional experience in corporate payroll, private healthcare practice, and hospital business environments.

Ellen is married to Sean McGrath, who works in the new Stem Cell Biobank and Disease Modeling Core with Anya Bilousova and Igor Kogut. Sean and Ellen are proud parents to 2-year-old Owen and a new baby girl, Joanna, born in December. Away from campus, Ellen enjoys hiking, trying to improve at skiing, and game nights with family and friends. She is excited to be involved with an organization that promotes leading-edge medical research, and that has so many exciting projects on the horizon.



**Mark Petrash, Ph.D.:** Mark Petrash became Associate Director of the Gates Center as of July 1, 2017. As professor and vice chair of research in the Department of Ophthalmology since 2008, Petrash retains his current position while amplifying his involvement with the center, with which he has become quite familiar over the past few years. He was our 2015 internal self-study reviewer, a key collaborator in the center's successful partnership with the Department of Ophthalmology to raise \$10 million to establish an ocular stem cell and regeneration program and recruit Valeria Cantor-Soler, Ph.D., as its director. Further, Petrash is a longtime Gates Center member, a member of our Gates Grubstake Scientific Investment Advisory Committee (SIAC) and an enthusiastic

mentor for our Gates Summer Internship Program since its creation in 2015.

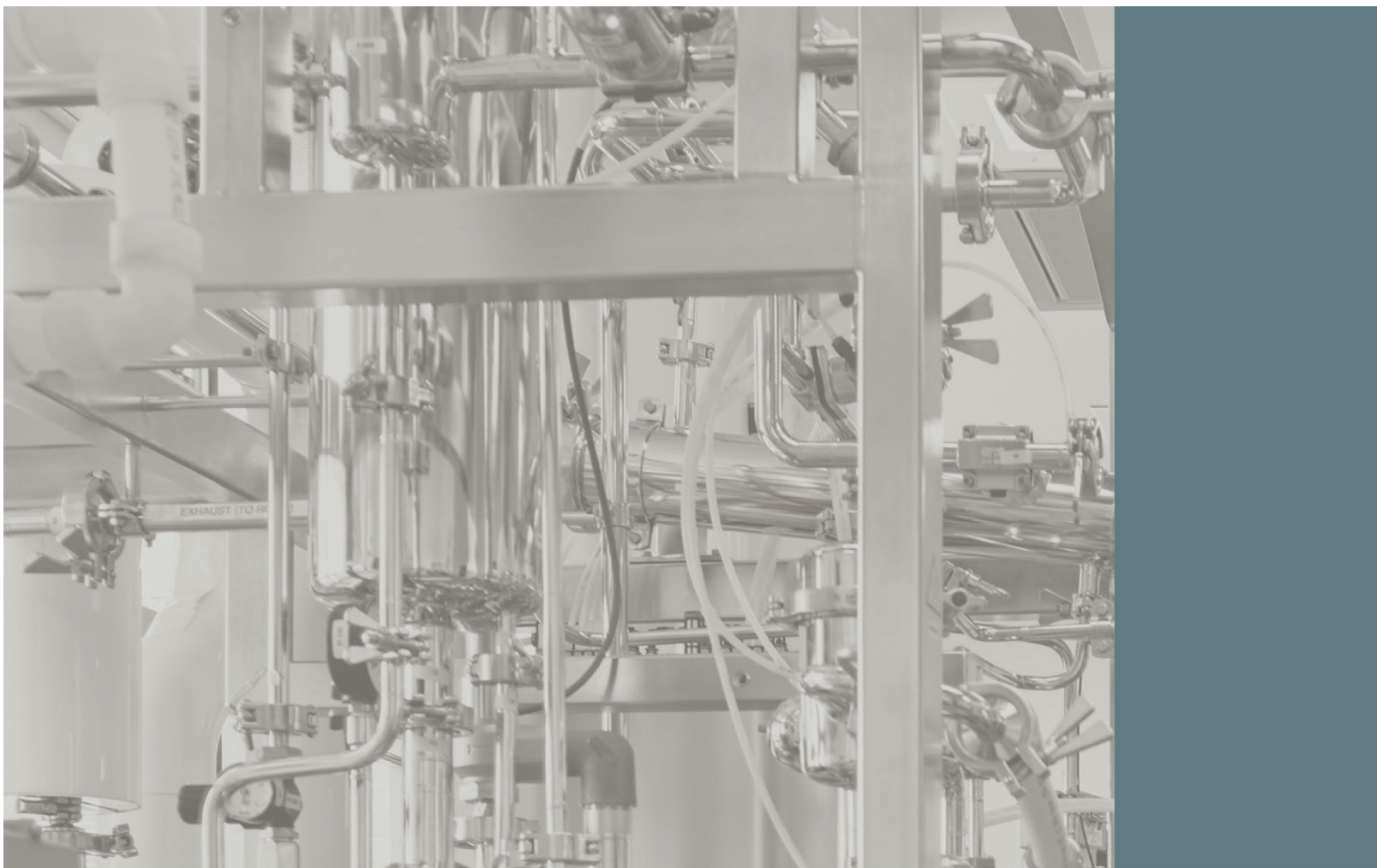
A Texas native, Mark earned his B.S. in Zoology from the University of Texas, Austin, and his Ph.D. in Human Biological Chemistry and Genetics from the University of Texas Medical Branch in Galveston. Following a postdoctoral fellowship in the

Department of Biochemistry at New York University, Mark became a research assistant professor of Ophthalmology at Emory University School of Medicine in Atlanta. In 1984, he and his family relocated to St. Louis, MO, where he joined the faculty of Washington University School of Medicine. Over the next 20 years at Washington University, Mark rose through the ranks to professor of Ophthalmology and Visual Sciences and professor of Genetics, prior to his recruitment to the University of Colorado Anschutz Medical Campus in 2008.

Mark is the recipient of numerous awards, including the 1988 Robert E. McCormick Research Scholar and 1997 Lew R. Wasserman Merit Awards from Research to Prevent Blindness, Inc., the 2000 Outstanding Faculty Mentor Award from Washington University's Graduate Student Senate of Arts & Sciences and the 2012 Distinguished Service Award from the Association for Research in Vision and Ophthalmology. In addition to his work as vice chair for research in the Department of Ophthalmology and new role at the Gates Center, he also serves the wider Anschutz Medical Campus on the Research Track Steering Committee and Strategic Infrastructure for Research Committee (SIRC).

Given Mark's distinguished professional career, charismatic leadership and devotion to his colleagues and students, and long list of inventions, intellectual property, patents and publications, the Gates Center considers itself extremely fortunate to add Mark and his talents to its midst and future.

Mark and his wife Kelly have three grown children, two of whom have followed him into the world of medicine as a doctor and critical care nurse, respectively.





# FINANCIAL OVERVIEW



The following financial statement reflects the operations of the Gates Center and of the Gates Biomanufacturing Facility, both of which have been the fortunate recipients of funding from a number of sources including the University of Colorado Foundation and President's Office, the CU Anschutz Chancellor's Office, the Gates Frontiers Fund, our hospital partners and private donors. Please note that we continue to collaborate with other centers, departments and divisions, as well as our hospital partners, and because of these collaborations, our financial statement does not fully capture the extent of our activities and philanthropic support. Likewise, research performed by individual Gates Center members is funded directly through federal and state research grants, private foundations and individual donations, along with targeted support from the Gates Center.

Overall, Gates Center expenditures are designed to fuel the research of the future. In addition to providing research support to its members, the Gates Center operates the Gates Biomanufacturing Facility and four core laboratory facilities (Biobank & Disease Modeling; Flow Cytometry; Morphology and Phenotyping; and Bioengineering), and it provides laboratory infrastructure to members for work done outside of the core facilities. Commercialization support, education and outreach, and marketing and development activities are also provided as part of the overall Gates Center mission.

# **GATES CENTER OPERATIONS**

2017 was the second year of operations under a five-year funding agreement between the Gates Frontiers Fund, the University of Colorado Foundation, the University of Colorado President's Office and the CU Anschutz Chancellor's Office. Additionally, the Gates Center facilitated approximately \$1.8 million in new philanthropic support for key initiatives described in more detail on pages 19-20, 28-29, 33 and 40-43.

Consistent with our mission and past priorities, center program support of \$721,053 was the largest expense category, totaling 29 percent of all spending for 2017. Investments in equipment and operations of the core facilities and the Gates Center laboratories totaled \$594,723 in 2017, which was 24 percent of expenses. The balance of our expenses were for marketing and development totaling \$530,526 (21 percent), center administration totaling \$389,380 (15 percent), and center enrichment, educational activities and commercialization support totaling \$285,939 (11 percent).

The Gates Center net of sources less expenditures for 2017 was a gain of \$78,379 for the calendar year ended 12/31/2017. Our fund balance for the Gates Center was \$159,177 at calendar year end.

# **GATES BIOMANUFACTURING FACILITY OPERATIONS**

In its third year of operations, the Gates Biomanufacturing Facility generated \$1,726,357 in revenue from a combination of outside for-profit companies and Anschutz-related laboratories. We also received an additional \$3,125,000 from our operating partners. With cost of goods sold and operating costs totaling \$5,238,907 and capital expenditures of \$240,764, the Gates Biomanufacturing Facility reported a net loss of \$628,313 for the calendar year ended 12/31/17. The GBF fund balance was \$131,365 as of calendar year end.





	2013	2014	2015	2016	2017
<b>Infrastructure and Operations Grants</b>					
Infrastructure and Operations Grants	\$2,150,000	\$2,003,100	\$2,010,330	\$2,547,617	\$2,600,000
<b>Gates Center Expenditures</b>					
Center Lab Operations	\$157,500	\$188,204	\$160,967	\$328,657	\$286,645
Center Core Facilities	\$197,750	\$277,826	\$458,498	\$166,039	\$308,078
Center Research Program Support	\$711,440	\$506,551	\$751,750	\$976,914	\$721,053
Marketing & Development	\$409,994	\$318,155	\$338,655	\$336,937	\$530,526
Center Admin/Maint/Supplies	\$243,107	\$317,948	\$336,792	\$376,593	\$389,380
Center Enrichment	\$28,000	\$53,198	\$18,539	\$30,375	\$56,286
Center Educational Activities	\$23,500	\$60,575	\$31,914	\$122,841	\$123,903
Center Extraordinary Expenses	\$327,866	\$18,027	\$22,000	\$0	\$0
Commercialization Support	\$151,307	\$111,224	\$62,266	\$102,433	\$105,750
<b>Total Expenditures</b>	<b>\$2,250,464</b>	<b>\$1,851,708</b>	<b>\$2,181,381</b>	<b>\$2,440,789</b>	<b>\$2,521,621</b>
<b>Center Sources - Expenditures</b>	<b>(\$100,464)</b>	<b>\$151,392</b>	<b>(\$171,051)</b>	<b>\$106,828</b>	<b>\$78,379</b>
<b>Gates Fund Balance</b>				<b>\$(31,544)</b>	<b>\$159,177</b>
<b>Gates Biomanufacturing Facility</b>					
GBF Customer Revenue			\$ 166,025	\$ 1,511,209	\$ 1,726,357
GBF Partner Support			\$ 1,376,750	\$ 1,535,000	\$ 3,125,000
<b>GBF Total Income</b>			<b>\$ 1,542,775</b>	<b>\$ 3,046,209</b>	<b>\$ 4,851,357</b>
GBF Operating, and Capitol Expenditures			(\$ 1,762,518)	(\$ 3,618,463)	(\$ 5,479,670)
<b>GBF Sources-Expenditures</b>			<b>(\$219,743)</b>	<b>(\$572,254)</b>	<b>(\$628,313)</b>
<b>GBF Fund Balance</b>				<b>\$ 248,522</b>	<b>\$ 131,366</b>

# ACKNOWLEDGEMENTS

## CHARLIE'S ANGELS

On the occasion of the second annual Charlie's Picnic on August 23, 2017, Diane Gates Wallach presented the first "Charlie's Angels Award" to perennial Gates Center boosters Rhondda and Peter Grant. Enthusiastically dedicated to the Gates Center over the years, Rhondda and Peter have performed countless acts of kindness, supporting individual Gates Center researchers, helping purchase essential pieces of equipment, hosting countless gatherings to introduce the center to family and friends, and helping launch and sustain the Gates Summer Internship Program for college undergraduates. We hope that this award will recognize all they have done to inspire and support us as we pursue Charlie Gates' vision of enabling safe and expedited translation of discovery into human therapies.



Rhondda and Peter Grant





**The Gates Center gratefully acknowledges the following individuals, foundations and organizations for supporting our research and mission during the 2017 year.**

Berenice Gates Hopper Family Fund	The Glendorn Foundation	Susan Bonsall Rosenberry
Dori Biester, Ph.D., FAAN	Rhondda and Peter Grant	Walter S. Rosenberry, III Charitable Trust
Janelle and Buck Blessing	Margaret Hoyt Hagerman	Rotary Club of Highlands Ranch
Balbi A. Brooks	Susan and William Hiatt, M.D.	Annalee and Wagner Schorr, M.D.
Children's Hospital Colorado	Joyce and Wayne Hutchens	Anita and Geoff Solich
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Yvette and Chris Frampton	Mary Lanius	University of Colorado Anschutz Medical Campus, Office of the Chancellor
Patrick Gaines	Gretchen and Charles Lobitz	University of Colorado Anschutz Medical Campus, School of Medicine
Deb Froeb and Tim Gardner	Daniel and Janet Mordecai Foundation	University of Colorado Foundation
Gates Frontiers Fund	Pema Foundation	University of Colorado Health
Gates Grubstake Fund	Kelly and Mark Petrash, Ph.D.	University of Colorado President's Office
Valerie Gates	Ann and Kevin Reidy	Lloyd Wade
Mary Gearhart	Daniel Ritchie	
	Betty and Dennis Roop, Ph.D.	

We are also grateful to volunteers such as Kathy Barrett Lee, who has put her talents to task to help us create a pleasant working environment for the Gates Center and the Gates Biomanufacturing Facility, and to Mike Perry, who has shared his expertise in the area of government and regulatory affairs to help us further this promising field. They stand among other friends on-and-off campus that kindly help us further Charlie Gates' vision and our mission.

To learn more about how you can play a role in accelerating research through philanthropic gifts, please reference the enclosed envelope, visit [giving.cu.edu/gatescenter](http://giving.cu.edu/gatescenter) or contact Allison Krebs at 303-724-6342 or [Allison.Krebs@ucdenver.edu](mailto:Allison.Krebs@ucdenver.edu)





Chuck and Gretchen Lobitz, Sheff Tulp



Meg Nichols, Janelle Blessing, Ed Nichols



Joy and Bill Mathews



Kim Muller



Antonio Jimeno, Janet Mordecai, Tom Flaig



Marshall Wallach, Will and Susan Hiatt



Brooks and Warren Stewart





Arlene and Mike Perry,  
Michael Verneris



Curt and Nancy Freed, Diane Wallach



Peter Grant and Dan Ritchie



John Moyski



Wag and Annalee Schorr



Rick Stoddard, Lia Gore, Bruce  
and Marcy Benson, Jena Hausmann



Valeria Canto-Soler and Diane Wallach



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For inquiries about the Gates Biomanufacturing Facility, please refer to the facility's website at [www.gatesbiomanufacturing.com](http://www.gatesbiomanufacturing.com) and/or contact Patrick Gaines or Tim Gardner.



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

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It was a lovely night on the occasion of the second annual Charlie's Picnic held in loving memory of Charles C. Gates.