



# 2018

## *Annual Report*

The Gates Center



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





Day two of "Zoobiquity Colorado: Connecting Human and Animal Health through Regenerative Medicine" took place on the Anschutz Medical Campus. Cohosted by the Gates Center for Regenerative Medicine and Colorado State University's College of Veterinary Medicine and Biomedical Science, the conference provided an opportunity to highlight the laboratory and clinical research of human and veterinary investigators, and foster ongoing and future collaborations.





# TABLE OF CONTENTS

*Letter from Director Dennis Roop, Ph.D.....4*

*Who We Are.....8*

*What We Do.....10*

*List of Members.....11*

*Collaboration Expands our Reach.....15*

*Select Member Publications and Honors.....21*

*Commercialization.....28*

*Core Facilities.....34*

*Gates Biomanufacturing Facility.....38*

*Education.....40*

*Outreach.....44*

*New Faces at the Gates Center.....46*

*Financial Overview.....50*

*Acknowledgements.....52*

*2018 Charlie's Picnic.....54*

*\*Cover photo: Sean McGrath, Ph.D. analyzes CRISPR/Cas9 cutting efficiency for RDEB (Recessive Dystrophic Epidermolysis Bullosa) genetic corrections at the Gates Center for Regenerative Medicine.*





# Gates Center for Regenerative Medicine

UNIVERSITY OF COLORADO **ANSCHUTZ MEDICAL CAMPUS**

Knowledge is the ultimate investment.

When we focus our attention on solving the greatest challenges in science and medicine, we reimagine the potential of human endeavor and expand the boundaries of the possible.

At the same time, we live in a world of limited financial resources, and unlimited desire from patients and their families to apply knowledge toward cures. The Gates Center for Regenerative Medicine was formed with the foundational support of entrepreneurs and academics alike, in order to pursue a wider return on that investment in knowledge.

We at the Gates Center, alongside our colleagues at the Anschutz Medical Campus and other key allies, are pleased to report that tangible returns on these investments propelled us through 2018 and beyond.

One of the best tools we have to leverage return on investment in regenerative medicine research was launched in 2014 in the spirit of our namesake, entrepreneur, business leader and philanthropist Charles C. Gates. The Gates Grubstake Fund awards significant financial resources to promising concepts and links researchers to invaluable help with commercialization from CU Innovations and business mentors.

Since launch, the Grubstake Fund has awarded \$3.5 million to Anschutz Medical Campus researchers. We are now learning from our partners at CU Innovations that those funded projects have attracted \$18 million in follow-on grants and investments, with millions more expected to close in early 2019. As researchers, finance isn't necessarily our first language, but a 5X return on investment easily translates across disciplines.

Even more importantly, we estimate that there are now 105 regenerative medicine projects underway on the Anschutz Medical Campus aimed at pushing basic science toward human treatments that may be eligible for Grubstake funding, and 25 have reached the product development stage. The



pipeline toward all-important clinical trials is filling up, constituting an important advancement in our mission. Read in more depth about the Gates Grubstake Fund starting on page 28.

When lab research projects are ready to be translated into human clinical trials, the Gates Biomanufacturing Facility (GBF) across the street from the campus is ready to provide the clinical grade cell therapies and protein biologics specified for the trials. In spring 2018 the GBF passed an important landmark by manufacturing its first clinical trial-grade product for direct infusion into patients.

The groundbreaking effort by the facility capped years of planning and assembling the requisite quality systems and trained teams to deliver its first cell therapies for use in cancer patients. The materials—manufactured for a clinical trial in multiple myeloma treatment by a private research firm—are based on the production of CAR-T cells that give the immune



system the ability to recognize and attack cancer cells. These CAR-T cells were shipped to the locations of clinical trials around the nation. Congratulations are due to GBF Executive Director Ryan Crisman, Director of Finance & Operations Tim Gardner, and their entire team. CU Anschutz Chancellor Don Elliman called the event “another important milestone in collaborative efforts at the CU Anschutz Medical Campus to be a leading bench-to-bedside research and treatment center.”

We are also thankful to report that bench science did not suffer as we accumulated other returns on investment. A highly efficient and safe technology to reprogram a patient’s diseased skin cells into stem cells developed by Gates members Ganna Bilousova, Ph.D. and Igor Kogut, Ph.D., was highlighted in the elite Nature Communications in February 2018. This unique reprogramming technology has enabled a number of successful grant applications and allowed us to focus on a wide variety of potential treatments—particularly where there are no readily accessible affected tissues. The Gates Center Stem Cell Biobank and Disease Modeling Core, founded around this technology, has both lowered costs and shortened research time for scientists across the nation and around the globe, successes you can read more about on page 36.

Last year also marked the previously-announced arrival of leading national cancer researcher Terry J. Fry, M.D., to the faculty of the University of Colorado School of Medicine and Children’s Hospital Colorado. Dr. Fry, also a Gates Center member, is a pioneer in the fast-expanding field of CAR-T cells as cancer-fighting weapons. According to Dr. Fry, the capabilities of the GBF and other collaborative efforts at Anschutz were critical factors leading to his decision to move his research team from the NIH to our medical campus.

During the year, the Gates Center added 17 new members from across CU Anschutz and other campuses, further extending our collaborations and research efforts. Among numerous accomplishments and contributions, individual Gates Center members stepped forward as mentors to help

us inspire the next generation of scientists and clinicians through our annual Gates Summer Internship Program.

As the Center focused on specific areas of technology, commercialization and production, we also finalized a new and ambitious strategic plan with the invaluable guidance of our Advisory Board and other key stakeholders. As part of this long-term planning, Gates Center leadership identified the most promising areas of research focus, and CU Innovations contributed a competitive review and analysis of other leading academic research centers to help spotlight areas we can be proud of and areas where we can continue to challenge ourselves.

Throughout these efforts, we are reminded that a crucial multiplier for our return on investment is the aforementioned collaboration that we work to inspire. The “Zoobiquity Colorado” conference in the fall of 2018 was a perfect example, itself a result of close collaboration with Colorado State University. The two-day, two-campus event explored how the human and animal medical sciences are informing each other to reach new understanding. As an example, the pipeline toward clinical trials now includes teams comprised of both animal and human orthopedic surgeons from both our campuses.

In other important collaborative efforts highlighted on page 18, the Epidermolysis Bullosa (EB) iPS Cell Consortium, of which the Gates Center is a part, received a \$3.8 million award from the U.S. Department of Defense (DOD). The grant will help move discoveries in stem cell-created skin grafts into the manufacturing stage—a crucial step toward initiating one of the first iPSC-based clinical trials in the US. The Consortium includes research teams from the Gates Center, Stanford University School of Medicine and Columbia University Medical Center. Members of this EB Consortium share in the dedication to find a permanent corrective therapy for this devastating, blistering skin disease and to the potential of applying it to other currently incurable monogenetic diseases.





Looking ahead to 2019 and beyond, another role we hope to continue to play at the Gates Center is to provide objective and reliable scientific information to the public about stem cells. Claims about the current medical applications of stem cells are proliferating, frequently based on unproven theories and untested premises. The FDA has begun to crack down on some domestic clinics making wildly unsupported medical claims, but “stem cell tourism” continues to draw customers to overseas clinics with even fewer restrictions on advertising. As Advisory Board member and Anschutz Bioethics Professor Marilyn Coors, Ph.D., noted in a presentation to our board this year, “We are all more convinced than ever of the promise of stem cells, and would hate to see public enthusiasm for further research diminished by exaggeration and perceived failure.”

All of these efforts and projects would not be possible without the dedication and generous support of our donors, members, friends, staff and on- and off-campus leadership, for whom we are most grateful. Special thanks go to members of our Gates Center Advisory Board (pictured on page 7), who literally and

figuratively challenge us to raise our sights and jump so high, and to Dori Biester, whose service on the board over the past five years has been over and above the call of duty.

Last summer we enjoyed getting together at our annual Charlie’s Picnic to celebrate our collective accomplishments and to honor our 2018 Charlie’s Angel and board member, Will Hiatt, M.D. We look forward to our picnic in August 2019 to do much the same—with thanks for past and future investments in knowledge delivering the promise of regenerative medicine to benefit patients.

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







## 2018 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



**CHARLES C. GATES** is shown here with V-belts invented in the early 1900's by his family's company, which revolutionized power transmission. He was an engineer, a visionary leader and a philanthropist, who foresaw the potential of regenerative medicine and asked his children and others to do everything possible to make it a reality. His legacy lives on at the Gates Center for Regenerative Medicine, inspiring our dedication to revolutionize the safe and expedited translation of research in stem cell biology and regenerative medicine into therapies and cures for people worldwide.

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



# WHO WE ARE



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

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

The Gates Center strategic plan embraces the following value drivers:

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



The Gates Center currently focuses research resources and recruiting efforts in the following areas of expertise:

**Platform Technologies** applied across multiple areas of medicine (see discussion of the Stem Cell Biobank and Disease Modeling Core on page 36)

**Applied Technology and Translational Programs in:**

- Cardiology
- Dermatology
- Neurology
- Oncology
- Ophthalmology
- Orthopedics
- Pulmonary science
- Wound healing

Dennis Roop, Ph.D., recruited from the Baylor College of Medicine in 2007, is the Center Director and coordinates a

talented array of 114 multi-institutional researchers from the Anschutz Medical Campus, CU Boulder, CU Denver, Colorado State University, Colorado School of Mines and National Jewish Health, as well as private industry. The Gates Advisory Board, comprised of community leaders and clinicians, provides counsel and additional support (see page 7).

Key to the success of the Gates Center is the partnership with the Gates Biomanufacturing Facility, a state-of-the-art manufacturing facility translating innovative research discoveries into safe and effective cell therapy and protein biologic products for human clinical trials. The GBF contains 7,000 square feet of “clean room” operated under FDA “Good Manufacturing Practice” guidelines, which assure proper design, monitoring and control of manufacturing processes and facilities. The GBF has proven essential in engagement of research talent present on the Anschutz Medical Campus as well as in talent recruitment nationwide.

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



Retiring Gates Center Advisory Board member Dori Biester with Allison Krebs



David Norris, M.D., Professor and Chairman, Department of Dermatology, has been a perennial champion and collaborator of the Gates Center.



Gates Summer Internship Program students listened to guest speaker during final day ceremonies held on August 10, 2018.

# WHAT WE DO

## Gates Center for Regenerative Medicine

Where leading-edge research comes to life.



**BENCH RESEARCH**



**REGULATORY &  
COMMERCIALIZATION AID**



**FUNDING**



**CLINICAL TRIALS**



**PATIENT BENEFIT**

### MISSION

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

### GATES CENTER BENEFITS

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

### RESEARCH CONSORTIUM

The Gates Center is a world-class consortium of 114 researchers, clinicians and private industry members from:



Boulder



University of Colorado  
Anschutz Medical Campus



Colorado  
State  
University



uchealth



Children's Hospital Colorado

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



# LIST OF MEMBERS

NAME	DEGREE(S)	POSITION	ACADEMIC INSTITUTION/AFFILIATES	PRIMARY (AND SECONDARY) APPOINTMENT(S)
Appel, Bruce	Ph.D.	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.	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
Belkind-Gerson, Jaime*	M.D., M.S.	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Pediatrics / Digestive Health Institute
Benam, Kambez*	Ph.D.	Assistant Professor	University of Colorado Anschutz Medical Campus	Departments of Medicine (and Bioengineering)/ Division of Pulmonary Sciences and Critical Care
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
Brown, Jeffrey*	Ph.D.	Senior Scientist	AlloSource	Research and Development
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
Crisman, Ryan*	Ph.D.	Executive Director	University of Colorado Anschutz Medical Campus	Gates Biomanufacturing Facility
D'Alessandro, Angelo*	Ph.D.	Assistant Professor	University of Colorado Anschutz Medical Campus	Department of Biochemistry and Molecular Genetics/ Division of Hematology
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	D.V.M., Ph.D.	Professor	Colorado State University	Department of Clinical Sciences
Ehrhart, Nicole	D.V.M.	Professor	Colorado State University	Department of Surgical Oncology

\* New members in 2018

NAME	DEGREE(S)	POSITION	ACADEMIC INSTITUTION/AFFILIATES	PRIMARY (AND SECONDARY) APPOINTMENT(S)
Ford, Heide	Ph.D.	Professor David F. and Margaret Turley Grohne Chair in Translational Cancer Research	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 Leopold Korn and Michael Korn Chair in Parkinson's Disease	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
Fry, Terry*	M.D.	Professor Robert J. and Kathleen A. Clark Endowed Chair for Pediatric Cancer Therapies	University of Colorado Anschutz Medical Campus	Departments of Pediatrics/ Hematology and Immunology
Garbe, Christopher*	B.A, M.B.A.	Director of Quality	University of Colorado Anschutz Medical Campus	Gates Biomanufacturing Facility
Gavin, Kathleen	Ph.D.	Assistant Professor	University of Colorado Anschutz Medical Campus	Department of Medicine/ Division of Geriatric Medicine
Ghosh, Moumita*	Ph.D.	Assistant Professor	National Jewish Health	Pulmonary, Critical Care & Sleep Medicine
Goodrich, Laurie	DVM, M.S., Ph.D.	Associate Professor	Colorado State University	College of Veterinary Medicine
Gore, Lia	M.D.	Professor The Ergen Family Chair in Pediatric Cancer	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
Hanson, Kirk*	Ph.D.	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Biochemistry and Molecular Genetics
Herson, Paco	Ph.D.	Principal Investigator	University of Colorado Anschutz Medical Campus	Department of Anesthesiology, Neuronal Injury Program
Hiatt, William	M.D.	Professor	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	Department of Medicine/ 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

\* New members in 2018



NAME	DEGREE(S)	POSITION	ACADEMIC INSTITUTION/AFFILIATES	PRIMARY (AND SECONDARY) APPOINTMENT(S)
Liechty, Kenneth	M.D.	Professor The Sandy Wolf Chair in Maternal Fetal Surgery	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	Department of Medicine /Division of Pulmonary
Majka, Susan*	Ph.D.	Professor	National Jewish Health, University of Colorado Anschutz Medical Campus	Department of Medicine/Pulmonary, Critical Care & Sleep 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
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
Nair, Devantha*	Ph.D.	Assistant Professor	University of Colorado Anschutz Medical Campus University of Colorado Boulder	School of Dental Medicine
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 Cleo Meador and George R. Scott Chair of Medicine in Hematology	University of Colorado Anschutz Medical Campus	Department of Medicine/Hematology
Plenter, Robert*		Senior PRA	University of Colorado Anschutz Medical Campus	Division of Pulmonary, Critical Care Medicine
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	Department of Medicine/Hematology
Refaeli, Yosef	Ph.D.	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Dermatology
Reyland, Mary*	Ph.D.	Professor	University of Colorado Anschutz Medical Campus	Departments of Craniofacial Biology/Cell Developmental Biology/Pathology

\* New members in 2018

NAME	DEGREE(S)	POSITION	ACADEMIC INSTITUTION/AFFILIATES	PRIMARY (AND SECONDARY) APPOINTMENT(S)
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
Salinas, Branden*	Ph.D.	Director of Protein Development and Manufacturing	University of Colorado Anschutz Medical Campus	Gates Biomanufacturing Facility
Sartorius, Carol	Ph.D.	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Pathology
Sclafani, Robert	Ph.D.	Professor	University of Colorado Anschutz Medical Campus	Department of Biochemistry and Molecular Genetics
Seefeldt, Matthew*	Ph.D.	Director of Cell Therapy	University of Colorado Anschutz Medical Campus	Gates Biomanufacturing Facility
Serban, Karina*	M.D.	Assistant Professor	National Jewish Health	Department of Medicine, Division of Pulmonary and Critical Care Medicine
Shellman, Yiqun*	Ph.D.	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Dermatology
Sherk, Vanessa	Ph.D.	Instructor	University of Colorado Anschutz Medical Campus	Department of Medicine/Endocrinology
Song, Kunhua	Ph.D.	Assistant Professor	University of Colorado 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 The La Cache Critical Care Endowed Chair	University of Colorado Anschutz Medical Campus	Department of Pediatrics/Critical Care
Sussel, Lori*	Ph.D.	Professor Sissel and Findlow Family Chair	University of Colorado Anschutz Medical Campus	Barbara Davis Center for Diabetes Pediatrics (Cell & Developmental Biology)
Terzian, Tamara	Ph.D.	Assistant Professor	University of Colorado Anschutz Medical Campus	Department of Dermatology
Thamm, Douglas	D.V.M.	Assistant Professor	Colorado State University	Department of Clinical Sciences
Torchia, Enrique	Ph.D.	Assistant Professor	University of Colorado Anschutz Medical Campus	Department of Dermatology
Verneris, Michael	M.D.	Professor The Barton Endowed Chair of Pediatric Bone Marrow Transplant	University of Colorado Anschutz Medical Campus	Department of Pediatrics/Hematology, Oncology and Bone Marrow Transplantation
Vladar, Eszter*	Ph.D.	Assistant Professor	University of Colorado Anschutz Medical Campus	Department of Medicine/Division of Pulmonary Sciences, Department of Cell & Developmental Biology
Wagner, David	Ph.D.	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Neurology
Walker, Lori	Ph.D.	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Medicine/Cardiology
Wang, Xiao-Jing	M.D., Ph.D.	Professor John S. Gates Endowed Chair in Stem Cell Biology	University of Colorado Anschutz Medical Campus	Department of Pathology
Wang, Zhijie	Ph.D.	Assistant Professor	Colorado State University	Department of Mechanical Engineering
Williams, Trevor	Ph.D.	Professor	University of Colorado Anschutz Medical Campus	Department of Craniofacial Biology 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 2018



# COLLABORATION EXPANDS OUR REACH

## ZOOBIQUITY COLORADO

Connecting Human and Animal Health  
through Regenerative Medicine

Oct. 5

Dr. Barbara Natterson-Horowitz, professor of medicine, UCLA Division of Cardiology, co-author of "Zoobiquity: The Astonishing Connection Between Human and Animal Health," with Dr. Mark Stetter, dean of the Colorado State University College of Veterinary Medicine and Biomedical Sciences at the Zoobiquity Colorado conference on Oct. 5, 2018. (John Eisele/CSU photo)

The Gates Center for Regenerative Medicine strove in 2018 to carry out one of the core philosophies of founding benefactors Charlie Gates and family: Find the best people and move forward together, as Director Dennis R. Roop, Ph.D., frequently sums it up.

Insightful and promising collaborations abounded at the Gates Center in 2018, from a unique multi-campus exploration of how physiological similarities among humans and the animal world can foster medical advances; to national financial underwriting of ongoing Epidermolysis Bullosa (EB) research; to commercialization teamwork pushing groundbreaking treatments to the cusp of human clinical trials.

## HUMANS HELPING ANIMALS, AND VICE-VERSA

Truly opening minds and expanding the idea of the possible was the fall 2018 "Zoobiquity Colorado" conference, co-created by the Gates Center at CU Anschutz and Colorado State University's College of Veterinary Medicine and Biomedical Sciences and focused on regenerative medicine. The inter-campus event drew nearly 200 people from across the country, Ireland, and a large contingent from Japan. Physicians, veterinarians, human and animal researchers, graduate students and more participated in tours and symposia at the CSU campus followed by a next-day event at CU Anschutz capped with a panel discussion on the "The Future of Regenerative Medicine," moderated by CBS News medical correspondent Max Gomez, PhD.

The phrase and brain-boosting properties of “Zoobiquity” were coined by Dr. Barbara Natterson-Horowitz, a professor of medicine at UCLA, and co-author Kathryn Bowers in their book “Zoobiquity: The Astonishing Connection Between Human and Animal Health.” Natterson-Horowitz has said, “Over centuries of modern human times, we’ve forgotten about how essentially animal we are.”

Kicking off the CSU portion of the conference, Dr. Wayne McIlwraith, University Distinguished Professor and director of the Orthopaedic Research Center at CSU, talked about being the only veterinarian in a class on human arthroscopic surgery at Purdue University in 1976. This was his first experience in translational research and medicine from a human patient to horse patients.

There were more than a few skeptics arguing against the use of this procedure in horses, initially. But McIlwraith helped silence those critics, after he operated on Spend a Buck, an American thoroughbred racehorse. Five months after the procedure, Spend a Buck won the Kentucky Derby by more than five lengths.

“That’s what convinced most of the equine racing world about the benefits of arthroscopy,” said McIlwraith. Now, the procedure is widely accepted for horses and has revolutionized care for equine patients in much the same way it did for humans.

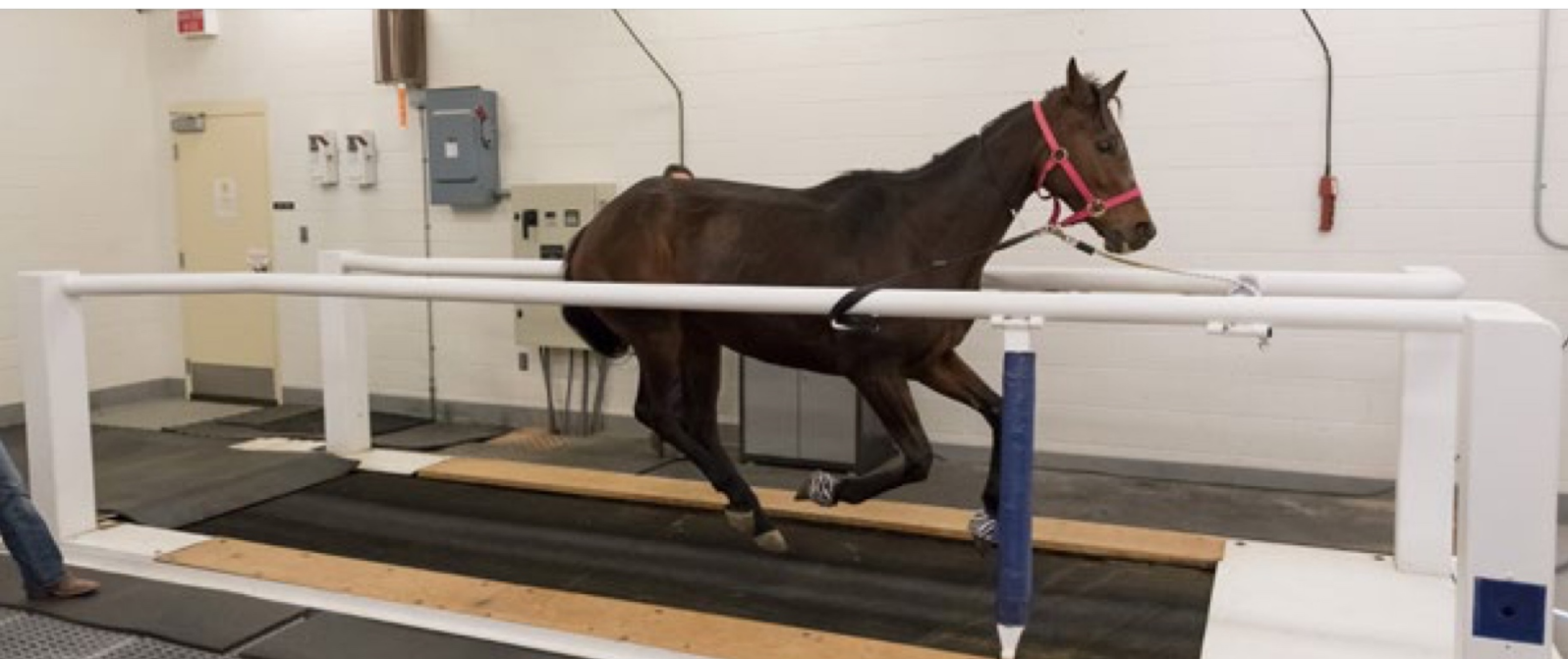
Dr. Laurie Goodrich, a CSU associate professor of orthopedics in the Department of Clinical Sciences, explored the question: Why do we need regenerative medicine?

She discussed cartilage injuries in horses and the need for new therapies that would provide faster bone healing in equine patients. Stem cell therapy has shown promise in horses to treat osteoarthritis, and to help with cartilage repair, fracture healing and tendinopathy, a disease that causes tenderness and pain in tendons.

“We still need comparisons between the different types of stem cells that exist,” Goodrich said. “We need larger and more clinical trials. We hope to treat our patients better, faster and more effectively.”

Dr. Steve Dow, professor of immunology in the Department of Clinical Sciences, and Dr. Terry Fry, co-director of the Human Immunology and Immunotherapy Initiative on the CU Anschutz Medical Campus, shared new insights into childhood cancer gained from clinical trials in dogs.

Fry acknowledged how far the field has come, while also highlighting what still needs to be explored. Although some patients with some tumors have dramatic responses, these responses are uneven and unpredictable, said Fry.



A horse runs on a high-speed treadmill at CSU’s Orthopaedic Research Center on day two of Zoobiquity Colorado.  
(John Eisele/CSU photo)



There are patients we know that are probably cured with a single infusion,” said Fry. “Some patients can be cured. But if you look at this the other way, more than half of the patients will relapse within a year.”

Dow said that dogs — companion animals that get cancer naturally, similar to humans — are a good model for using immunotherapy to treat cancer. Veterinarians from CSU are, in fact, working with clinicians at Children’s Hospital Colorado to implement a clinical trial for pediatric osteosarcoma.

Dogs get malignant cancers at about twice the rate as humans do. Osteosarcoma is a common cancer in humans and dogs: the tumor arises in the same sites in the bone with dogs and humans, progresses at the same rate and metastasizes in the same way.

Clinicians already know how to slow tumors from metastasizing with chemotherapy. Armed with that knowledge, CSU veterinarians in Dow’s lab — led by Assistant Professor Dan Regan — used Losartan, a drug that has been used to treat high blood pressure and kidney disease, in combination with

chemotherapy to treat osteosarcoma in dogs.

Dow said the team saw very positive results with this therapeutic combination, which prompted CSU to initiate a conversation with clinicians at Children’s Hospital Colorado. A pediatric clinical trial could start in early 2019, Dow said.

Dow is also the recipient of a Gates Grubstake Fund award for promising treatments in chronic wound infections in animals that mimic troublesome, antibiotic-resistant MRSA infections in human joints. Grubstake’s further inter-campus collaborations toward commercialization have been a tremendous help, Dow said. CU Anschutz orthopedic surgeons will be partners in upcoming clinical trials for the treatment.

“For us as veterinarians, it’s nice to see the value of the animal model recognized, while it’s also nice to work with our medical colleagues on the physician side,” Dow said. “Our goal is to treat both humans and animals, and if we can accomplish both that’s a huge win for all of us.”



Keynote Speaker Frank Barry from the National University of Ireland Galway



Forty veterinarians and medical doctors from Japan attended Zoobiquity Colorado.



CBS Medical Correspondant Max Gomez

## COLLABORATING FOR EB PROGRESS AND REGENERATION KNOWLEDGE

Scientists from the Gates Center are part of a consortium awarded \$3.8 million from the U.S. Department of Defense (DOD) to move discoveries in stem cell-created skin grafts into the manufacturing stage, bringing further hope to victims of debilitating inherited skin diseases.

The major grant for the Epidermolysis Bullosa (EB) iPS Cell Consortium, which includes research teams from CU Anschutz, Stanford University School of Medicine and Columbia University Medical Center, will move production of stem cells into the Gates Biomanufacturing Facility.

The grant follows recent awards for the same investigators by the 21st Century Cures Act and the California Institute of Regenerative Medicine, discussed in our 2017 Annual Report. The backing will boost research that could not only benefit EB sufferers, but also countless patients with severe chronic skin wounds.

### 'CUTTING-EDGE SCIENCE'

In announcing the new grant, DOD reviewers issued one of the most emphatic research endorsements possible, saying, "This study is based on the strongest cutting-edge scientific rationale in the field of wound care and dermatology. It is also a collaborative effort among top physician-scientists, scientists, health care providers, epidermolysis bullosa patients, families, and charities across the United States."

One evaluator wrote: "The proposed research has the highest probability of success of bringing gene-corrected tissue to patients in the hospital ..." Roop often points out that EB may represent an ideal platform from which to test an iPSC-based therapy. It is an orphan disease and it can be devastating, sentencing patients to a life of severe pain and disability and even early death. Further, the skin is readily accessible, easy to monitor and to excise in the event of an adverse event. If deemed safe and effective, iPSC therapies could then be expanded to treat monogenetic diseases affecting internal organs, in which the difficulty of monitoring adverse effects would make them very unlikely first targets.



Zoobiquity Colorado's panel on the Future of Regenerative Medicine (left to right): Dennis Roop, Ph.D.; Ryan Crisman, Ph.D.; Mike Perry, D.V.M., Ph.D.; Sue VandeWoude, D.V.M. and CBS Medical Correspondent Max Gomez, Ph.D.

The DOD award will allow the EB research team to further investigate best manufacturing practices for larger-scale production of stem cell-created skin grafts, utilizing the unique RNA-based reprogramming and gene editing technology developed by Gates Center investigators and the state-of-the-art resources of the GBF. The goal now is to move the technology from the laboratory into clinical trials.

Roop has talked frequently about behind-the-scenes collaborations and networks that have furthered the EB consortium's work, of which he is a key part. In 2016 the EB Charities, composed of foundations formed by families of children suffering from the disease\*, challenged research teams from the University of Colorado and Stanford and Columbia Universities to collaborate rather than compete in finding a cure for EB. The teams' willingness to collaborate within the EB iPS Cell Consortium has been rewarded by EB Charities' initial and continued funding, leading to public support outlined above and fervent hope for future success.

Three years ago, Roop was presenting data at Harvard and seeking ways to improve homing of stem cells into injured tissue. Robert Sackstein, M.D., a Harvard professor of dermatology, offered to solve the problem and sent reviews and papers over the following months.

*\*EB Charities (the EB Research Partnership (EBRP), the Los Angeles-based EB Medical Research Foundation, and the London-based Cure EB Charity—formerly SOHANA Research Fund)*



Yvette Pita Frampton joined the Gates Center Advisory Board about that time. As fate would have it, she had studied piano as a child with Sackstein's mother. She contacted Sackstein about the work of the Gates Center, and Sackstein said he would welcome further collaboration with Roop and the Center.

Sackstein is a bone marrow transplant surgeon who had a patient die after a transplant at the beginning of his career, and he began to focus on how blood stem cells know to home into bone marrow. He discovered an enzyme that decorates the surface of cells--much like a piece of Velcro-- enabling the cells to leave the blood vessel and go to the bone marrow or areas of inflammation.

This was also a time when another Advisory Board member, Wag Schorr, M.D., asked Roop if it might be possible to create a therapy for Ehlers-Danlos Syndrome (EDS), from which his granddaughter suffers. EDS is characterized by slackened skin and hyper-mobile joints that dislocate easily. Schorr offered to help get this project off the ground.

Since then, Roop and his colleagues, Drs. Bilousova and Kogut and members of their laboratory have found what he calls "one of the most amazing things I've seen in my career." The team recently induced inflammation in a mouse's ear and then introduced green mesenchymal stem cells into the blood vessel. Using live imaging technology, the researchers watched as the green cells stopped in the red vessel of the living mouse, and then moved out into the tissue and the site of inflammation.

The implications of this data are complex, and show the possibility of giving cells systemically to kids with EB as well as for treating other diseases such as EDS and lung inflammation. Without the collaboration and helpful interventions of board members like Wag and Yvette, these discoveries might never have been made.

## **COLLABORATION DISTINGUISHES THE GATES CENTER WAY**

Valeria Canto-Soler, Ph.D., offers similar conclusions when talking about the progress of her pioneering research into stem cells' ability to grow new retinal material that could cure a form of macular degeneration. Since arriving at the Gates Center from Johns Hopkins University in 2017, Canto-Soler's lab has made faster-than-expected progress toward clinical trials. The expert advice and coaching from her Gates Grubstake Fund award and other collaborations have been key to that progress, she said.

"I am a basic researcher; we are not trained for developing clinical products," Canto-Soler explained. "We are not trained to move a basic research product through the pipeline. I've been extremely pleasantly surprised about the infrastructure support we have through the Gates Center and Anschutz Medical Campus and CU Innovations -- to allow a product so ambitious, curing blindness in patients with AMD, to really support it so it can move steadily toward the clinic. I couldn't imagine a year and a half ago that today I would have been able to learn as much as I have, and feel we are really pushing forward our bench product to get it into the clinic."

Many thanks to the following Gates Center members who made presentations at  
**ZOOBIQUITY, COLORADO:**

Steve Dow, D.V.M., Ph.D. | Nicole Ehrhart, D.V.M. | Terry Fry, M.D.  
Laurie Goodrich, D.V.M., Ph.D. | Karin Payne, Ph.D. | Dennis Roop, Ph.D.





Drs. Emily Warshauer and Julio Salas in front of Dr. Salas' first dermatology clinic in Monterrey, Mexico

## COLLABORATION HEADED SOUTH

In 2017, Emily Warshauer, M.D., a faculty member in the Department of Dermatology, helped make a fascinating discovery. Genetic analysis of several Colorado Epidermolysis Bullosa (EB) patients suggested that they may be related to hundreds of EB patients in Mexico who share the same founder mutation—and may well be descended from a group of Sephardic Jewish families who fled the Spanish Inquisition 300 to 400 years ago. During 2018, Dr. Warshauer in collaboration with Adam Brown, founder of the Avotaynu DNA Project with expertise in Jewish population genetics, and other scientists, genealogists and historians, expanded the study to include EB patients in Latin America. Genealogical tests of new EB samples gathered by clinicians in Mexico, Chile, Columbia, Argentina and Paraguay revealed many with substantial Sephardic Jewish ancestry.

This research project was initially proposed by Steve Berman, M.D., founder of the EB Center of Excellence at the Children's Hospital Colorado, and includes a collaboration with Julio Salas, M.D., of Monterrey, Mexico. In 1994, Dr. Salas along with some local dermatologists and families with EB began a support group to serve six families. The organization now numbers more than 500 families across the country. In Fall 2018, Salas visited the Gates Center to discuss his research and patients, and later hosted Dr. Warshauer, who traveled to visit patients requiring wound care, hand reconstructive surgeries, squamous cell carcinoma surgeries, esophageal dilation and other treatments for their needs.

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.



# SELECT MEMBER PUBLICATIONS AND HONORS\*

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

Using zebrafish spinal cord as a model, Dr. Appel and his colleagues discovered that gradients in the concentration of signaling molecules instruct neural progenitor cells either to develop as myelinating oligodendrocytes or to persist as oligodendrocyte precursor cells (Ravanelli et al., *Developmental Biology*, 2018). These findings address a long-standing problem in vertebrate neural development of how apparently similar populations of progenitors produce different kinds of neurons and glia.

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

In this paper, Drs. Niswander and Artinger identify the epigenetic regulators required for growth and differentiation of craniofacial cartilage and bone in both zebrafish and mice (Sen et al., *J Dev Biol*, 2018). This study provides insight into how cranial neural crest cells are regulated to give rise to the different shapes and sizes of the bone and cartilage in the craniofacial skeleton and how genetic alterations of these regulators may result in craniofacial defects.

**James Bamburg, Ph.D.,** *Professor, Department of Biochemistry and Molecular Biology, Colorado State University*

Following the analysis of four different stroke models in mouse brains, Dr. Bamburg and his colleagues discover that cofilin-actin rod pathology develops around the site ischemic injury in all four models (Won et al., *PLoS One*, 2018). Therapeutic approaches that prevent the aggregation of cofilin-actin rods may reduce synaptic loss after stroke.

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

In collaboration with Dr. Redenti, at City University of New York, Dr. Canto-Soler demonstrates that retinal progenitor cells release extracellular vesicles (EV) containing mRNA, miRNA and proteins associated with multipotency and retinal development (Zhou et al, *Scientific Reports*, 2018). They also confirmed that EV can transfer their cargo to other retinal progenitor cells, thus identifying a novel mechanism involved in differentiation and fate determination during retinal development.

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

Activating mutations in FMS-like tyrosine kinase 3 (FLT3) are one of the most frequently observed genetic defects in acute myeloid leukemia (AML). Although FLT3 inhibitors have shown impressive anti-leukemic activity in clinical trials, sustained remissions using these inhibitors as a monotherapy have not been achieved. In this study, Dr. DeGregori reports that the combined use of FLT3 inhibitors with a glutaminase inhibitor results in significantly improved survival in a patient-derived xenograft AML mouse model (Gregory et al., *Exp Hematol*, 2018).

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

Using patient-derived xenografts from melanoma, colon, and pancreatic cancer tissues, Dr. Fujita and her colleagues discovered that CDK1, a master regulator of the cell cycle, was upregulated in tumor-initiating cells (Cancer Res., 2018). They also discovered that CDK1 was a novel regulator of the pluripotent stem cell transcription factor Sox2. These findings suggest that the interaction between CDK1 and Sox2 may be a new therapeutic target for several types of cancer.

**Kathleen Gavin, Ph.D., Assistant Professor, Division of Geriatric Medicine, Susan Majka, Ph.D., Professor, Division of Pulmonary, Critical Care & Sleep Medicine, National Jewish Health, and Dwight Klemm, Ph.D., Professor, Division of Pulmonary and Critical Care Medicine**

Drs. Gavin, Majka and Klemm report that loss of ovarian hormones influences the production and distribution of adipocytes in adipose tissue arising from bone marrow-derived cells in mice (Front Endocrinol., 2018). If translatable across species, the production of bone marrow derived adipocytes may be a mechanism by which abdominal body fat increases in estrogen-deficient postmenopausal women.

**Igor Kogut, Ph.D., Assistant Professor, Department of Dermatology, Dennis Roop, Ph.D., Professor, Department of Dermatology, Ganna Bilousova, Ph.D., Assistant Professor, Department of Dermatology**

Drs. Kogut, Roop and Bilousova report the development of a clinically safe approach that consistently reprograms healthy and disease-associated patient's skin cells into induced pluripotent stem cells (iPSCs) with an unprecedented efficiency (Nature Communications, 2018). This breakthrough in developing a highly-efficient reprogramming method, that avoids the use of viral vectors, may allow FDA approval for one of the first iPSC-based clinical trials in the US.

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

In this study, Drs. Norris and Shellman report that the use of a combination of BH3 mimetics against members of the BCL-2 family of cell survival factors are effective in inducing cell death of melanoma-initiating cells (Cell Death Dis., 2018). Of clinical relevance, they showed that melanoma samples taken from patients that had relapsed from current treatments, such as anti-PD-1 immunotherapy, were also killed by this combination therapy.

**Eric Pietras, Ph.D., Assistant Professor, Division of Hematology, and James Hagman, Ph.D., Professor, Department of Immunology, National Jewish Health**

In this paper, Drs. Pietras and Hagman report a novel role for ZFP521 in regulating the numbers of hematopoietic stem and progenitor cells, common lymphoid progenitors, and B and T cell precursors (Mol Cell Biol., 2018). These findings suggest that ZFP521 may be a novel target for cancer therapies.

**Christopher Phiel, Ph.D., Assistant Professor, Department of Integrative Biology, CU Denver**

Dr. Phiel identifies glycogen synthase kinase-3 (GSK-3) as a novel regulator of the RNA demethylase, FTO (fat mass and obesity-associated protein) at the protein level (J Biol Chem., 2018). This study provides the first evidence for how RNA methylation is regulated in mammalian cells and identifies a putative novel mechanism by which GSK-3 activity regulates stem cell pluripotency.

**Holger Russ, Ph.D., Assistant Professor, Barbara Davis Center for Diabetes/Microbiology and Immunology Department**

Dr. Russ is a co-author of this paper, which describes for the first time the development of cell culture conditions that closely mimic events occurring during pancreatic islet organogenesis and  $\beta$  cell maturation (Nat Cell Biol. 2018).  $\beta$  cells grown under these conditions exhibit robust glucose-stimulated insulin secretion.



**Kunhua Song, Ph.D., Assistant Professor, Division of Cardiology**

Using cardiomyocytes (CMs) derived from induced pluripotent stem cells generated from patients suffering from Danon disease, Dr. Song reports that these CMs exhibit profound defects in autophagic fusion, as well as mitochondrial and contractile abnormalities (Proc Natl Acad Sci U S A, 2018). Correction of the mutation in the lysosomal-associated membrane protein 2 (LAMP-2) gene, which is associated with Danon disease, rescued the Danon phenotype.

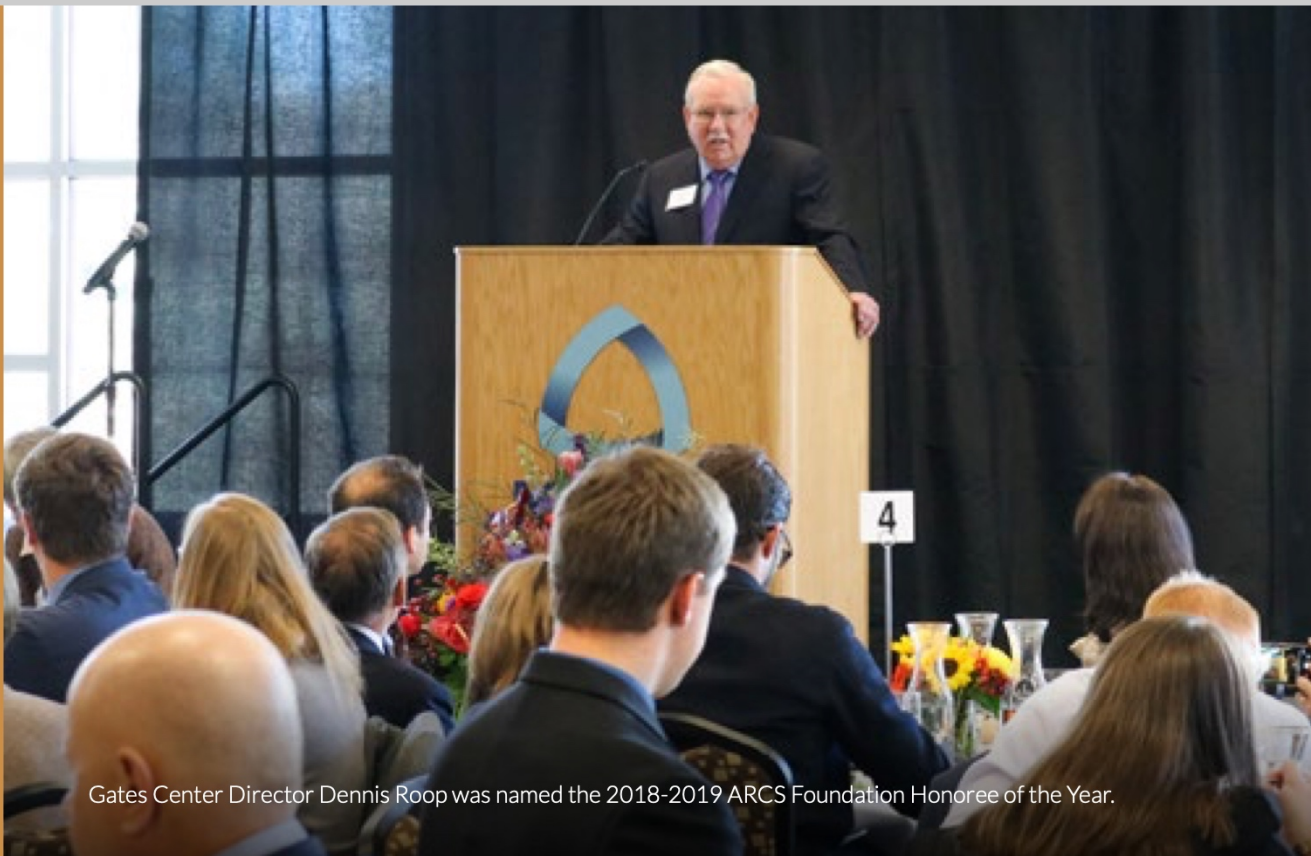
**Michael Verneris, M.D., Professor, Department of Pediatrics**

In acute lymphoblastic leukemia patients that relapse to chimeric antigen receptor (CAR) therapy against CD19, Dr. Verneris and his colleagues discovered genetic mutations in CD19 that result in loss of expression of CD19 on the cell surface (Nat Med., 2018). This loss of CD19 expression advocates for a combination CAR approach against an additional surface antigen in addition to CD19.

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

In this report, Drs. Wang and Jimeno demonstrate that the use of both human hematopoietic and mesenchymal stem cells enhances engraftment and immune cell trafficking in an allogeneic humanized mouse model of head and neck cancer (Mol Carcinog., 2018). This improved humanized mouse model more accurately recapitulates the human tumor microenvironment in the original patient's tumor and may aid in the development of more effective immune therapies for these cancers.

# HONORS



Gates Center Director Dennis Roop was named the 2018-2019 ARCS Foundation Honoree of the Year.

**Kambez Benam, D.Phil., Assistant Professor, Departments of Medicine and Bioengineering,** received the Society of Toxicology (SOT) Inhalation and Respiratory Specialty Section's Young Investigator Award in recognition of his highly innovative research efforts and contributions to the pulmonary toxico-pathology field.

**Neil Box, Ph.D., Associate Professor, Department of Dermatology,** received the Daneen and Charles Stiefel Investigative Scientist Award at the American Skin Association's spring gala at the Plaza Hotel on April 10, 2018. This award recognized Dr. Box's unique status as an emerging leader in melanoma research, important contribution to the understanding of melanoma risk mediated via genetic factors and environmental exposure, dedication to educating a new generation of melanoma investigators and skill and dedication as a teacher and mentor.



**William Hiatt, M.D., Professor, Cardiology and CPC Clinical Research,** is the recipient of the American Heart Association's 2018 Clinical Research Prize Award. He was also recognized at a celebration on October 30, 2018 announcing the William R. Hiatt Endowed Chair in Cardiovascular Research created in his honor.

Will Hiatt, M.D. with granddaughter Sydney, who held his hand to give him courage to get through his remarks at the dedication ceremony of the William R. Hiatt Endowed Chair Celebration on October 30, 2018

**Kenneth Liechty, M.D., Professor, Department of Surgery/Pediatric Surgery,** was elected 2021 Wound Healing Society President.

**Susan Majka, Ph.D., Professor, Pulmonary, Critical Care & Sleep Medicine, National Jewish Health and Anschutz Medical Campus,** was named the Vanderbilt University Medical Center Institute for Clinical & Translational Research Investigator of the Month in July 2018.

**Dennis Roop, Ph.D., Professor, Department of Dermatology,** was recognized on November 13, 2018 as the 2018-2019 ARCS Foundation Honoree of the Year. Chartered in 1976 and dedicated to advancing science and technology, the ARCS Colorado Chapter has raised and awarded over \$4 million in scholar awards to outstanding students at in-state colleges and universities pursuing scientific, engineering and medical degrees. Blake Snyder, a fourth-year student at CU's School of Medicine, was designated the ARCS Honorary Dr. Dennis Roop Scholar. Dennis will be honored at ARCS' annual gala scheduled for May 3, 2019.



Blake Snyder was designated the ARCS Honorary Dr. Dennis Roop Scholar.



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*Thanks to the Barbara Davis Center, we are optimistic for the future of all who suffer Type 1 diabetes. The Sissel and Findlow families are proud to support the research being conducted, especially around regenerative medicine, as we believe there will be solutions found to help future generations who experience this complicated disease.*

*- Mary and George Sissel*

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**Lori Sussel, Ph.D., Professor, Barbara Davis Center for Diabetes, Pediatrics (Cell & Developmental Biology)** was named the first holder of the Sissel & Findlow Family Endowed Chair in the Barbara Davis Center for Diabetes at a reception on February 13, 2018. Established first as a professorship in 2010 with gifts from benefactors including the Children's Diabetes Foundation and the Gates Frontiers Fund, this endowment was completed thanks to a generous commitment from Mary and George Sissel, whose twin grandson suffers from Type 1 diabetes. The Sissels join previous benefactors whose goals were to enable the pursuit of new methods for treating childhood diabetes and to move promising new developments in stem cell research from the laboratory to the clinic more quickly than before.

(left to right) George Sissel, Lori Sussel, Ph.D. and Mary Sissel at Sissel & Findlow Family Endowed Chair reception at the Barbara Davis Center for Diabetes on February 13, 2018

**Holger Russ, Ph.D., Assistant Professor, Barbara Davis Center for Diabetes/Microbiology and Immunology Department**, received the Young Investigator Award from the Human Islets Research Network (HIRN) NIH consortium and the Culshaw Junior Investigator Award in Diabetes.

**Wagner Schorr, M.D., Gates Center Advisory Board member**, received the CU School of Medicine's Distinguished Service Award for his work in nephrology and service to the medical community at the Anschutz Medical Campus' May 2018 alumni weekend.

*\*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 Campus.*

# GRANT AWARDS

PRINCIPAL INVESTIGATOR(S)	AGENCY/SPONSOR	AMOUNT AWARDED	TITLE	FUNDING PERIOD
Appel, Bruce	National Institutes of Health	\$427,625	Mechanisms of Neuron-Glia Synaptic Communication	09/01/18 - 08/31/20
Artinger, Kristin/ Co-I Prekeris, Rytis	National Institutes of Health	\$408,185	The mechanism regulating actin dynamics and polarized membrane transport during invadopodia formation.	02/1/18 - 01/31/22
Bamburg, James	National Institutes of Health	\$187,550	Fluorescence Microscope for automated large array scanning and 3D imaging	05/15/18 - 05/14/19
Bamburg, James	National Institutes of Health	\$150,000	PrPc and NOX-dependent signaling in dementia- Supplemental award	08/15/18 - 03/31/20
Benam, Kambez H.	U.S. Food and Drug Administration	\$3,445,344	Toxicity and Carcinogenicity Profiling of Emerging Tobacco Products	09/2018 - 09/2021
Benam, Kambez H.	University of Colorado Pulmonary Innovation Award	\$16,667	3D-Printed Personalized Human Lung Airway for Treatment of Tracheobronchial Stenosis	09/2018 - 09/2021
Benam, Kambez H.	University of Colorado Cancer Center Career Enhancement Award	\$50,000	Micro-engineered Lung Small Airway for Modeling Lung Cancer and Therapeutic Development	05/2018 - 04/2019
Boyle, Kristen	American Diabetes Association	\$600,000	Umbilical cord-derived stem cell metabolism: Understanding mechanisms for childhood obesity risk	01/01/18 - 12/31/20
Boyle, Kristen	National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases	\$1,677,087	Epigenetic programming of infant mesenchymal stem cells: mechanisms for obesity and diabetes risk in humans	07/25/18 - 06/30/23
Bilousova, Ganna / Kogut, Igor / Roop, Dennis	California Institute for Regenerative Medicine Cell Therapy/Biologic award (PI: Anthony Oro; Stanford University)	\$556,825	Engineering skin grafts for dystrophic epidermolysis bullosa patients using gene-corrected iPSC-derived cells.	03/01/18 - 09/30/20
Bilousova, Ganna / Kogut, Igor / Roop, Dennis	EB Charities	\$281,489	Developing a Therapeutic Approach for Delivering Stem Cells Systemically to Treat Fragile Internal Epithelia in Recessive Dystrophic Epidermolysis Bullosa Patients	12/01/18 - 11/30/19
Bilousova, Ganna / Kogut, Igor / Roop, Dennis	EB Charities	\$276,254	Testing a "Spray on Skin" Approach as an Alternative Method for Delivering Keratinocytes and Fibroblasts derived from Gene-edited induced Pluripotent Stem Cells (iPSCs) to Recessive Dystrophic Epidermolysis Bullosa Patients	12/01/18 - 11/30/19
Bilousova, Ganna / Kogut, Igor / Roop, Dennis	Department of Defense	\$3,786,877	Translating a Stem Cell-Based Therapy for Epidermolysis Bullosa into the Clinic	09/15/18 - 09/14/21
Canto-Soler, Valeria	Gates Grubstake Fund	\$350,000	Stem Cell-Derived Retinal Transplant to Treat Dry AMD	01/01/18 - 12/31/21
Canto-Soler, Valeria	National Institutes of Health, National Eye Institute	\$375,000	Patterning Genes in Retinal Development	02/01/18 - 01/31/23
Degregori, James	National Institutes of Health, National Cancer Institute	\$108,750	Targeting MCJ/DNAJC15 and the mitochondrial electron transport chain in acute myeloid leukemia	07/01/18 - 06/30/20
Degregori, James	American Association for Cancer Research	\$488,168	Microenvironment-mediated Clonal Evolution and Risk of Lung Adenocarcinoma	09/01/18 - 08/31/21
Degregori, James	Leukemia and Lymphoma Society	\$223,616	Therapeutic Targeting of AML Stem Cells	10/01/18 - 09/30/23
Degregori, James	National Institutes of Health, National Cancer Institute	\$66,660	Therapeutic targeting of autophagy-dependent cancer	11/01/18 - 10/31/19
Degregori, James	National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases	\$280,000	Impact of IL-1 signaling on hematopoietic stem cell function and emergence of clonal hematopoiesis	12/01/18 - 11/30/23
Fry, Terry	National Institutes of Health Cancer Moonshot	\$2,452,238	Multispecific targeting incorporating cytokine receptor pathways in high risk pediatric acute leukemias to improve durability of adoptive cell therapy-induced remissions	10/01/18 - 08/31/23
Gavin, Kathleen	Boettcher Foundation	\$235,000	Biomarkers and phenotype of bone marrow-derived adipocytes in humans	07/01/18 - 06/31/21
Hagman, James	National Institutes of Health	\$162,666	Regulation of Humoral Immunity by SR Protein Kinase 3	05/14/18 - 04/30/20



PRINCIPAL INVESTIGATOR(S)	AGENCY/SPONSOR	AMOUNT AWARDED	TITLE	FUNDING PERIOD
Hagman, James	National Institutes of Health	\$444,583	Chd3 Conditional Knockout Mice: A New Tool for Studies of Lymphocyte Epigenetics	11/15/18 - 10/31/20
Krebs, Melissa/ Payne, Karin	National Institutes of Health, National Institute of Arthritis and Musculoskeletal and Skin Diseases	\$353,717	Engineering a Biopolymer Hydrogel to Inhibit Osteogenesis: Implications for Growth Plate Repair	05/01/18 - 04/30/20
Krebs, Melissa	CU School of Medicine/Children's Hospital Colorado	\$20,000	Sustained Release Zwitterionic Gels for Pediatric Wound Healing	05/01/18 - 04/30/19
Krebs, Melissa/ Diercks, David / Navarre-Stichler, Alexis	National Science Foundation	\$999,700	MRI: Acquisition of a Raman Imaging-Scanning Electron Microscope / Focused Ion Beam Instrument for Correlative Analysis of Materials Across Multiple Length Scales	09/01/18 - 08/31/20
Liechty, Kenneth	CU School of Medicine/Children's Hospital Colorado	\$10,000	Sustained Release Zwitterionic Gels for Pediatric Wound Healing	05/01/18 - 04/30/19
Lu, Shi-Long	Colorado Office of Economic Development and Int'l Trade Advanced Industry Award	\$130,000	HNKlear, a saliva-based molecular test for head and neck cancer	07/01/18 - 06/30/20
Lu, Shi-Long	SPARK Colorado Grant	\$100,000	Development of non-invasive molecular test for head and neck cancer recurrence	09/01/18 - 08/31/20
Majka, Susan	National Institutes of Health, National Heart, Lung, and Blood Institute	\$2,443,705	Role of Lung MSC in Emphysema	04/01/18 - 03/31/22
Majka, Susan	Department of Defense Tuberous Sclerosis Complex Research Program	\$711,000	Lung MSC Regulate Angiogenesis and Repair During Fibrosis	09/30/18 - 09/29/21
Olson, Jeffrey	Colorado Advanced Industry Accelerator Award	\$165,000	Intravitreal Drug Delivery System	10/2018 - 09/2020
Payne, Karin	Gates Grubstake Fund	\$350,000	Bioresorbable 3-D Printed Personalized Implant for Cartilage Regeneration in Pediatric Growth Plate Injuries	01/01/18 - 12/31/21
Phiel, Christopher	National Institutes of Health, National Institute of General Medical Sciences	\$466,499	The Regulation of mRNA Methylation by Glycogen Synthase Kinase-3	05/01/16 - 04/30/19
Pietras, Eric/ D'Alessandro, Angelo	Golfers Against Cancer	\$45,000	Interleukin-1 as a metabolic regulator of AML pathogenesis	10/01/18 - 09/30/19
Russ, Holger	National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases	\$1,541,680	Improving human pluripotent stem cell derived beta cell transplantation using genetic lineage tracing	09/30/18 - 07/31/22
Russ, Holger	National Institutes of Health, National Institute of Allergy and Infectious Diseases	\$466,500	Stress induced changes to the human beta cell proteome	04/01/19 - 03/31/21
Russ, Holger	The Colorado Clinical & Translational Sciences Institute	\$20,000	Induced Pluripotent Stem Cell-Derived Human Motor Neurons for Modeling and Treatment of Amyotrophic Lateral Sclerosis and Other Human Motor Neuron Diseases.	05/01/18 - 04/30/19
Russ, Holger	University of Colorado Anschutz Medical Campus Skin Disease Research Center	\$20,000	Determine the role of FOXN1 in human skin.	01/01/18 - 12/31/18
Russ, Holger	CU School of Medicine RNA Bioscience Initiative	\$10,000	Elucidating human beta cell subtype regulation and interconversion in health and disease.	01/01/18 - 12/31/18
Russ, Holger	NIH/NIDDK/ HIRN	\$231,000	Investigating the human pancreatic beta cell transcriptome in health and disease.	06/01/18 - 05/31/20
Russ, Holger	Peter J. Culshaw	\$100,000	Designing Immune Privileged Beta Cells for Cell Therapy of Autoimmune Diabetes	09/01/18 - 08/31/20
Shellman, Yiqun	University of Colorado School of Medicine	\$50,000	Academic Enrichment Fund	12/01/18 - 11/30/19
Shellman, Yiqun	University of Colorado-SDRC Pilot Grant	\$20,000	The therapeutic potential of SASH1 in melanoma	02/01/18 - 07/30/18
Song, Kunhua	National Institutes of Health	\$194,375	Mechanisms for cell signaling in the control of cardiomyogenesis	09/15/18 - 08/31/19
Verneris, Michael	Hyundai Hope on Wheels	\$300,000	Targeting Pediatric Sarcoma with IL-15 Producing, CAR Expressing NK cells	09/30/18 - 09/30/20
Wang, Xiao-Jing	National Institutes of Health, National Institute of Dental and Craniofacial Research	\$1,511,070	Proprietary biologic treatment to heal skin wounds	09/18/18 - 08/31/20
Wang, Xiao-Jing	National Institutes of Health, National Institute of Dental and Craniofacial Research	\$585,209	Elucidating Mechanism of Immune Evasion in Head and Neck Cancers	08/09/18 - 07/31/23
Zamora, Martin	Gates Grubstake Fund	\$350,000	Clinical Development of Autologous CD117+ Progenitor Cell Therapy for Solid Organ Transplantation	01/01/18 - 12/31/21
TOTAL AWARDS =		\$20,870,020		

# COMMERCIALIZATION

## GRUBSTAKE RESEARCH FUND HITS RICH VEINS

The Gates Grubstake Fund made enormous strides in 2018 in guiding the promising basic science at Anschutz Medical Campus toward commercialization and tangible benefits for patients.

The Grubstake Fund, with multiple awards of about \$350,000 each year, is meant to bridge the “valley of death” funding gap that separates a promising medical concept from production and a business model that will make a difference in human lives.

It’s working.

The Gates Center and the CU Innovations Office, its Grubstake Fund collaborator, report that by 2018, the cumulative \$3.5 million in Grubstake awards had already produced about \$18 million of follow-on funding from partners seeking to help develop and commercialize the concepts.

That “5X” return is remarkable in any financial setting. For the Gates Center, it is confirmation that the mission of collaboration and entrepreneurship in the name of medical advancement is now producing results.

“The Grubstake Fund program has been so game-changing as far as impact and getting research to patients,” said Kim Muller, managing director of CU Innovations. “We are looking at using that model for all therapeutic areas around campus.

We almost feel we have an ethical obligation to do it.”

To date, there are 105 ongoing regenerative medicine projects on campus with potential to compete for Grubstake awards, of which 25 have reached the product development stage. As word spreads of the program’s opportunities for researchers, being selected for the handful of awards has become increasingly competitive.

Diane Gates Wallach, co-chair of the Gates Center Advisory Board, said the 2018 progress report indicates the Grubstake Fund is fulfilling the original concept of the awards as a bridge between bench science and human treatments. The philanthropy of Charles C. Gates and the Gates family provided the foundation of the Gates Center in 2006.

“It’s very consistent with my dad’s philosophy of taking a chance early on with great ideas,” Wallach said. “You know you’re going to drill a dry hole now and then, but you’ve got to try. I think he’d be thrilled if he could see all this creativity. It’s exactly what he’d hoped.”

The Grubstake Fund is focused on accelerating research in the field of regenerative medicine with the potential for direct patient impact. Research eligible for awards includes projects having proof of concept data supporting development as:



- Treatments (e.g. biologics, small molecules, cell therapies)
- Diagnostics, platforms and research tools (e.g. biomaterials, scaffolds, therapeutic targets, cell expansion methods)
- Devices (e.g. drug delivery, implants, restoration)
- Cell biology and tissue engineering

The Grubstake Fund goes a significant way toward addressing a gap between academia and “the real world” that has existed since the founding of medical schools. Researchers are constantly trying to broaden the impact of their work to help more than an individual patient. Yet when they have a promising concept, their scientific training lacks the background in regulatory approvals and how to access the capital required to prove a concept’s commercial value.

“They’ve never had to intersect with the private sector,” Muller explained. “There’s no education in medical school or at work that helps them prepare for that.”

“A lot of scientists have great ideas and they recognize the scientific importance of what they work on,” said Gates Center Associate Director Mark Petrash, Ph.D., who is also a professor and director of research in the School of Medicine’s Ophthalmology Department. “But what they don’t recognize is the commercial potential of the discoveries they make in their laboratories.”

The Grubstake Fund typically awards three researchers each year with a multi-year grant. The selection process -- overseen by a Scientific Investment Advisory Committee of subject matter experts and institutional investors -- gives weight to projects that appear within three to five years of launching a clinical trial. In addition to funding, the structure set up by the Gates Center, CU Innovations and other supporters provides:

- Access to the resources of the “Startup Toolbox” developed by Gates Center Advisory Board member Ann Sperling and colleagues.
- Mentoring by business experts on- and off-campus, for pathway and business plan development.
- Coaching through the regulatory process required by the Food & Drug Administration and other compliance offices in drug or device development.
- Access to SPARK Colorado run through CU Innovations.

Members of the public who read casually about venture capital in hotbeds like California’s Silicon Valley may assume there are financiers with suitcases full of ready cash hovering around all Ph.D.s. But that kind of capital tends to move in when an idea is ready for mass commercialization, innovation experts said. Before that stage, scientists need money for lab assistants and regulatory help to show that something seen under a microscope has real promise as a treatment.

“When you are at the proof of concept translational stage, that’s where most VCs aren’t going to invest,” said the Gates Center’s Entrepreneur in Residence Heather Callahan, who also serves as portfolio manager at CU Innovations bringing the expertise of an Executive MBA, a law degree and a Ph.D. in biochemistry. “That’s why this was the perfect place in the trajectory of invention to start putting money.”

The money and the mentoring have moved a growing portfolio of projects toward initial clinical trials in the next two to three years.

Dr. Kenneth Liechty is using a 2016 Grubstake Fund award to broaden research into anti-inflammatory mechanisms he discovered as a leading pediatric surgeon at Children’s Hospital Colorado and the University of Colorado School of Medicine. Liechty, the Sandy Wolf Chair in Maternal Fetal Surgery, has perfected techniques for repairing spina bifida and fluid on the lungs *in utero*.

Wounds *in utero* heal with limited inflammation and no scarring. Liechty and others have attempted to isolate those mechanisms to benefit adult patients. People living with diabetes, for example, suffer from excessive inflammation and wounds that don’t heal.

The team designed and produced a therapeutic nanoparticle they believed could be efficacious, and tested it in a model employing diabetic mice. Their wounds healed at the rate of non-diabetic skin. “If you can limit injury, you can promote tissue regeneration, and that’s what the Gates Center is all about,” Liechty said.

That’s when Liechty applied for a Grubstake award, to take the model to larger animals, and to support the arduous process of filing for FDA Investigational New Drug status.

"The Gates Center has been phenomenally helpful in accelerating our work," Liechty said. The Grubstake model and the Gates Biomanufacturing Facility address three keys to the drug commercialization process, he said: "It's one thing to say, 'Okay, we can manufacture things.' Or another thing to say, 'We have people who know the ins and outs.' And another to say, 'How do you pay for it?' We're a relatively new campus for that kind of idea, and this is what's needed to really jumpstart this."

The call for applications for the Grubstake awards also gives the university and the Gates Center another opportunity to promote the kind of cross-disciplinary and cross-campus collaboration that leads to some of the most potent research. Grubstake awardee Steven Dow, DVM, Ph.D., of Colorado State University is a prime example.

The Gates Center membership includes researchers at CSU and other Colorado institutions beyond the Anschutz Medical Campus, and Dow is a professor and Director of CSU's Center for Immune and Regenerative Medicine. He was a featured speaker at the Gates Center and CSU Zoobiquity Colorado Conference in 2018, drawing together collaborators studying how human and animal medicine can share discoveries for the good of both.

Dow works with a type of stem cell (mesenchymal stem cells) that has proven useful for treating wounds and chronic wound infections. Work began with chronic staph infections in mouse models mimicking antibiotic-resistant MRSA infections that develop in human knees and other implants after surgery. The activated cells then proved to be efficacious in a clinical trial in dog patients with post-surgical infections treated at the CSU Veterinary Teaching Hospital.

The Gates Center Director, Dennis Roop, Ph.D., encouraged Dow's group to apply for Grubstake funding, which they received in 2015, an award Dow calls "transformational."

The expertise of the Gates Biomanufacturing Facility staff has been particularly helpful as part of the Grubstake education process, Dow said, knowing they can produce clinical trial-size amounts of activated cells "in our backyard."

Dow has also lined up the infectious disease and orthopedic surgery teams at the School of Medicine and UHealth who will be key to human trials, while drawing on CU Innovations for the complex regulatory steps.

The assistance network is "moving our work pretty efficiently from bench – the mouse studies – to our 'bedside', which is dogs, and eventually into human clinical trials," he said.

The annual Grubstake award process has helped everyone involved with the Gates Center and wider campus research efforts keep an eye on the true significance of the scientific pursuit, Petrash said.

"This is an important part of the mission of the university, to not only do good research but to make it of practical use to society."

The next Grubstake Award application process will begin in June 2019, with written applications due at the end of August. Interested applicants are encouraged to reach out to the Gates Center's Entrepreneur in Residence, Heather Callahan, for guidance.

### **\$18M IN FOLLOW-ON-FUNDING - SO FAR** 5X Return on Investment - 2014-2018



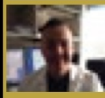
✓ **Antonio Jimeno** – 2014 Award  
"Humanized mouse cancer model"  
\$4.0 million



✓ **Xiao-Jing Wang** – 2014 Award  
"Smad7 fusion protein for oral mucositis"  
\$3.5 million BDEG/SBIR/STTR Phase I & II Funding



✓ **Ganna Bilousova & Igor Kogut** – 2015 Award  
"High efficiency generation of iPSCs"  
\$6.4 million NIH, DOD, and philanthropy



✓ **David Wagner** – 2016 Award  
"Peptide inhibitor of CD40 for autoimmune diseases"  
\$4.0 million STTR Phase I & II Funding



✓ **Jeff Olson** – 2017 Award  
"Ophthalmic implant to prevent macular degeneration"  
\$165,000 AIA Funding



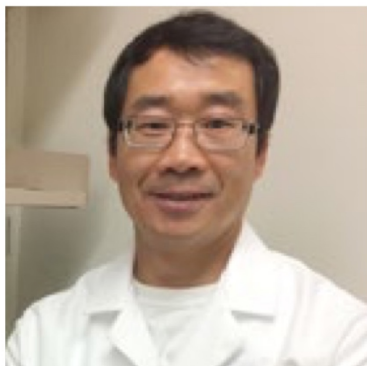
# 2018 GATES GRUBSTAKE FUND UPDATE

## 2018 GATES GRUBSTAKE AWARDEES:



### **PREVENTION AND TREATMENT OF PULMONARY FIBROSIS, KEN LIECHTY, M.D.**

Acute lung injury leading to Acute Respiratory Distress Syndrome (ARDS) causes 150,000 adult ICU admissions and 75,000 deaths annually in the US. Currently, treatment for ARDS is palliative, and does not address the underlying causes. Dr. Ken Liechty and his team have shown that their nanoparticle therapy is able to regenerate healthy lung tissue in a mouse model of acute lung injury. The Grubstake Award will allow them to develop an inhaled version of the nanoparticle therapy and do the additional safety studies required prior to a clinical trial in ARDS patients.



### **HEART REGENERATION BY CONVERSION OF NON-MYOCYTES INTO FUNCTIONAL CARDIOMYOCYTES, KUNHUA SONG, PH.D.**

Eight million Americans suffer a heart attack annually; that is 3% of adults in the US. The annual cost for treating heart attacks is \$12 billion, making it the most expensive condition treated in hospitals in the US. Even worse, 30-40% of heart attack patients develop heart failure, accounting for about 50% of all heart failure patients. The five-year survival rate for heart failure patients is only 50%. Despite the development of various therapies and medical devices such as the Left Ventricular Assist Device, the five-year survival rate has not changed in the past 20 years. Dr. Kunhua Song and his team have discovered a way to regenerate healthy cardiac cells from the fibrotic tissue causing heart failure using a gene therapy approach. The Grubstake Award will allow them to complete their animal studies and begin preparing to file an IND to enter clinical trials.



### **GENERATION OF ENGRAFTABLE HEMATOPOIETIC STEM CELLS FROM INDUCED PLURIPOTENT STEM CELLS, MIKE VERNERIS, M.D.**

Bone marrow transplants are a high risk, expensive procedure (>\$13 billion) used to treat leukemia, lymphoma, and genetic diseases. Two thirds of patients receive transplants from unrelated donors, which causes delays to find matching donors, and increases the complications and cost associated with the procedure. Recently, scientists have discovered how to create induced pluripotent stem cells (iPS cells) from a patient's own cells, expand them, and convert them to bone marrow cells. However, these cells have not been successful at engrafting into the bone marrow in mouse models, indicating they would not be effective in a bone marrow transplant in patients. Dr. Verneris and his team have discovered that adding a small molecule during the conversion of the iPS cells allows engraftment of the cells in the mouse model. The Grubstake Award will allow them to confirm their initial finding in animal models, and to determine the most promising small molecule for clinical and commercial use.

## 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

### 2017

- Karin Payne, Ph.D.: Bioresorbable 3-D printed personalized implant for cartilage regeneration in pediatric growth plate injuries
- Valeria Canto-Soler, Ph.D.: Stem cell-derived retinal transplant to treat dry-AMD
- Martin Zamora, Ph.D.: Clinical development of autologous CD117+ progenitor cell therapy for solid organ transplantation



CU Innovations Managing Director Kim Muller



2017 Grubstake Fund awardee Marty Zamora and colleague Robert Plenter





Gates Center Entrepreneur in Residence Heather Callahan and 2017 Awardee Valeria Canto-Soler



2017 Awardee Karin Payne and collaborator Nancy Miller, M.D.

Gates Grubstake Fund investment decisions are made on a competitive basis by members of the Scientific Investment Advisory Committee (SIAC):

- **Mark Brunvand, M.D.**, former *Director of Unrelated Donor Transplantation*, Colorado Blood Cancer Institute; Medical Director for Transplantation, Cigna
- **William Hiatt, M.D.**, *Professor*, Division of Cardiology, University of Colorado Anschutz Medical Campus; President, CPC Clinical Research; member, Gates Center Advisory Board
- **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., FACPVT**, *Chief Executive Officer*, Avita Medical Ltd.; Managing Director, Bioscience Managers Pty Ltd
- **J. 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 Center Advisory Board
- **Robert Traver, J.D.**, *Patent Attorney*, Sheridan Ross

# 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.

## 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, which can rapidly isolate and collect unique types of cells.

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

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

### THE FOLLOWING WERE PROVIDED IN 2018:

- We received additional funding from the School of Medicine, the Gates Center, the Cancer Center, and the CU RNA Initiative to purchase a new Sony MA900 cell sorter. This instrument will enable us to establish a customer-operated cell sorting service at an economical price.
- We added a new spectral analyzer, the Cytex Aurora, which captures the spectral “fingerprints” of cellular fluorescence tags across the visible light spectrum, rather than using a narrow band of fluorescence for each tag. This innovation permits the use of more than 20 tags for each sample in a user-friendly manner.
- We added two new software analysis packages, De Novo FCS Express and Astrolabe, which allow researchers to more fully explore their complex data sets including expanded graphical and statistical features.
- We continue to deploy an enthusiastic, engaged and expert team to consult with and instruct members in basic and advanced flow cytometry techniques.
- We continue to offer educational workshops and presentations to promote the optimal use of flow cytometry.



## 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 consultations 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.

### THE FOLLOWING WERE PROVIDED IN 2018:

- We provide expert consultation on the generation and interpretation of tissue histology.
- We are the only research facility on the Anschutz Medical Campus with expertise in skin and appendage histology.
- We continue to expand our customer base within and outside of UC Anschutz.
- We continue to interface with board-certified dermatopathologists to provide our customers with expert advice on skin pathology.

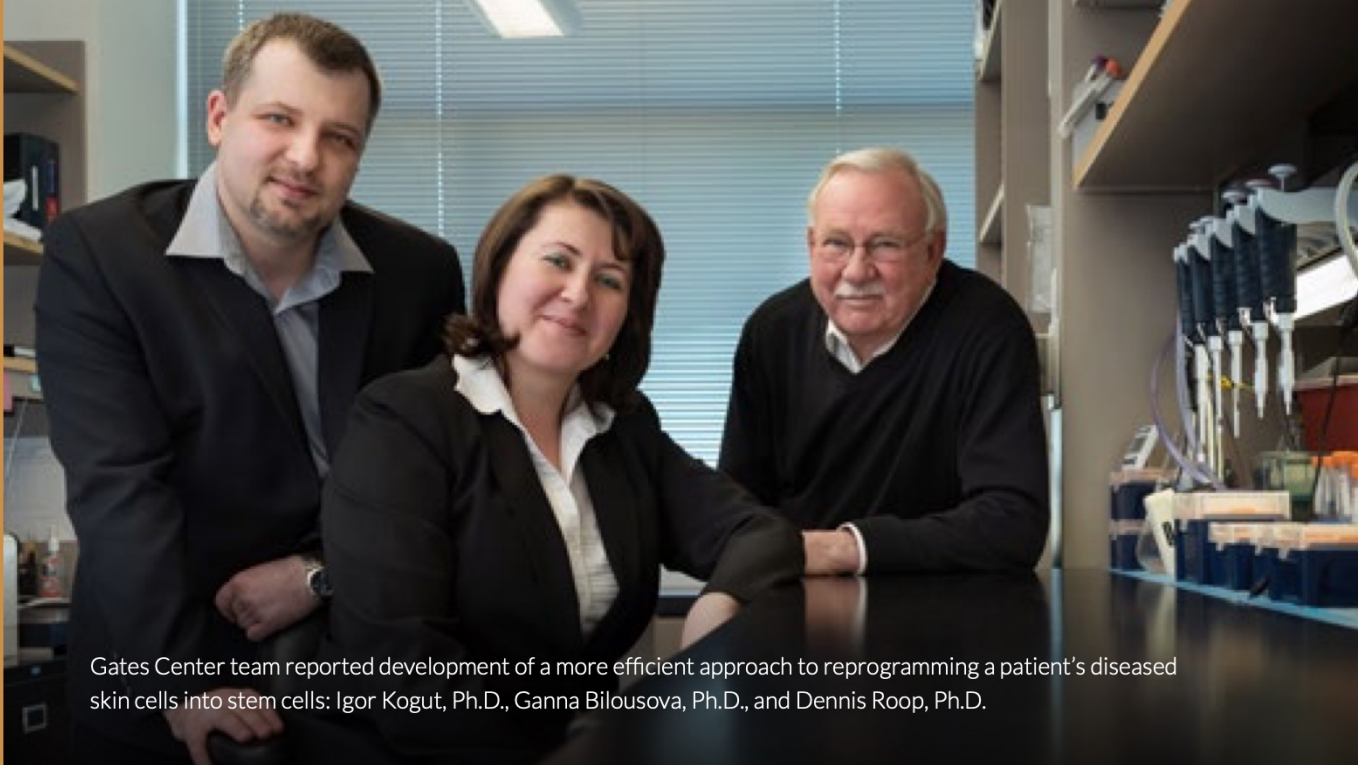
## BIOENGINEERING CORE

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 also provide 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., 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).

### THE FOLLOWING WERE PROVIDED IN 2018:

- We are an integral part of the CU Anschutz Medical Campus animal facility that generates genetically engineered mice for the CU Anschutz community and customers from other universities.
- Our ability to attract customers from outside institutions demonstrates our competitiveness and expertise as a transgenic mouse facility (e.g. University of Wyoming, University of Alaska, Florida Atlantic University, Northwestern University, CSU, CU Boulder, University of Oregon and Columbia University)
- We continue to expand our service repertoire and improve the efficiency of our technology (e.g. crispr/cas modification of mouse embryos by in vitro electroporation).
- We develop new technology to advance research in the area of ectodermal stem cell biology (e.g. mouse amniotic sac injections with viral vectors to genetically modify ectodermal surface stem cells).



Gates Center team reported development of a more efficient approach to reprogramming a patient's diseased skin cells into stem cells: Igor Kogut, Ph.D., Ganna Bilousova, Ph.D., and Dennis Roop, Ph.D.

## STEM CELL BIOBANK AND DISEASE MODELING CORE

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

This core, which is co-directed by Drs. Bilousova and Kogut, achieved significant progress and recognition in 2018, helping to advance the cause of effective treatment for some of the world's most debilitating and intractable diseases. The core, which offers complete services related to the production of high-quality human iPSCs from patient-derived somatic cells, also found success in building further collaborations with numerous departments on campus. Additionally, it inspired donors to contribute toward the "iPSC Discovery Platform" and the "Director's Innovation Fund" to support various research projects described on page 36. Twelve projects in the center's research pipeline are attributable to the core facility, which is making iPSC lines safely and efficiently at one-third the cost charged by others. In addition to serving on-campus research, the core is producing cell lines for research teams at Stanford University, Columbia University, and universities in France, among other nations.

“

*We have been using reprogrammed induced pluripotent stem cells produced by Dr. Bilousova and Dr. Kogut in order to study the development of heart defects. They have been able to use cells from amniotic fluid, collected at birth from infants with specific congenital heart defects and cells collected from urine from subjects with Down syndrome. Both of these are non-invasive methods of cell collection, allowing us to study cell lines from many infant and pediatric subjects. This core is easy to work with, fast, and reasonably priced. Cells we have obtained from this core expand very quickly and we have been able to differentiate these into cardiomyocytes and other heart cells with high efficiency.*

*- Jeff Jacot, Ph.D.*

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*My vision is a seamless transition between Anschutz and Boulder. We do not plan to generate iPSCs – you do this extremely well and the patient resources are at Anschutz – but instead to expand the scope of iPSC studies by creating a hub in Boulder for life scientists with new biological insights and to develop innovative platforms alongside engineers for differentiation and organoid formation. Then, when projects move forward to potential clinical application, this would pass back down to Anschutz and the GMP facility.*

*- Lee Niswander, Ph.D.*



## **FOLLOWING IS A LIST OF SOME OF THE CLIENTS WITH WHICH THE CORE HAS COLLABORATED DURING 2018:**

### **ANSCHUTZ MEDICAL CAMPUS**

**Linda Crnic Institute for Down Syndrome:** iPSCs from renal epithelium: differentiate into different adult lineages

**Mike Verneris, M.D.:** iPSCs from renal epithelium: differentiate into natural killer cells

**Jeffrey Jacot, Ph.D.:** iPSCs from cells isolated from amniotic fluid: differentiate in cardiomyocytes

**Holger Russ, Ph.D.:** iPSCs from thymic epithelium: differentiate into thymic epithelium

**Peter Dempsey, Ph.D.:** iPSCs from fibroblasts: differentiate into intestinal organoids

**Valeria Canto-Soler, Ph.D.:** iPSCs from fibroblasts: differentiate into miniature human retinas that sense light

**Huntington Potter, Ph.D.:** iPSC lines from patients with Alzheimer's disease: differentiate into neurons to model a neuronal phenotype in Alzheimer's

**Tim Benke, M.D., Ph.D.:** iPSCs from patients with specific neurogenetic diseases (epilepsy)\* \*\*

**Ellen Elias, M.D.:** iPSCs from patients with Ehlers-Danlos Syndrome \*

**Susan Boackle, M.D.:** iPSCs from patients with lupus to elucidate the role of specific nucleotide polymorphisms in disease progression

### **BOULDER CAMPUS CLIENTS**

**Lee Niswander, Ph.D.:** A new Stem Cell Research and Technology Resource Center the goal of which is to expand the scope of iPSC studies by creating a hub in Boulder for life scientists to develop innovative platforms alongside engineers for differentiation and organoid formation.

**William Old, Ph.D.:** iPSCs from individuals with Down Syndrome and iPSC lines with DYRK1A knockout: differentiate into neuronal organoids

**Michael Stowell, Ph.D.:** iPSCs from individuals with Alzheimer's Disease: differentiate into neurons, astrocytes and neuronal organoids

### **EXTERNAL CLIENTS**

**Bertha Chen, M.D., and Vittorio Sebastiano, Ph.D. (Stanford):** RNA reagents for the production of iPSCs to treat women with urinary incontinence (CIRM funded)

**Vittorio Sebastiano, Ph.D. (Stanford):** RNA reagents to achieve tissue rejuvenation

**Clifford Folmes, Ph.D. (Mayo Clinic Cancer Center, Arizona):** Reprogramming RNA reagents and iPSCs to assess changes in mitochondria metabolism during cellular reprogramming

**Alain Hovnanian, M.D., Ph.D. (University Paris Descartes - Sorbonne Paris Cité, Paris, France):** RNA reagents to generate genetically corrected iPSCs for the treatment of skin blistering diseases

**Tony Oro, M.D., Ph.D. and Angela Christiano, Ph.D. (EB iPS Cell Consortium, Stanford and Columbia Universities):** RNA reagents to generate genetically corrected iPSCs for the treatment of skin blistering diseases \*

\* Projects funded through philanthropic donations to the iPSC Discovery Platform

\*\* Project partially funded through the Director's Innovation Fund

# GATES BIOMANUFACTURING FACILITY



2018 Gates Biomanufacturing Facility staff at a holiday get-together: (BACK ROW, left to right) Matthew Seefeldt, Timothy Gardner, Krutika Patel, Jessica Freeman, Deepa Vadakkan, Christopher Baclasky, Russell Marians, Branden Salinas (MIDDLE ROW, left to right) Mitchell Fraller, Bertina Minjares, Sandra Jernberg, Sonja Giguere, Paul Lemaire, Emily Yuan, Matthew Brenton (FRONT ROW, left to right) David Hahn, Rebecca Mallo, Caylee Martens, Kaela Siahpush, Aashrit Donthi, Christopher Garbe, Ryan Crisman (Not Pictured: Kevin Ash, Sarah Carter, Christopher Freedman, Graciela Gamez, Roger Giller, Jordan Krause, Felicia Lanzarone, Sadhna Mehra, Jackie Nelson, Thomas Street)



## Charles C. Gates Biomanufacturing Facility

UNIVERSITY OF COLORADO **ANSCHUTZ MEDICAL CAMPUS**

2018 was a pivotal year at the Gates Biomanufacturing Facility (GBF) as we produced our first clinical-grade material for use in a Phase 1 multiple myeloma CAR-T cell clinical trial. This is a major milestone for a Good Manufacturing Practice (GMP) facility and positions the GBF to compete with the top echelon of universities manufacturing products for university-sponsored clinical trials. The GBF's ability to produce materials for clinical trials is the result of significant effort by our team to build and implement a strong quality management system that two third-party quality audits

have now reviewed and approved. We now have a top-tier facility combined with an experienced leadership team that understands the intricacies of doing clinical trials in leading-edge cell therapies, as well as more traditional protein biologics.

With our first Phase 1 GMP run in cell therapy behind us, we began the technology transfer process for production of materials for a CD19 CAR-T trial, which will be the first cell therapy clinical trial sponsored by the CU School of Medicine



(SOM) in connection with a trial at UCHealth. This project is a collaboration with the SOM Clinical Research Administration Office (CRAO), SOM Division of Hematology and the UCHealth Bone Marrow Transplant Clinic. This clinical trial will pave the way for many university-sponsored clinical trials in the future. With the help of our Medical Director, Roger Giller M.D., we are also in the process of establishing procedures for providing a similar product for patients at Children's Hospital Colorado. Dr. Terry Fry, Director of Cancer Immunotherapy, described the unique nature of this campus-wide coordination, stating that "It certainly facilitates cross fertilization and collaboration when you have adult and children's hospital research programs and a GMP facility all on one campus. That's sort of an unbelievable opportunity."

After a few iterations, the GBF finalized its governance structure with the first meeting of the Gates Biomanufacturing Advisory Board in June 2018. The Advisory Board consists of the Chancellor of the Anschutz Medical Campus, the Dean of the School of Medicine, leadership from our funding partners—UC Health, Children's Hospital Colorado, and the Gates Frontiers Fund, along with other campus staff and volunteers with expertise in GMP manufacturing and clinical

trial operations. We also have a Finance Advisory Committee in place consisting of the Chief Financial Officers of the Anschutz Chancellor's office, School of Medicine, UCHealth and Children's Hospital Colorado. This new structure provides a clear decision-making process that allows us to evaluate risks and make appropriate operating and financial decisions in a timely manner. This governance structure distinguishes us from most other universities run by combinations of committees, and provides a competitive advantage for our clients.

It has taken considerable financial resources to build the facility, hire and retain the talented team, and maintain the quality system and the equipment used for operations. Our funding partners have been unwavering in their commitment to quality and their financial support of the facility. None of our success to date would have been possible without this ongoing support.

Looking forward, we are in a great position to achieve our mission, which is "to accelerate the translation of scientific discoveries into human clinical trials as safely, efficiently, and cost effectively as possible according to high quality standards."

GATES FRONTIERS FUND

uchealth

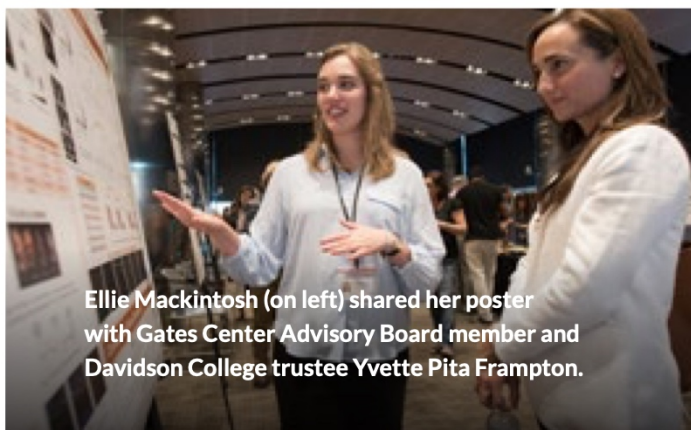


Protein Suite

Cell Therapy

# EDUCATION

## THE GATES SUMMER INTERNSHIP PROGRAM



Ellie Mackintosh (on left) shared her poster with Gates Center Advisory Board member and Davidson College trustee Yvette Pita Frampton.

*"Having worked with my fellow interns, I can assure you that the contributions to the Gates Summer Internship Program (GSIP) are helping to develop the next generation of physicians and scientists who have major goals to push regenerative medicine forward. Thank you for investing in our development and our futures." - Ann Lyons*

The quote above reflects the appreciation of the college undergraduates who participated in the Gates Summer Internship Program during the summer of 2018. These young people are grateful for the myriad opportunities they found on the Anschutz Medical Campus, and cognizant of the many sources of support that made their experience possible.

In 2015, a generous gift from Gates Center friends Rhondra and Peter Grant helped establish the GSIP program for 12 students to further the dream of the Gates Center to encourage exceptional college undergraduates to pursue careers in stem cell biology and regenerative medicine. Thanks to wonderful, continued support from the Grants and others, the program has grown substantially and has benefited both our students and the laboratories in which they have worked. Last summer, our nationwide applicant pool swelled to 206 from 135 the year before, and 18 interns and three affiliate students participated in the fourth year of the 11-week program. Students assigned to the labs of individual Gates Center mentors pursued a variety of research topics and therapies across the Anschutz Medical Campus. The addition

of affiliate mentors Jeff Jacot Ph.D., from the Department of Bioengineering and Holger Russ, Ph.D., from the Barbara Davis Center for Diabetes further diversified the portfolio of lab and project opportunities available.

In addition to working in their respective laboratories, students attended biweekly seminars focused on an array of career development and research topics, including newly added presentations on intellectual property and commercialization. Additionally, interns with aspirations to go to medical school shadowed clinicians in the Division of Medical Oncology. They also gathered together for on- and off-campus social activities such as rafting, and volunteered for the annual Mallets for Melanoma Polo Event – all organized by our program directors and staff and volunteers from the Colorado Melanoma Foundation. The summer ended with the annual closing day ceremony, featuring guest speaker Richard Duke, Ph.D. sharing his "Musings of a Serial Biotech Entrepreneur," along with a poster session and reception to share these students' exceptional work with faculty, family and donors. We were particularly pleased with the survey conducted at the program's end in which 100% of the interns said that they would recommend the program to others, and 100% of the mentors wanted to participate in the 2019 program.

We at the Gates Center join these current and former students in thanking those who have made the Gates Summer Internship Program possible, including our academic partners Davidson and Middlebury Colleges and the University of Colorado Denver. We also want to acknowledge the researchers and clinicians listed along with their lab staffs who kindly agree to take GSIP interns under their wings during the summer and the nurse, Krista Treichel, and the clinicians in the Cutaneous Oncology Clinic who provided shadowing opportunities to interns focused on medical school. We are particularly appreciative of the instances in which our mentors and others continue to advise and support former GSIP students as they consider and apply for prospective jobs and advanced degrees, as shown by the messages included in this Education section. Finally, we want to thank the hard-working directors of our



program, Tamara Terzian, Ph.D., Neil Box, Ph.D., and Enrique Torchia, Ph.D., and especially our interns, who have given us great hope for the future of the field. As School of Medicine Dean John Reilly Jr., M.D., said at the GSIP closing day ceremony,

*"We hope that you have seen the allure of being a part of an academic campus and that we have helped satisfy your curiosity as to how we might move the field of regenerative medicine forward to make a positive impact on humans. We have tried to pique your interest in science, discovery and health, and would love to see you back on campus in a few years!"*

INTERN	UNDERGRADUATE INSTITUTION	MENTOR	DEPARTMENT/FACILITY
Anne Lyons*	University of Colorado Denver/ Anschutz Medical Campus	Jeffrey Jacot, Ph.D.	Department of Bioengineering
Austin Schoppe	University of Texas, San Antonio	Ganna Bilousova, Ph.D.	Department of Dermatology
Drake West	University of Wisconsin, LaCrosse	Yiqun Shellman, Ph.D.	Department of Dermatology
Eleanor Mackintosh*	Davidson College	Tamara Terzian, Ph.D.	Department of Dermatology
Grant Wilson	Azusa Pacific University	Antonio Jimeno, M.D., Ph.D.	Department of Medicine/Medical Oncology
Halley Herbst	University of Colorado Boulder	Peter Dempsey, Ph.D.	Department of Pediatrics
Hiba Anwar	University of Colorado Boulder	Mayumi Fujita, M.D., Ph.D.	Department of Dermatology
James Gonzalez	Texas A&M University	Tamara Terzian, Ph.D.	Department of Dermatology
Joseph Gerlach	Cornell University	Kristin Artinger, Ph.D.	Department of Craniofacial Biology
Joseph O'Brien*	Middlebury College	Holger Russ, Ph.D.	Barbara Davis Center for Diabetes
Khoa Nguyen	University of Colorado Boulder	Xiao-jing Wang, M.D., Ph.D.	Department of Pathology
Lisa Blackmer-Raynolds	Colby College	Curt Freed, M.D.	Department of Medicine/ Clinical Pharmacology and Toxicology
MacKenzie Walz	Regis University	Paco Herson, Ph.D.	Department of Anesthesiology, Neuronal Injury Program
Madeline Maloney	Middlebury College	Neil Box, Ph.D.	Department of Dermatology
Madison Weber	Bard College	Mark Petrash, Ph.D.	Department of Ophthalmology
Molly Murphy	University of Notre Dame	Shi-long Lu, M.D., Ph.D.	Department of Otolaryngology
Renee Woods	University of Colorado Denver	Michael Verneris, M.D.	Department of Pediatrics/Hematology, Oncology and Bone Marrow Transplantation
Ryan Lupi	Virginia Polytechnic Institute	Lori Walker, Ph.D.	Department of Medicine/Cardiology
Sydney Marchando	Colorado School of Mines	Torchia, Enrique	Department of Dermatology
Zachary Feuer	Rensselaer Polytechnic Institute	Karin Payne, Ph.D.	Department of Orthopedics
Zachary Trottier	Carleton College	Stanca Birlea, M.D., Ph.D.	Department of Dermatology

2018 Gates Summer Internship Program (GSIP) participants and affiliate students (BACK ROW back row, left to right) Zachary Trottier, Grant Wilson, Zachary Feuer, Austin Schoppe, Mackenzie Walz, Ellie Mackintosh, Madeline Maloney, Austin Hensley, Khoa Anh Nguyen, Joseph Gerlach, Ryan Lupi, Halley Herbst (FRONT ROW, left to right) Joe O'Brien, Renee Woods, Lisa Blackmer-Raynolds, Anne Lyons, Sydney Marchando, Madison Weber, Molly Murphy, Hiba Anwar (not shown: Drake West)



Hi Gates Center,

*I wanted to give you a quick life update as my GSIP experience has truly been so impactful in shaping my career path and aspirations.*

*I couldn't have gotten my current job without the skills I gained through GSIP and the PI whom I worked with has been an outstanding mentor, supporting me as I applied to jobs and now to school. I was undecided throughout college if I wanted to pursue a career in research, medicine, both, or perhaps neither, but experiencing the interdisciplinary, collaborative community at Anschutz, hearing the faculty lectures, and seeing the amazing potential of translational research at an academic medical center definitely helped shape my aspirations.*

*Regardless, I wanted to say how grateful I was to spend Summer 2016 in Colorado--writing medical school applications has caused me to reflect on my sources of inspiration and motivation and GSIP was a constant theme.*

*Thanks again to you and everyone who makes the program possible!*

Best,

Emma Office, GSIP Class of 2016



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

In 2018, the Gates Center continued its 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.

As explained by Dr. Appel, "CSD students and faculty have common interests in understanding the molecular and cellular mechanisms that underlie development, disease, stem cell biology and regeneration—a common curiosity that promotes extensive interaction among labs and creates a fantastic intellectual environment." The Gates Center is proud to be associated with this fine program, which helps attract and train talented candidates in the regenerative medicine field.

During the year, Gates Center support helped 11 students travel to the following scientific conferences: Keystone Symposium on Endoderm Development and Disease, Taos, NM;

Association of University Anesthesiologists Annual Meeting, Chicago, IL; Genetics Society of America – 2018 Ciliate Molecular Biology Meeting, Washington, D.C.; Gordon Research Conference on Cell Polarity Signaling, West Dover, VT; Gordon Research Conference for Visual System Development, Il Ciocco, Italy; *Population, Evolutionary, and Quantitative Genetics Conference, Madison, WI*; International Society for Stem Cell Research (ISSCR) 2018, Melbourne Australia; GRC Neural Development: Generating Diverse Cells and Networks in the Nervous System, Newport, RI; Society of Craniofacial Genetics and Developmental Biology, La Jolla, CA and the American Society for Cell Biology Annual Meeting, San Diego, CA.

Additionally, Gates Center funding enabled a CSD student representative to attend a STEM undergraduate conference; education outreach activities organized by CSD students; a recruitment trip to undergraduate campuses by CSD Associate Director Jeff Moore; two graduate courses run by CSD faculty; the annual Bootcamp training for summer interns run by CSD students; and, one outside seminar speaker.

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




*I am happy to hear that George Lampe whom I mentored from the GSIP class of 2016 landed a great opportunity at Memorial Sloan Kettering, a world-class cancer center. I consider this a really positive and very tangible outcome of the GSIP experience. Please share with the directors and others.*

- J. Mark Petrash, Ph.D., Professor and Vice Chair, Department of Ophthalmology







Parkinson's pioneer researcher Curt Freed, M.D. received funding for a clinical trial and student stipend from the Glendorn Foundation.

## GLENDORN FOUNDATION SPURS RESEARCH AND ENABLES INTERNSHIP PROGRAM

Four years ago, a gift from the Glendorn Foundation toward the emerging field of ocular stem cell research helped kick off the Gates Center's collaborative effort with the Department of Ophthalmology to raise \$10 million for the launch of Cellsight, the ocular stem cell program. In 2017, a subsequent gift from the foundation in support of research and stipends for Gates Center interns helped fuel the continued growth of this program, as well as training of the next generation of scientists and clinicians under the charismatic leadership of world-class researcher Valeria Canto-Soler, Ph.D., and her colleagues.

Similar to previous efforts to kick off new research and to enable a Gate Center intern to be involved in cutting-edge investigations, the Glendorn Foundation awarded a grant in 2018 to Curt R. Freed, M.D. (see photo). The grant was immediately matched by Mrs. Hoehle, a long-standing supporter of Dr. Freed's work, to initiate a study to see if a simple fatty acid sold as a food supplement had the potential to stop the progression of Parkinson's disease. The fatty acid is named butyrate. The idea stemmed from Dr. Freed's 2011 discovery that a related drug called phenylbutyrate could keep Parkinson's from developing in mice that had been genetically programmed to get the disease. Adding phenylbutyrate to the animals' drinking water starting in mid-life, before Parkinson's developed, stopped the disease from ever occurring. Dr.

Freed's group found that the drug worked by turning on a protective gene called DJ-1. Higher DJ-1 activity in all brain cells prevented deposits of abnormal proteins. Instead of forming deposits in the brain, misfolded forms of the alpha-synuclein protein were pushed out into the bloodstream, where they could be eliminated. Testing the same drug in people with Parkinson's disease showed the same benefit.

Because phenylbutyrate is an expensive drug, Dr. Freed's group tested similar but cheaper alternatives. They discovered that the fatty acid butyrate was just as effective as phenylbutyrate. The aim of the project funded by the Glendorn Foundation and Mrs. Hoehle has been to see if butyrate taken orally by people with Parkinson's disease will lead to an increase in the plasma concentration of the alpha-synuclein protein. While the study is not yet complete, preliminary evidence indicates that butyrate is working in people as it had in mice.

Success in these human experiments could lead to larger human clinical trials to see if butyrate can stop the progression of Parkinson's disease. The food supplement is more than 100 times less expensive than phenylbutyrate. If butyrate can stop Parkinson's, it would be a cheap and widely available drug to prevent this disabling disease and a major contribution to American medicine.

# OUTREACH



**Gates Center Advisory Board member Rick Stoddard has been a wonderful champion for all things Gates Center.**

Making connections kept the Gates Center and our affiliated Gates Biomanufacturing Facility (GBF) remarkably busy in 2018, as the staff grew and product manufacturing for clinical trials kicked off officially in the spring. In past years, we have enjoyed welcoming school groups and visitors for tours of the Gates Center and the GBF as well as presenting to outside organizations and clubs. In 2018, we did much of the same, while focusing on reaching across campus to faculty researchers who might be contemplating a clinical trial, producing biomanufactured goods or looking for Gates Center benefits such as commercialization support or access to the Gates Grubstake Fund. We also strengthened our collaboration with Colorado State University's School of Medicine and Veterinary Science as we prepared for the Zoobiquity Colorado conference in October. Finally, center staff responded to the constant flow of inquiry regarding

the availability and advisability of stem cell treatments, and shared updates on Gates Center's operations and research with elected officials and the media.

Thanks to Dennis Roop, Charlie Wall, Michael Ferreros and members of the GBF staff, we arranged for on-campus presentations and tours for individuals and groups from: the Colorado Leaders, Interns, Mentors in Business (CLIMB) program; Colorado Early Colleges; Colorado School of Mines; CU Boulder President's Leadership Class; CU Science Discovery Program; Friends School Boulder, and Kent Denver School, among others. In the meantime, Gates Center Advisory Board member and former Chair of Children's Hospital Colorado Foundation Rick Stoddard continued as our tireless champion introducing clinicians, researchers and hospital foundation members to the potential of our new reprogramming technology and Stem Cell Biobank and Disease Modeling Core, and to the capabilities of the GBF. Additionally, we conducted a campus survey to garner insight as to those on our Anschutz Medical Campus who are currently involved in regenerative medicine, as well as to those who might like to be. This feedback provided useful suggestions as to how our facilities and staff might best serve our members and the entire campus—much of which we incorporated into the strategic plan that we finalized in the fall.

As mentioned under "Collaboration," planning and overseeing the Zoobiquity Colorado conference provided a unique opportunity to deepen our ties with the College of Veterinary Medicine and Biomedical Sciences at Colorado State University, and to reach out to other human medicine and veterinary contacts. In conducting research for our strategic plan, we looked at 15 academic regenerative medicine centers across the country and found that we are among only four out of 15 affiliated with a veterinary school, providing both



our institutions with a distinct advantage. As we noted in last year's annual report, 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. The intention of this cross-disciplinary conference was to bridge that gap and to create conversations and relationships between human and veterinary colleagues confronted with similar clinical challenges. We deem our joint efforts with CSU to have done just that and look forward to continuing our partnership, outreach and mutual progress toward therapies and cures.

Additionally, the Gates Center receives frequent inquiries about stem cell treatments, obviously inspired by the advertising wraps that regularly encase copies of the newspaper and ads that pop up on the internet. Purportedly, there are now hundreds of clinics across the country advertising fat-derived stem cell therapy treatments for ailments ranging from sports injuries and Alzheimer's to paralysis and neurodegenerative conditions, as well as numerous clinics abroad making equally unsupported claims. Following a Channel 7 investigative report on local stem cell clinics, Gates Center's Entrepreneur in Residence Heather Callahan and Biomanufacturing Facility Executive Director Ryan Crisman gave a televised interview, sharing their concern over the safety and efficacy of these treatments that have not been proven in carefully conducted clinical trials. Clinic operators generally insist that fat-derived stem cells generated from their patients should not be subject to the same kind of regulations as other treatments, but the FDA is increasingly alarmed. The FDA has made headlines in the past year with crackdowns on clinic operators making unscrupulous claims, and the Colorado public often turns to us for context. Currently, the only stem cell therapies approved by the FDA use cells from bone marrow or cord blood to treat cancers of the blood and bone marrow. We will continue to voice our concern over this situation to our elected officials, the FDA and the public.

Finally, prior to the holidays Gates Center staff was privy to a harmonic convergence that reminded us of the potential of adhering to the highly regulated, FDA-compliant clinical trials process to achieve our mission of treatments and cures. Fox

31 filmed a touching interview at the Gates Biomanufacturing Facility featuring our new campus recruit Terry Fry, M.D., GBF Executive Director Ryan Crisman and Bill Brennan, a lymphoma patient who successfully underwent CAR-T cell therapy last spring after two unsuccessful rounds of chemotherapy (see link <https://kdvr.com/2018/12/19/mans-terminal-cancer-disappears-one-month-after-treatment-at-uchealth/> Man's terminal cancer disappears one month after treatment at UCHealth). Ironically, recent CU Anschutz recruit Terry Fry is a CAR-T cell pioneer, and Ryan Crisman worked until recently at Juno Therapeutics, which manufactured the cells for the clinical trial at UCHealth (University of Colorado Hospital) in which Bill Brennan participated. It was beyond touching to have these peripherally connected individuals come together to celebrate Brennan's new lease on life. We are inordinately proud that the Gates Center's affiliate Gates Biomanufacturing Facility is among the few facilities in the country now capable of producing CAR-T cell products for clinical trials to benefit patients like Bill Brennan.



Kent Denver senior Lily Dines and Senior Manager, GMP Manufacturing, Mitchell Fraller, are unrecognizable gowned up for a tour of the facility.

# NEW FACES AT THE GATES CENTER



**Roger Giller, M.D.:** Effective July 2018, Roger Giller joined the Gates Center's Gates Biomanufacturing Facility as Medical Director with over 30 years of experience in laboratory research, clinical research and patient care in the fields of human bone marrow transplantation and other forms of cellular therapy. Coupled with his intimate familiarity with the Anschutz Medical Campus as a professor of pediatrics and attending physician at Children's Hospital Colorado, he was an ideal choice.

Roger was an undergraduate at Northwestern University, where he became interested in medicine and medical research. He attended medical school at the Medical College of Wisconsin and spent his internship, residency and fellowship at the University of Colorado and Children's Hospital Colorado. As a young researcher and clinician, he left Colorado to help begin the pediatric bone marrow program at the University of Iowa. He returned to Denver in 1993 to found the Pediatric Bone Marrow Transplant Program at Children's Hospital Colorado, which he directed until 2016. During that time, the program carried out nearly 1000 transplants for a range of malignant and noncancerous conditions in infants, children, adolescents and young adults. An active clinical research program was established involving local investigators as well as national and international collaborators, and external regulatory certification of the Program thru the Foundation for Accreditation of Cellular Therapy (FACT) was continuously maintained.

Roger has an interesting historical perspective going back to the 1970's. He recalls as a college and medical student being involved in preclinical bone marrow transplant research conducted in mice and dogs, and the early days of trying to understand both the rejection and acceptance of foreign tissue and the role and power of the immune system to protect and to cause disease. He now has knowledge of and experience administering leading-edge therapies such as immunotherapy, which keeps him enthusiastic about brighter futures for difficult patients. Several years ago he worked with recent Anschutz Medical Campus recruit Terry Fry, M.D. to enroll a little boy suffering from intractable leukemia in a clinical trial at the National Cancer Institute. Following a transplant, the young boy has been in remission for three years—something that would have not been possible five years ago.

According to Roger, the current Anschutz Medical Campus is an increasingly exciting place to be as it continues to evolve and develop resources—particularly its human resources. He feels that science leading to innovation needs brilliant researchers and clinicians working together with different strategies, approaches and knowledge of disease, and that the Gates Center is key to promoting that sort of collaboration. Likewise, he believes that the development and manufacture of novel cellular and protein therapies destined for early phase human trials depends on the resources and procedures that only a facility such as the Gates Biomanufacturing Facility can provide.

Roger thinks we are just at the beginning and that we can develop technology to take on some of the most challenging medical problems. We are thrilled to have him join our team.



Roger lives in Denver with his wife, Jill, a small business owner dealing in Native American arts. They have one son, Dan, who is a Lieutenant in the U.S. Navy and married to Nichole, a medical epidemiology researcher. Outside medicine, Roger enjoys outdoor Colorado --- cycling, hiking, skiing, fishing badly and gardening hopefully --- as well as travel, the arts and their 25-year-old couples' book club.



**Jessica Taylor Heard:** Jessica Taylor Heard began working at the Gates Center as administrative assistant in August 2018. An Alabama native, she moved to Colorado in the spring with her husband, who serves in the U.S. Air Force.

Jessica graduated from the University of South Alabama in Mobile, AL, where she obtained her bachelor's degree in communication studies. With experience as a camp counselor, community director of student housing, Alabama National Guard family readiness support assistant and office manager and event coordinator for Spring Hill College, Jessica brings a gracious, capable and unflappable spirit to the Gates Center, which is welcome, indeed.

Jessica loves to travel and enjoys the outdoors, so she and her husband are particularly glad to have relocated to Colorado and are looking forward to exploring the state. Happily, she also likes to decorate, which will come in very handy when the Gates Center moves into a new office in late 2019! Overall, we are delighted to have Jessica in our midst to coordinate the Gates Summer Internship Program and to help support the Gates Center's smooth operation and team.



**Branden Salinas, Ph.D.:** Branden Salinas joined the Gates Center as the Gates Biomanufacturing Facility's Director of Protein Development and Manufacturing in April 2018. Branden brings over 10 years of experience working in big pharma at companies such as Centocor/Janssen Pharmaceuticals and Novo Nordisk Pharmaceutical Industries, where he helped advance several new therapies for multiple myeloma, rheumatoid arthritis and diabetes in both early and late stages of development.

A native of Austin, Texas, Branden earned his B.S. in Chemical Engineering from the University of Texas, Austin. Following an advisor's suggestion that he might be interested in pursuing pharmacological research, Branden was referred to Dr. Theodore Randolph at the University of Colorado Boulder, where he proceeded to earn his master's and Ph.D. in Chemical and Biological Engineering.

While at CU Boulder pursuing his doctoral research, Branden had the opportunity to work on industry sponsored projects under the mentorship of Dr. Randolph who is considered "a world authority in protein stabilization and supercritical fluid technology..."

Branden is dedicated to the GBF's mission of translating scientific discoveries into human clinical trials as safely, efficiently, and cost effectively as possible. He relishes the altruism of working within a non-profit affiliated with a university. He also enjoys the interpersonal and technical challenges of working closely with academic investigators alongside his "super motivated and productive" protein team and GBF staff, many of whom come from industry backgrounds, as well.

Prior to moving to Colorado to attend graduate school, Branden grew up vacationing with his family at a beloved mountain cabin built by his great-grandfather in 1950—a place he can now enjoy with his wife and three daughters. We are enormously glad to welcome Branden back to the Centennial State and to the Anschutz Medical Campus, where we can now boast of a growing biotech sector capable of attracting the likes of him and his colleagues.



**Michael Tortoro:** Michael Tortoro joined the Office of Advancement in the fall of 2018. Michael joins the staff with seven years of experience in nonprofit fundraising. His previous position was with the Doheny Eye Institute, an affiliate of the UCLA Health academic medical center. At Doheny he developed strong relationships with donors and faculty in support of vision research programs. He earned a Bachelor's degree in political science and economics from the University of California, Irvine.

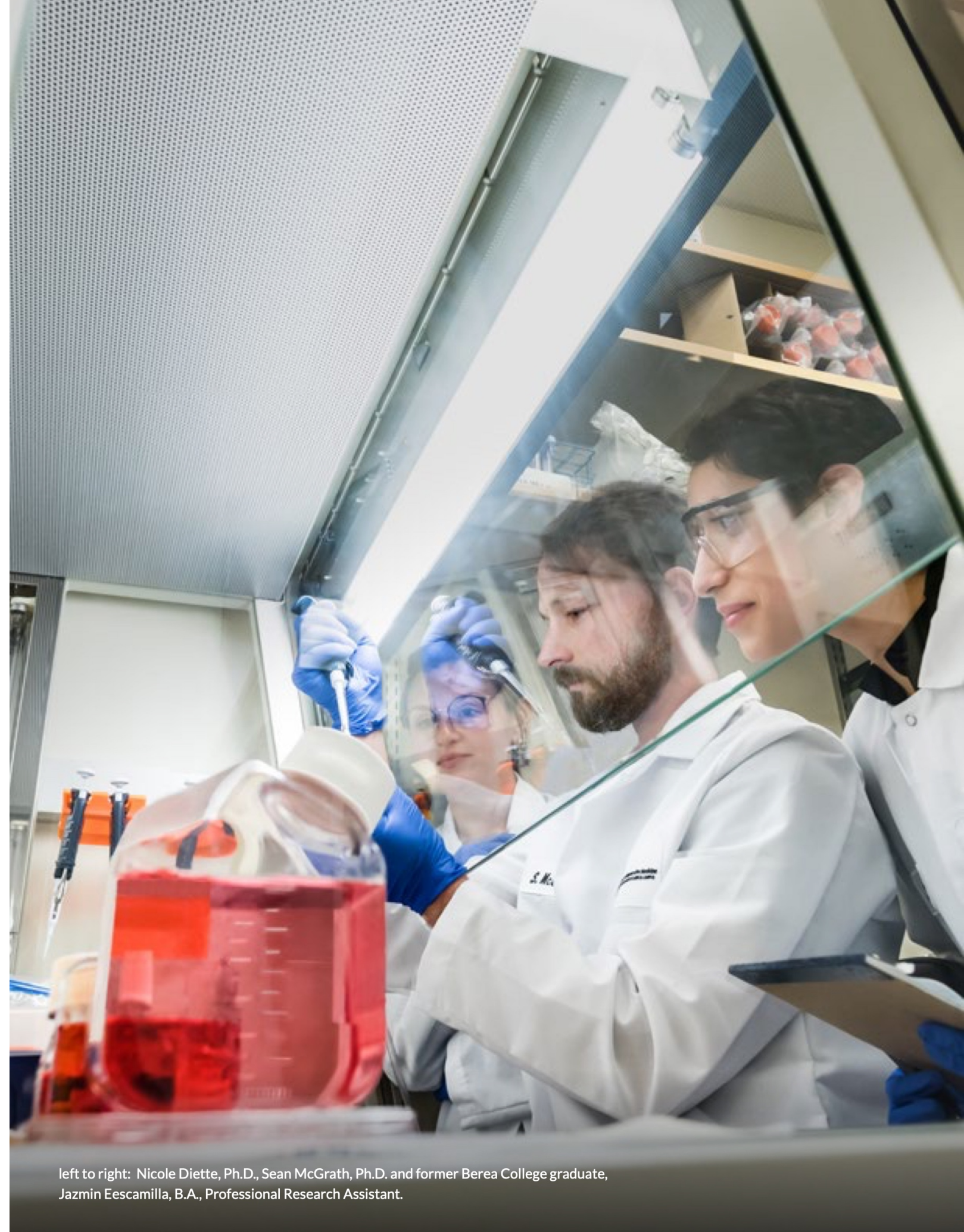
Michael believes medical research has a transformational impact on society, and he is excited to help advance the innovative work at the Gates Center.

Before moving to Colorado, Michael was a lifelong Southern California resident. He is eager to explore Colorado along with his wife, Gwendolyn, and their young son, William.



Makara Han, B.A., who grew up in Cambodia, attended Berea College in Kentucky and spent the summer of 2018 as a Gates Center intern, recently joined the Gates Center as a Professional Research Assistant following his graduation from Berea.





left to right: Nicole Diette, Ph.D., Sean McGrath, Ph.D. and former Berea College graduate, Jazmin Eescamilla, B.A., Professional Research Assistant.





# FINANCIAL OVERVIEW

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

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

## GATES CENTER OPERATIONS

This past year we moved from calendar year reporting to fiscal year reporting to be consistent with the University's reporting period. This change in accounting periods means that FY 2018 cannot be compared directly with prior calendar year statements.



Fiscal Year 2018 was the third year of operations under a five-year funding agreement between the Gates Frontiers Fund, the University of Colorado Foundation, the University of Colorado President's Office and the CU Anschutz Chancellor's Office. Additionally, the Gates Center was a critical partner in garnering over \$1.8 million in new philanthropic support for key initiatives described in more detail throughout this report.

Consistent with our mission and past priorities, center program support of \$1,072,416 was the largest expense category, totaling 36 percent of all spending for 2018. This amount was higher than prior years as we fulfilled long-term commitments made to key campus investigators. Investments in equipment and operations of the core facilities and the Gates Center laboratories totaled \$580,161 (20%) in 2018, which was consistent with prior years. The balance of our expenses was for marketing and development totaling \$554,373 (19 percent), center administration totaling \$474,671 (16 percent), and center enrichment, educational activities and commercialization support totaling \$257,238 (9 percent).

The Gates Center net of sources of income less expenditures was a loss of (\$211,274) for the fiscal year ended 6/30/2018—primarily due to higher research program support. Our committed funding is sufficient to meet our expenses and research funding obligations through December 2020.

	2014	2015	2016	2017	2018
<b>Infrastructure and Operations Grants</b>					
Gates Frontiers Fund	\$1,000,000	\$1,000,000	\$1,200,000	\$1,200,000	\$1,200,000
University of Colorado Foundation	\$1,000,000	\$1,000,000	\$600,000	\$600,000	\$600,000
University of Colorado Presidents Office			\$600,000	\$600,000	\$600,000
Philanthropy	\$3,100	\$10,330	\$147,617	\$200,000	\$327,585
Infrastructure and Operations Grants	\$2,003,100	\$2,010,330	\$2,547,617	\$2,600,000	\$2,727,585
<b>Gates Center Expenditures</b>					
Center Research Program Support	\$506,551	\$751,750	\$976,914	\$721,053	\$1,072,416
Lab Operations and Core Facilities	\$466,030	\$619,465	\$494,696	\$594,723	\$580,161
Marketing & Development	\$318,155	\$338,655	\$336,937	\$530,526	\$554,373
Center Admin/Maint/Supplies	\$317,948	\$336,792	\$376,593	\$389,380	\$474,671
Center Enrichment, Education and Commercialization	\$243,024	\$134,719	\$255,649	\$285,939	\$257,238
Total Expenditures	\$1,851,708	\$2,181,381	\$2,440,789	\$2,521,621	\$2,938,859
Center Sources - Expenditures	\$151,392	(\$171,051)	\$106,828	\$78,379	(\$211,274)

# ACKNOWLEDGEMENTS

## CHARLIE'S ANGELS

On August 22, 2018, at the annual Charlie's Picnic, Will Hiatt, M.D., became the second recipient of the "Charlie's Angel" award. Initiated in 2017, the award honors special individuals who play unusual and often quiet roles, helping the Gates Center thrive.

In conferring the award, Diane Gates Wallach explained its genesis. Her father Charlie Gates loved the long running television series "Charlie's Angels," featuring athletic, intelligent women solving the world's problems in creative ways. They were strong, persistent individuals who were even stronger as a team. They could make a splash when needed, but avoided publicity and rode quietly into the sunset after the good deed was done. As Diane explained, these types of

"angels" inspired her father and others to step out, be bold, take risks and to care.

Much like Peter and Rhondda Grant, who received the first award for their incredible early and ongoing leadership support of the Gates Summer Internship Program, Will Hiatt is an obvious award recipient. As Charlie Gates' doctor and family friend, he knew the real Charlie very well. Further, it was he who actually sparked Charlie's interest in stem cells that inspired the dream to create a center for regenerative medicine right here in Colorado. Will Hiatt, said Diane, was an angel here at the beginning and has been an advocate for the growth of the Center every step along the way.



Will Hiatt's family joined in the surprise award presentation: (left to right) Mike Wazylenky, Susan Hiatt, Kelsey Wazylenky, Will Hiatt and Diane Gates Wallach



**The Gates Center gratefully acknowledges the following individuals, foundations and organizations for supporting our research and mission during the 2018 year through philanthropic gifts toward initiatives including the Director’s Innovation Fund, the Gates Summer Internship Program, The iPSC Discovery Platform and Startup Toolbox:**

Joan Anderson	Rhondda and Peter Grant	Daniel Ritchie
Anonymous Donor	Susan and William Hiatt, M.D.	Betty and Dennis Roop, Ph.D.
The Berenice Gates Hopper Family Fund	Patricia Singleton Hoehle	Walter S. Rosenberry, III Charitable Trust
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Janelle and Buck Blessing	Mary Sue and Gary Horgan	Annalee and Wagner Schorr, M.D.
Balbi A. Brooks	Joyce and Wayne Hutchens	Lisa and Steven Shinn
Darlene and Arnold Brown	Illumina Inc.	The Solich Fund
Children’s Hospital Colorado	Allison and Jeff Krebs	Anita and Geoff Solich
Marguerite Childs and Thomas Detmer Jr.	Monty and Frank Kugeler	Ann Sperling
Jill Cowperthwaite and Charles Jones	Mary Lanius	Janie and Rick Stoddard
Paula Crowley	Penny Lewis	Diane Thompson
Diana and Bruce Davis	Gretchen and Charles Lobitz	A. Sheffield Tulp
Stephanie Foote and Lloyd Wade	Betsy and Peter Mangone	UCHealth
Yvette and Chris Frampton	Joy and William Mathews	University of Colorado Anschutz Medical Campus, Office of the Chancellor
Deb Froeb and Tim Gardner	Sue Ann and Richard Miles	University of Colorado Anschutz Medical Campus, School of Medicine
Patrick Gaines	John Moyski	University of Colorado President’s Office
Gates Frontiers Fund	Dennis O’Hanlon	
Gates Grubstake Fund	Pema Foundation	
Glendorn Foundation	Kelly and Mark Petrash, Ph.D.	
	Ann and Kevin Reidy	

As in years past, we would like to thank photographer and Denver native Edward DeCroke. He has provided the majority of photographs within this report, and we would be hard-pressed to tell our Gates Center story without his talent and good humor.

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)





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Marshall Wallach, Judy and Bill Hays



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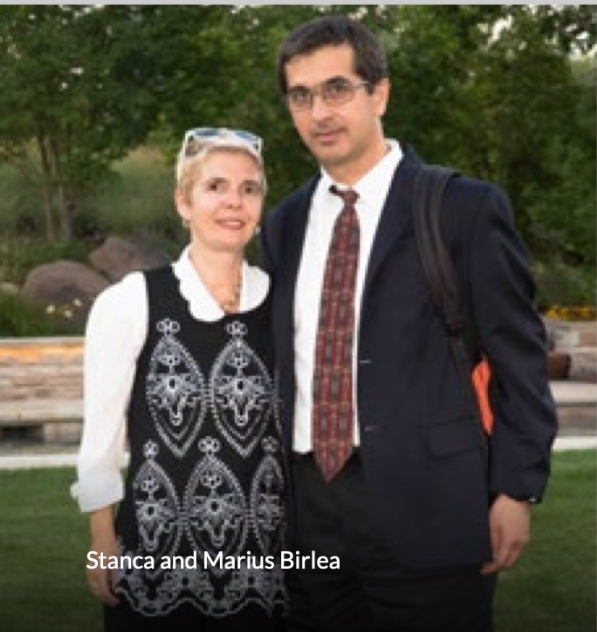




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