





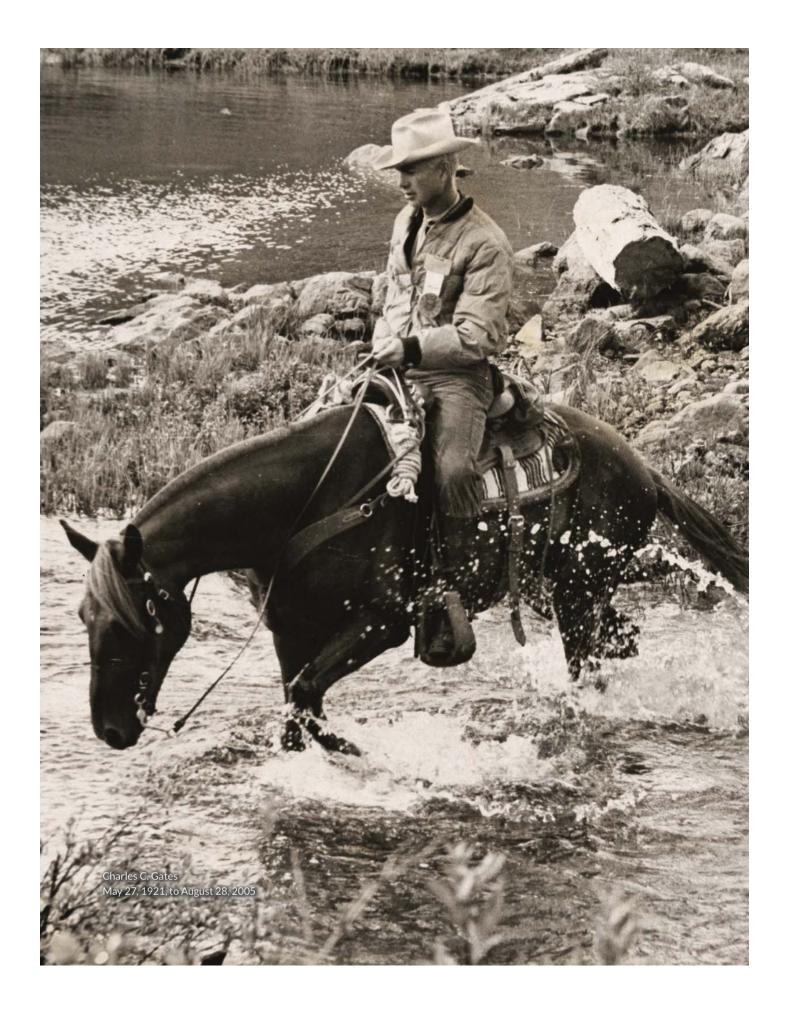


The Grand Opening of the Gates Biomanufacturing Facility was held on Tuesday, April 6, 2015. Attendees included (left to right): Gates Center Director Dennis Roop, PhD, Chancellor Don Elliman, CU President Bruce Benson, Diane Gates Wallach, Senator Michael Bennet, School of Medicine Dean John Reilly,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



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When wagon trains headed west and came to a challenging creek, pioneers would "throw their hats" to the other side. Hats were indispensable for protection from the sun, insulation from the cold, shelter from the rain, a way to water their horses and more. Figuratively, tossing a hat to the other side absolutely committed a pioneer to ford the stream, retrieve the hat, and continue the journey westward.

To entrepreneur and philanthropist Charles C. Gates, in whose memory the new Gates Biomanufacturing Facility was dedicated on April 6, 2015, throwing the hat symbolized a commitment to take the risks necessary to keep moving toward a goal.

Toward the end of his life, he foresaw a future in regenerative medicine and exhorted his children and others to bring it to fruition. We are grateful for the legacy of his vision, which lives on at the Gates Center for Regenerative Medicine, and for the generous commitments that were made to make the Charles C. Gates Biomanufacturing Facility a reality.

## WHO WE ARE

Established in 2006 with a generous gift in Charles Gates' memory, the Gates Center for Regenerative Medicine is a world-class consortium headquartered on the University of Colorado Anschutz Medical Campus—the only comprehensive academic health sciences center in Colorado, the largest academic health center in the Rocky Mountain region, and one of the newest education, research and patient care facilities in the world. Home to 21,000 employees, more than 4,000 degree-seeking students and two nationally recognized hospitals that handle 1.7 million patient visits each year, CU Anschutz trains the health sciences workforce of the future and fuels the economy.

Operating within this interconnected campus, the Gates Center brings together outstanding medical researchers and clinicians, grant and philanthropic funding, three state-of-theart core scientific facilities and the Gates Biomanufacturing Facility, along with sophisticated commercialization support, and education and outreach designed to accelerate discoveries into clinical practice as quickly as possible.

From the beginning, the major focus of the Gates Center has been adult stem cells. Recent research has proven that adult stem cells, also referred to as differentiated stem cells, can be reprogrammed into embryonic-like stem cells, referred to as induced Pluripotent Stem Cells (iPS cells), and then differentiated into virtually any cell type in the body. For example, Gates Center researchers have biopsied skin cells from individual patients, reprogrammed those cells into iPS cells and corrected their underlying genetic defect. The long-term goal is to return genetically corrected iPS cell-derived adult stem cells to the patient from which they were derived. In this way, the Gates Center's clinical pathway is leading toward a new paradigm of personalized medicine in which an individual's own cells can be used to cure a number of diseases and conditions.

Professor Dennis Roop, PhD, was recruited from the Baylor College of Medicine in January 2007 to lead the Gates Center by establishing a critical mass of faculty, clinicians, students, research staff and administrators to execute its mission. The Gates Center is a multi-institutional consortium whose membership, as of the end of 2015, was comprised of 88 members from the University of Colorado Anschutz Medical Campus and CU Boulder campus, Colorado State University, Colorado School of Mines, National Jewish Health and private industry. In addition to being multi-institutional, the Gates Center is also multidisciplinary, with members investigating regenerative therapies and stem cell treatments in the areas of cardiology, dermatology, immunology, neurology, oncology, ophthalmology and orthopedics.

Therapies under development include immunotherapies for cancer and viruses, stem cell therapies for inherited skin diseases, macular degeneration, Parkinson's disease and cardiovascular disease, as well as stem cell therapies to repair bone and cartilage.

The Gates Center for Regenerative Medicine is helping bolster the Anschutz Medical Campus' growing reputation as a global medical destination. Among other efforts, the Gates Center launched the Gates Biomanufacturing Facility in spring 2015, in which future cellular therapies and protein-based biologics are being manufactured for human trials under the highest FDA standards. The Gates Biomanufacturing Facility is one of six combined cell therapy and protein manufacturing facilities in the United States and the only one of its kind within an 800-mile radius. It will enable the safe and expedited translation of discovery into human therapies for people worldwide.

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## WHAT WE DO



## LIST OF MEMBERS

NAME	DEGREE(S)	POSITION	ACADEMIC INSTITUTION/AFFILIATES	PRIMARY (& SECONDARY) APPOINTMENT(S)	
Appel, Bruce	PhD	Professor Diane G. Wallach Chair in Pediatric Stem Cell Biology	University of Colorado Department of Pediatrics/ Anschutz Medical Campus Developmental Biology		
Artinger, Kristin	PhD	Associate Professor	University of Colorado Department of Craniofacial Bio Anschutz Medical Campus School of Dental Medicine		
Ayers, Reed	PhD	Professor	Colorado School of Mines	Metallurgical & Material Engineering	
Bailey, Susan	PhD	Professor	Colorado State University	Department of Environmental and Radiological Health Sciences	
Baker, Christopher	MD	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Pediatrics/Pulmonology	
Bamburg, James	PhD	Professor	Colorado State University	Department of Biochemistry and Molecular Biology	
Barlow, Linda*	PhD	Professor	University of Colorado Anschutz Medical Campus	Department of Cell and Developmental Biology	
Bernt, Kathrin	MD	Assistant Professor	University of Colorado Anschutz Medical Campus	Department of Pediatrics Hematology, Oncology & Bone Marrow Transplantation	
Bilousova, Ganna	PhD	Assistant Professor	University of Colorado Anschutz Medical Campus	Department of Dermatology	
Birlea, Stanca	MD, PhD	Assistant Professor	University of Colorado Anschutz Medical Campus	Department of Dermatology	
Box, Neil	PhD	Assistant Professor	University of Colorado Anschutz Medical Campus	Department of Dermatology	
Boyle, Kristen*	PhD	Assistant Professor	University of Colorado Anschutz Medical Campus	Department of Pediatrics	
Bruckner, Anna*	MD	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Dermatology	
Brzezinski, Joseph	PhD	Assistant Professor	University of Colorado Anschutz Medical Campus	Department of Ophthalmology	
Burnham, Ellen	MD, MS	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Medicine/ Pulmonary Sciences and Critical Care	
Chick, Wallace	PhD	Assistant Professor	University of Colorado Anschutz Medical Campus	Department of Cell and Developmental Biology	
Dannemiller, Elisa	MD, MBA		Sharklet Technologies, Inc.		
De Langhe, Stijn	PhD	Associate Professor	National Jewish Health Department of Pediatr		
DeGregori, James	PhD	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	PhD	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Pediatrics	
Dow, Steven	PhD	Professor	Colorado State University	Department of Microbiology, Immunology and Pathology and Department of Clinical Sciences	
Ehrhart, Nicole	VMD, Diplomate, ACVS	Professor	Colorado State University	Department of Surgical Oncology	
Ford, Heide	PhD	Professor	University of Colorado Anschutz Medical Campus  Department of Pharmacology		
Franco, Santos	PhD	Assistant Professor	University of Colorado Department of Pediatrics/ Anschutz Medical Campus Developmental Biology		
Freed, Brian	PhD	Professor	University of Colorado Department of Medicine/ Anschutz Medical Campus Allergy and Clinical Immunolog		
Freed, Curt	MD	Professor	University of Colorado Department of Medicine/ Anschutz Medical Campus Clinical Pharmacology and Toxicolo		
Friedman, Jed	PhD	Professor	University of Colorado Anschutz Medical Campus	Department of Pediatrics	
Fujita, Mayumi	MD, PhD	Professor	University of Colorado Department of Dermatology Anschutz Medical Campus		

<sup>\*</sup> New members in 2015

NAME	DEGREE(S)	POSITION	ACADEMIC INSTITUTION/AFFILIATES	PRIMARY (& SECONDARY) APPOINTMENT(S)	
Goodrich, Laurie*	DVM, MS, PhD	Associate Professor	Colorado State University	College of Veterinary Medicine	
Gore, Lia*	MD	Professor The Robert J. and Kathleen A. Clark and Ergen Family Endowed Chairs	University of Colorado Anschutz Medical Campus	Department of Pediatrics/Hematology, Oncology & Bone Marrow Transplantatio	
Hagman, James	PhD	Professor	National Jewish Health	Department of Immunology	
Hiatt, William	MD	Professor Novartis Endowed Chair in Cardiovascular Research	University of Colorado Anschutz Medical Campus	Department of Medicine/Cardiology	
Huang, Hua	MD, PhD	Professor	National Jewish Health	Integrated Department of Immunology	
Janssen, William	MD	Associate Professor	National Jewish Health	Division of Pulmonary, Critical Care and Sleep Medicine	
Jimeno, Antonio	MD, PhD	Professor Daniel and Janet Mordecai Chair in Cancer Stem Cell Biology	University of Colorado Anschutz Medical Campus	Department of Medicine/ Medical Oncology	
Kahook, Malik*	MD	Professor Slater Family Endowed Chair in Ophthalmology	University of Colorado Anschutz Medical Campus	Department of Ophthalmology	
King, Karen	PhD	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Orthopedics	
Klemm, Dwight	PhD	Professor	University of Colorado Anschutz Medical Campus	Department of Medicine/ Pulmonary Sciences	
Koch, Peter	PhD	Professor	University of Colorado Anschutz Medical Campus	Department of Dermatology	
Kogut, Igor	PhD	Instructor	University of Colorado Anschutz Medical Campus	Department of Dermatology	
Koster, Maranke	PhD	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Dermatology	
Krebs, Melissa	PhD	Assistant Professor	Colorado School of Mines	Chemical & Biological Engineering	
Lee, Katherine	PhD	Assistant Professor	University of Colorado Anschutz Medical Campus	Department of Pediatrics/ Infectious Disease	
Liechty, Kenneth*	MD	Professor	University of Colorado Anschutz Medical Campus	Department of Surgery/Pediatric Surgery	
Long, Carlin	MD	Professor	University of Colorado Anschutz Medical Campus	Department of Medicine/Cardiology	
Lu, Shi-Long	MD, PhD	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Otolaryngology	
Lyons, Traci	PhD	Assistant Professor	University of Colorado Anschutz Medical Campus	Department of Medicine/ Medical Oncology	
Magin, Chelsea	PhD	Director of Product Development	Sharklet Technologies Inc.		
Malkoski, Stephen	MD, PhD	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Medicine/Pulmonary Sciences and Critical Care	
Mandava, Naresh*	MD	Professor Sue Anschutz-Rodgers Endowed Chair in Retinal Diseases	University of Colorado Anschutz Medical Campus	Department of Ophthalmology	
Masterson, Joanne	PhD	Assistant Professor	University of Colorado Anschutz Medical Campus	Department of Pediatrics	
McCurdy, Carrie	PhD	Assistant Professor	University of Colorado Anschutz Medical Campus	Department of Pediatrics/Neonatology	
Meng, Xianzhong	MD, PhD	Professor	University of Colorado Anschutz Medical Campus	Department of Medicine/Cardiology	
Neff, Tobias	MD	Assistant Professor	University of Colorado Anschutz Medical Campus	Department of Pediatrics/Hematology, Oncology & Bone Marrow Transplantation	
Niswander, Lee	PhD	Professor	University of Colorado Anschutz Medical Campus	Department of Pediatrics/ Developmental Biology	
Norris, David	MD	Professor	University of Colorado Anschutz Medical Campus	Department of Dermatology	
Olwin, Bradley	PhD	Professor	University of Colorado Boulder	Department of Molecular, Cellular and Developmental Biology	
Ormond, David Ryan*	PhD	Assistant Professor	University of Colorado Department of Neurosurgery/ Anschutz Medical Campus Translational Clinical Research		

<sup>\*</sup> New members in 2015

NAME	DEGREE(S)	POSITION	ACADEMIC INSTITUTION/AFFILIATES	PRIMARY (& SECONDARY) APPOINTMENT(S)	
Patel, Vikas*	MD	Professor	University of Colorado Anschutz Medical Campus  Department of Orthopedi		
Payne, Karin	PhD	Assistant Professor	University of Colorado Anschutz Medical Campus	Department of Orthopedics	
Payne, Thomas*	PhD	Assistant Professor	University of Colorado Department of Dermatolo		
Perraud, Anne-Laure*	PhD	Associate Professor	National Jewish Health, University of Colorado Anschutz Medical Campus	Department of Biomedical Research/ Immunology and Microbiology	
Phiel, Christopher*	PhD	Assistant Professor	University of Colorado Denver	Department of Integrative Biology	
Pietras, Eric*	PhD	Assistant Professor	University of Colorado Anschutz Medical Campus	Department of Medicine/Hematology	
Petrash, Mark, J.	PhD	Professor	University of Colorado Anschutz Medical Campus	Department of Ophthalmology	
Porter, Christopher	MD	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Pediatrics/Hematology, Oncology & Bone Marrow Transplantation	
Refaeli, Yosef	PhD	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Dermatology	
Reynolds, Susan	PhD	Associate Professor	National Jewish Health	Department of Pediatrics	
Ribera, Angeles	PhD	Professor	University of Colorado Anschutz Medical Campus	Department of Physiology and Biophysics	
Roop, Dennis	PhD	Professor Charles C. Gates Endowed Chair in Regenerative Medicine and Stem Cell Biology	University of Colorado Anschutz Medical Campus	Department of Dermatology	
Sartorius, Carol	PhD	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Pathology	
Sclafani, Robert*	PhD	Professor	University of Colorado Anschutz Medical Campus	Department of Biochemistry and Molecular Genetics	
Sherk, Vanessa*	PhD	Fellow	University of Colorado Anschutz Medical Campus	Department of Medicine/Endocrinology	
Song, Kunhua	PhD	Assistant Professor	University of Colorado Anschutz Medical Campus	Department of Medicine/Cardiology	
Soranno, Danielle*	MD	Assistant Professor	University of Colorado Anschutz Medical Campus	Department of Pediatrics	
Stenmark, Kurt	MD	Professor	University of Colorado Anschutz Medical Campus	Department of Pediatrics/Critical Care	
Terzian, Tamara	PhD	Assistant Professor	University of Colorado Anschutz Medical Campus	Department of Dermatology	
Thamm, Douglas	VMD	Assistant Professor	Colorado State University	Department of Clinical Sciences	
Torchia, Enrique	PhD	Assistant Professor	University of Colorado Anschutz Medical Campus	Department of Dermatology	
Wagner, David	PhD	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Neurology	
Walker, Lori*	PhD	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Medicine/Cardiology	
Wang, Xiao-Jing	MD, PhD	Professor John S. Gates Endowed Chair in Stem Cell Biology	University of Colorado Anschutz Medical Campus	Department of Pathology	
Williams, Trevor	PhD	Professor	University of Colorado Anschutz Medical Campus	Department of Craniofacial Biology and Cell and Structural Biology, School of Dental Medicine	
Wilusz, Carol	PhD	Professor	Colorado State University Department of Microbiology, Immunology and Pathology		
Wilusz, Jeff	PhD	Professor	Colorado State University	Department of Microbiology, Immunology and Pathology	
Yi, Rui	PhD	Associate Professor	University of Colorado Boulder	Department of Molecular, Cellular and Developmental Biology	
Zhang, Qinghong	PhD	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Dermatology	
Zhou, Wenbo	PhD	Associate Professor	University of Colorado Anschutz Medical Campus	Department of Medicine/ Clinical Pharmacology and Toxicology	

<sup>\*</sup> New members in 2015



Dennis Roop was the featured guest at a June 27 Spotlight Health-Aspen Ideas Festival luncheon that included 20 of the country's top leaders in health care as well as journalists Judy Woodruff, co-anchor of the PBS NewsHour, and Corby Kummer, senior editor of *The Atlantic* magazine.

In the words of the late Charles C. Gates, "You never do your best work alone." This statement is both a reflection of our first nine years and a mandate for our future. As we round the corner on our first decade on the Anschutz Medical Campus, the Gates Center for Regenerative Medicine has built an indelible foundation on the tenets of collaboration, determination and multidisciplinary teamwork.

The year 2015 marked the culmination of three years of careful planning and execution leading to the official opening of the Gates Biomanufacturing Facility on April 6 with a celebration that drew a crowd of more than 250 guests and dignitaries. As the only current Good Manufacturing Practices (cGMP) facility within an 800-mile radius capable of manufacturing stem cell therapies and biologics, the Gates Biomanufacturing Facility is among the most dynamic public/private partnerships on the Anschutz Medical Campus. The facility's capital infrastructure was made possible thanks to the generosity of private contributions totaling just over \$8 million. Further, Children's Hospital Colorado, UCHealth, the University of Colorado School of Medicine and the Gates Frontiers Fund united to contribute \$8 million toward the first

five years of operational support. Such a shared investment in this state-of-the-art facility represents a concerted effort and a commitment to ushering in the new frontier of cell-based personalized medicine on the Anschutz Medical Campus. We were particularly proud that an article published on the April 6, 2015 CU Anschutz Today website was named one of Today's top five stories of 2015. See "Game Changer: Gates Biomanufacturing Facility helps further propel CU Anschutz, Colorado into world-class medical destination" (http://cuanschutztoday.org/).

Inside this year's report we are pleased to feature the Gates Center's partnership with the Department of Ophthalmology and the \$10 million funding initiative to establish the Ocular Stem Cell and Regeneration (OSCAR) Program. This new endeavor is designed to transform age-related macular degeneration research and treatment by drawing upon the collective expertise and collaborative research taking place at the UCHealth Eye Center and the Gates Center for Regenerative Medicine. This ambitious initiative, detailed on page 14, began with a generous \$5 million 1x1 challenge from the Gates Frontiers Fund and quickly gathered momentum among friends and benefactors passionate about the future of eye care.

As we prepared last winter for the grand opening of the new facility, the Gates Center also completed a required self-study and, a month later, welcomed a team of external reviewers for a two-day site visit. We were gratified by the reviewers' final report summary, which read in part:

The center has made a dramatic, positive impact on the School of Medicine and the entire medical campus. The recent addition of an outstanding Biomanufacturing Facility, which enables the production of therapeutic proteins and cells, elevates the Gates Center into the Top 5 Regenerative Medicine Centers/Institutes in the U.S. The review team commends the university and community for partnering to establish the Gates Center and recommends continued, strong support. In the next five years, there is a high probability that next-generation therapeutics will be developed in the Center and tested in clinical trials...

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In September 2015, the Gates Center launched a robust strategic planning process. Taking another cue from the vision of the center's namesake, Charles C. Gates, we were encouraged to throw our hat across the creek and invite a pioneering team of thought-leaders to join us for a retreat focused on forging a path toward the year 2020. With an ultimate focus on patient outcomes, the Gates Center mirrors the School of Medicine's mission to improve function, relieve suffering and increase longevity of the people we help serve on the Anschutz Medical Campus.

Joining the Gates Advisory Board and staff in this important ongoing effort are four individuals to whom we express our appreciation and welcome to the Gates Center family. First, John J. Reilly Jr., MD, who began his tenure as the new dean of the University of Colorado School of Medicine in April 2015. Prior to joining CU, Dr. Reilly was the Jack D. Myers Professor and Chair for the University of Pittsburgh's Department of Medicine. Next, Jena Hausmann was appointed president and CEO of Children's Hospital Colorado in May, after 11 years on the Children's Hospital senior leadership team, including holding the interim president and CEO position from January 1 to April 30, 2015. We also welcome Jack Finlaw who became president and CEO of the University of Colorado Foundation in November 2014, and joined the Gates Center's strategic planning efforts in 2015. Well-known to the citizens

of Denver and Colorado, Jack served as a member of the Honorable John Hickenlooper's leadership team from 2003 to 2014, as chief legal counsel to Governor Hickenlooper from 2011 to 2014 and director of Denver's Theater and Arenas Division and chief of staff during Hickenlooper's tenure as mayor of Denver. Finally, we welcome Will Cook, who was named president and CEO of University of Colorado Hospital in July 2015. Cook comes to us from UPMC (University of Pittsburgh Medical Center), where he most recently served as senior vice president of UPMC's Health Services Division, chief operating officer of physician services and president of UPMC Mercy.

As we celebrate our 10th anniversary year in 2016, we invite you to visit the Anschutz Medical Campus for a tour of our facilities and to explore ways that you can become involved in our mission.

Sincerely,

Dennis R. Roop, PhD

Director, Gates Center for Regenerative Medicine

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



September 2015 Gates Center Strategic Planning Retreat with Gates Advisory Board, guests and staff: (BACK ROW, left to right) Jack Finlaw; Kevin Reidy; Scott Arthur; Karin Payne, PhD; Will Hiatt, MD; Xiao-Jing Wang, MD, PhD; Antonio Jimeno, MD, PhD; Don Elliman; John Reilly, Jr., MD; Will Cook; Rick Stoddard; Mark Petrash, PhD (MIDDLE ROW, left to right) Kimberly Muller; Steve VanNurden; Dennis Roop, PhD; Marilyn Coors, PhD; Wag Schorr, MD; Jena Hausmann, Ann Sperling; Dori Beister, PhD, FAAN; Janelle Blessing (FRONT ROW, left to right) Diane Gates Wallach, Patrick Gaines, Tim Gardner, MBA; Jill Cowperthwaite; Allison Krebs, MBA; Mike Perry, DVM, PhD, FACVPT

# GATES CENTER MEMBER SPOTLIGHT:

CU Department of Ophthalmology



Developing Mouse Eye (Courtesy of Tatiana Eliseeva, BS and Joe Brzezinski, PhD): Retinal stem cells (green) produce photoreceptors (purple). Photoreceptors die in diseases like age-related macular degeneration. Photoreceptors derived from patient-specific induced Pluripotent Stem (iPS) cells could be used to treat macular degeneration. This image is displayed in the Gates Biomanufacturing Facility.

Age-related macular degeneration (AMD) is the leading cause of blindness among Americans age 50 and older. More than 2 million Americans suffer from AMD, and the number of people affected is expected to increase 77% over the next 15 years. AMD involves breakdown of the macula, the part of the retina that is responsible for sharp central vision. Macular rods and cones are nourished by pigmented epithelial cells, which allow them to respond to light and send electrical signals through the optic nerve to the brain. Degeneration of these macular cells leads to compromised central vision, reducing one's ability to live independently and enjoy the visual world. The body does not have a natural way to heal or replace the retinal cells that are affected by AMD, and current treatments only slow the progressive cell loss that leads inevitably to reduced vision and blindness.

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There is real hope for stem cell therapy for AMD, and real possibilities that critical advances can be achieved through the partnership of laboratory investigators and clinicians in the Department of Ophthalmology and the Gates Center. The Macular Degeneration Program at the UCHealth Eye Center is internationally recognized as a leading center of clinical, teaching and research excellence. Faculty experts in AMD, led by Department of Ophthalmology Chair Naresh Mandava, MD, the Sue Anschutz-Rodgers Chair in Retinal Diseases, annually treat 20,000 AMD patients and perform over 6,000 complex AMD procedures and surgeries. AMD patients travel from across the United States and from outside the country to receive care from Dr. Mandava and his team at the UCHealth Eye Center.

The Department of Ophthalmology, in partnership with the Gates Center for Regenerative Medicine, is uniquely positioned to make stem cell therapy a reality for patients with AMD. In their quest to develop cures for AMD, Naresh Mandava, MD, and J. Mark Petrash, PhD, Vice Chair for Research in the Department of Ophthalmology, have built a team of experts to tackle challenges that must be overcome

in order to develop a successful stem cell-based therapy. The team includes Joseph A. Brzezinski, PhD, Assistant Professor of Ophthalmology, whose work focuses on genes that encode molecular switches that influence growth of rod and cone photoreceptors in the retina. Anne Lynch, MD, head of the ocular epidemiology program, is also working with Dr. Mandava and other retina experts in the UCHealth Eye Center to produce a registry of AMD patients. This resource will be invaluable in efforts to clarify steps in the disease and thus identify individuals who could most benefit from therapeutic transplant of retinal cells. Finally, Malik Kahook, MD, the Slater Family Endowed Chair in Ophthalmology, plays a key role in moving research discoveries from the lab to the clinic.

Research capabilities in age-related macular regeneration and ocular stem cell research have been bolstered by the creation of a \$10 million funding initiative to establish the Ocular Stem Cell and Regeneration (OSCAR) Program, a program designed to transform age-related macular degeneration research and care by drawing upon the collective expertise and collaborative research taking place at the UCHealth Eye

Center and the Gates Center for Regenerative Medicine. This ambitious initiative began with a generous \$5 million challenge grant from the Gates Frontiers Fund and quickly gathered momentum among friends and benefactors passionate about the future of eye care. Support from benefactors Lyda Hill, the Glendorn Foundation, LGA Foundation and several members of the Gates family is fueling research into the promise of stem cells for patients battling the disease.

According to Petrash, "With leadership gifts from the Gates Frontiers Fund and other visionaries in our community, we have a tremendous opportunity to take the next giant step toward making ocular stem cell therapy a reality for patients with AMD." Recruitment of the director of the Ocular Stem Cell and Regeneration Program will be made possible by these generous gifts. Additional resources already in place, including core laboratories and expertise in the Gates Center for Regenerative Medicine and the new Gates Biomanufacturing Facility, will strengthen our ability to attract top talent to our program. The clustering of state-of-the-art research laboratories, literally steps away from the UCHealth Eye Center and Gates Biomanufacturing Facility, will make the University of Colorado Anschutz Medical Campus a fully integrated site for producing therapeutic stem cells and surgically delivering them into the eyes of patients.



## **RESEARCH SPOTLIGHT:**

Select Honors and Publications\*



#### **PUBLICATIONS**

**Bruce Appel, PhD,** *Professor, Pediatrics,* recently published a paper in *Genes and Development* that overturns a longstanding dogma about the origin of motor neurons and oligodendrocytes, the myelinating cell type of the brain. Dr. Appel showed that these cells do not arise from a common stem cell as previously thought, but rather from different origins in the developing nervous system. This work has implications for methods that aim to produce motor neurons or oligodendrocytes from induced pluripotent cells for therapeutic use.

**Kristin Artinger, PhD,** Associate Professor of Craniofacial Biology, School of Dental Medicine, published a report in the journal Developmental Biology using live imaging to demonstrate the mechanism responsible for the migration of neural crest cells during the development of zebrafish. This study reveals a novel role for the putative Sonic hedgehog receptor and cell adhesion regulator, cdon, in zebrafish neural crest migration. Understanding the mechanisms that regulate normal neural crest cell migration during development may provide insight into the causes of craniofacial birth defects, as well as the abnormal migration of cancer cells in melanoma.

Kathrin Bernt, MD, and Tobias Neff, MD, Assistant Professors of Pediatrics, Division of Hematology, Oncology & Bone Marrow Transplantation, have a paper that was accepted for publication in The Journal of Clinical Investigation reporting that high levels of Meningiona-1 (MN1) cooperate with the normal form of the histone methyltransferases, MLL1, to transform bone marrow cells into leukemia cells. High levels of MN1 are associated with the poor survival of acute myeloid leukemia patients, with almost 80% dying within two to three years. This study demonstrates that MN1 leukemia cells respond to a new class of drugs that was developed to treat MLL1-mutant leukemias and represents an important step toward new therapies for a group of patients for whom conventional approaches offer little chance of cure.

**Stanca Birlea, MD, PhD,** Assistant Professor, Dermatology, published data in the Journal of Investigative Dermatology on the study of melanocyte stem cell populations that emerge from the hair follicle bulge to regenerate the epidermis devoid of pigment cells in vitiligo patients. This study provides insight into the process of repigmentation that will eventually allow the design of better treatments for vitiligo based on melanocyte stem cell activation and mobilization. This paper was selected as a "Featured Article" and was one of the journals "Top Ten" downloaded papers in 2015.

**James DeGregori, PhD,** *Professor, Biochemistry and Molecular Genetics*, published experimental evidence in the *Journal of Clinical Investigation* suggesting that age-associated inflammation contributes to the development of leukemia through the selection of cells harboring oncogenic mutations. Dr. DeGregori and his colleagues showed that increasing inflammation in young mice resulted in B cell progenitor defects similar to those seen in aged mice. Conversely, reducing inflammation in aged mice preserved B cell progenitor fitness and reduced selection of oncogene-expressing progenitors, preventing leukemogenesis.

**Heide Ford, PhD,** *Professor, Pharmacology,* recently published data in *Nature Communications* documenting a novel mechanism negatively regulating TP53 (p53), a tumor suppressor gene that is mutated in 50% of all human cancers. The pro-tumorigenic/metastatic Six1 homeoprotein decreases p53 levels through a mechanism that does not involve the negative regulator of p53, MDM2. Instead, Six1 regulates p53 via a dual mechanism involving upregulation of microRNA-27a and downregulation of ribosomal protein L26 (RPL26). Thus, Dr. Ford and her colleagues have identified a competitive mechanism of p53 regulation, which may have consequences for drugs aimed at reinstating p53 function in tumors through inhibition of the p53/MDM2 interaction.

Antonio Jimeno, MD, PhD, Professor of Medicine, Division of Medical Oncology, and Yosef Refaeli, PhD, Associate Professor of Dermatology, published a report in Oncogene describing a proof-of-principle model that utilized Dr. Refaeli's novel technology for expanding human hematopoietic stem and progenitor cells (HSPCs) [Bird et al, PLoS One, 2014] to reconstitute the radiation-depleted bone marrow of NOD/SCID/IL2rg(-/-) (NSG) mice with human allogeneic HSPCs. Following the transplantation of human tumor tissue onto these mice, it was possible to identify human immune and stromal cells arising from the donor HSPCs in the transplanted tumor's microenvironment. This study paves the way for developing patient-derived xenograft models containing both tumor and immune/stromal cells from the same patient.

Shi-Long Lu, MD, PhD, Associate Professor, Otolaryngology, has a paper that was accepted for publication in Oncogene that provides insight into how overexpression of the gene encoding the phosphatidylinositol-4, 5-bisphosphate 3-kinase catalytic subunit alpha (PIK3CA) drives head and neck squamous cell carcinoma (HNSCC) invasion and metastasis. Amplification and mutation of the PIK3CA gene are among the most common genetic alterations in human HNSCC. Using a genetically engineered mouse model in which the wild-type PIK3CA gene is overexpressed in head and neck epithelium, Dr. Lu and his colleagues discovered that overexpression of PIK3CA alone was not sufficient to initiate HNSCC formation; however, it significantly increased tumor susceptibility in an oral carcinogenesis mouse model by increasing the number of cancer stem cells in these tumors. Molecular analysis of this model revealed that progression of PIK3CA-driven HNSCC was facilitated by increased levels of 3-phosphoinositide-dependent protein kinase (PDK1). An examination of human HNSCC clinical samples revealed that both PIK3CA and PDK1 protein levels correlated with tumor progression, thus highlighting the significance of this pathway.

**Lee Niswander, PhD,** *Professor, Pediatrics*, published an article in *eLife* describing a potential treatment that could minimize muscle damage in patients with central core disease. Using a mouse model that mimics the human disease connected to weakness in skeletal muscle, known as central core disease, Dr. Niswander and her colleagues discovered that muscle weakness in these mice is caused by defects that result in the leakage of potassium ions from the muscle cells. Treating these mice with an existing drug called glibenclamide reversed the disease symptoms by reducing the leakage of potassium ions from the muscle cells, thus suggesting a potential treatment for the human disease.

**Kunhua Song, PhD,** Assistant Professor of Medicine, Division of Cardiology, published an article in Nature Communications documenting that the efficiency of direct reprogramming of fibroblasts into cardiomyocytes by forced expression of cardiomyogenic factors, GMT (GATA4, Mef2C, Tbx5) or GHMT (GATA4, Hand2, Mef2C, Tbx5) can be dramatically increased by up to 60% by inhibiting pro-fibrotic signaling. These findings provide new insights into the molecular mechanisms underlying cardiac conversion of fibroblasts and could enhance efforts to generate cardiomyocytes for clinical applications.

#### **HONORS**

Antonio Jimeno, MD, PhD, Professor of Medicine, Division of Medical Oncology, was named the first Daniel and Janet Mordecai Chair in Cancer Stem Cell Biology, which is supported by a generous gift of \$2 million from the Daniel and Janet Mordecai Foundation to the Gates Center for Regenerative Medicine. Janet Mordecai is a 1965 graduate of the University of Colorado College of Nursing. She established the CU College of Nursing's first endowed chair in rural health—the Daniel and Janet Mordecai Endowed Chair in Rural Health Nursing in 2007. Daniel Mordecai was a graduate of the University of Denver and was a successful owner of US Nursing—a national nurse staffing agency. At the time of the announcement, Janet Mordecai said: "First and foremost, I am pleased to support Dr. Jimeno's pursuit of some of the most cutting-edge scientific cancer research, realizing that the results of this research will have broader application to other fields of medical research as well. I was drawn to Dr. Jimeno's innovative cancer screening models when I began supporting his research in 2012, and I am very encouraged by the collaborative team of students, technicians, researchers and clinicians that he has assembled."

**Douglas Thamm, VMD, DACVIM,** Associate Professor of Oncology at Colorado State University, was the 2015 recipient of the Asa Mays, DVM Award for Excellence in Canine Health Research. Dr. Mary Smith, chair of the American Kennel Club (AKC) Canine Health Foundation's Grants Committee, presented the award to Dr. Thamm at the 2015 National Parent Club Canine Health Conference in St. Louis, Missouri. During the presentation, Dr. Smith said, "In addition to being a leading researcher, Dr. Thamm is also a great partner to the AKC Canine Health Foundation. He frequently contributes to our podcasts, educational materials, and volunteers his time and expertise to our peer review process." The foundation has awarded Dr. Thamm nearly \$240,000 for his work involving novel targeted therapies for animal and human cancer and ways to integrate these therapies with existing treatments. The Asa Mays, DVM Award for Excellence in Canine Health Research is presented to investigators who demonstrate meritorious advancements identifying, characterizing, and treating canine diseases and ailments.

\*This list highlights only a few of numerous Gates Center member publications and honors.



PRINCIPAL INVESTIGATOR(S)	SPONSOR	AMOUNT AWARDED	TITLE	
Appel, Bruce	National Institutes of Health	\$875,000	Genetic analysis of oligodendrocyte specification	
Appel, Bruce	National Institutes of Health	\$875,000	Mechanisms guiding axon selection for myelination in vivo	
Artinger, Kristin/ (multi PI) Niswander, Lee	National Institutes of Health	\$1,615,000	Function of chromatin modifiers in cranial neural crest development	
Bamburg, James	National Institutes of Health	\$1,380,042	PrPc- and NOX dependent signaling in dementia	
Bernt, Kathrin	National Institutes of Health	\$2,035,253	The role of H3K79 methylation in IDH-mutant leukemia	
Box, Neil	National Institutes of Health	\$233,250	The role of keratinocyte p53 in development of pigmented lesions	
Box, Neil	Health Research Inc Rosewell Park Division	\$8,442	KLR9-TXNRD2 Axis in melanoma progression and metastasis	
DeGregori, James	CCTSI Independent Faculty Award	\$60,000	Analyzing changes in human hematopoietic mutational landscapes with age	
De Langhe, Stijn	March of Dimes	\$324,999	Role of Integrin linked kinase in regulating epithelial cell lineage commitment during lung development	
Ford, Heide	Golfer's Against Cancer Pilot Grant	\$50,000	Identifying the role of the Six1/Eya transcriptional complex in Myc-driven Group3	
Franco, Santos	Boettcher Foundation	\$225,000	Origins and functions of inhibitory interneuron diversity in the cerebral cortex	
Franco, Santos	Colorado Clinical and Translational Sciences Institute	\$30,000	Novel Interactors of the Reelin signaling pathway and their potential roles in healthy brain function and Alzheimer's disease pathology	
Freed, Brian	US Department of Health and Human Services	\$3,600,000	The University of Colorado Cord Blood Bank	
Fujita, Mayumi	CU Boulder	\$20,000	Homozygously deleted chromosomal changes in metastatic melanoma	
Lu, Shi-Long	Whedon Cancer Foundation	\$104,605	Methylated microRNAs as biomarkers for early detection of head and neck cancer	
Lu, Shi-Long	Head and neck cancer Specialized Programs of Research Excellence (SPORE) pilot grant	\$25,000	DNA methylation of microRNA as a biomarker for HNSCC recurrence and second primary malignancy	
Malkoski, Stephen	National Institutes of Health	\$699,750	Targeting defective DNA pathways in Smad4 deficient lung cancer	
Neff, Tobias	Sidney Kimmel Foundation	\$200,000	Tumor suppressor function of Ezh2 in acute leukemia	
Neff, Tobias	Hyundai Hope on Wheels	\$250,000	Chd4 as a therapeutic target in acute leukemia	
Niswander, Lee	National Institutes of Health	\$1,035,000	Transcriptional control of epithelial behaviors that drive mammalian neural tube closure	
Niswander, Lee/ Miller, Nancy	National Institutes of Health	\$225,000	Familial idiopathic scoliosis: gene discovery and functional studies	
Niswander, Lee	CCTSI Center for NeuroScience Award	\$30,000	Investigating the cellular and molecular roles of GCN5 in corticostriatal development and obsessive-compulsive phenotypes	

PRINCIPAL INVESTIGATOR(S)	SPONSOR		TITLE		
Roop, Dennis/ Norris, David	National Institutes of Health	\$1,684,303	Training in Immunodermatology		
Olwin, Bradley	Crnic Grand Challenge Grant	\$100,000	Mechanisms of muscle dysfunction in Down syndrome		
Payne, Thomas	Colorado Office of Economic Development & International Trade	\$225,342	Validation of cGMP manufacturing of cell-therapy products at the University of Colorado Gates Biomanufacturing Facility		
Porter, Chris co-PI/ Vibhakar	National Institutes of Health	\$43,515	Targeting Wee1 in MYC driven medulloblastoma		
Sartorius, Carol	National Institutes of Health	\$250,000	Estrogen receptor composition of disseminated breast cancer using multiparame imaging		
Sartorius, Carol	Cancer League of Colorado	\$60,000	Targeting breast cancer stem cells by inhibiting glucose metabolism		
Terzian, Tamara	Dean's Academic Enrichment Funding AEF Bridge Funding	\$50,000	p53 in skin cancers		
Thamm, Douglas	Asa Mays Excellence in Canine Health Research Award	\$240,000	Novel targeted therapies for animal and human cancer		
Wang, Xiao-Jing	TTO/State of Colorado	\$100,000	Developing novel biologics to treat oral mucositis and diabetic wounds		
	Total Awards =	\$16,654,501			



## COMMERCIALIZATION



The Gates Center is committed to bringing the world's brightest innovators together to accelerate the movement of regenerative medicine into clinical trials and commercialized therapies.

As a team, we encompass the dynamic creativity, scientific intelligence and industry experience needed to realize the true potential of breakthrough technologies. To that end, we strive to help our members translate their discoveries into commercialization opportunities for the benefit of the inventor, the University of Colorado and our community as a whole.

Highlights from our 2015 efforts include the following:

#### Allander Biotechnologies

Allander Biotechnologies, LLC, formed in 2014, is a start-up company fostered by the Gates Center for Regenerative Medicine, which has developed biologics to treat at least four diseases:

- Oral mucositis: a frequent side effect for cancer patients undergoing radiation and chemotherapy.
- Psoriasis: the most prevalent autoimmune disease in the U.S., with as many as 7.5 million Americans and 125 million people worldwide affected.

- Chronic wounds: including foot ulcerations caused by diabetes, pressure ulcerations caused by spinal cord injuries, contralateral limb ulcers caused by amputation, venous ulcers caused by poor blood circulation and acute wounds caused by surgeries and burns. These chronic wounds affect 6.5 million patients.
- Fibrotic diseases: including hypertrophic scars and keloids, which affect up to 100 million patients per year in developed countries.

With the help of the Gates Center, Allander reached its seed-round fundraising goal to establish investment funds during 2015. These funds will be used for research and development, patent applications, office actions and professional consulting services. The first patent application, "Therapeutic applications of Smad7," was awarded in the United States on July 21, 2015, (US Patent 9084746) and in China on December 8, 2015. The second patent application, "PTD-SMAD7 THERAPEUTICS" for the United States (US2014/0288006 A1) and PCT (PCT/US2014022052), has been filed at the nationalization stage. In addition to private investment, Allander's research and development are supported by commercialization grants from the state of Colorado, Gates Frontiers Fund and the National Institutes of Health (NIH) Small Business Innovation Research and Small Business Technology Transfer programs. The company's first technical milestone is to be able to scale up production of its biologics from the laboratory scale to commercialization scale. This work involves producing high-yield and high-purity biologics, and the development of analytical tools to test biological activities for future quality control of the products. Allander is working closely with the Gates Biomanufacturing Facility to develop these processes.

#### Gates Grubstake Fund

The Gates Grubstake Fund (GGF) was incorporated as a private 501(c)(3) foundation on August 6, 2015. The mission of the GGF is to provide translational research funding for projects and teams affiliated with the Gates Center for Regenerative Medicine through direct grants and endowment distributions. Grants such as these fuel early-stage research initiatives that can otherwise lag due to their inability to attract national-level funding. The intent is to make approximately three grants per year, totaling \$750,000 to \$1 million per year.

A Scientific Investment Advisory Committee (SIAC) was established to evaluate grant proposals and make recommendations for funding to the director of the Gates Center and the board of the GGF. The first grant review meeting of the SIAC was held on December 9, 2015. The SIAC members are as follows:

- Michael Bristow, MD, PhD Professor of Medicine, Division of Cardiology, University of Colorado Anschutz Medical Campus
- William Hiatt, MD Professor, Division of Cardiology, University of Colorado Anschutz Medical Campus; President, CPC Clinical Research
- Ryan Kirkpatrick Partner, Colorado Impact Fund
- Kyle Lefkoff Founder and General Partner, Boulder Ventures
- Kimberly Muller Director of Technology Licensing, University of Colorado
- Michael Perry, DVM, PhD, FACVPT Senior Vice President and Chief Scientific Officer, Global Business Development & Licensing, Novartis AG
- Mark Petrash Professor and Vice Chair, Department of Ophthalmology, University of Colorado Anschutz Medical Campus
- Ann Sperling Senior Director, Trammell Crow Company; Member, Gates Advisory Board

The following projects received Grubstake grants in 2015:

- 1. Induced Pluripotent Stem Cell Services as a Platform for Clinical Research, Ganna Bilousova, PhD, and Igor Kogut, PhD.
- 2. Antimicrobial Stem Cell Therapy for Infected Diabetic Foot Ulcers, Steven Dow, DVM, PhD, and Mary Ann DeGroote, MD.
- 3. Structural Living Bone Allografts to Enhance Bone Formation in Orthopedic Surgery, Karin Payne, PhD, and Vikas Patel, MD.



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

The success of these cores in providing quality service with a quick turnaround time is illustrated by the fact that, in addition to being utilized by Gates Center members, they are utilized by investigators in 15 different departments, divisions and centers within the School of Medicine and in the following: the Skaggs School of Pharmacy and Pharmaceutical Sciences and the CU School of Dental Medicine, National Jewish Health, CU Boulder and Colorado State University. In addition, the Bioengineering Core has users from outside of Colorado that include the University of Alaska Fairbanks, the University of Alabama at Birmingham, Thomas Jefferson University, the University of Lausanne (Switzerland) and Stony Brook University.

The cores operate on a cost-recovery basis, and are largely financially independent, with a combined operating budget of \$1,439,195 in 2015. However, the cores receive some additional annual support from the Gates Center operating budget (\$97,689 from Gates/CU Foundation matching funds) and from Academic Enrichment Funds provided by the Dean of the CU School of Medicine (\$150,000).

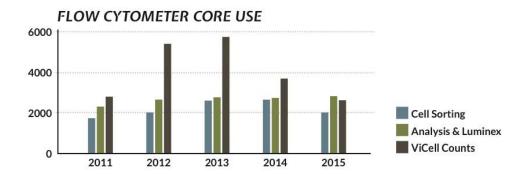
The core operating budget is not designed to cover equipment purchases, or to replace, update or expand capacity. Additional equipment purchases supported by the Gates Frontiers Fund/CU Foundation matching funds during 2015 totaled \$59,671.

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

1

#### Flow Cytometry Core

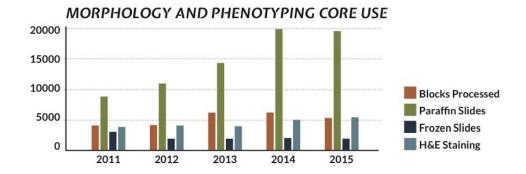
Flow cytometry and cell sorting allow for the rapid identification and isolation of individual stem cells within a mixed population. The recent addition of a CyTOF2 mass cytometer to the Flow Cytometry Core enables stem cell researchers to deeply profile cell populations, using 30 to 40 markers on each cell. The core has established a CyTOF2 supply center, from which users will be able to buy smaller quantities than are available through commercial vendors. This will allow investigators to initiate projects employing mass cytometry at much lower costs than they would otherwise. Another new cytometer, the Yeti, provides researchers with a state-of-the-science traditional flow cytometer employing five lasers and 28 color detectors. The Yeti offers researchers greater analysis options on a traditional flow cytometry platform.



2

#### Morphology and Phenotyping Core

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

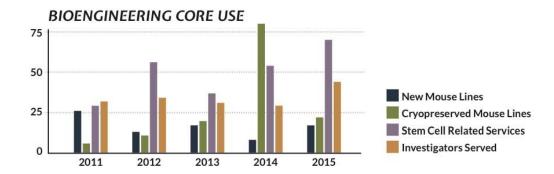


#### **Bioengineering Core**

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 to produce conventional and Bacterial Artificial Chromosome (BAC) transgenic mice and mouse Embryonic Stem (ES) cell injections to produce mice with modified genes, cryo-preservation of embryos and embryo re-derivation. We also conduct "gene targeting" experiments in ES cells that allow the introduction of a deletion or a targeted mutation into a disease promoting gene.

With the advent of induced Pluripotent Stem Cell (iPS cell) technology, researchers can now reprogram adult cells into cells that have the ability to become 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 iPS cells from various species used in biomedical research (e.g., human, mouse, dog, horse).

In 2015, the Bioengineering Core served 44 investigators from several universities (CU Denver, CU Boulder, CSU, University of Lausanne (Switzerland), Stony Brook University and the University of Alaska in Fairbanks. In 2015, our services included the generation of 14 genetically engineered mouse lines, the cryo-preservation of 22 mouse lines and 70 stem cell-related services (e.g., gene targeting in mouse embryonic stem cells, iPS cell generation and iPS cell differentiation into defined cell types). Note that projects such as the generation of a mouse line consist of several services. The total number of services rendered in 2015 was 332.







# GATES BIOMANUFACTURING FACILITY





#### Mission

The Gates Biomanufacturing Facility at the University of Colorado Anschutz Medical Campus provides process development, scale up and cGMP manufacturing services to academic researchers, clinicians and private companies.

We utilize our expertise in cell-based therapies, protein biologics, quality assurance, process development and manufacturing to help translate bench-scale processes to optimized clinical-ready manufacturing processes and perform product manufacturing for early-phase clinical trials.

### **GRAND OPENING APRIL 6, 2015**

New Aurora medical production lab could keep top Anschutz talent from going elsewhere.

Researchers at the University of Colorado Anschutz Medical Campus cut the ribbon on a new on-campus facility April 6 that is expected to thrust Aurora's health mecca to the national forefront of adult stem cell and proteinbased biologic research.

- Aurora Biz AURORA | April 8, 2015







The vision of the Gates family is being realized at the Gates Center, which took a giant step forward last month when it opened the Gates Biomanufacturing Facility. It not only will help provide cell-based therapies for patients with cancer, cardiovascular disease, HIV, influenza, skin diseases and others, but also furthers CU Anschutz as one of the world's leading academic medical facilities and a major health care destination. Fittingly, one of the cell-based therapies being developed at the facility will help address the macular degeneration that afflicted my friend Charlie Gates.

-University of Colorado President Bruce Benson, May 10, 2015



Within one week of the grand opening, the Gates Biomanufacturing Facility began performing process development services for a publicly traded pharmaceutical company based in Colorado. By year's end 2015, the facility had performed process development services for three different companies and two CU Anschutz Medical Campus researchers. This early customer activity underscored the anticipated urgency for such a facility. Going into 2016, our staff was in discussions with a number of qualified prospects who were interested in both process development and cGMP production.





The Gates Biomanufacturing Facility was able to provide my company with high-quality, active, preclinical material under a tight timeline after other Contract Manufacturing Organizations (CMOs) had failed. The team took real ownership of the project and dealt with every challenge professionally, creatively, and in a timely fashion. They were an invaluable resource for accelerating the development of our therapeutics.

- Geoff Davis, PhD, Angelica Therapeutics



"

The Gates Biomanufacturing Facility is a valuable resource for the Anschutz Medical Campus. The team was responsive, conducting thorough fermentation and downstream protein purification experiments. The facility's efficiency in helping us scale our early-stage processes accelerated our ability to conduct preclinical research.

"

- Jan P. Kraus, PhD, Professor, Pediatrics/Cell and Developmental Biology

During 2015, our team grew from its "start-up" group, consisting of Dennis Roop and four directors to a year-end total of 10. The new employees are:

Jordan Krause MSc - Processing Supervisor - Senior PRA
Brittany Robinson MSc - Processing Supervisor - Senior PRA
Sonja Giguere - PRA
Jessica Freemen - PRA
Laura Titter - Materials Specialist

#### **Oversight Committee**

While the Gates Biomanfacturing Facility is operated by the Gates Center for Regenerative Medicine at the University of Colorado School Of Medicine, it receives strategic direction from an Oversight Committee consisting of the following people:

Don Elliman, Chancellor, University of Colorado Anschutz Medical Campus

Jena Hausmann, President and CEO, Children's Hospital Colorado

Will Cook, President and CEO, University of Colorado Hospital

Terri Carrothers, Senior Vice Chancellor, Finance and Administration, University of Colorado Anschutz Medical Campus

Steve VanNurden, President and CEO, Fitzsimons Redevelopment Authority

Wag Schorr, Advisory Board Member, Gates Center for Regenerative Medicine

Neil Krauss, Director of Initiatives and Outreach, Chancellor's Office, University of Colorado Anschutz Medical Campus

Erin O'Brien, Associate University Counsel, University of Colorado

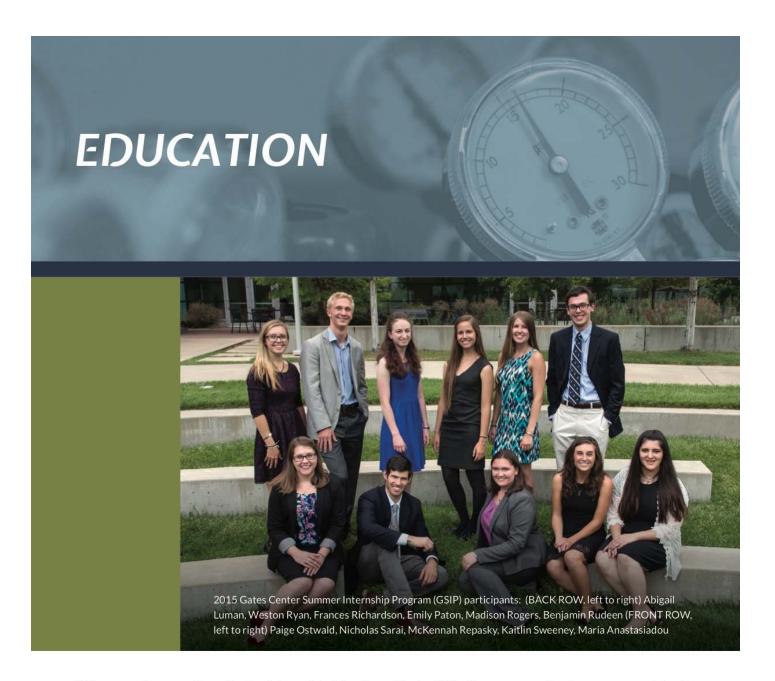
Alison Lakin, PhD, RN, LLB, LLM, Assistant Vice Chancellor for Regulatory Compliance, University of Colorado Anschutz

**Medical Campus** 

Dennis Roop, PhD, Director, Gates Center for Regenerative Medicine

We held our second Oversight Committee meeting on November 20, 2015. The Oversight Committee reviewed our financial statements through September 30, 2015 and discussed our business development strategy, staffing plans and progress toward being ready for cGMP manufacturing in 2016.

The Gates Biomanufacturing Facility's funding comes from a combination of the five-year operating fund commitments made by its partners (Children's Hospital Colorado, UCHealth, the University of Colorado School of Medicine and the Gates Frontiers Fund) and fee-for-service from CU researchers and outside companies.



With an ongoing commitment to inspiring and training the next generation of scientists and clinicians, the Gates Center both augmented and strengthened its educational program during the 2015 calendar year.

Thanks to a generous gift from longtime Gates Center friends Rhondda and Peter Grant, the center inaugurated the Gates Center Summer Internship Program (GSIP) in June 2015. Designed and run by three dedicated Gates Center faculty members—Tamara Terzian, PhD, Neil Box, PhD, and Enrique Torchia, PhD, and Gates Center Lab Manager

Charles Wall—the program aspires to encourage outstanding undergraduates to consider careers in stem cell and regenerative medicine research in an academic or industry setting by providing state-of-the-art training opportunities at the Gates Center.

In June, the center welcomed 12 undergraduates who were selected on a competitive basis from across the country and assigned to 12 Gates Center member labs. In addition to the 11-week full-time program, GSIP interns attended a Gates Center orientation, weekly lectures, a field trip to the new

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Gates Biomanufacturing Facility, along with conducting a presentation of their work on August 14, 2015, at a poster session and reception, to which family, friends, donors and Gates Center members were invited.

Given the success of the first summer in operation, an additional seven Gates Center faculty members signed up in fall 2015 to participate in the 2016 program, joining the 11 who participated during the first summer. As a result of this increased number of faculty participants and national interest from undergraduate applicants and various colleges and universities, along with wonderful support from Rhondda and Peter Grant and Monty and Frank Kugeler, plans were well underway by the end of the year to expand the program to accommodate up to 24 students.

Following up on recommendations made by the Gates Center's self-study reviewers in the spring, the center also took steps to increase its support of and integration with the Graduate Program in Cell Biology, Stem Cells and Development Graduate Program, directed by Bruce Appel, PhD, Gates Center member and Diane G. Wallach Chair in Pediatric Stem Cell Biology. Initiated in 2007, 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. Beginning in January 2016 through 2021, the Gates Center will support two graduate student fellowships per year, as well as provide funds to be used at Dr. Appel's discretion toward graduate student travel grants to attend stem cell-related conferences, graduate student recruitment—particularly for underrepresented minorities, and a summer boot camp. Dr. Appel feels that this additional support will have a tremendous impact on the program.

Finally, Gates Center members Ganna Bilousova, PhD, and Karin Payne, PhD, recently designed and taught a Special Topics Bioengineering course (see photo below). With the field of bioengineering on the rise, and no other courses focused on using stem cells for tissue engineering available, Drs. Bilousova and Payne felt it was important to familiarize students with the application of stem cells in regenerative medicine and in tissue engineering, including the integration of stem cells into damaged tissues. Taught in fall 2015 with visiting instructors Igor Kogut, PhD, Danielle Sorrano, MD, and Thomas Payne, PhD, the course attracted bioengineering graduate students, a chemistry undergraduate and individuals from several other departments, who audited the course. Given the compelling topic and the clear interest on campus, Drs. Bilousova and Payne look forward to expanding the course's credit hours to allow for a more in-depth discussion of the topics.



## OUTREACH



The 2015 year was an extraordinary one in the life of the Gates Center and its ability to reach out to the community, schools, and elected officials, as well as to patients and their families.

Celebrating the grand opening of the Gates Biomanufacturing Facility on April 6, 2015, (see Gates Biomanufacturing Facility on page 28) provided the Gates Center a unique opportunity to showcase the center and the new facility to guests and elected officials and to thank our partners who helped make this critical addition to the University of Colorado Anschutz Medical Campus possible: Children's Hospital Colorado, UCHealth, the University of Colorado School of Medicine and the Gates Frontiers Fund. A month later, thanks to the encouragement of Gates Advisory Board member Janelle

Blessing, the Gates Center was able to host a similar evening on campus for the Colorado chapter of the Young Presidents' Organization and World Presidents' Organization (YPO/WPO). Groups of YPO/WPO members and their friends then came out to campus to visit the new facility at various times throughout the remainder of the year, as did other interested individuals and groups, such as the Colorado chapter of Achievement Rewards for College Scientists Foundation, Inc.

Whether on or off campus, the year also enabled the center to share its mission and work with a variety of individuals and groups. Students and teachers came to the center for presentations and tours from Mackintosh Academy, Vail Mountain School, Aurora Public Schools, CU Science Discovery, Stanley British Primary and Arapahoe High School.

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Additionally, Gates Center faculty members Neil Box, PhD, Tamara Terzian, PhD, and others who founded the Colorado Melanoma Foundation in 2013, promoted skin cancer and melanoma awareness at their annual fundraisers, one of which was Mallets for Melanoma in partnership with the Denver Polo Club, as well as in schools and at other community events such as the 9Health Family Fair. During this action-packed year, Center Director Dennis Roop and others were also invited to speak at the Tower Club, the Aspen Ideas Festival and the Tuesday Morning Group, among others.

Thanks to the University of Colorado Office of Government Relations, the Gates Center was invited to make a presentation before the State House Health and Services Committee in March 2015, welcomed six elected state and federal officials to the grand opening of our Gates Biomanufacturing Facility and worked with Colorado delegation offices and the Alliance for Regenerative Medicine regarding regenerative medicine legislation under consideration in the U.S. Congress. Thanks to our membership in Washington, DC-based Research America, the Gates Center was featured in the organization's summer newsletter and included in a stakeholders group working with the FDA, which has offered to confer with the center as we take a regenerative medicine product from development through manufacturing.

Lastly and importantly, the Gates Center had occasion throughout the year to confer with various groups of patients, the ultimate focus of our center's mission. One particular highlight involved a laboratory visit in July 2015, hosted by the research teams of Maranke Koster, PhD and Peter Koch, PhD. The laboratory visit was primarily aimed at individuals affected by ectodermal dysplasias (inherited disorders that involve genetic abnormalities in the skin, hair, nails, limbs, teeth and other appendages) and their families. In the morning, patients donated skin biopsies that are being used to analyze the molecular and cellular abnormalities that underlie ectodermal dysplasias. These biopsies were obtained by Anna Bruckner, MD and Arelis Burgos, MD, two clinicians who practice dermatology at Children's Hospital Colorado. The second part of the day consisted of a tour of the research facilities. Patients and family members learned about current research regarding the disease mechanisms underlying ectodermal dysplasias and actively participated in discussions relating to these disorders. In addition, hands-on activities for children and adults, designed to foster their interest in life sciences, were provided. The research day was a great success, as well as instrumental in advancing research into these rare genetic disorders. The event was partially funded by the Gates Center for Regenerative Medicine, the Department of Dermatology, and the National Foundation for Ectodermal Dysplasias.





**Julie Clarke:** Julie Clarke joined the Gates Center in March 2015 to assist its investigators and staff in a myriad of ways. A Minnesota native, Julie moved to Colorado after college and undoubtedly prefers Colorado's winters. Her background is business administration, working in account management, marketing and sales. Prior to joining the University of Colorado, she worked for the Cherry Creek School District's Directors of Mental Health, Early Childhood, Special Education and School Safety Design Teams, coordinating several programs for students and families district-wide. In 2013, she came to the University of Colorado Anschutz Medical Campus to work for the dermatology clinic, supporting the clinic and faculty. Julie has always

been interested in research related to health issues and is thrilled now to be a part of the Gates Center. Additionally, she cherishes spending time with her two busy children, who are just beginning their careers, as well as reading, drawing and exploring the genre of independent movies.



**Marilyn Coors:** Marilyn Coors joined the Gates Advisory Board in September 2015. She is associate professor of bioethics at the Center for Bioethics and Humanities and the Department of Psychiatry at the University of Colorado Anschutz Medical Campus. She holds a PhD in bioethics, and the ethical issues in clinical genetics and genomic research are the foci of her research, teaching and professional service.

Research interests pursued by Dr. Coors include the ethics of human genetic modification, informed consent in genomic research, and the use of genomic information in behavioral

genetics. As the Director of Research Ethics for the Colorado Clinical and Translational Science Institute, she is directly involved in research ethics consultation and cross-disciplinary ethics education. Dr. Coors is an affiliate member of the University of Colorado Division of Substance Dependence and a faculty fellow of the University of Colorado Institute of Behavioral Genetics.

Dr. Coors received her undergraduate education from Cornell University, where she majored in biological sciences. She then attended the University of Denver, earning a MS in cytogenetics, an MA in ethics and religion, and a PhD in bioethics. Coors is chairperson of the Ethical, Legal & Social Issues Working Group of the Alpha-1 Foundation, serves on the Advisory Board of the Alpha-1 Medical and Scientific Advisory Committee and the Board of Directors of the COPD Foundation Patient-Powered Research Network. She is a superb addition to the Gates Advisory Board.

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Allison Krebs: As of January 2015, Allison Krebs joined the Gates Center for Regenerative Medicine as director of development. A Colorado native and member of the advancement staff since 2012, Allison arrived on campus with more than eight years of local fundraising experience at the Clyfford Still Museum, Denver Art Museum and Denver Museum of Nature & Science. Since then, she has successfully forged relationships with benefactors, faculty and community members in support of a variety of research, particularly in the area of cancer. Allison earned a bachelor's degree in business from Colorado State University and an MBA from the University of Denver. She and her husband, Jeff, had their first child in September

2014 and are expecting another in May. Her engaging manner and dedication to advancing medical research have made her a very welcome addition to the center's team.



**Rick Stoddard:** Rick joined the Gates Advisory Board in the spring of 2015. Currently serving as chair of the Children's Hospital Colorado Foundation, Rick also serves as a member of the Children's Hospital Colorado Board and the Health System Board.

After a twelve-year legal career as a merger and acquisition attorney in Denver, Rick became the chairman and CEO of Kaiser Steel Corporation in 1988 and successfully brought Kaiser out of a Chapter 11 bankruptcy and restored the medical benefits of 7,500 Kaiser Steel retirees. Kaiser (then called Kaiser Ventures) developed several new businesses including real

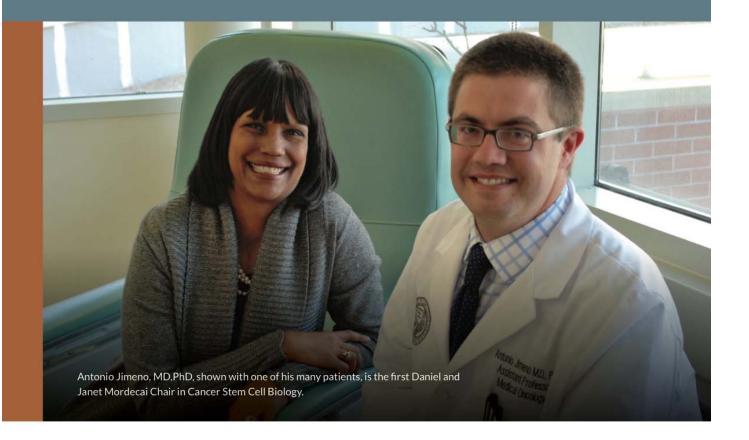
estate and water development, NASCAR Speedways, recycling and waste management, private prisons, military training and landfill development. Rick remains the Managing Liquidation Director of Kaiser, whose final projects include a pumped storage hydroelectric project and mining.

Rick received his Bachelor of Business Administration in 1972 from the University of Iowa and his Juris Doctor from Georgetown University Law Center in 1976. In 1992, Rick was named Entrepreneur of the Year in the Turnaround Category in Southern California by INC. Magazine, Merrill Lynch and Ernst & Young.

Rick lives in Denver with his wife, Janie, and together they have six adult children. We welcome the expertise and close association to Children's Hospital Colorado that he brings to our midst.



## FINANCIAL OVERVIEW



The research done by Gates Center members is funded directly through federal and state research grants, private foundation grants, philanthropic gifts for research and Gates Center research support.

The Gates Center operating budget funds a portion of the three core laboratory facilities (Flow Cytometry, Morphology and Phenotyping and Bioengineering), along with commercialization support, education and outreach programs, and marketing and development efforts. The Gates Center operating budget is in turn supported through grants from the Gates Frontiers Fund and the University of Colorado Foundation (see Gates Center Operations on page 40).

The Gates Biomanufacturing Facility's funding comes from a combination of the five-year operating fund commitments made by its partners (see Gates Center Operations) and fee-for-service from CU researchers and outside companies.



#### **GRANTS**

Between January 2007 and the end of the 2015 calendar year, Gates Center members had received a total of over \$135 million in research grant funding, approximately three quarters of which was from the National Institutes of Health (NIH). The balance was from the Department of Defense, Veterans Affairs Administration, American Cancer Society, the Dermatology Foundation, partnering hospitals and others. In 2015, individual Gates Center members were awarded over \$16 million in new funding detailed

in the table on pages 20 to 21. Given the variations in grant award numbers that occur from year to year as most awards are paid out over a three to five-year period, and the cuts in overall federal spending, the Gates Center will continue to seek research funding alternatives to make its members less dependent on the NIH and other federal funding sources.

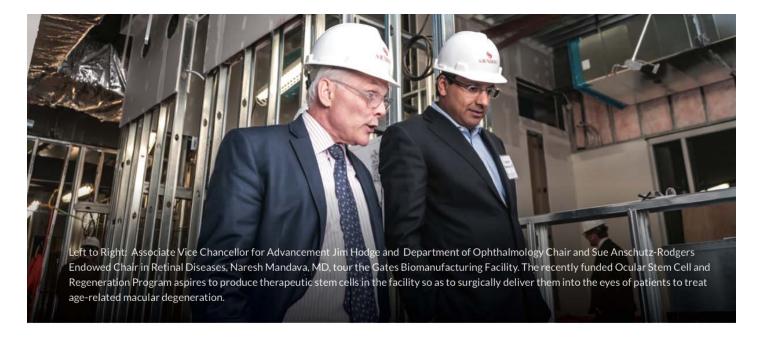


#### PHILANTHROPY

The Gates Center for Regenerative Medicine is grateful to the individuals, foundations and corporations who give so generously in support of our mission. While federal grants and industry sponsorships will always be critical to our success, philanthropic support is very often the accelerator of innovative, scientific discoveries that fall outside traditional public and private organizational funding parameters.

In 2015, the Gates Center was the grateful beneficiary

of \$4,374,888 in philanthropic support from benefactors listed on page 43. Unlike the previous year, when the majority of the funds raised provided critical support for the renovation and equipping of the Gates Biomanufacturing Facility, funds raised in 2015 were primarily directed toward the Ocular Stem Cell and Regeneration Program, basic research, the Gates Summer Internship Program and the Daniel and Janet Mordecai Endowed Chair for Cancer Stem Cell Biology.



#### **GATES CENTER OPERATIONS**

In 2015, the Gates Center finalized a five-year funding agreement between the University of Colorado Foundation, the University of Colorado President's Office and the Gates Frontiers Fund to support the Gates Center for Regenerative Medicine's basic research, general operations, education and outreach programs, and technology upgrades through the year 2020.

Consistent with its mission of providing research funding, core equipment and services to its members, along with fundraising assistance and commercialization support, the center's top expense categories in 2015 were Program and Research Support \$752,000 (34%), Core Operations and Core/Center Equipment \$618,000 (28%), Marketing and Development \$339,000 (16%) and Center Administration \$336,000 (15%). The balance of expenses totaling 7% includes Education, Enrichment, Strategic Planning Consulting and Patent Expense.

As of December 30, 2015, the center's combined fund balance was \$28,525.

#### GOING FORWARD

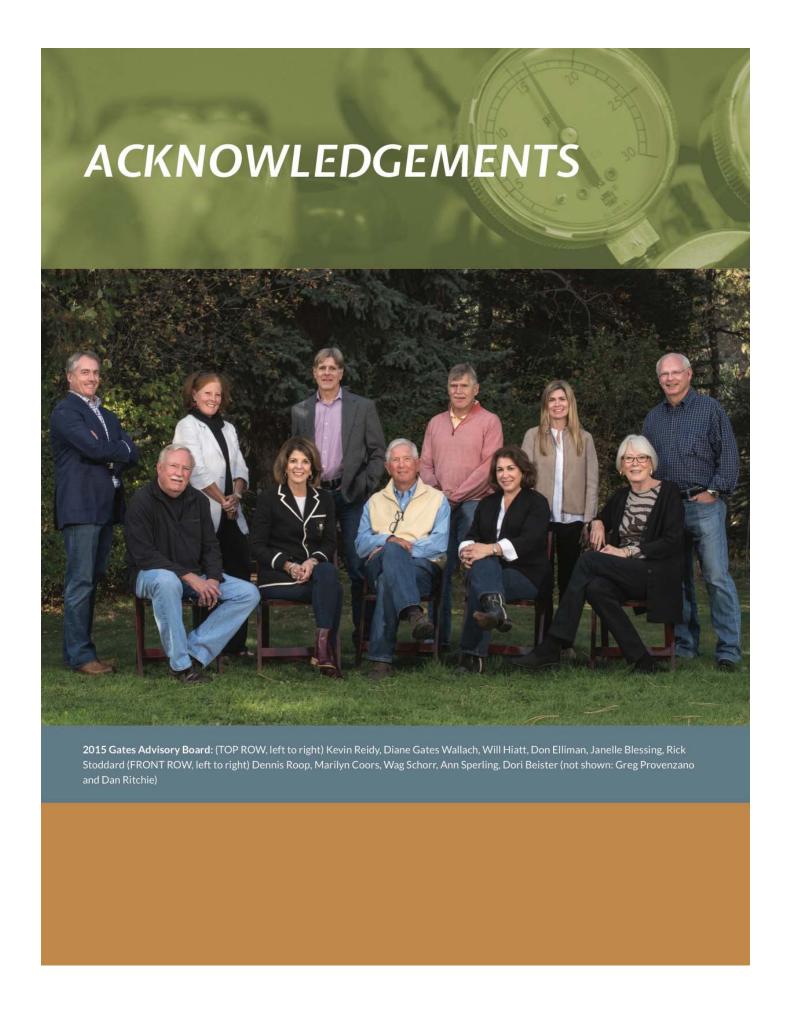
- We will continue to strategically leverage private contributions and pre-clinical investments to accelerate Gates Center member research and help us remain competitive for increasingly scarce federal funding.
- We have an excellent track record of matching benefactor intent with research opportunities, and we will continue to market our most promising research to a broader philanthropic community.
- The Gates Center will leverage operational support from the CU Foundation, the University of Colorado President's
  Office and the Gates Frontiers Fund to stimulate recurring and diversified revenues and other sources of funding to
  support our operations beyond the year 2020.
- The Gates Center will strive to remain ahead of the technology curve in our core facilities, which are among the key resources we provide for our members.

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### **GATES CENTER FINANCIALS**

	2012	2013	2014	2015
Infrastructure and Operations Grants	***			
Gates Frontiers Fund	\$1,000,000	\$1,000,000	\$1,000,000	\$1,000,000
CU Foundation	\$1,000,000	\$1,000,000	\$1,000,000	\$1,000,000
Interest/gifts received on Gift Account			\$3,100	\$10,330
Fund to cover equity fund expenses		\$150,000	\$-	\$ -
Infrastructure and Operations Grants	\$2,000,000	\$2,150,000	\$2,003,100	\$2,010,330
Expenditures				
Center Equipment	\$414,055	\$157,500	\$188,204	\$160,967
Center Core Facilities	\$201,777	\$197,750	\$277,826	\$458,498
Center Research Program Support	\$651,381	\$711,440	\$540,729	\$751,750
Marketing & Development	\$271,856	\$409,994	\$318,155	\$338,655
Center Admin/Maintenance/Supplies	\$243,287	\$243,107	\$317,948	\$336,792
Center Enrichment	\$26,165	\$28,000	\$53,198	\$18,539
Center Educational Activities	\$20,580	\$23,500	\$60,575	\$31,914
Center Extraordinary Expenses	\$ 37,650	\$327,866	\$18,027	\$22,000
Center Patent Expenses	\$-	\$151,307	\$111,224	\$62,266
Total Expenditures	\$1,866,751	\$2,250,485	\$1,885,907	\$2,181,382
Sources - Expenditures	\$133,249	\$(100,485)	\$117,193	\$(171,052)
Fund Balance	\$248,418	\$60,138	\$199,577	\$28,525



The Gates Center gratefully acknowledges the following individuals, companies and organizations for supporting our research and mission through their generous gifts of time, talent and treasure during the 2015 calendar year.

#### BENEFACTORS

Allander Biotechnologies, LLC Rhondda and Peter Grant The William H Anderson Foundation Inc Margaret Hoyt Hagerman

Janelle and Buck Blessing Lyda Hill

Kelly Bowles The Berenice Gates Hopper Family Fund

Virginia Bowles Allison and Jeff Krebs Balbi A. Brooks Monty and Frank Kugeler Darlene and Arnold Brown LGA Family Foundation

The Caulkins Family, in loving memory of George P. Caulkins, Jr. Gretchen and Charles Lobitz

Jill Cowperthwaite and Charles Jones Mary Jo McGlashan Daniel and Janet Mordecai Foundation Dennis M. O'Hanlon Marguerite Childs and Thomas Detmer, Jr. Marilyn Pooley First Western Financial, Inc. Ann and Kevin Reidy The Foote Wade Family Fund Betty and Dennis Roop

Virginia Foote Sanskriti Saxena Deb Froeb and Tim Gardner **Tschudy Schmidt Gates Frontiers Fund** A. Sheffield Tulp Mary Gearheart **UBS Foundation USA** 

The Glendorn Foundation University of Colorado Foundation

#### **VOLUNTEERS**

Marty Williams Tee Cowperthwaite AIA Eric Peterson Susan Bonsall Rosenberry Brendan Young Hobson Feltus

Kathy Stokes Kathy Barrett Lee Sandra Walton Michael S. Perry, DVM, PhD, FRCVS

To learn more about how you can accelerate research through private gifts, please contact Allison Krebs at 303-724-6342 or allison.krebs@ucdenver.edu.





## **CONTACT US**

Dennis R. Roop, PhD, *Director* 303-724-3050 dennis.roop@ucdenver.edu

Jill Cowperthwaite, Director of Marketing and External Relations 303-724-6143 jill.cowperthwaite@ucdenver.edu

Allison Krebs, MBA, *Director of Development* 303-724-6342 allison.krebs@ucdenver.edu

Patrick Gaines, Executive Director 303-724-6141

Tim Gardner, MBA, Chief Financial Officer 303-884-9056 timothy.gardner@ucdenver.edu

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



Gates Center for Regenerative Medicine Mail Stop 8320 | 12800 East 19th Avenue | Aurora, CO 80045 P: 303-724-3050 | F: 303-724-3051 | gatescenter.org