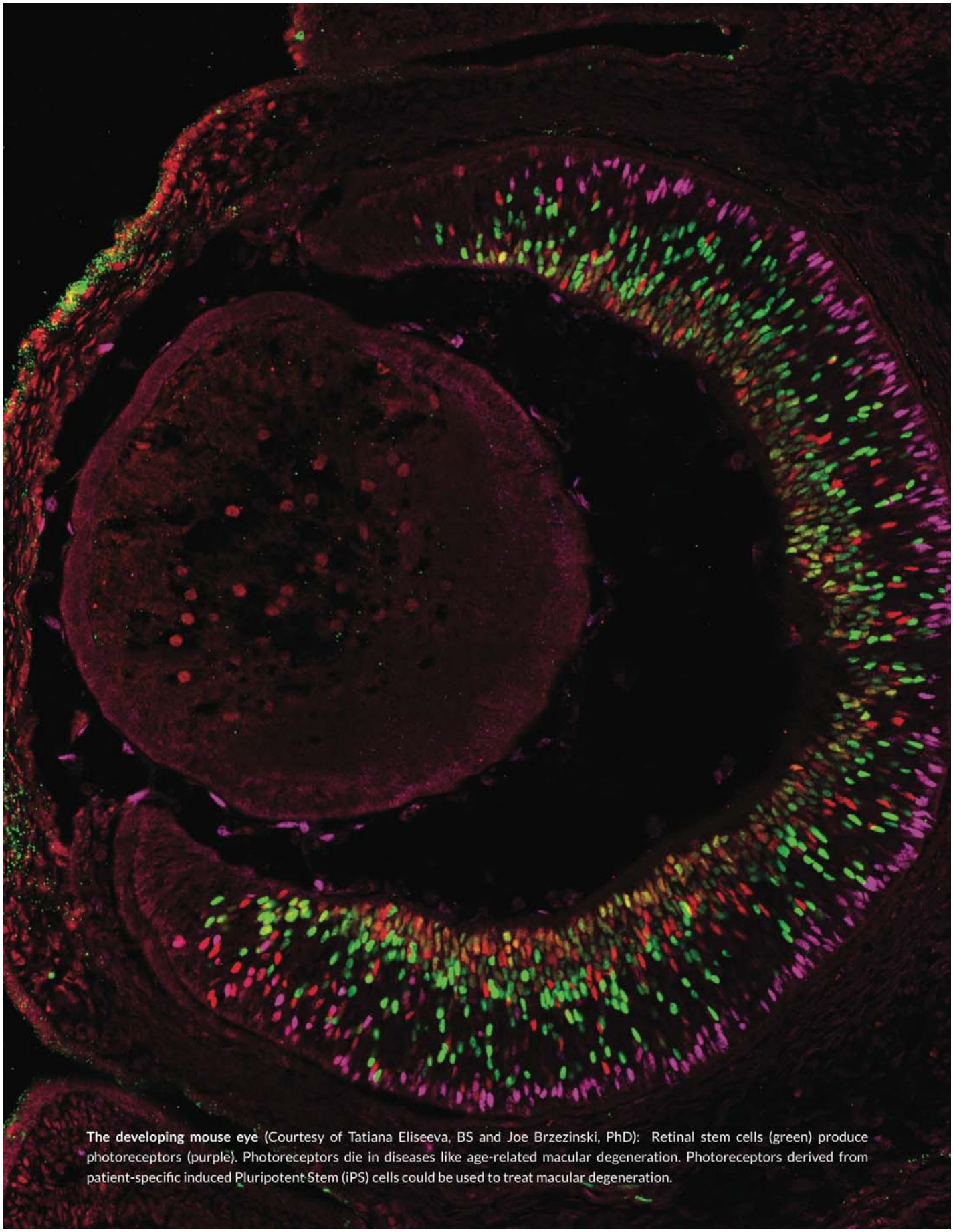
2014 Annual Report

The Gates Center

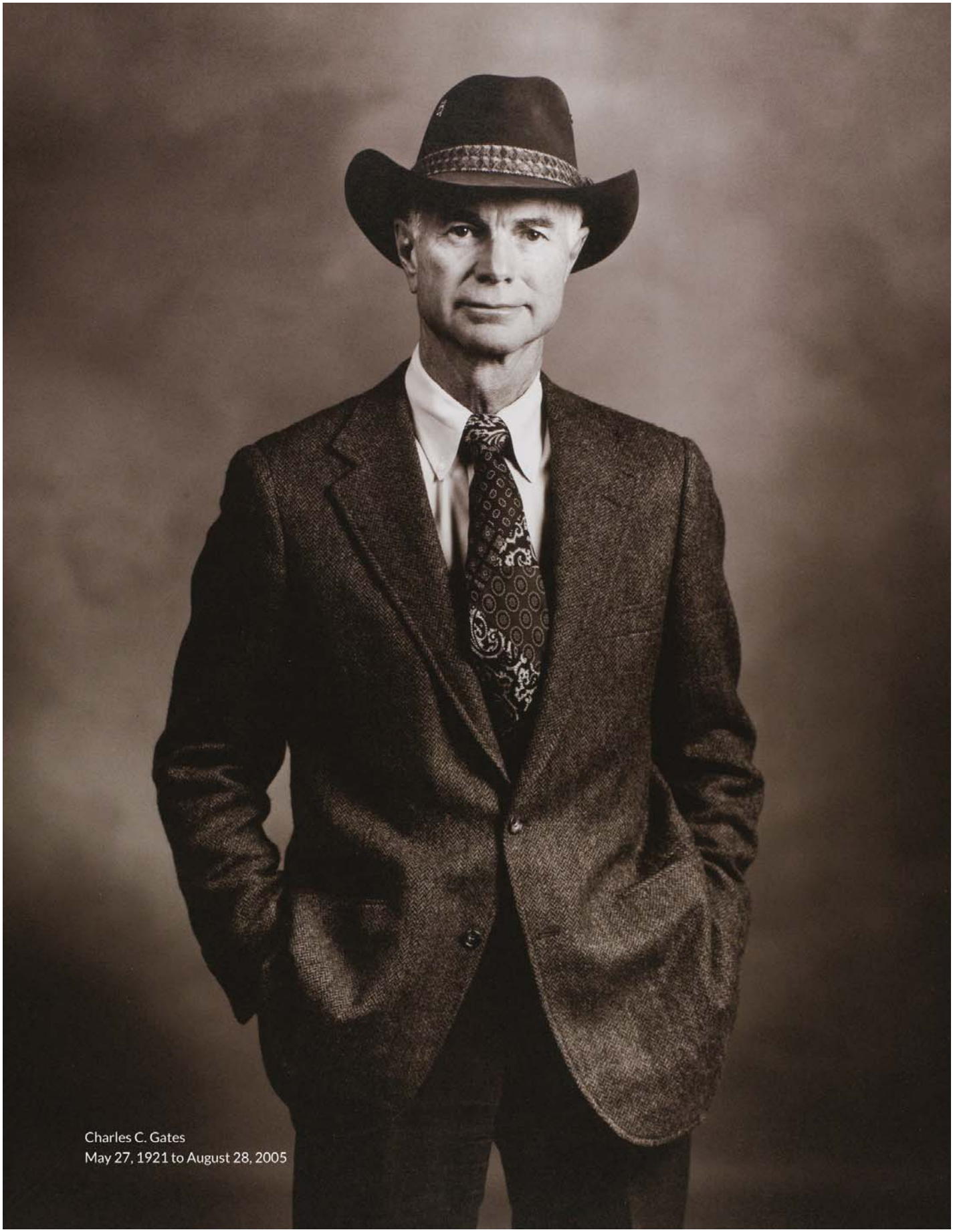
Gates Center for Regenerative Medicine

UNIVERSITY OF COLORADO | ANSCHUTZ MEDICAL CAMPUS



The developing mouse eye (Courtesy of Tatiana Eliseeva, BS and Joe Brzezinski, PhD): Retinal stem cells (green) produce photoreceptors (purple). Photoreceptors die in diseases like age-related macular degeneration. Photoreceptors derived from patient-specific induced Pluripotent Stem (iPS) cells could be used to treat macular degeneration.

CONTENT



THE VISION

Left to right: Gates Advisory Board co-chairs Don Elliman, Diane Gates Wallach and Dan Ritchie.

"Charles C. Gates, our father, led a wonderful entrepreneurial life. He was above all an innovator who always felt that things could be better. A problem solved was a life improved. When he heard about regenerative medicine, a light went on, and he said, 'This is the future!' His vision was to find the right solutions to move forward research on regenerative medicine. The Gates Center for Regenerative Medicine is the legacy of his vision, and this pioneering effort bears his name."

~ Diane Gates Wallach and John Gates

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 largest comprehensive academic health care center between Chicago, Texas and the West Coast, serving an estimated 1,000,000 patients per year.

The Gates Center brings together outstanding medical researchers and clinicians, grant and philanthropic funding, four state-of-the-art core scientific facilities and sophisticated commercialization support, along with 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 (iPSCs), 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 iPSCs and corrected their underlying genetic defect. The long-term goal is to return genetically corrected iPSC-derived adult stem cells to the patient from which they were derived. In this way, the Gates Center's clinical pathway is leading toward a new paradigm of personalized medicine, in which an individual's own cells can be used to cure a number of diseases and conditions.

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 currently comprised of 74 members from the University of Colorado Anschutz Medical Campus and CU Boulder campus, Colorado State University, Colorado School of Mines 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 dermatology, orthopedics, cardiology, ophthalmology, neurology, oncology and immunology.

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

The Gates Center for Regenerative Medicine is helping bolster the Anschutz Medical Campus's growing reputation as a global medical destination. Among other efforts, the Gates Center launched its fourth core facility—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 one of six combined cell therapy and protein manufacturing facilities in the United States and is 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.

WHAT WE DO

The year 2014 can be summed up in one word: collaboration! Since its founding in 2006, the Gates Center for Regenerative Medicine has been built on collaboration among scientists, clinicians and educators. This year we made great progress in broadening our collaborative reach to include new friends, volunteers and donors, as well as leaders in our community and beyond. We also spent 2014 carefully plotting a course for the spring 2015 launch of what we consider to be the key missing link in the creation of the most robust biotech and healthcare ecosystem in Colorado history: the Gates Biomanufacturing Facility.

Last year also marked the arrival of three dynamic leaders on the Anschutz Medical Campus, all of whom will help accelerate the Gates Center's progress in the coming years. Don Elliman, who once served as the Gates Center's executive director and had been splitting duties as chancellor of both the medical and downtown campuses, was named chancellor of the CU Anschutz Medical Campus in September 2014. Chancellor Elliman continues to serve on the Gates Center's Advisory Board, where he has been co-chair since 2012. We are also pleased to welcome Elizabeth "Liz" Concordia as CEO of University of Colorado Health. Concordia comes to us from the University of Pittsburgh Medical Center where she served as the executive vice president and the president of UPMC's hospital and community services division. We are proud to partner with University of Colorado Health in helping bolster and extend Colorado's reputation as a global medical destination. Finally, we are delighted to welcome Scott Arthur as vice chancellor for advancement on the CU Anschutz Medical Campus. Arthur's most recent appointments were executive director of constituent giving at Nationwide Children's Hospital Foundation in Columbus, Ohio, and a major gifts officer for the Mayo Clinic in Rochester, Minnesota. Philanthropy has been essential to the Gates Center's progress since day one and has helped our investigators leverage more than a 10-fold return in the form of federal support. We look forward to working with Scott and his team as we bring in new friends and partners to pursue even greater opportunities in the months and years to come.

In closing, I want to thank Dr. Richard Krugman, longtime dean of the University of Colorado School of Medicine, for his faith and formidable efforts to ensure the Gates Center's success. Dr. Krugman's spring 2015 retirement coincided with the April 2015 grand opening of the Gates Biomanufacturing Facility, which he and other campus collaborators helped make a reality. We wish him well in his future endeavors and ongoing efforts to protect and preserve the lives of children.

As you read the enclosed updates and peruse our new website at GatesCenter.org, we invite you to send us your questions and to come see us in the coming year.

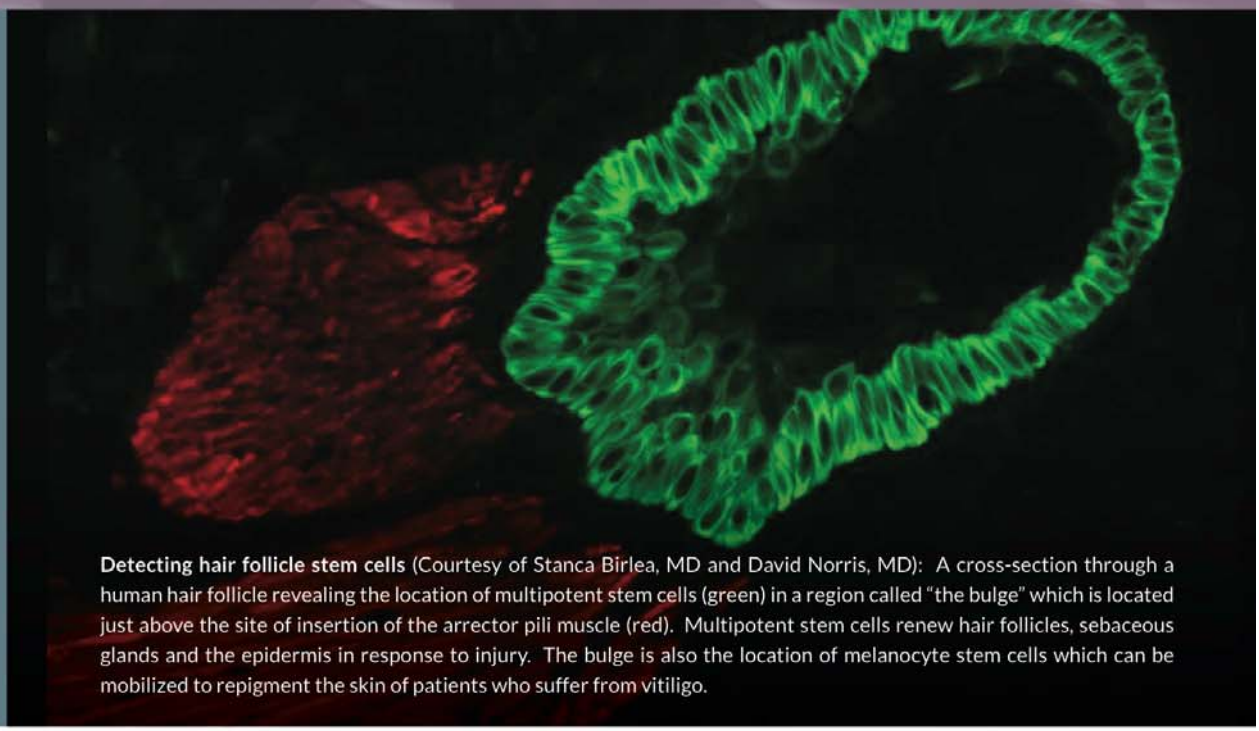
Sincerely,

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

Dennis Roop, PhD, listens to Adam Klafter, of Atlanta, GA, describe his skin condition, called epidermolytic hyperkeratosis. Dr. Roop's lab is working on a cure for Adam, utilizing the Gates Biomanufacturing Facility (see page 22).

GATES CENTER MEMBER SPOTLIGHT:

CU Department of Dermatology



Detecting hair follicle stem cells (Courtesy of Stanca Birlea, MD and David Norris, MD): A cross-section through a human hair follicle revealing the location of multipotent stem cells (green) in a region called "the bulge" which is located just above the site of insertion of the arrector pili muscle (red). Multipotent stem cells renew hair follicles, sebaceous glands and the epidermis in response to injury. The bulge is also the location of melanocyte stem cells which can be mobilized to repigment the skin of patients who suffer from vitiligo.

As of December 31, 2014, the Gates Center for Regenerative Medicine included 74 members from multiple departments and divisions within the University of Colorado School of Medicine, along with our consortium institutions, CU Boulder, CSU and School of Mines, and private industry. In the 2014 Annual Report, we are pleased to highlight our collaborations with the CU Department of Dermatology. Subsequent annual reports will focus on other collaborators. Please see page 13 for an update on individual members' honors and publications in 2014, as well as a chart summarizing center members' grants awarded during the 2014 calendar year on page 15.

Use of Stem Cells to Correct Skin Disease

In 2006, Shinya Yamanaka, MD, PhD, discovered that one can induce normal adult skin cells to become pluripotent stem cells, and this has provided staggering opportunities for correcting human genetic disease without using embryonic stem cells. Drs. Anya Bilousova, Igor Kogut and Dennis Roop are currently generating induced Pluripotent Stem Cells (iPSCs) from patients with inherited skin fragility syndromes using methods that do not require viral vectors, and determining whether genome editing techniques can be used to correct the genetic defects in these patient-specific iPSCs. The ultimate goal is to return keratinocytes derived from genetically corrected iPSCs to the patient as an autograft. Drs. Bilousova and Kogut, both

in the CU Department of Dermatology, are collaborating to devise optimal approaches for iPSC generation to treat human diseases. The skin diseases that are the best targets for this approach are epidermolysis bullosa. This is a family of hereditary skin diseases in which mutations in the genes that produce key structural proteins lead to extensive blistering of the skin. When the defective proteins produced in this disease cause full-thickness blisters of the skin, they can lead to a life of intense suffering and early death. The second candidate disease for treatment is epidermolytic hyperkeratosis, a disease in which mutations in the key structural protein keratin lead to painful and disabling lesions of the hands and feet. Being able to correct these diseases would not only be a "proof of principal" that gene editing of iPSCs can cure, but would also spare these children severe disability and death.

Other Stem Cell Research in Dermatology

A number of important ongoing projects in regenerative medicine are also being developed in the Gates Center and the CU Department of Dermatology. These projects have applications in vitiligo, a common, psychologically devastating autoimmune disease that induces spotty depigmentation of the skin, and Alopecia Areata, another autoimmune skin disease that targets pigmented hairs and produces patchy to complete hair loss. In addition, Drs. Xiao-Jing Wang and Qinghong Zhang are studying the biochemical control of psoriasis, oral mucositis, and other inflammatory diseases, as well as the role of these pathways in skin cancer induction and progression. Finally, Drs. Wang, Refaeli and Zhang are collaborating on testing the potential of using the Tat-Smad7 fusion protein in the treatment of chronic wounds.

Cancer Stem Cells in Dermatology

CU investigators are at the forefront of discovering protocols that can be used to directly identify and characterize melanoma stem cells to develop new treatment strategies and new targeted drug combination therapies. In addition, our investigators are studying how mutations in genes impact stem cells that influence skin pigment.

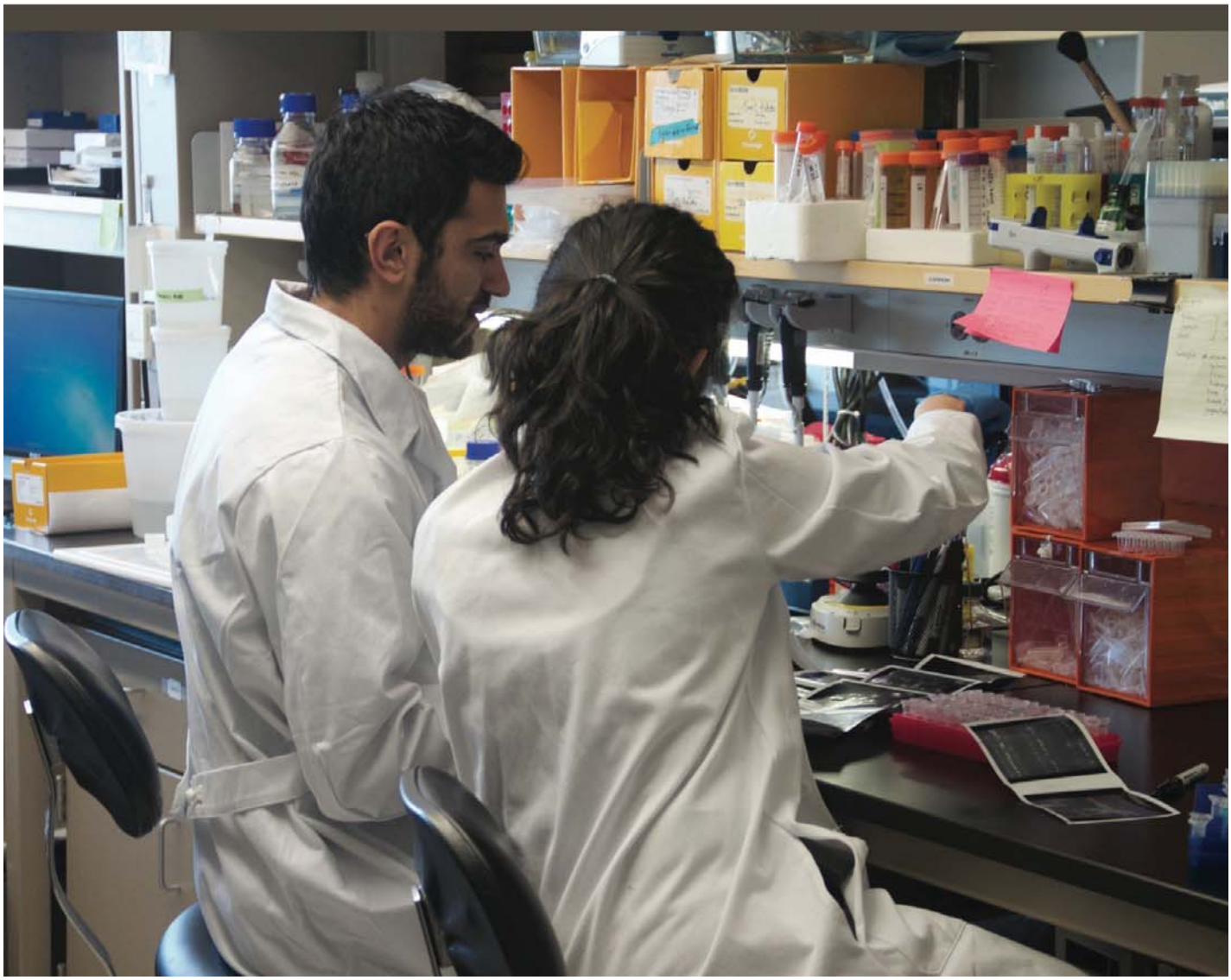
David A. Norris, M.D., Professor and Chairman, Department of Dermatology

It has been a great pleasure to participate in the establishment and growth of the Gates Center for Regenerative Medicine, and 2014 clearly saw some of our greatest accomplishments. Above all, the translation of discoveries to new human therapies moved much closer to reality with the build-out of the new Gates Biomanufacturing Facility. Likewise, collaborations thrived, under the leadership of Dennis Roop, between the center and multiple departments in the CU School of Medicine, including important achievements that accelerated stem cell research in the CU Department of Dermatology. These include the continued operation of the state-of-the-art Gates Center research laboratory cores, the expertise of a growing body of scientists and clinicians, grants and awards from federal sources, foundations and individuals, and seed funding that will push groundbreaking bench research into clinical therapeutics in the Gates Biomanufacturing Facility. As one of a number of departments that has benefitted tremendously from a close affiliation with the Gates Center, I want to congratulate Dennis Roop and the Gates Center's leadership for the great accomplishments of 2014 and their indispensable role in making these and future successes possible.

Role of Dermatology Administration in supporting the Gates Stem Cell Center

Department of Dermatology Chair David Norris has worked closely with Gates Center Director Dennis Roop over the past eight years. He has worked to foster the collaborative culture of the Gates Center and to coordinate interactions with other departments and with the CU School of Medicine, campus and system administration. He has also been an active partner in multiple research projects, and his department has provided resources to help maintain the research productivity and momentum of members of the dermatology faculty in the Gates Center laboratories.

The administration of the CU Department of Dermatology has also worked hard to create an effective partnership with the Gates Center's administrative team, which is crucial to addressing the ongoing challenges and opportunities related to funding, space, personnel and new translational research approaches for the future.



RESEARCH SPOTLIGHT:

Honors and Publications

Xiao-Jing Wang, MD, PhD,
giving the William Montagna Lecture

Christopher Baker, MD, *Assistant Professor, Pediatrics-Pulmonary,* received a three-year grant from the NIH on December 1, 2014, that will support his research into how complications of pregnancy interfere with stem cells in the blood of premature babies that help the lungs to develop normally. This project may lead to novel treatments for respiratory complications commonly seen in these medically fragile children.

Stanca Birlea, MD, PhD, *Assistant Professor, Dermatology,* received the American Skin Association Scholar Award in Vitiligo/Pigment Cell Disorders in December 2014 for a project titled "Harnessing the power of regenerative medicine for vitiligo treatment." This award is intended to honor, reward and support research in vitiligo for active investigators. Primary emphasis is given to researchers with a strong career goal within the field of dermatology, who are dedicated to the furtherance of knowledge concerning vitiligo/pigment cell disorders and focused on new discoveries in the basic or translational medical sciences that impact the understanding or treatment of vitiligo/pigment cell disorders.

Neil Box, PhD, Assistant Professor, *Dermatology,* published data on November 19, 2014, in *Cancer Epidemiology, Biomarkers & Prevention,* a journal of the American Association for Cancer Research (AACR), that establishes a link between genetic factors and different ultraviolet exposure measures in children, such as the number of waterside vacations or sunburns, and the resultant biomarkers of melanoma risk, as in the number of freckles or moles that develop during childhood. The research paper was selected for press release by AACR and was the subject of national press coverage.

Mayumi Fujita, MD, PhD, *Professor, Dermatology,* an investigator in both the Gates Center and the University of Colorado Cancer Center, published an original article in the *Proceedings of the National Academy of Sciences* reporting the activity of a recently discovered communication molecule of the body's immune system, Interleukin 37 or IL-37. It has been known to limit inflammation, and the current study reports its activity in the adaptive immune system: IL-37 inhibits the ability of the immune system to recognize and target new antigens.

William Hiatt, MD, *Professor of Medicine, Division of Cardiology,* was honored by the American Heart Association as one of six 2014 Distinguished Scientists on November 16, 2014. These annual awards recognize AHA/ASA members for significant, original and sustained scientific contributions that have advanced the association's mission to build healthier lives, free of cardiovascular diseases and stroke. CPC Clinical Research, of which Dr. Hiatt is president, is dedicated to running clinical trials that translate stem cell discoveries into FDA-approved therapies to treat a variety of disorders. CPC is currently running several stem cell trials in peripheral artery disease and wound healing.

Antonio Jimeno, MD, PhD, *Professor of Medicine, Division of Medical Oncology,* was named full professor on July 1, 2014, one of the youngest professors in the history of the University of Colorado School of Medicine.

Karin Payne, PhD, *Assistant Professor, Orthopedics,* was featured in a November 2014 5280 magazine story on exciting medical innovations. She's been working with Melissa Krebs, PhD, from the Colorado School of Mines Department of Chemical and Biological Engineering on a project that could affect how we treat growth-plate injuries in children.

Yosef Refaeli, PhD, *Associate Professor, Dermatology,* published an article in *PLOS ONE* on August 29, 2014, reporting the breakthrough discovery of a process to expand production of stem cells used to treat cancer patients. These findings could have implications that extend beyond cancer, including treatments for inborn immunodeficiency and metabolic conditions, and autoimmune diseases.

Kunhua Song, PhD, *Assistant Professor of Medicine, Division of Cardiology,* who specializes in regenerative medicine and heart development/disease, was one of seven early-career scientists joining the ranks of Boettcher Investigators in the Class of 2014 Webb-Waring Biomedical Research Program. Boettcher Investigators are awarded grants that cover three years of research, with a goal of establishing themselves and becoming competitive for federal and private support. The Webb-Waring Biomedical Research Program was created in 2008 as a result of an innovative agreement among the Boettcher Foundation, the Webb-Waring Foundation for Biomedical Research and the University of Colorado. Through the program, the Boettcher Foundation now invests more than $1.5 million each year into efforts to increase Colorado's competitiveness in biomedical science.

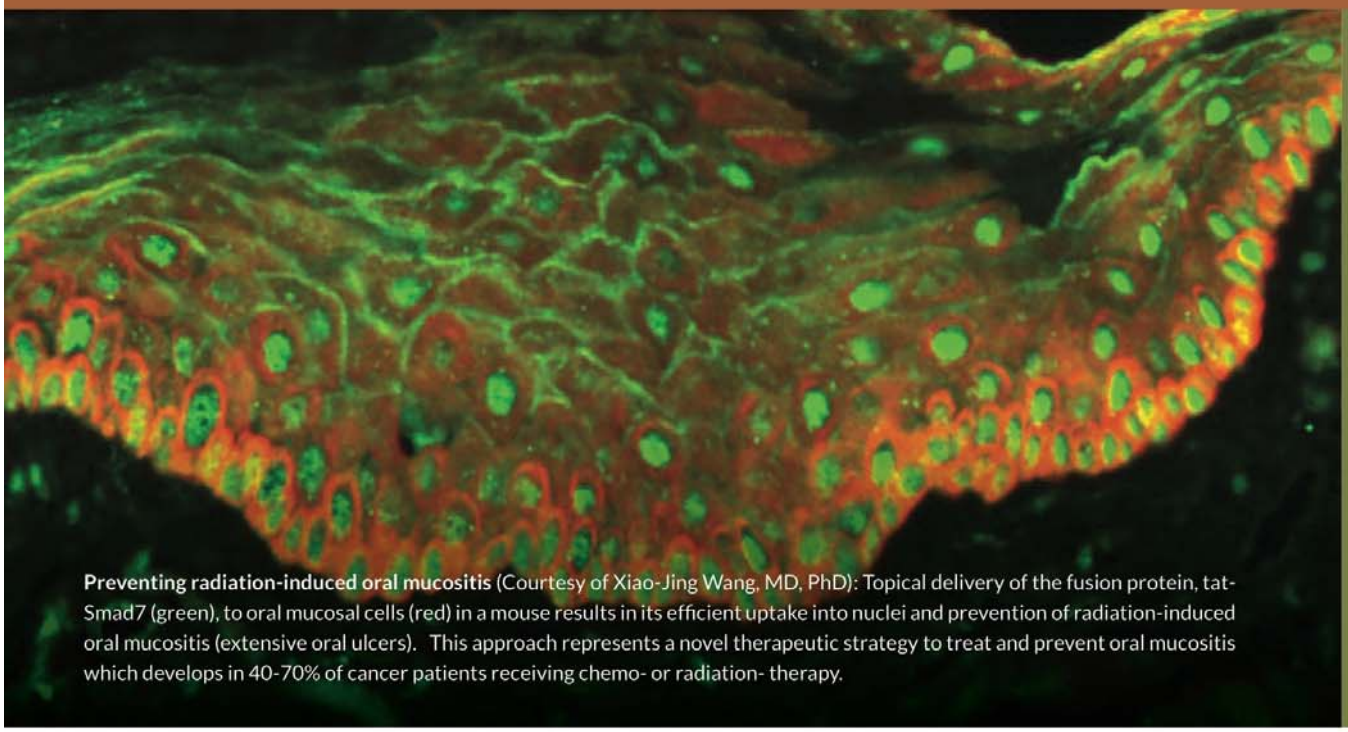
Xiao-Jing Wang, MD, PhD, *Professor, Pathology,* (see photo on page 13) received the William Montagna Lecture Award at the annual meeting of the Society for Investigative Dermatology on May 10, 2014. Given annually at the society's annual meeting, this award is intended to honor and reward young active investigators. Primary emphasis is given to researchers in skin biology. According to Gates Center Director Dennis Roop, "She gave an outstanding lecture, and we are all very proud of her." In her inimitable style, Xiao-Jing responded, "To get the record complete, Dennis won the same award 22 years ago, so I'm just slow in catching up with him!" Xiao-Jing is currently the John S. Gates Endowed Chair and director of the head and neck cancer research program, professor in CU Department of Pathology, and holds joint appointments in the departments of otolaryngology, dermatology, and craniofacial biology.

GRANT AWARDS

PRINCIPLE INVESTIGATOR	SPONSOR	AMOUNT AWARDED	TITLE
Artinger, Kristin	National Institutes of Health	$200,000	The role of Sash1 in melanocyte development and disease
Baker, Christopher	National Institutes of Health	$1,320,750	Impaired angiogenesis after maternal complications of pregnancy
Baker, Christopher	Dean's Academic Enrichment Funding AEF Bridge Funding	$100,000	Impaired angiogenesis after maternal complications of pregnancy in preterm birth
Birlea, Stanca	American Skin Association	$120,000	Harnessing the power of regenerative medicine for vitiligo treatment
Box, Neil, PhD	Colorado Clinical and Translational Sciences Institute Award	$30,000	Chemoprevention of skin cancer-toward a better sunscreen
Brzezinski, Joseph	Department of Defense	$249,979	Programming retinal stem cells into cone photoreceptors
Brzezinski, Joseph	National Institutes of Health	$1,941,876	Mechanisms of cell-fate specification and competence regulation in photoreceptors
DeGregori, James	National Institutes of Health	$946,860	SPORE in Lung Cancer
DeGregori, James	National Institutes of Health	$225,000	Nrf2-mediated impaired hematopoietic stem cell fitness following irradiation
De Langhe, Stijn	Pulmonary Fibrosis Foundation	$50,000	Role of Wnt and Fgf signaling in alveolar epithelial regeneration after bleomycin
De Langhe, Stijn	National Institutes of Health	$1,888,592	HL-role of c-Myc in myofibroblast differentiation in pulmonary fibrosis
Ford, Heide	Cancer League of Colorado	$60,000	Developing stapled peptides for breast cancer therapy
Ford, Heide	Alex's Lemonade Stand Foundation	$250,000	Targeting the Six1/Eya transcriptional complex to inhibit pediatric sarcoma
Ford, Heide	National Institutes of Health	$435,000	Developing cancer therapies through targeting the Six1/Eya transcriptional complex
Friedman, Jed	National Institutes of Health	$2,071,000	Randomized trial of diet in GDM: metabolic consequences for mother and offspring
Goodrich, Laurie	AlloSource	$324,904	The evaluation of laser-enhanced cartilage discs for the regeneration of chondral defects in the equine model- in vivo.
Goodrich, Laurie	AlloSource	$14,193	The evaluation of laser enhanced cartilage discs for the regeneration of chondral defects in the equine model- Pilot
Goodrich, Laurie	Grayson Jockey Club Research Foundation	$109,476	Contrast enhanced CT for detection of cartilage injury
Huang, Hua	National Institutes of Health	$1,250,000	Cell-fate specification: basophils vs. mast cells
Jimeno, Antonio	National Institutes of Health	$1,400,000	Oral cancer stem cells
Koch, Peter	Shipley Foundation	$525,000	Monocyte targeted immunotherapy for cancer
Koch, Peter	Dean's Academic Enrichment Funding AEF Bridge Fund	$50,000	Bridge funding
Koch, Peter/ Koster, Maranke	National Institutes of Health	$917,617	Elucidating the molecular pathology of ectodermal dysplasias caused by TP63 mutations
Koster, Maranke	Nat'l. Fdn Ectodermal Dysplasias	$25,000	Developing methods for generating full thickness, healthy replacement skin for AEC patients

PRINCIPLE INVESTIGATOR	SPONSOR	AMOUNT AWARDED	TITLE
Lu, Shi-Long	University of Colorado Cancer Center	$17,000	Development of methylated microRNAs as biomarkers for head and neck cancer
Neff, Tobias	University of Colorado Cancer Center	$30,000	Cancer League of Colorado grant award
Niswander, Lee	Cancer League of Colorado	$60,000	Grhl2 developmental network to identify novel suppressors of EMT in breast cancer
Niswander, Lee	National Institutes of Health	$410,868	Phenotyping embryonic lethal knockout mice with neural crest and neural defects
Payne, Karin	Musculoskeletal Transplant Foundation	$100,000	Revitalization of bone allograft with induced pluripotent stem cells to enhance spinal fusion
Refaeli, Yosef	Private Sponsor	$100,000	Ebola vaccine development
Roop, Dennis/ Norris, David	National Institutes of Health	$3,108,176	Molecular analysis, modeling and correction of skin diseases core center (P30)
Terzian, Tamara	American Cancer Society Institutional Research Grant	$30,000	The role of mutant p53 in tumorigenesis
Terzian, Tamara	Colorado Clinical and Translational Sciences Institute Award	$20,000	Identifying the genetic determinants of giant congenital nevi
Terzian, Tamara	Dermatology Foundation	$20,000	p53 in photoprotection
Wagner, David	State of Colorado	$178,000	Testing a drug as a treatment option for MS
Wang, Xiao-Jing	National Institutes of Health	$2,506,362	Identifying oral cancer stem cell properties by the microenvironment
Wang, Xiao-Jing	National Institutes of Health	$194,672	Testing Smad7-based biologics for treating chronic wounds
Wang, Xiao-Jing	National Institutes of Health	$186,330	Smad7 use in oral mucositis treatment
Yi, Rui	National Institutes of Health	$1,622,285	Genetic analysis of microRNA functions in skin stem cells in vivo
Zhang, Qinghong	National Institutes of Health	$69,300	Crosstalk between metabolism and inflammation in pulmonary hypertension
	Total Awards =	$23,108,240	

COMMERCIALIZATION



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

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

As a team, we encompass the dynamic creativity, scientific intelligence and industry experience needed to realize the true potential of breakthrough stem-cell 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 2014 efforts include the following:

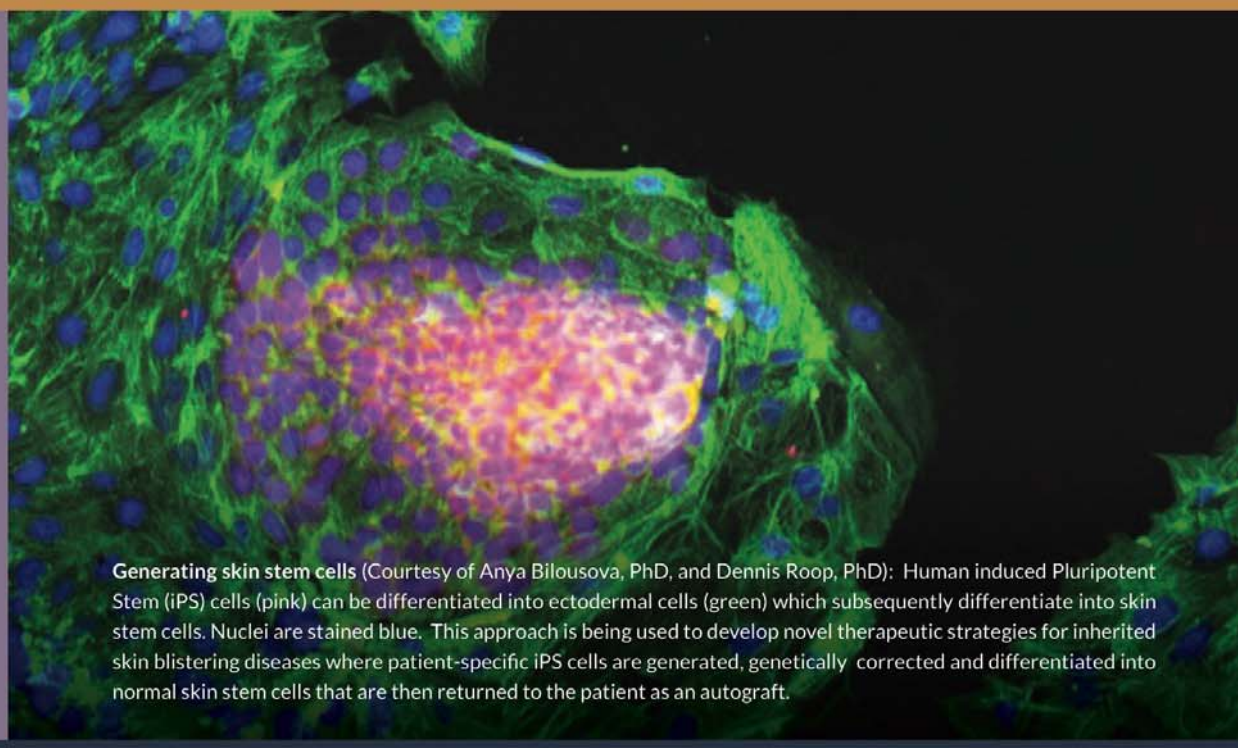
Dr. Xiao-Jing Wang and her colleagues have developed a fusion protein (biologic) that can be used to regenerate mucosal tissue damaged during radiation or chemotherapy treatments for cancer. Oral mucositis is a seriously debilitating condition, and its avoidance is a frequent reason for modifying cancer treatments to less optimal regimens. There is currently no approved treatment for regeneration of mucosal tissue; the only available drug is approved for prevention of damage. This drug has been shown less effective than Dr. Wang's fusion protein in head-to-head tests in animals.

In 2014 the patent for Tat-Smad7 was issued in the US, and additional patent applications were filed in Canada and Hong Kong, along with an international Patent Cooperation Treat patent application. Also in 2014, Allander Technologies, a Colorado LLC, was formed to commercialize this technology, and at year's end Allander and the University of Colorado Technology Transfer Office had reached substantive agreement on terms for a worldwide, exclusive license to the technology.

Drs. Ganna Bilousova, Igor Kogut and Dennis Roop have developed a non-genetic method for reprogramming adult skin cells into iPSCs. This method is based on the use of RNA and does not involve the controversial use of viral vectors. This novel method will greatly accelerate the clinical application of iPSC-based therapies. The first anticipated use of cells derived from iPSCs will be for patients with inherited skin blistering diseases. A provisional patent has been filed, and early discussions have been initiated with a major pharmaceutical company for licensing this technology.

In an effort to help Gates Center members learn more about the intricacies of commercialization, the Gates Center hosted two presentations in its 2014 Commercialization Toolkit Seminar and Q&A Series:

- The first, titled "Why Patent Inventions - What You Need to Know" led by Director of Intellectual Property Heather Callahan, was held on April 24, 2014.
- The second, titled "Corporate Structure for Start-ups: Pros and Cons" led by Director of Finance and Operations Tim Gardner and Sage Law Group Partner Rex O'Neal, was held on July 10, 2014.



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

CORE FACILITIES

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

The success of these cores in providing quality service with a quick turnaround time is further illustrated by the fact that in addition to being utilized by Gates Center members, they are utilized by investigators in 15 different departments, divisions or centers within the School of Medicine and in the following: the Schools of Pharmacy and Dentistry, National Jewish Health, UC 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, and Thomas Jefferson University.

The cores are operated on a cost-recovery basis, and are largely financially independent, with a combined operating budget of $1,423,210 in 2014. However, the cores receive some additional annual support from the Gates Center operating budget ($110,000 from Gates/CU Foundation matching funds) and from Academic Enrichment Funds provided by the dean of the CU School of Medicine ($150,000).

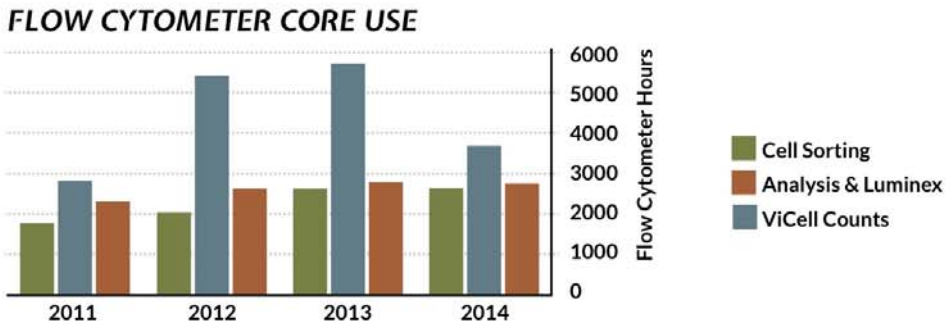
The core operating budget is not currently designed to cover equipment purchases to replace, update or expand capacity. Additional equipment purchases were supported by the Gates Frontiers Fund/CU Foundation matching funds between 2011 and 2014 totaling $398,097.

In addition, the five-year Skin Diseases Research Core Center grant to Drs. Norris and Roop, which was awarded in September 2009 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. The 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 also serves as the administrative assistant for the center. This grant was renewed for five more years in September 2014.

A brief description of these core facilities and graphic summaries illustrating their use by both Gates Center members and non-members from 2011-2014 is as follows:

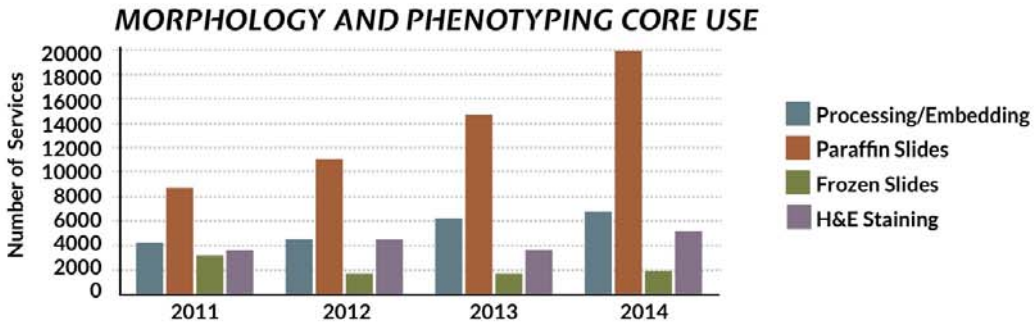
1 Flow Cytometry Core

The techniques of flow cytometry and cell sorting allow for the rapid identification and isolation of individual stem cells within a mixed population. The Flow Cytometry Core added two new pieces of equipment in 2014 that will greatly improve the core's ability to accomplish this goal; a Beckman Coulter AstriosEQ cell sorter and a Fluidigm CyTOF mass cytometer. Partially funded by the Gates Center, the Astrios EQ cell sorter improves the resolution of differences between cell subsets including very small particles and can quickly (50,000 cells/second) collect up to six subsets of cells simultaneously. The AstriosEQ allows us to rapidly find and collect the rarest of stem cells in sufficient numbers for further analysis. The center also partially funded the CyTOF2 mass cytometer, which is the first CyTOF in the Rocky Mountain region. The CyTOF2, a combination flow cytometer and mass spectrometer, detects rare earth metal tags linked to up to 40 different antibody markers to deeply define cell populations on a cell-by-cell basis.



2 Morphology and Phenotyping Core

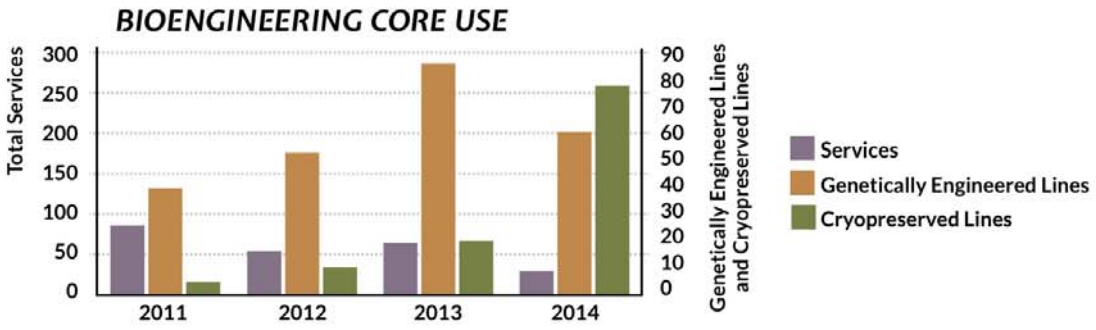
The ability of doctors and researchers to analyze diseased tissue microscopically using histological approaches is a powerful tool necessary for the understanding of disease. The Morphology and Phenotyping core provides qualitative and quantitative evaluation of tissue (e.g. skin) and appendages (e.g. hair follicles), which requires precise and reproducible orientation of tissue sections. Users submit sample biopsies following advice from the core's histotechnicians, who contribute anatomic expertise to organizing collection protocols and to verifying the histopathological classification of specimens collected. In addition, the core owns the equipment necessary to process and section submitted tissue samples, and employs a histology technician trained in processing samples.



3 Bioengineering Core

Generation of genetically modified (i.e., transgenic) animals is a powerful tool for understanding the in vivo role of genes and mutations in disease or in tissue maintenance. The Bioengineering Core provides pronuclear injections to produce conventional and Bacterial Artificial Chromosome (BAC) transgenic mice, mouse Embryonic Stem Cell (ES) cell injections to produce mice with deleted genes (e.g. knockout) or mice carrying a targeted mutation (e.g. knockin mice), 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 targeted mutation into a disease promoting gene.

With the advent of induced Pluripotent Stem Cell (iPSC) 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 can introduce reprogramming factors into normal and diseased cells from human and mouse origin in order to generate custom-designed iPSCs lines. iPSCs from other species, including canine and equine, have recently been generated as well. The Bioengineering Core is currently using both lentiviral- and sendai-viral vector systems to deliver reprogramming factors to cells. Both systems are efficient, with the latter system having the advantage to generate iPSCs with a non-DNA-integrating vector system such that no trace of the original reprogramming factors remain in the final iPSC cell line; hence they do not possess any foreign DNA that could cause disease if used in a patient.



GATES BIOMANUFACTURING FACILITY

The Gates Biomanufacturing Facility's new bioreactor, which will enable the production of protein-based biologics for early-phase clinical trials

In the 2013 Annual Report, we described the Gates Center's planning and early implementation of the Gates Biomanufacturing Facility, a new core facility designed to manufacture FDA-approved cellular therapies and protein-based biologics for early-phase clinical trials. Among other efforts, the Gates Center obtained philanthropic gifts totaling $4.3 million from eight donors to cover a budgeted renovation and construction amount of $4.26 million. Further, the Gates Frontiers Fund and one other donor provided a total of $4.1 million to cover equipment purchases for the facility. On November 10, 2014, we hosted more than 70 guests from the CU Anschutz Medical campus and greater Denver/Aurora community for an evening of "Cellular Cocktails: an inside look at the future of stem-cell therapies and regenerative medicine." By the end of 2014, the facility was beginning to take shape with about 60% of the initial renovation having been completed - well on its way for the facility's grand opening in April 2015.

GATES BIOMANUFACTURING FACILITY PARTNERS

The lead time required for researchers and biotech companies to guide their research toward manufacturing can amount to several months to a few years. For this reason, we knew it was critical to create a five-year runway of operating support from key partners on the Anschutz Medical Campus who will help drive innovation and test the therapies and drugs produced in the Gates Biomanufacturing Facility. In early 2014, the Gates Center obtained five years of lease costs and essential operating expenses totaling $7.3 million from the following partners:

University of Colorado Anschutz Medical Campus

GATES FRONTIERS FUND

School of Medicine
UNIVERSITY OF COLORADO | ANSCHUTZ MEDICAL CAMPUS

Children's Hospital Colorado

UNIVERSITY of COLORADO HEALTH

We are grateful to the generous donors below who also helped make the Gates Biomanufacturing Facility a reality:

The Caulkins Family, in loving memory of George P. Caulkins, Jr.
Children's Hospital Colorado
Gates Frontiers Fund
Monty and Frank Kugeler
LGA Family Foundation
Daniel L. Ritchie
Walter S. Rosenberry III Charitable Trust
Mrs. Thomas Taplin
Temple Hoyne Buell Foundation

Left to right: Matt Seefeldt, Gabe Orosco and Thomas Payne

GATES BIOMANUFACTURING FACILITY MANAGEMENT TEAM

Director of Cell Therapy – Thomas Payne, PhD

Tom joined the Gates Center for Regenerative Medicine in October 2012. From 2006 to 2012, Tom served as the research and development manager for Cook MyoSite, Inc., in Pittsburgh, PA. His responsibilities encompassed the manufacture and clinical application of an autologous cell therapy product and the management of personnel, laboratories and projects within Cook's research and development department. Tom also participated in the design, development and initiation of two first-in-human clinical trials for the catheter-based delivery of skeletal muscle-derived stem cells as a treatment for acute and chronic heart failure. Tom earned his BS in molecular biology and mathematics at Benedictine University, his PhD in bioengineering from Swanson School of Engineering, University of Pittsburgh, and completed his postdoctoral research at the University of Pittsburgh's Department of Orthopedic Surgery.

Director of Protein Chemistry – Matthew Seefeldt, PhD

Matt completed his doctoral studies in protein stability at the University of Colorado in collaboration with Dr. Theodore Randolph, with a focus on the effects of high pressure on protein structure, stability and refolding. Matt co-founded BaroFold, Inc. in 2009, to help companies create novel protein therapeutics, accelerate therapeutic protein development and manufacture follow-on biologics where access to a novel process technology is critical. Over the years Matt has become a leading global expert in protein refolding, having worked on approximately 150 proteins to date. His experience at BaroFold working with outside Commercial Manufacturing Organizations to develop multiple proteins uniquely qualifies him to assist our customers with their process development and scale-up projects.

Director of Quality – Gabriel Orosco

Gabe joined the Gates Biomanufacturing Facility in August 2014 with 18 years of experience in quality assurance, manufacturing and operations. Prior to joining the GBF, Gabe was the senior director of biopharmaceuticals for Dohmen/Reglera, an outsourced pharmaceutical and medical device commercialization consultancy where he worked for 6 1/2 years. In industry, Gabe worked with Sandoz/Novartis on the remediation of global sites in facilities, validation, computer systems and quality systems. Gabe has held the following leadership roles: senior director of biopharmaceuticals, director of quality assurance, director of contract manufacturing operations, director of engineering, facilities and maintenance, senior validation engineer - computer system validation. Gabe earned his BS in mechanical engineering at California State University, Fullerton.

CFO and Business Development – Timothy Gardner

Tim joined the Gates Center for Regenerative Medicine in December 2013. He brings 25 years of business experience in technology, manufacturing and financial service companies. Prior to joining the Gates Center, Tim was the CFO and Vice President-Business Development at Boulder Ionics, a specialty chemical manufacturer providing electrolytes for advanced energy storage. At BI, he negotiated three rounds of financing including a $4.3 million venture capital investment and established a joint development agreement with JSR Energy. Prior to joining BI, he was a founding partner with Cache Creek Partners, a consulting partnership that accelerates growth and profitability for midsize companies. Tim served as president of the board of trustees at St. Anne's Episcopal School for six years and is currently chairman of the board of the Southwestern Foundation. He was also a board member at the Kempe Children's Foundation from 1984 to 1992. He received his bachelor's degree from the University of Colorado and his MBA from the Kellogg School of Management at Northwestern University.

GATES BIOMANUFACTURING FACILITY DESCRIPTION

The Gates Biomanufacturing Facility (GBF) is a 14,000 square foot production laboratory for the manufacturing of pharmaceutical and cellular products. The facility is designed and organized according to the Food and Drug Administration's (FDA) current Good Manufacturing Practice (cGMP) standards for all pharmaceutical manufacturers, including quality control and quality assurance programs. Adherence to strict FDA standards ensures that the Gates Biomanufacturing Facility maintains systems that assure proper design, monitoring and control of manufacturing processes. In addition to strong quality management systems, this also includes obtaining appropriate quality raw materials, establishing robust operating procedures, detecting and investigating product-quality deviations and maintaining reliable testing laboratories. This formal system of controls helps prevent instances of contamination, mix-ups, deviations, failures and errors.

The Gates Biomanufacturing Facility operates as a cost-neutral service center within the University of Colorado School of Medicine and serves academic, clinical and commercial researchers, both Colorado-based and nationwide, looking to translate their discoveries into clinical-grade products suitable for investigational use in humans. The facility provides the required space, equipment, regulatory compliance and process expertise for the safe development and manufacture of biologic drugs (proteins) and cell-based products. To enable the processing of multiple product lines simultaneously, the facility is comprised of multiple individual clean rooms to provide adequate segregation of different product lines.

The Gates Biomanufacturing Facility is located in Bioscience Park Center, which is located on the north side of Montview Boulevard, one block north of the Gates Center research labs. For more information, please go to GatesBio.org.

The GBF provides the following services: process development, scale-up, manufacturing of both cell therapy- and protein-based products to cGMP standards, and process documentation. The focus is on delivering these services to: academic researchers, clinicians and early-stage biotechnology companies.

The impact of this facility will be significant and wide ranging. First and foremost, it will enable the Anschutz Medical Campus to remain competitive among national peers and maintain our presence as a top-ranking academic medical center, capitalizing on the new wave of advanced biologic and stem cell-based therapies that require a regulatory-compliant manufacturing facility to initiate human clinical trials. It will also bind the campus together by completing a medical ecosystem that begins with basic research and flows through manufacturing, clinical trials and new standards of patient care. This facility will also enhance the University of Colorado, Children's Hospital Colorado and the University of Colorado Health system to attract worldwide top talent in stem cell therapies.

GATES BIOMANUFACTURING FACILITY FLOOR PLAN

- **Cell Therapy Manufacturing** (blue)
- **Protein Manufacturing** (orange)
- **Cryogenic & Material Storage** (brown)
- **Utilities** (purple)
- **Quality Control Lab** (dark blue)
- **Cell Development Lab** (green)
- **Protein Development Lab** (green)
- **Quality Assurance** (yellow)

EDUCATION

As an academic medical center and citizen of a larger bioscience ecosystem that we are trying to build, the Gates Center has reached out and collaborated to provide education regarding stem cell biology and regeneration in a variety of ways. These include: a graduate-level program, lectures to medical students, mentoring summer interns, outreach efforts and center tours and, most recently, a summer school for international trainees.

Shortly after the stem cell program was initiated in 2007, we worked with the director of an existing graduate program - "Cell Biology and Development" - to create a new integrated graduate program titled "Graduate Program in Cell Biology, Stem Cells and Development (CSD)," which is currently directed by Bruce Appel, PhD, Gates Center member and holder of the Diane G. Wallach Chair in Stem Cell Research. The combined program was 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 make fundamental discoveries of how cells function and how cells in embryos form the different tissues of the body. The faculty and students are linked by their common interest in understanding cells in the contexts of development, regeneration and disease.

Throughout the 2014 year, many members of the Gates Center faculty also participated in teaching Core Courses, which are required for all biomedical-science PhD students, including CSD students. In addition to Core Courses, two well-attended and evaluated stem-cell-specific courses were taught: "Stem Cells and Development: An Integrated Approach" and an advanced-level graduate course titled "Stem Cells and Stem Cell Technology in Biomedical Research."

Ultimately, the Gates Center's mission is to develop treatments for debilitating diseases, and our scientists work collaboratively with clinicians as they pursue their research with this goal in mind. As a result, there is a greater focus on medicine and the clinic than in many other academic institutions. This is reflected in the two lectures on stem cells for medical students taught annually by Dr. Roop: "Stem Cells and Differentiation" to first-year medical students and "Stem Cells, Science and Evolving Therapies" to fourth-year medical students.

In an effort to inspire another generation of scientists, the Gates Center reaches out to undergraduate (and occasionally high school) students through the summer intern program. As of the end of 2014, 51 student interns have been mentored through the Gates Center, the majority of whom received paid positions through Gates Center donor funds. 18 students participated during the 2014 year.

One of the highlights of the 2014 year included the creation of the "Gates Center Summer Internship Program," made possible with a generous gift from Peter and Rhondda Grant. The goal of this selective program is to encourage outstanding undergraduates to consider careers in stem cell research in

an academic or industry setting by providing state-of-the-art training opportunities in stem cell research laboratories at the Gates Center.

In fall 2014, a committee of Gates Center faculty was formed to choose up to 14 highly qualified undergraduates to work full time for eleven weeks during the summer of 2015. Selected GSIP fellows will attend an orientation, biweekly lectures given by Gates Center faculty and a field trip to the Gates Biomanufacturing Facility. They will also present their work at the end of their internship at a poster or oral session.

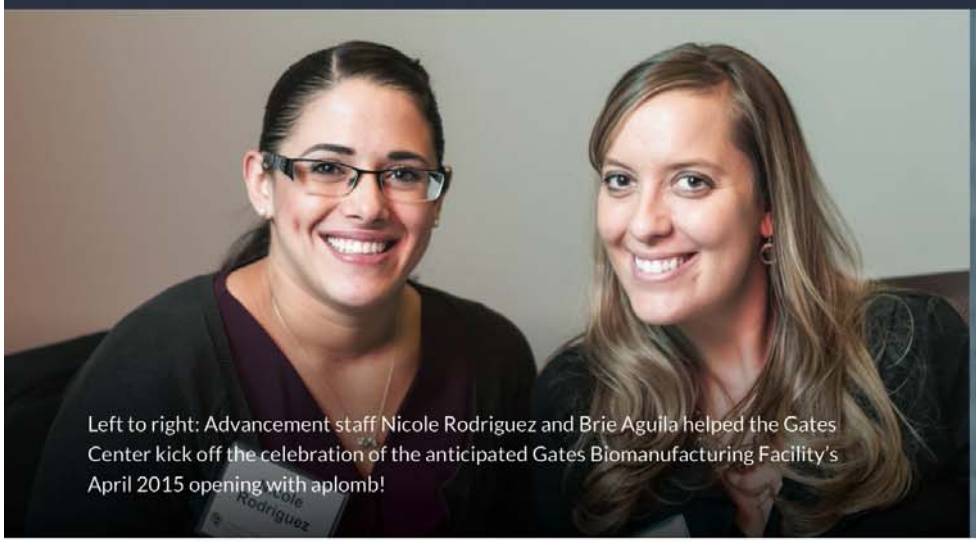
Another tremendous achievement of the 2014 year involved the formation of a Global Skin Diseases Research Consortium as part of the renewal application for our National Institute of Arthritis and Musculoskeletal and Skin Diseases - funded Skin Diseases Research Center, involving the following institutions:

- Columbia University Medical Center Skin Diseases Research Center, New York
- The Department of Dermatology, Keio University School of Medicine, Japan
- Dundee University Centre for Dermatology and Genetic Medicine, Scotland
- Collaborative Research Center, Department of Dermatology, University of Cologne, Germany
- Skin Research Institute of Singapore, A*STAR, Singapore

The consortium will sponsor a biannual summer school for PhD students and postdocs to rotate among the six institutions, the exchange of PhD students and postdocs to learn new techniques and approaches, and the promotion of collaborative projects between laboratories within the participating institutions. It was a great honor for the University of Colorado Anschutz Medical Campus to host the first biannual summer school from July 28-30, 2014, focused on stem cells.

The University of Colorado Anschutz Medical Campus hosted the Global Skin Diseases Research Consortium's first biannual summer school in July 2014, focused on stem cells.

OUTREACH



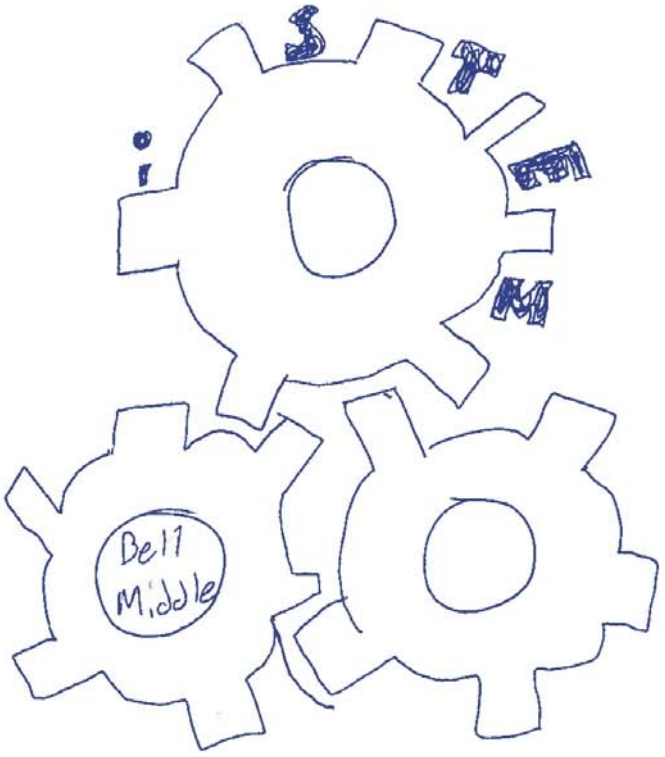
Left to right: Advancement staff Nicole Rodriguez and Brie Aguila helped the Gates Center kick off the celebration of the anticipated Gates Biomanufacturing Facility's April 2015 opening with aplomb!

We have striven to reach out to the community to share our mission and research, to make new friends and to garner support. Outreach efforts have included numerous onsite visits for individuals, groups, clubs, inquisitive and enthusiastic elementary and high school students, and elected officials, typically including presentations about the center and tours of our laboratory. During 2014, the Gates Center welcomed 258 visitors on campus during 17 events. We also hosted a "Cellular Cocktails" hard hat celebration in November 2014 to introduce people to the Gates Biomanufacturing Facility in anticipation of its opening in spring 2015.

Outreach efforts in 2014 included visits to individuals, schools, Eclectics, and the Conifer and Littleton Rotary Clubs (totaling 586 people) to provide presentations on stem cell biology and the Gates Center mission. As in previous years, we received invitations not just to address groups, but also to return with updated presentations to organizations such as Rotary Clubs that seem to faithfully monitor our progress.

Our new interactive website launched at the beginning of April 2015, and we added the Gates Biomanufacturing Facility to our Gates Center tour menu, as well. With these new tools, we expect to widen our promotional reach substantially.

We would like to thank those who have helped facilitate these opportunities, which have enabled us to introduce the center and our work to accelerate stem cell technology and regenerative medicine to improve peoples' lives. Sincere appreciation also goes to Eric Peterson in Washington, D.C., who, in addition to our university government-relations staff, has devoted many hours toward promoting the Gates Center and the promise of regenerative medicine with our elected officials and beyond.

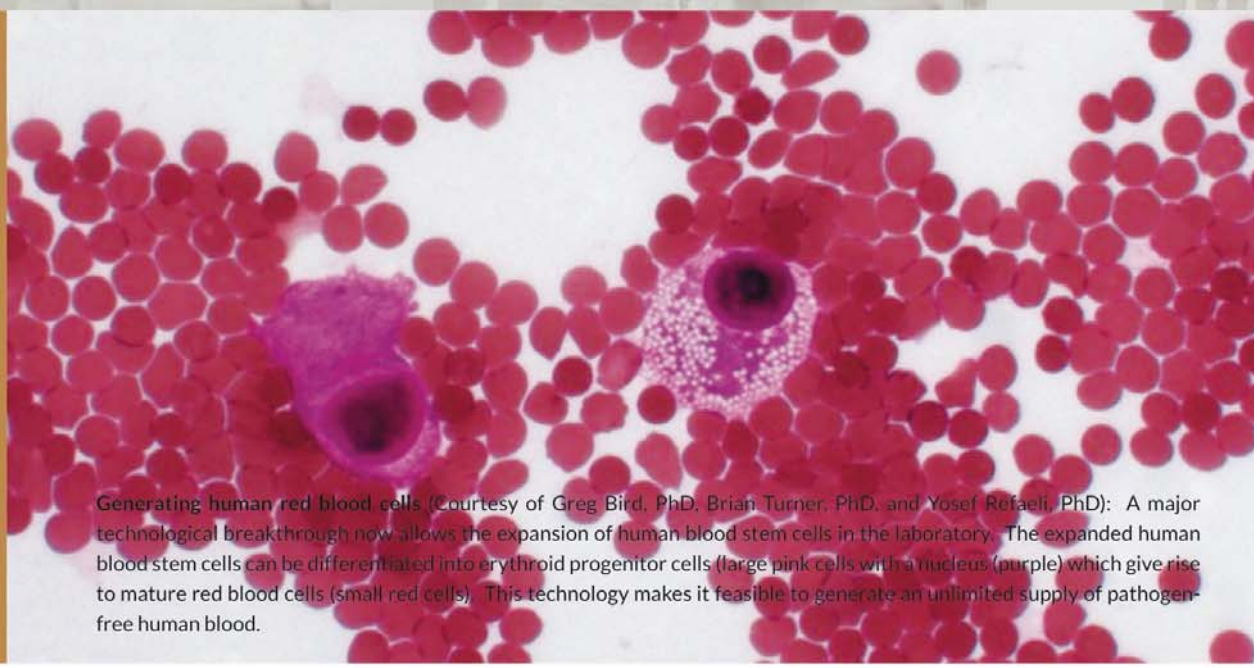


Thank you so much for letting us come visit. I learned a lot! I can't believe that cancer cells can last 20 years! Or that you can multiply cells to see more about them! Or that you can just freeze cells, then comeback. Or that you guys may one day cure cancer. It was so much fun. Maybe I will be working there one day. Who knows?

- Emily
ISTEM at Bell Middle School

Bell Middle School students visited the Gates Center in 2014 and looked to the future of stem cell research.

NEW FACES AT THE GATES CENTER



Generating human red blood cells (Courtesy of Greg Bird, PhD, Brian Turner, PhD, and Yosef Refaeli, PhD): A major technological breakthrough now allows the expansion of human blood stem cells in the laboratory. The expanded human blood stem cells can be differentiated into erythroid progenitor cells (large pink cells with a nucleus (purple) which give rise to mature red blood cells (small red cells). This technology makes it feasible to generate an unlimited supply of pathogen-free human blood.

The Gates Center is committed to doing everything possible to accelerate scientific discovery in stem cell research into new areas of treatment, and that includes helping attract a critical mass of scientists with complementary scientific expertise, as well as skilled professionals and community leadership to collaborate in translating laboratory research to clinical and commercial use. During the 2014 year, the Gates Center welcomed the following individuals to its team:

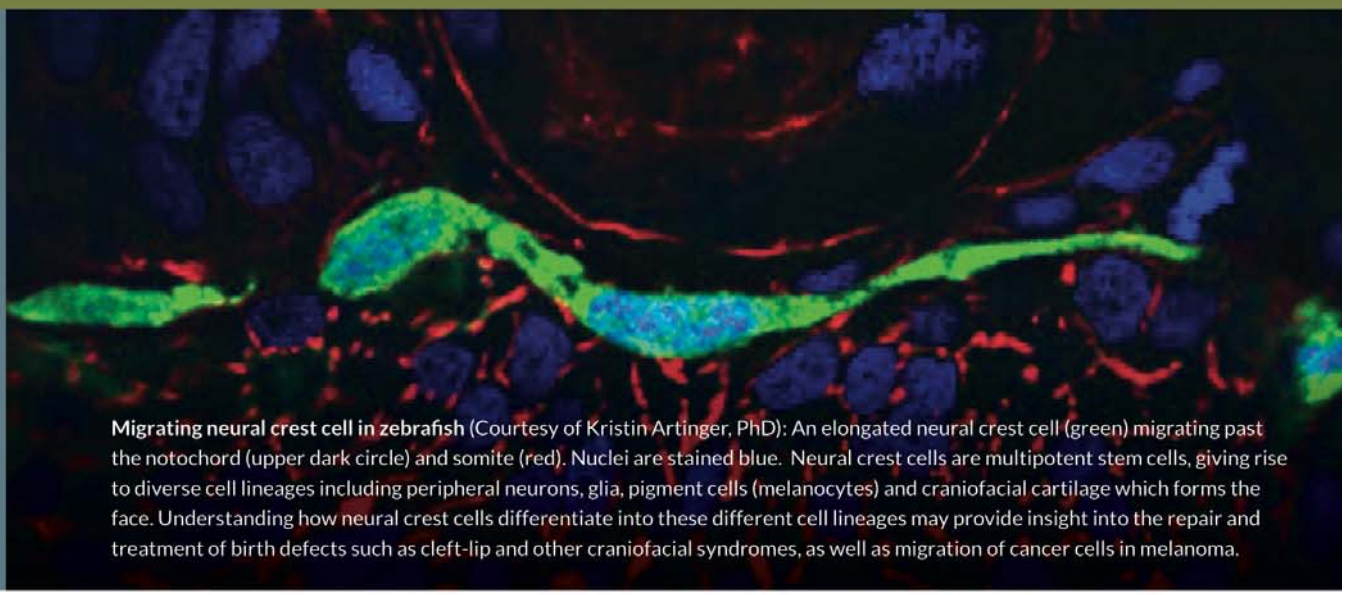
Janelle Blessing: Janelle Blessing, who grew up in Littleton and graduated from Fort Lewis College, joined the Gates Center Community Advisory Board in fall 2014. A strong advocate of conservation, she performed field research for Fort Lewis College and Oak Ridge National Laboratory for three summers during college, assessing the effects of the Yellowstone fires of 1989. Janelle's diverse interests and capabilities have also led her into the fields of medicine and finance, respectively, as a registered nurse at Swedish Medical Center and Boulder Community Hospital and then as a financial planner. She has served on the boards of the Family Learning Center and Pikes Peak Community Foundation,

and is active with the Denver Botanic Gardens and the Denver Art Museum. Currently, Janelle also serves on the Colorado board of trustees for The Nature Conservancy. Janelle enjoys traveling, biking and skiing and has found a special niche in endurance competitions, having participated in two Ironmans, the Leadville Trail 100 Mountain Bike Race and the New York City marathon, among others. Janelle and her husband, Buck, live in Denver with their two young daughters.

Elizabeth "Liz" Kelly: In October 2014, Liz Kelly joined the Gates Center as research administrative manager. Completing her bachelor's and master's degrees in anthropology at the University of Tennessee and the University of Cincinnati respectively, Liz began her career in academia at the University of Cincinnati, where she worked for 13 years with the College Conservatory of Music's Preparatory Department program, the controller's office on the medical campus and the central grants office. She was then named a grant specialist in the department of molecular genetics, where she supported 25 principal investigators and ended up running the department. Following a move to Colorado, Liz joined the University of Colorado Department of Pediatrics and spent three years overseeing grant applications and post-award activities for 54 investigators.

Charles "Charlie" Wall: Charlie Wall arrived in September 2014 to fill the position of lab manager for the Gates Center, bringing 26 years of experience working in academic and private science and a broad array of life experiences to share. Charlie attended the University of Colorado Boulder, graduating with a bachelor's degree in molecular, cellular and developmental biology. After several years of working in biotech in Los Angeles, Charlie returned to Denver and moved professionally back and forth between the University of Colorado Health Sciences Center and National Jewish Health. Working at National Jewish Health in Gordon Keller's lab focusing on mouse embryonic stem cells and hematopoiesis, Charlie got in on the ground floor of stem cell research. Having worked since 2004 with Uwe Staerz, PhD, CSO, as a research associate and scientist at Greffex Inc. in the Fitzsimons BioScience Park Center, Charlie is thrilled now to be in the position to support the science going on in the Gates Center labs and to see all that is being done to translate this work into human therapies. He simply wonders what else will revolutionize this world and revels in the promise of all the young people with whom he now has the pleasure to work.

FINANCIAL OVERVIEW



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

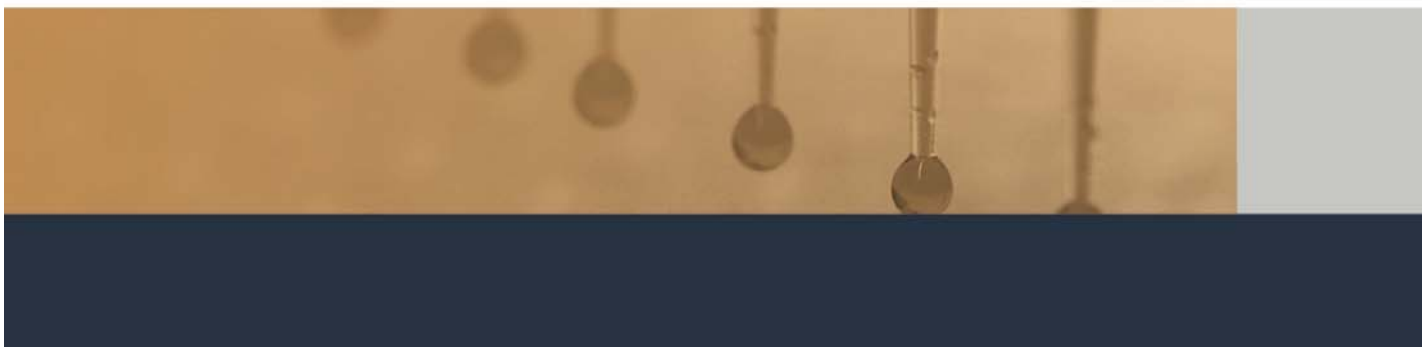
The research done by Gates Center members is funded directly through federal and state research grants, private foundation grants, philanthropic gifts for research and Gates Center research support.

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 below).

The Gates Biomanufacturing Facility's funding comes from a combination of the five-year operating fund commitments made by its partners (see page 23) and fee-for-service from CU researchers and outside companies.

GRANTS

As of December 31, 2014, Gates Center members had received a total of over $118 million in research grant funding, 76% of which was from the National Institutes of Health. The balance was from the Department of Defense, Veterans Affairs Administration, American Cancer Society, the Dermatology Foundation, partnering hospitals and others. In 2014, individual Gates Center members were awarded over $23 million in new funding detailed in the table on page 15. As the graph above shows, 2014 awards increased over prior years, which can be misleading because most awards received are paid out over a three to five-year period. Due to cuts in overall federal spending, the Gates Center remains genuinely concerned about prospects for the renewal of these grants at the end of three to five years and will continue to seek research funding alternatives that will 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 described in the "Grants" section above 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 2014, the Gates Center was the grateful beneficiary of $9,839,728 in philanthropic support from donors listed under our "Acknowledgements" section on page 39. These funds provided critical support for the renovation and equipping of the Gates Biomanufacturing Facility, and helped generate new and expanded research in the areas of macular degeneration, cancer stem cell therapies, development of more effective drug screening models and scholarships for the Gates Center's summer internship program. We also received support for the Director's Discovery and Translation Fund, which enables the Gates Center to provide bridge funding to move promising research closer to clinical trials at the Gates Biomanufacturing Facility.

GATES CENTER OPERATIONS

In 2011, the Gates Center received commitments from the Gates Frontiers Fund and the University of Colorado Foundation in the amount of $5 million each to be paid over a period of five years. This $2 million per year of annual funding has covered the Gates Center's operations, but is scheduled to end in December 2015. At the encouragement of both the Gates Frontiers Fund and CU Foundation, the Gates Center had initial discussions regarding renewing these grants for another five years. A second five-year grant for $12 million was approved subsequent to year end.

Consistent with its mission of providing core equipment and services to its members, along with research funding, fundraising assistance and commercialization support, the center's top expense categories in 2014 were Salaries $951,000 (50%), Core

Operations and Equipment $400,000 (21%), and Program and Research Support $360,000 (19%). The balance of expenses totaling 10% includes Education, Enrichment, General Operations and Marketing and Development.

As of December 30, 2014, the center's combined fund balance was $450,000. This amount was sufficient to cover anticipated expenses through 2015 when combined with the final grant payments from the Gates Frontiers Fund and CU Foundation during this period.

GOING FORWARD

- Federal grant funding is becoming increasingly scarce and competitive, so in the future, we will be more reliant on philanthropic contributions and early stage investments to fund Gates Center member research.
- We have an excellent track record of matching donors with research requirements, and we will continue to broaden our donor network.
- The Gates Center has relied on the Gates Frontiers Fund and the CU Foundation for operating support and will do so through 2020. From 2020 and beyond, we will have to find recurring revenues and other sources of funding to support our operations.
- One of the key services we provide our members is access to the state-of-the-art equipment contained in our core facilities. We need to continually enhance and upgrade this equipment.

	2011	2012	2013	2014
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
Fund to cover equity fund expenses			$150,000	$ -
Infrastructure and Operations Grants	$2,000,000	$2,000,000	$2,150,000	$2,003,100
Expenditures				
Center Salary and Benefits Total	$946,037	$733,242	$1,024,952	$951,031
Center Equipment Total	$134,719	$414,055	$157,500	$188,204
Center Maintenance/Supplies Total	$44,643	$68,452	$53,00	$34,243
Center Enrichment Total	$24,665	$26,165	$28,000	$53,198
Center Educational Activities Total	$20,580	$20,580	$23,500	$60,575
Marketing & Development Total	$2,257	$2,257	$102,500	$8,369
Center Core Facilities Total	$277,554	$160,000	$135,000	$212,411
Center Program Support Total	$42,000	$442,000	$470,833	$359,847
Center Consulting Fees Total	$ -	$ -	$225,200	$18,027
Center Patent Filing Fees Total	$ -	$ -	$30,000	$ -
Total Expenditures	$1,492,455	$1,866,751	$2,250,485	$1,885,907
Sources - Expenditures	$507,545	$133,249	$(100,485)	$117,193
Fund Balance	$115,169	$248,418	$60,138	$449,577

ACKNOWLEDGEMENTS

Gates Advisory Board members, guests and staff: (BACK ROW, left to right) Scott Arthur, Ann Sperling, Dori Biester, Janelle Blessing, Jill Cowperthwaite, Rick Stoddard, Allison Krebs, Kevin Reidy, Patrick Gaines, Xiao-Jing Wang, Tim Gardner (FRONT ROW, left to right) Dennis Roop, Diane Gates Wallach, Dan Ritchie, Don Elliman

The Gates Center gratefully acknowledges the following individuals, companies and organizations for supporting our research and mission through their generous gifts of time, treasure and talent during the 2014 calendar year.

Donors to the Gates Biomanufacturing Facility listed below are also acknowledged on page 23.

GATES ADVISORY BOARD as of December 31, 2015

Diane Gates Wallach, *Co-Chair*
Dan Ritchie, *Co-Chair*
Don Elliman, *Co-Chair*
Dori Biester, PhD, FAAN
Janelle Blessing
William Hiatt, MD
Wayne Hutchens
Greg Provenzano
Kevin Reidy
Wagner Schorr, MD
Ann Sperling

DONORS

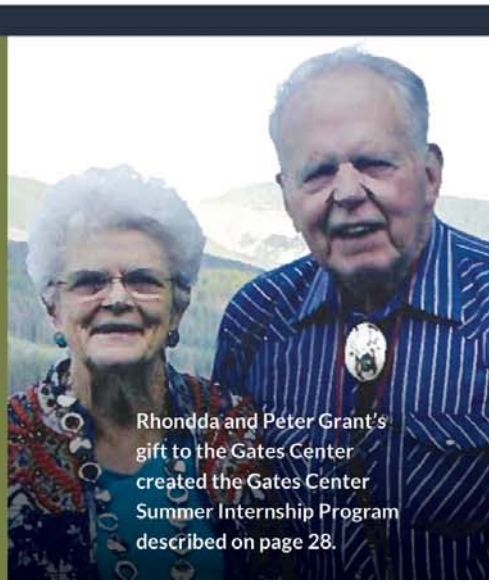
The William H. Anderson Foundation, Inc.
Arrow Electronics, Inc.
Balbi A. Brooks
Arnold and Darlene Brown
The Caulkins Family, in loving memory of George P. Caulkins, Jr.
Children's Hospital Colorado
Dennis and Beverly Christine
John and Margaret De Leon
Denver Eclectics LLC
E. Thomas Detmer Jr. and Marguerite Childs
Virginia Foote
Alexandra Gage
Timothy Nelson Gardner and Deborah Froeb
Gates Frontiers Fund
Mary J. Gearhart
Glendorn Foundation
Peter and Rhondda Grant
The Berenice Gates Hopper Family Fund
Monty and Frank Kugeler
LGA Family Foundation
Peter and Betsy Mangone
Daniel and Janet Mordecai Foundation
Richard Oglesby, MD, and Nancy Oglesby
Dennis M. O'Hanlon
Gordon and Pamela Parker
Thomas and Karin Payne
Daniel L. Ritchie
Walter S. Rosenberry III Charitable Trust
Timothy and Julie Rugg
Sanskriti Saxena
Mrs. Thomas Taplin
A. Sheffield Tulp

VOLUNTEERS

The Bawmann Group
Tee Cowperthwaite
Peter and Rhondda Grant
Joy Godesiabois Mathews
Kathy Barrett Lee
Eric Peterson
Ann Benson Reidy
Susan Bonsall Rosenberry
Jerry Winterrowd
Marty Williams
Sandra Walton
Joe Wood

To learn more about how you can play a role in accelerating research through private gifts, please contact Allison Krebs at 303-724-6342 or Allison.Krebs@ucdenver.edu

left to right: John Warner, Missy Dorn Warner, Warren Stewart, Brooks Stewart. As trustees of the Glendorn Foundation, Missy and Brooks worked with the Gates Center to help facilitate a grant toward the Ocular Stem Cell Program and its work on age-related macular degeneration research.



Rhondda and Peter Grant's gift to the Gates Center created the Gates Center Summer Internship Program described on page 28.

CONTACT US

Dennis R. Roop, PhD, *Director*
303-724-3050

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
Patrick.Gaines@ucdenver.edu

Tim Gardner, MBA, *Chief Financial Officer*
303-884-9056
Timothy.Gardner@ucdenver.edu

For inquiries about the Gates Biomanufacturing Facility, please contact Patrick Gaines or Tim Gardner.

School of Medicine
UNIVERSITY OF COLORADO
ANSCHUTZ MEDICAL CAMPUS

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