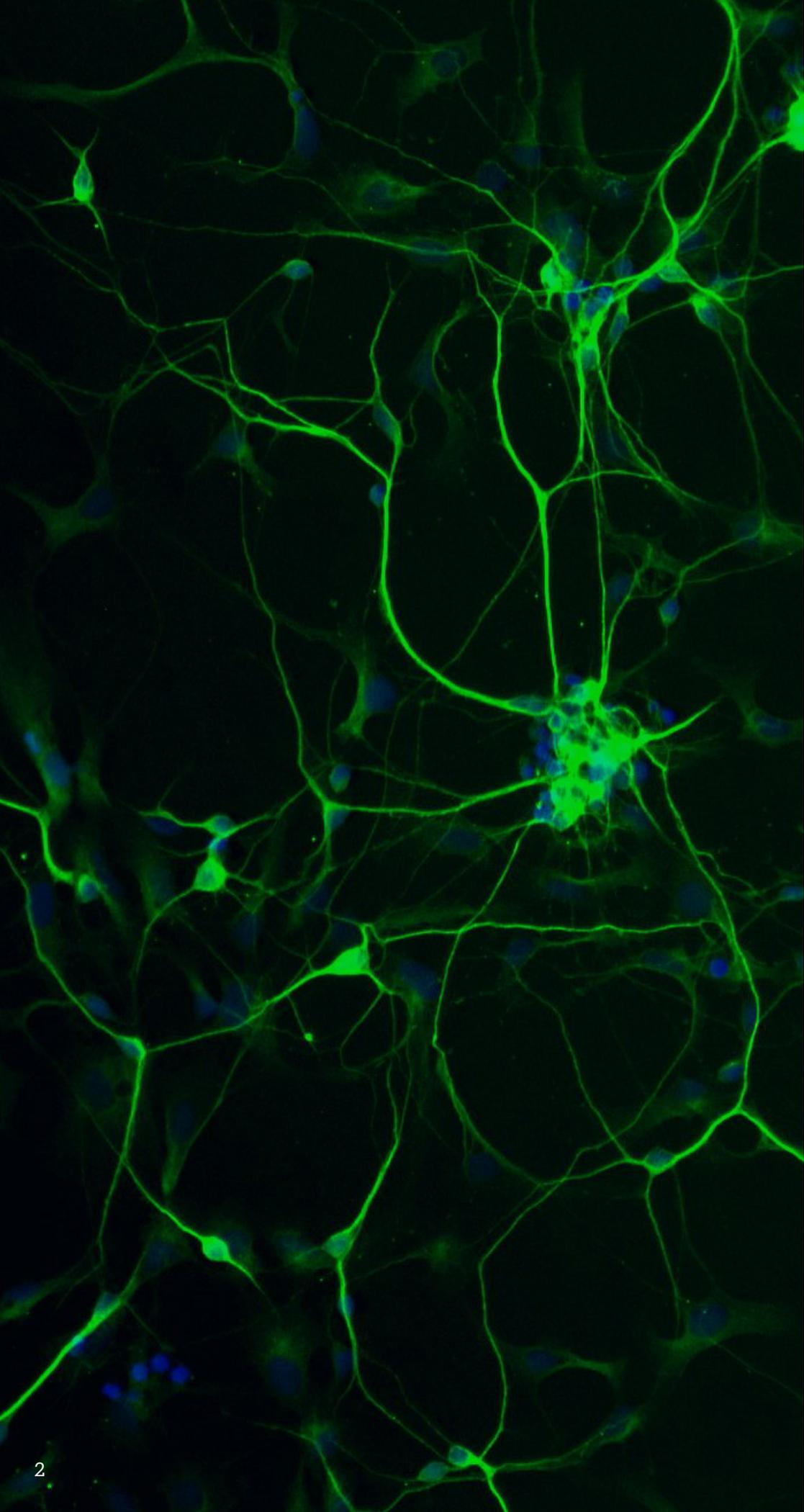


WE FUEL INNOVATION AND SAVE LIVES

UCSF's Program for Breakthrough
Biomedical Research (PBBR)

Leading the way from curiosity to cures





**TRANSFORMATIVE BASIC
SCIENCE BREAKTHROUGHS
BEGIN WITH PBBR**

PBBR: SUPPORTING INVESTIGATIONS THAT CHALLENGE CONVENTIONAL WISDOM

UCSF scientists lead the global armada fighting human disease – commanding the charge behind many of the greatest biomedical victories the world has ever witnessed.

In one decade alone, three of our boldest young faculty members pursued provocative ideas that ultimately earned each of them the Nobel Prize, while a fourth member laid the groundwork for what would become Genentech, Inc., an international leader in drug development.

Today, no other program in the world supports these kinds of brilliant scientists like UCSF's Program for Breakthrough Biomedical Research (PBBR). A beacon for the most courageous among our investigators, PBBR

provides funding for only those ideas that challenge conventional wisdom and could never qualify for funding from increasingly conservative grant sources like the National Institutes of Health (NIH). This unique program dares our scientists to dig deeper, ask tougher questions, and invent novel approaches that defy the status quo.

At UCSF, our investigators stand ready to change the health care conversation from "There's nothing we can do" to "We have answers." Yet they face a mounting, multifaceted funding crisis, with a rapidly evaporating fiscal wellspring from the NIH and other grant sources.

PBBR alone provides the fiscal struts to support these scientists as they build their extraordinary bridges to discovery.

Now more than ever, PBBR requires the partnership of sophisticated investors who understand that in risk, there can be transformative, lifesaving rewards.

"The Program for Breakthrough Biomedical Research benefits our bold scientists who are willing to step outside of their comfort zones. It drives innovation and encourages projects for which results may be less predictable but hold extra promise for discovery. I cannot speak highly enough of the program and its achievements, which allow the best and the brightest to go further with their research, take bigger risks, and explore new scientific frontiers."

UCSF Chancellor Sam Hawgood
Arthur and Toni Rembe Rock Distinguished Professor

WE VISUALIZE DARING IDEAS WE GIVE RAPID FUNDING WE GET REVOLUTIONARY RESULTS

Backed by PBBR, UCSF's researchers are limited only by their imaginations.

HIGH-RISK, HIGH-REWARD TRANSFORMATIVE CHANGE

"Play it safe." These words of "advice" are given all too often to young investigators who are encouraged to stay well inside the established scientific boundaries in order to appear a safe bet to ever more conservative funders. Wary of the career threats posed by stepping outside the norm, most budding scientists are encouraged to shy away from posing the bold, unorthodox questions that originate outside the box but may lead to revolutionary advances. PBBR enables the best and the brightest to become the exceptions to these constraints on transformative change.

Twenty years ago, PBBR turned the traditional funding model on its head and never looked back. Though the majority of other grant programs require lengthy applications and multiple revisions, PBBR applications are no longer than two pages. And while most funding decisions can take at least a year to come in, PBBR decisions are made within 30 days.

We're not your run-of-the-mill funders

In a departure from traditional funders that favor conservative proposals led by well-established investigators with demonstrated success, the PBBR faculty selection committee chooses only those startup ideas that challenge generally accepted theories and have potential for transformational effects. Thus, PBBR's relatively modest grants reap rich rewards: Many of the nascent, low-budget projects have off-the-charts return on investment.

We build the momentum

Funded primarily by private philanthropy, PBBR represents a mere 0.5 percent of UCSF's overall research budget, but the

program has unrivaled leverage. Why? Because hundreds of faculty members have used PBBR grants to turn their unconventional ideas into exciting projects that later successfully compete for grants from the NIH and other major funding sources – opening the doors to improving treatments and developing cures for real people with real diseases.

We guarantee you'll see double

The Sandler Foundation doubles the impact of every gift to the program by matching current-use gifts to PBBR.

Now in its 21st year, PBBR's projects have generated over 3,000 peer-reviewed scientific publications, almost 90 patents, and more than 300 NIH research grants. Astoundingly, PBBR award winners have made discoveries that produced more than \$1.4 billion in subsequent follow-on funding and an additional \$347 million in indirect costs coverage for the campus.

THE HUMAN BENEFITS DERIVED FROM BASIC SCIENCE RESEARCH GRANTS

The chart below includes a small sample of the many basic science breakthroughs by UCSF faculty members that have transformed the world's understanding and treatment of human disease.



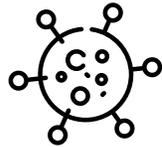
Recombinant DNA technology

Created the biotechnology industry, leading to the invention of new drugs for heart disease, cancer, diabetes, asthma, arthritis, and more



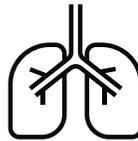
The first oncogene, traced to its origin in animals

Transformed cancer therapy by revealing the genetic basis of cancer and myriad targets for lifesaving drugs



The prion

Revealed a new, unsuspected mechanism for the cause and spread of brain diseases, including Alzheimer's and Parkinson's



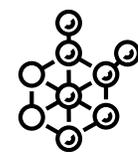
The role of pulmonary surfactant

Confirmed that synthetic surfactants can rescue premature newborns from lethal respiratory distress



The telomerase enzyme

Identified associations between telomere length and diseases of the heart, cancer, and diabetes, plus aging and longevity



Cell engineering technology

Shaped a new, innovative field of safer, more effective live cell therapies using molecular programming and engineering



PROFILES IN SCIENCE

Programming cells to cure disease

A mechanical engineer by training, **Hana El-Samad, PhD**, was drawn to explore biology at UCSF by the bold, risk-taking philosophy fueled by PBBR funding. Support from the program allowed her to apply her engineering background to understand how cells communicate and correct for disturbances. El-Samad's work has revolutionary implications for medicine, demonstrating that our own cells might one day be reprogrammed to deliver smart drugs.

Innovating new autoimmune treatments

Alex Marson, MD, PhD, received support from PBBR to develop a gene-editing tool for engineering cells to boost targeted immune responses. He also helped develop

a genomic algorithm to predict the risk of developing Alzheimer's disease, type 1 diabetes, and multiple sclerosis. Marson's work has expanded scientists' understanding of autoimmune disorders and advanced novel cell and gene therapies for treating them.

Increasing health span and rejuvenating the brain

With early support from PBBR, **Saul Villeda, PhD**, has led groundbreaking studies into slowing and reversing the symptoms of aging – including neurodegeneration and cognitive dysfunction. Villeda has identified chemicals in blood that reverse age-related decline, examined the role of the immune system in the aging process, and investigated how to reduce cognitive dysfunction in the aging population.

“Building synthetic feedback control with modular architecture and predictable operation can be an immensely powerful biotechnology tool.”

Hana El-Samad, PhD
Sandler Fellow 2005-2008



“Gene-engineered human T cells hold great potential for the next generation of cell-based therapies for cancer, autoimmunity, and infectious diseases.”

Alex Marson, MD, PhD
Sandler Fellow 2010-2016



“We understand the molecular mechanisms that drive certain aspects of aging, and we can target them. We don’t think of the symptoms of aging as inevitable anymore.”

Saul Villeda, PhD
Sandler Fellow 2012-2016

CHAMPION INNOVATION: SUPPORT PBBR

We need visionary funders to support our visionary thinkers.

Unorthodox science is difficult to fund. That’s why we need you. You are reading this because you understand the crucial importance of giving unconventional ideas a place to grow. In their early stages, radical concepts that challenge the status quo may be dismissed as unproven, impractical, or impossible. We believe you know that breakthroughs begin when atypical ideas are given a chance to

flourish. History shows that some of the most counterintuitive ideas have had the biggest impact on science and medicine, transforming disciplines and creating entirely new fields of study.

Gifts at all levels fund innovative new stars.

Support the Program for Breakthrough Biomedical Research at UCSF.

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