



# We fuel innovation and save lives

UCSF's Program for Breakthrough  
Biomedical Research (PBBR)

Leading the way from curiosity to cures



University of California  
San Francisco

Transformative  
basic science  
breakthroughs  
begin with  
PBBR

# PBBR: Lighting the world's way to transformative basic science breakthroughs

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 is providing the fiscal struts to support these scientists as they build their extraordinary bridges to discovery.

*"The Program for Breakthrough Biomedical Research benefits our bold scientists who are willing to step outside of their comfort zone. 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



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

We visualize  
daring ideas

We give  
rapid funding

We get  
revolutionary  
results

# Daring ideas, rapid funding, revolutionary results

“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 threaten the conventional wisdom but may lead to revolutionary advances. PBBR enables the best and the brightest to become the exceptions to these constraints on transformative change.

## Backed by PBBR, UCSF’s researchers are limited only by their imaginations

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 who favor conservative proposals led by well-established investigators with demonstrated success, the PBBR faculty selection

committee chooses only those startup ideas that challenge conventional wisdom 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% 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.

To date, PBBR projects have generated more than 1,500 scientific publications, at least 60 patents, and over \$1 billion in subsequent funding for its PIs. Also, PBBR has produced more than \$200 million to support UCSF research through indirect cost recovery, and the program has led to some 300 NIH awards.

## 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.

Basic Science Breakthrough	Transformative Impact on 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.

# Profiles in courage



***“PBBR allowed me to connect a core basic science question to a clinical dilemma.” — David Rowitch, MD, PhD***

## **Replacing myelin in a first-ever clinical trial**

A neonatologist, scientist, and former PBBR grantee, UCSF's David Rowitch is among a handful of doctors around the world using stem cells to treat devastating diseases in newborns and young children. In 2006, Dr. Rowitch received a grant from PBBR to explore a fundamental idea: He believed that the central nervous system development and neurological diseases shared common mechanisms.

Building on his background in developmental biology, this basic research helped lay the foundation for the world's first clinical trial of neural stem cells to treat Pelizaeus-Merzbacher disease (PMD), a condition caused by a defective X-linked gene that leads to insufficient myelin in the brain. Children with PMD are unable to walk, talk, eat, or breathe normally, and those with severe PMD progressively deteriorate until death at 10 to 15 years of age. Not only did the clinical trial show signs of myelin production in the brains of children with PMD, it also gave hope to the millions of patients around the world who suffer from multiple sclerosis, cerebral palsy, and other myelination disorders. Says Dr. Rowitch, “Some of the world's most devastating neurological diseases have a chance at a cure, thanks in large part to PBBR.”



***“Venturing into the hypothalamus was considered by some to be scientific suicide.” — Holly Ingraham, PhD***

## **Altering behavior through a single gene**

Cellular and molecular physiologist Holly Ingraham recalls both excitement and apprehension: She was preparing her application for a PBBR grant to begin asking how the hypothalamus and neuroendocrine system affected how we eat, defend ourselves, and reproduce. She remembers asking herself, “How would I be competitive for NIH funding when their peer-review system is inherently averse to risk-taking? How would I attract trainees to work in this area? And how would I get money to generate preliminary data so that we might begin publishing in this area?”

These are common concerns for investigators at the beginning of their careers because most traditional funding sources reward incremental steps instead of bold leaps. A PBBR grant allowed Dr. Ingraham to take the plunge into uncharted territory and follow her instincts. She has now published extensively in this area, presented on the topic at a National Society of Neuroscience symposium, and earned a major grant where it was suggested that her results were potentially transformative. Today, a handful of labs, including Dr. Ingraham's, are fully committed to understanding how neuroendocrine circuits develop and control behavior. The latest results suggest that we can dramatically change behavior, such as decreasing anxiety and increasing exploratory behavior, by eliminating just one gene from one hypothalamic region. “In the end, PBBR was essential to getting my lab headed down the right path,” Dr. Ingraham notes.



***“An infusion of money at the right time, at the right place, for the right thing, can have a dramatic effect.” — Joe DeRisi, PhD***

## **Detecting any virus in existence**

The global impact of UCSF microbiologist and PBBR grantee Joe DeRisi's ViroChip is measured in what *hasn't* happened. The device holds DNA samples of every known virus on the planet (currently 22,000). Within minutes, the ViroChip can detect any virus — like severe acute respiratory syndrome (SARS), which Dr. DeRisi helped the U.S. Centers for Disease Control and Prevention identify in 2003 — leading to its isolation and containment, and potentially preventing a pandemic.

Since SARS, several new viruses have been identified by the ViroChip, including some associated with diseases like gastroenteritis and severe respiratory disease, two of the biggest killers of children under five years of age. Dr. DeRisi believes the technology will be a lens to a whole new viral frontier. “PBBR provides an indispensable spark that ignites new ideas,” he says.

# Champion innovation: Support PBBR

## **We need visionary funders to support our visionary thinkers**

Visionary thinking is difficult to fund. That's why we need you. You are reading this because we believe you understand the crucial importance of giving an unconventional idea a place to grow. In their early stages, radical ideas that challenge the status quo may be dismissed as unproven, impractical, or impossible. We believe you know that giving atypical ideas a chance to flourish is the path to breakthroughs. You know that history shows some of the most counterintuitive ideas have had the biggest overall impact on science and medicine, transforming disciplines and creating entire new fields of study.

We strive to offer a unique array of awards to meet the broad aspirations of our fearless donors and the expansive needs of UCSF's visionary thinkers.

Priority funding areas include:

### **Biomedical Discovery Fund**

Named for the donor and existing in perpetuity, these endowment funds support innovative basic science projects at UCSF through the PBBR program.

### **New Frontiers Research**

These awards sponsor research projects at levels of risk and innovation that substantially exceed those supported by the NIH.

### **Technologies, Methodologies, and Cores**

These awards emphasize invention and development of new, shared resources for the scientific community, at UCSF and beyond.

### **Emerging Talent**

PBBR supports two initiatives for young scientists:

- **Postdoctorate Independent Research Program**

Knowing that many of the next generation's scientific leaders reside in UCSF's postdoc community, PBBR supports independent-minded young researchers who want to explore an innovative project outside the constraints of their home laboratory.

- **Sandler Fellows Program**

This novel initiative provides funding for a small cohort of MDs or PhDs, for whom a period of independence – free of the limitations of a postdoctoral traineeship and the demands of assistant professorship – would give full voice to their extraordinary creativity.

Support the Program for Breakthrough Biomedical Research at UCSF.

For more information, please contact:

**Michael Faber**

michael.faber@ucsf.edu

415-476-2617



# PROGRAM FOR BREAKTHROUGH BIOMEDICAL RESEARCH

For more information on how you can support the Program for Breakthrough Biomedical Research at UCSF today, please contact:

**Michael Faber**  
michael.faber@ucsf.edu  
415-476-2617