



HARVARD
MEDICAL SCHOOL



Giovanni Armenise-Harvard Foundation Dean's Basic Science Grant

Benefactor Report
October 2025



GIOVANNI ARMENISE- HARVARD FOUNDATION FOR SCIENTIFIC RESEARCH

Philanthropic support is essential to advancing innovative research at Harvard Medical School. The Giovanni Armenise-Harvard Foundation Dean's Basic Science Grant provides crucial resources for faculty scientists, enabling them to pursue a wide array of ambitious projects on the HMS Quad. Over the coming years and decades, this support will continue to be instrumental in driving groundbreaking discoveries and developing therapies that have the potential to transform patient care.

In a landscape marked by significant uncertainty—particularly regarding federal funding—support from the Giovanni Armenise-Harvard Foundation Dean's Basic Science Grant is more important than ever. It empowers pioneering scientists, including leaders such as Stuart Orkin, Arlene Sharpe, Gordon Freeman, David Corey, Bob Datta, and Isaac Chiu, to advance research into understudied questions, rare diseases, and bold early-stage concepts. Philanthropy not only encourages innovative exploration but also helps sustain later-stage, larger-scale projects that are vital for translating discoveries into real-world advances.

The research progress and achievements highlighted here are a testament to the impact of this generosity.

Research at Harvard Medical School

For more than 200 years, discoveries at Harvard Medical School have driven innovations in medicine and the life sciences, leading to groundbreaking treatments for a wide range of illnesses as well as new strategies to address health inequities and rising health care costs. Today, HMS's community spans 12,000 faculty members and 15 affiliated hospitals. HMS scientists unravel disease biology while clinical researchers advance patient care—all propelling medicine forward through collaboration and the relentless exchange of ideas.

The Orkin Laboratory



Stuart Orkin, MD '72

Stuart H. Orkin, MD '72, is the David G. Nathan Distinguished Professor of Pediatrics at Harvard Medical School and an HHMI Investigator at Boston Children's Hospital. Across decades of work, the Orkin lab has defined the molecular basis of human blood disorders and the mechanisms that govern blood cell development.

In December 2023, CASGEVY, a treatment for sickle cell disease and transfusion-dependent anemia, reached a milestone that began many years earlier in the Orkin lab. Sickle cell disease is the result of a mutation in the gene that makes hemoglobin, the protein in red blood cells that carries oxygen through the blood. Dr. Stuart Orkin and his colleagues determined that hemoglobin comes in two forms: a fetal form, which functions normally even in sickle cell patients, and an adult form, which the disease affects. Shortly after birth, the human body shuts down production of fetal hemoglobin, and sickle cell patients begin producing abnormal adult hemoglobin.

Dr. Orkin had the idea of switching the body's production of fetal hemoglobin back on in sickle cell disease patients. Working with one of his MD-PhD students, **Vijay Sankaran, MD '09, PhD '10** (now Jan Ellen Paradise, MD, Professor of Pediatrics at Harvard Medical School), patient samples from the National Institutes of Health, and a team in Sardinia, Italy, he identified the gene that suppresses production of fetal hemoglobin: BCL11A. Orkin's and Sankaran's 2008 paper in *Science*, "Human Fetal Hemoglobin Expression Is Regulated by the Developmental Stage-Specific Repressor BCL11A," inaugurated a new era of sickle cell disease research (<https://tinyurl.com/2008paper>).



Vijay Sankaran, MD '09, PhD '10

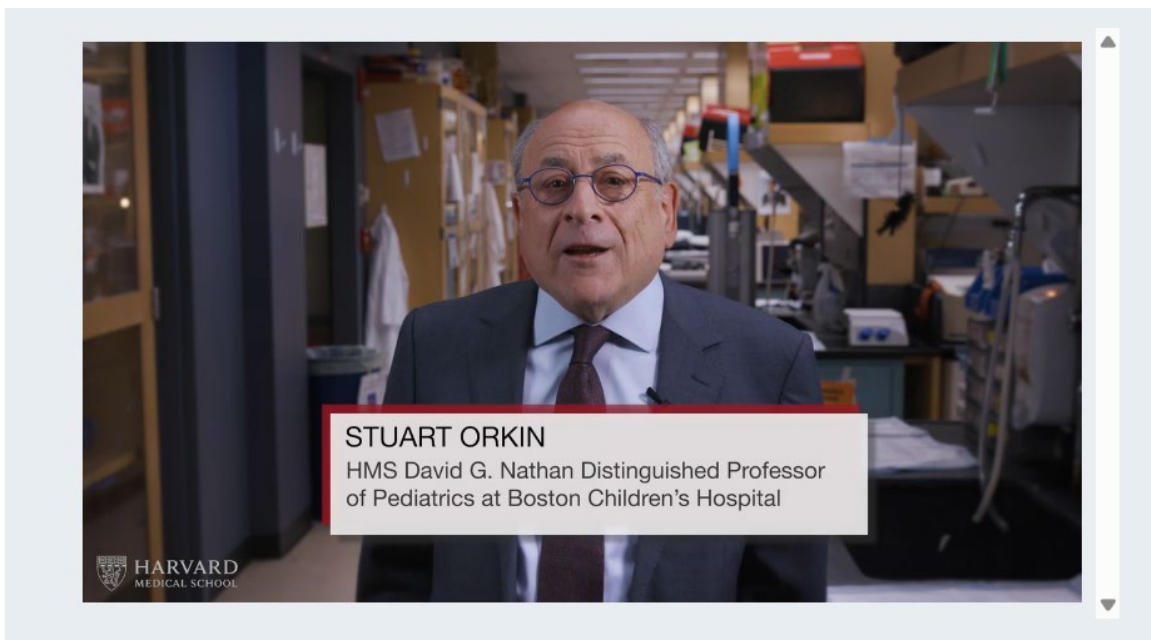


Daniel Bauer, MD, PhD

Five years after that breakthrough, another member of the Orkin lab, **Daniel Bauer, MD, PhD** (like Sankaran, now Donald S. Fredrickson, MD, Associate Professor of Pediatrics at Harvard Medical School), identified a DNA sequence in BCL11A that, when removed, drastically reduced the gene's activity. From there, the Orkin lab's discoveries moved toward clinical applications. David Altshuler, MD'94, PhD'94, had been another of Sankaran's professors; having moved full-time to Vertex Pharmaceuticals (where he is now chief scientific officer), he sought to capitalize on the Orkin lab's research. After another decade of work, Vertex made history with the launch of CASGEVY.



Video: The First CRISPR Medicine for Sickle Cell Disease: How a genetic insight paired with gene editing technology led to a life-changing new therapy



Watch here: <https://tinyurl.com/MakingMedEp1>

Arlene Sharpe, MD '82, PhD '81 and Gordon Freeman, PhD '79



Arlene Sharpe, MD'82, PhD'81, the Kolokotronis University Professor at Harvard University and chair of the Department of Immunology at Harvard Medical School, and **Gordon Freeman, PhD '79**, professor of medicine at Dana-Farber Cancer Institute and Harvard Medical School, have been married for 47 years. They have been scientific collaborators for just as long, dedicating their careers to investigating the immune system and teasing out the secrets that have made effective cancer immunotherapy possible.

Arlene Sharpe, MD'82, PhD'81
Gordon Freeman, PhD'79

In the early 2000s, Drs. Sharpe and Freeman, alongside other colleagues, discovered that some cancers eluded detection and destruction by the immune system by hijacking an immune pathway called PD-1/PD-L1. They found that by blocking either of the two molecules, PD-1 or PD-L1, or deleting the genetic instructions that lead the body to produce them, they could enhance T-cell immune activity against cancer. In animal models, they were able to restore the body's ability to find and fight tumors.

Ira Mellman, PhD, then vice president of cancer immunology at the biotechnology company Genentech, took up the task of designing anti-PD-1 and anti-PD-L1 therapies, using Dr. Sharpe's and Dr. Freeman's research, that could improve the human immune system's ability to resist cancer. Mellman's team led their candidate through clinical trials and eventually brought the drug, now known as Tecentriq, to FDA approval in the United States.

Today, similar drugs—immune checkpoint inhibitors—have greatly expanded and improved oncologists’ arsenals and changed the lives of enormous numbers of cancer patients. Before the widespread availability of such therapies, few patients survived metastatic melanoma for more than two years. In a recent long-term study following up on clinical trials, researchers found that half of patients with advanced melanoma who were treated with checkpoint inhibitors were still alive after 10 years.



Video: Medicines That Unleash the Immune System To Fight Cancer: The story behind the development of immune checkpoint inhibitors, fulfilling the promise of cancer immunotherapy



Watch here: <https://tinyurl.com/MakingMedEp2>

David Corey

The laboratory of **David Corey, PhD**, Bertarelli Professor of Translational Medical Science at Harvard Medical School, is developing strategies to treat hereditary deafness. The Corey lab focuses on common forms of hereditary deafness and two forms of Usher syndrome—a condition causing both deafness and blindness—as they work toward clinical treatments.

Dr. Corey has spent nearly 50 years studying how hair cells in the inner ear contribute to hearing and deafness. A decade ago, he realized that the tools and knowledge his lab had developed over the years finally had the potential to turn basic science into clinical cures for deafness—a goal he had never dreamed was possible.

NIH grants have fueled the Corey lab’s decades-long progress, pushing clinical treatments closer to reality. Dr. Corey warns, *“If the funding is cut back...there are going to be fewer cures, they’re going to take longer to get there—there just won’t be the medicines that there might have been otherwise.”*



David Corey, PhD

Sandeep Robert “Bob” Datta, MD '04, PhD '04



The laboratory of HMS neurobiology professor Sandeep **Robert “Bob” Datta, MD '04, PhD '04**, studies how the brain processes information related to smell, which for the mice neurobiologists work with is the most important of the five senses. He and his colleagues dissect the basic neural mechanisms that give order and structure to complex natural behaviors, and investigate how olfactory and motor systems influence each other to give animals a full account of the world around them.

Bob Datta, MD '04, PhD, '04

The Datta lab identified a heretofore-unknown class of odor receptor that had the strange characteristic of also being genetically implicated, when mutated, in decreasing the risk of Alzheimer’s disease. Having studied these receptors, the team determined how they work: the wild-type receptor “smells” inflammation and promotes the recruitment of T cells into the brain in the later stages of disease, accelerating neurodegeneration. The team is currently studying this phenomenon in a mouse model of Alzheimer’s. By knocking out or knocking down the relevant gene (i.e., stopping or decreasing its expression), Dr. Datta and his colleagues can completely prevent late-stage Alzheimer’s symptoms—even if the brain already contains extensive amyloid plaque.

In another project, Dr. Datta’s team used machine-learning methods for analyzing behavior to investigate how behavior evolves over an organism’s lifespan, and discovered that mouse behavior embodies an aging clock: With just 15 minutes of video of a mouse, researchers can tell how old that mouse is, give or take two weeks. By analyzing the behavior of a mouse any older than one year, they can accurately predict when it will die, even when this will occur more than a year later. This, Dr. Datta believes, shows that behavior is a key analytic for determining functional age—the discovery has important implications for the use of behavior as a metric for health.

Isaac Ming-Cheng Chiu, AB '02, PhD '09

Isaac Ming-Cheng Chiu, AB '02, PhD '09, is a professor of immunology at HMS. His lab focuses on the neuroimmune mechanisms underlying pain, host defense, and neurodegeneration.

Recent Chiu lab alumnus Dylan Neel’s PhD thesis work, “Gasdermin-E Mediates Mitochondrial Damage in Axons and Neurodegeneration,” formed the basis of some of the lab’s most promising recent work on neurodegenerative illness. Dr. Neel studied amyotrophic lateral sclerosis (ALS), better known as Lou Gehrig’s disease—an invariably fatal motor neuron disease that causes death in most patients within two to five years of diagnosis. His team found that, in the course of the disease, the protein Gasdermin-E starts an inflammatory cascade, opening pores in mitochondria and causing axon degeneration and ultimately neuron death.

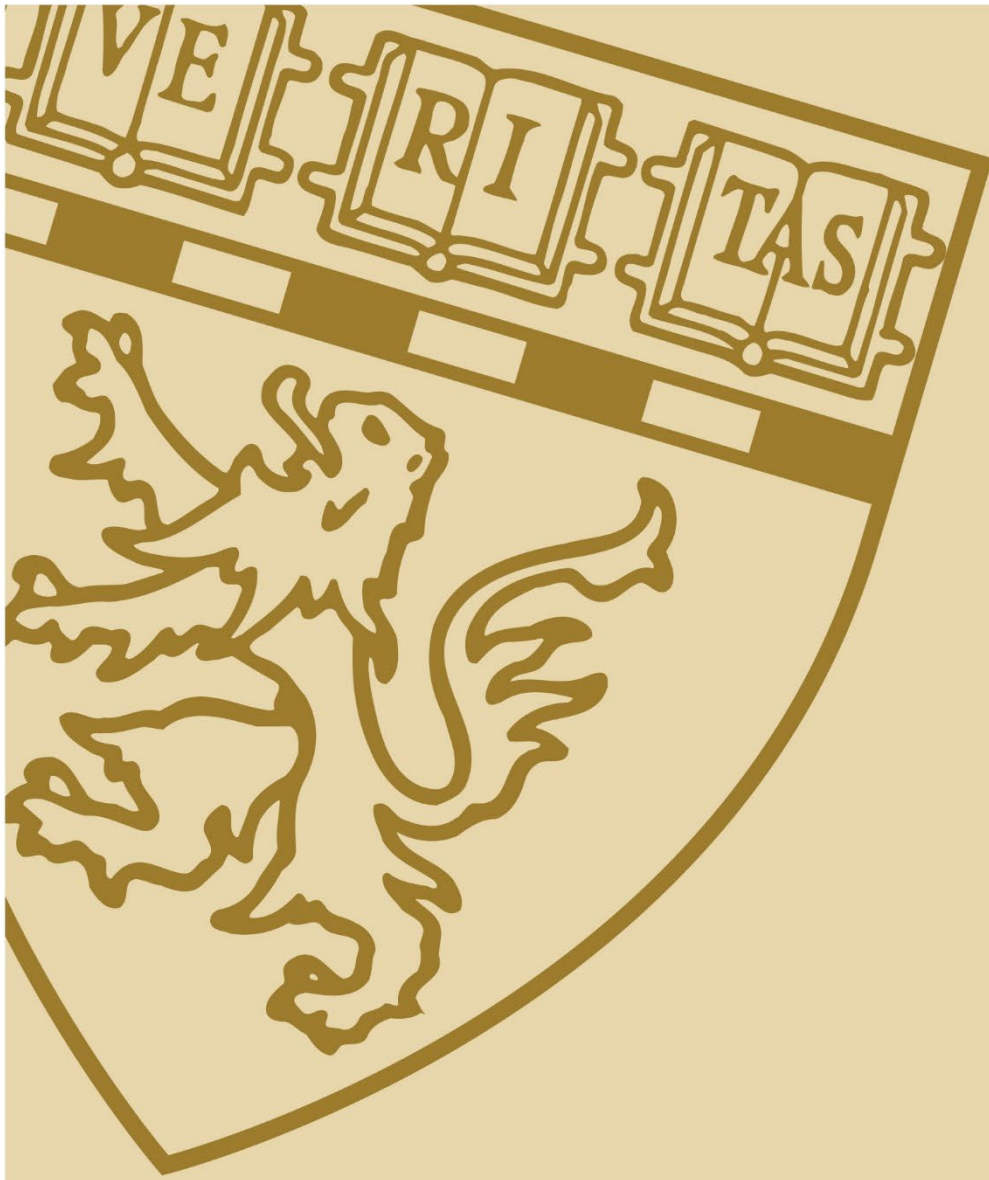
By genetically inhibiting Gasdermin-E production, Chiu lab researchers found that they could prevent axon loss in motor neurons derived from ALS patients and ameliorate disease in a mouse model of ALS. In the latter case, the mice lived longer and experienced less motor dysfunction, less motor neuron loss, and reduced neuroinflammation. The lab is presently working on new knockdown methods and studying Gasdermin-E’s role in both human stem cell and mouse



Isaac Chiu, AB '02, PhD, '09

models of Alzheimer's disease. Suppressing Gasdermin-E expression will hopefully prove relevant to the treatment of not just ALS and Alzheimer's, but cortical diseases, dementia, and many other neurodegenerative illnesses.

The Chiu lab also continues to study the links between pain, itch, and microbial infection, investigating the question of whether microbes contribute to chronic pain and looking at nociception in the skin. Their work with mouse models has been promising: when researchers treat mice with antibiotics, the animals experience less chronic pain. The team is looking into the mechanism behind chronic pain in Lyme disease and investigating how Botox—which blocks the body's local response to nerve signals—can treat infection. They also proved for the first time that *Staphylococcus aureus*, a bacterial pathogen associated with itchy skin diseases, secretes a protease that directly activates sensory neurons, driving itch and causing skin damage.



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