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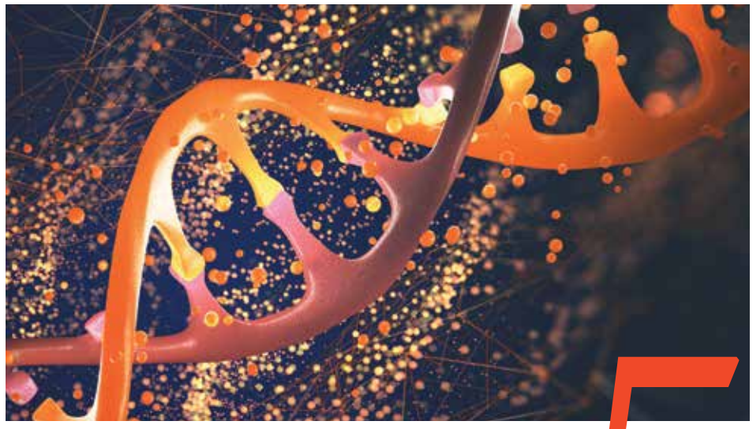

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Crossroads

With Dr. Richard Merkin

The unique perspective of Richard Merkin, M.D., as Innovation, Technology, Legislation and Care Delivery come together to impact the future of population health

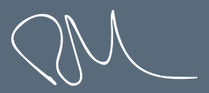
To Imagine What's Possible Is Our Motivation

For centuries early scientists and researchers have recorded their ideas, unique methods and countless attempts to create what they perceived to have been impossible at the time. Years later, advancements in modern science and technology provide the opportunity for breakthrough ideas to come to life and pave the way to cure diseases that scientists and scholars of old could only imagine possible.

We must continue to encourage and support ideas that push the limits and boundaries of what we know so that future generations can succeed in making today's incurable diseases a thing of the past.

In our two-part feature article, we spotlight the efforts and extraordinary research being done by scientists from the Innovative Genomic Institute at the University of California, Berkeley. Dr. Jennifer Doudna and her team at IGI are working diligently to find ways to administer and deliver safe methods to some of the world's incurable diseases. And in the process of doing so, also find a cure for sickle cell disease.

As we continue to strive for good health and well-being during an ongoing health crisis, I encourage everyone to get vaccinated and stay current on vaccines so that we can protect ourselves, our families and our community from potential exposure to new and more resistant variants. I want to thank everyone for their continued support and commitment to caring for and serving our various communities. I appreciate all of your efforts throughout the year and look forward to a healthy and promising new year.



Richard Merkin, M.D.
President and CEO of HPN

Richard Merkin, M.D.
Healthcare visionary Richard Merkin, M.D., has spent the last 40 years implementing a successful, workable business model to address the needs and challenges of affordable managed healthcare.

USE OF CRISPR GENOME EDITING TECHNOLOGY

AT INNOVATIVE GENOMICS INSTITUTE

USING CRISPR GENOME EDITING TECHNOLOGY FOR SAFER CURES AND SICKLE CELL DISEASE

AT UC BERKELEY'S INNOVATIVE GENOMICS INSTITUTE

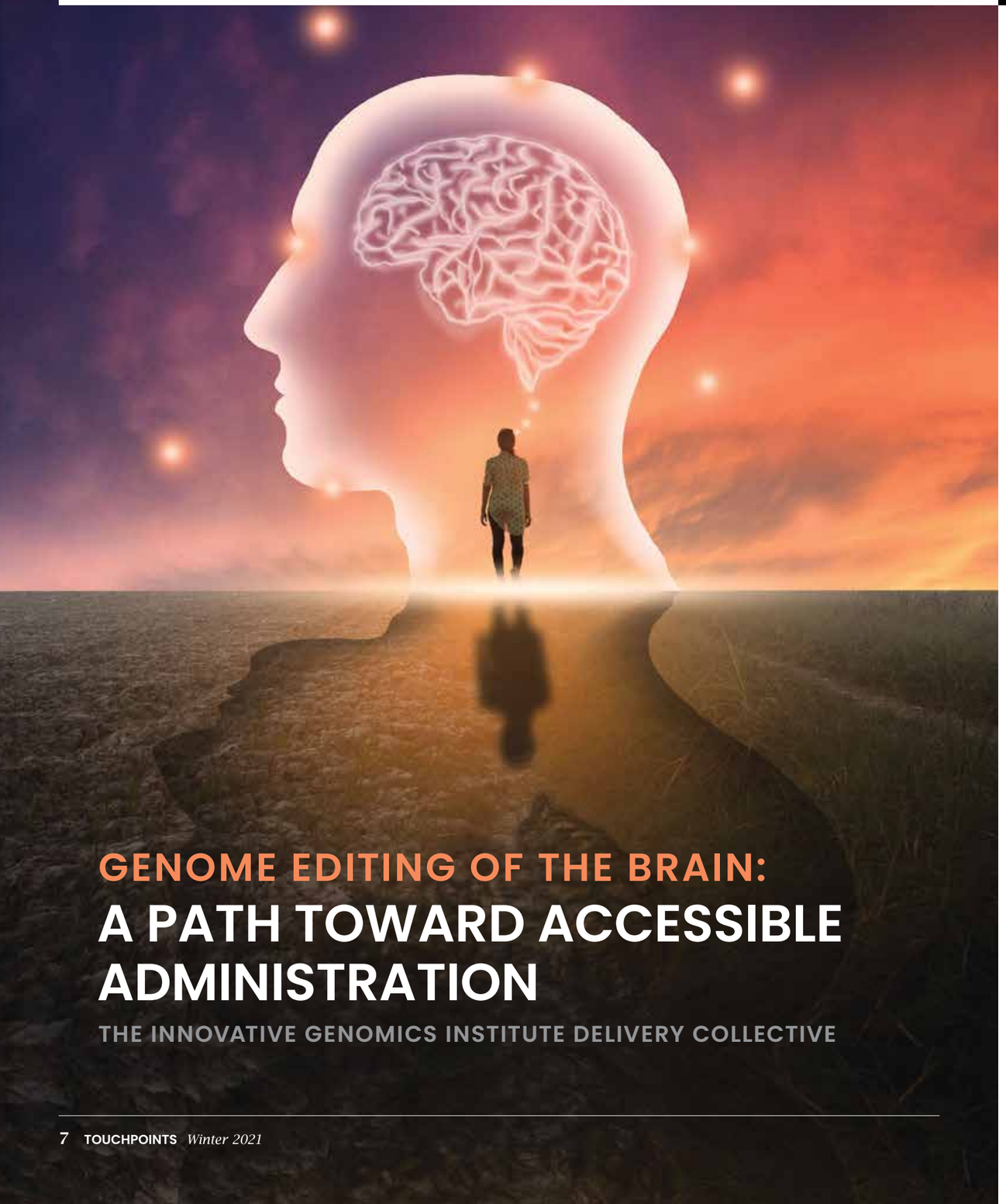
Some of the world's leading scientists working at the University of California, Berkeley have dedicated many years to push forward the boundaries of science and technology in their mission to find cures for some of the world's most complicated diseases.

Under the guidance of Jennifer Doudna, Ph.D., founder of Innovative Genomics Institute (IGI) and 2020 Nobel Prize winner in Chemistry, two separate IGI teams would tackle finding ways to safely administer therapeutics for some of the world's most incurable diseases, including sickle cell disease.

The IGI Delivery Collective team is trying to find a method to administer nontoxic genome editing enzymes into cells so that they're tailored to enter specific cell types that require repair. One option is to deliver CRISPR-derived genome editing enzyme Cas9 in the form of an RNA-protein (RNP) complex. This approach is ideal for use in the brain as Cas9 RNP can be diffused through brain tissue as seen in previous mouse models. This form of gene editing could potentially treat neurological diseases, such as Alzheimer's and Huntington's, as well as opioid addiction; all affecting millions of people each year. The availability of a gene editing delivery vehicle that is both safe and effective would have significant impact clinically, and on the many lives it could save.

Working closely with the IGI Delivery Collective team, the IGI CRISPR Cures team has its very own focus and strategy on finding a cure for sickle cell disease. While the use of CRISPR genome editing is an option, one of the greatest challenges still remain being able to apply direct-to-patient, or "in vivo" administration, along with other factors. To administer cures in this way comes with high risk, will require many technical resources and can be extremely expensive.

In our two-part feature article, IGI teams share the history of their research and the potential expected outcome and impact it will likely have if and when these cures become successful.



GENOME EDITING OF THE BRAIN: A PATH TOWARD ACCESSIBLE ADMINISTRATION

THE INNOVATIVE GENOMICS INSTITUTE DELIVERY COLLECTIVE

In our first in-depth Q&A session with the IGI Delivery Collective team, scientists share detailed insights into their techniques using therapeutic genome editing of the brain, how it is administered and the potential impact it will have on treating various neurological conditions.

Q: When did the initial research begin?

A: At the Innovative Genomics Institute, we have collectively been working on delivering genome editing enzymes for therapeutic purposes since 2014. Individual IGI investigators have been working on genome editing since its conception, and much of their research was foundational for establishing tremendous therapeutic potential and safety of genome editing.

Q: Can you elaborate on what is unique about these two engineered Cas9 RNP systems?

A: All current experimental genomic neurotherapeutics rely on viruses to deliver the therapeutic cargo, and this raises persistent concerns about undesired effects, such as insertion of the virus into the patient's DNA and immune system attack on the neurons. In key contrast, our approaches take a major step away from that and toward nonviral methods. Developing nonviral strategies for delivering genome editing enzymes has been challenging because it requires packaging them such that they can diffuse through brain tissue, then enter the neurons, and make their way into the nucleus where their target, the patient's DNA, resides. If successful, our experiments will demonstrate for the first time that nonviral genome editing in brain tissue without brain surgery is possible.

We are taking a stepwise approach to this extraordinarily ambitious, yet tractable, goal. The first strategy we are developing is focused on editing neurons after direct delivery to the brain. This method of delivery is highly effective, however the need for an intracranial injection is a limitation in some disease settings. The second strategy focuses on genetic correction of neurons after an intravenous injection. For the second strategy, we are working to develop genome editing enzymes that can cross the blood-brain barrier. This is not an easy challenge by any means, but the interdisciplinary team of experts we have assembled at the IGI has a track record of solving difficult problems through innovation.

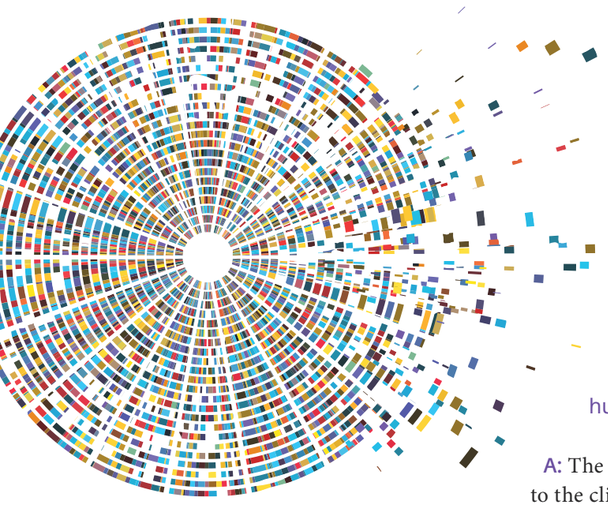
Two decades of progress in genetic diagnostics have given clinicians the ability to identify the genetic root cause of many severe diseases of the brain. If our efforts succeed, it will give clinicians the ability to use CRISPR and repair such disease-causing mutations in situ.

Q: How would this technology impact the future of biomedicine?

A: Genome editing has tremendous potential for treating neurologic diseases. We know that age-related neurodegeneration (e.g., Alzheimer's, Parkinson's and ALS), as well as neurodevelopmental disorders (e.g., autism spectrum disorders and seizure disorders) can be caused by mutations in single genes. CRISPR is a uniquely powerful tool for repairing such mutations but, for the moment, challenges associated with delivery are preventing this exciting class of therapeutics from having a clinical impact. If we can overcome the hurdles of delivering genome editing enzymes into neurons, it will pave the way for a wide variety of new therapies for incurable neurodegenerative and neurodevelopmental diseases.

Q: What are some of the major challenges with genome editing?

A: There are two major challenges associated with genome editing in neurons. First, we need to be able to cross the blood-brain barrier — which evolved to prevent something like CRISPR-Cas9 from crossing it — and access neurons. In addition, genome



> "The brain is definitely in the "hard to access" category, and our work at the IGI strives to enable safe and effective genome editing in the body's most complex organ."

editing may have unintended effects on the neurons. Our initial studies point to paths to address both of these challenges, but much interdisciplinary work lies ahead.

Q: How has partnering with Heritage Medical Research Institute (HMRI) assisted with the development of these two additional aspects of technology?

A: HMRI has been an essential partner for these studies. The outcome of the research we are conducting is too uncertain to obtain funding from traditional sources. It is telling that gene editing in the brain is not a major area of focus for biotechnology companies. We are thrilled that HMRI appreciates the immense potential impact of our efforts.

Q: How soon can you expect to begin human clinical trials?

A: The timeline for CRISPR to the clinic for any given disease is currently four to five years, but only after the delivery and safety issues have been solved; these challenges are the focus of our HMRI-funded effort. We are innovating in-parallel on engineering novel types of CRISPR enzymes, and new ways to intervene with neurologic disease at the molecular level. This parallel-track effort aims to accelerate the path of HMRI-funded innovation to the clinic, so that once delivery techniques become available, we're ready with a suite of targeted therapies to take to clinical trials through our partners at University of California, San Francisco.

Q: What would the successful result of this research mean for you personally?

NIREN MURTHY: I have been working in the area of drug delivery for the past 20 years. My long-term career goals are to develop delivery vectors that can improve human health. If successful, the experiments in this proposal will demonstrate that brain tissue can be efficiently edited nonvirally, and these results will dramatically accelerate the timeline for performing brain genome editing clinical trials. This would be very exciting.

ROSS WILSON: This is an incredibly exciting time for neurologic research. CRISPR's basic research applications are accelerating target discovery for neurodegenerative disease, but knowledge of these genetic targets will be fruitless unless it is enabled by delivery technology tailored to the brain. With this urgent need in mind, we aspire to have CNS-specific delivery technology ready for deployment as soon as this new wave of targets has been identified.

JENNIFER DOUDNA: As a scientist, I have focused my career on developing fundamental understanding of biological systems, work that led us to CRISPR genome editing technology. I'm excited by the opportunity to bring this technology to bear on neurologic disorders. The challenge for us now is to develop the tools and techniques we need to perform neurologic editing in ways that will be safe, effective and ultimately widely accessible and affordable to people who need it most.

Q: Is there any additional information that you would like to share?

A: Currently, therapeutic genome editing has proven successful in two contexts. The first success story involved editing of bone marrow stem cells, which are hard to access and must be edited in the context of transplantation. The second clinical success was in the liver, which is easier to access via intravenous delivery of the genome editing reagents.

The brain is definitely in the "hard to access" category, and our work at the IGI strives to enable safe and effective genome editing in the body's most complex organ. The ultimate goal of our work is to enable genome editing of the brain, following an intravenous administration of our editing reagents. This is an ambitious goal, but we are confident that it is attainable. As we work toward this goal, our efforts will also enable safe and efficient genome editing of the brain via direct injection into the relevant tissue, which will facilitate the development of revolutionary cures. Although access may be limited due to the complexities of administration in this case, it will still represent a major leap forward in terms of our ability to deliver CRISPR cures for diseases of the brain.

Ross Wilson, Ph.D.

Assistant Adjunct Professor at the University of California, Berkeley; Scientific Director of Therapeutic Delivery at the Innovative Genomics Institute

Ross Wilson is an assistant adjunct professor at the University of California, Berkeley, where he serves as the scientific director of therapeutic delivery at the Innovative Genomics Institute. Dr. Wilson is working to enable widespread clinical use of genome-editing enzymes, which is currently limited by the difficulty in delivering enzyme therapeutics to the cells in need of correction. To address this need, the Wilson lab relies on protein/RNA engineering to create effective methods of administration that will facilitate targeted delivery to specific cells, tissues or organs. Due to their desirable safety properties and relative ease of manufacture, nonviral platforms are a central focus of Wilson lab efforts. Development of these novel tools will help accelerate translation of genome editing strategies from the lab to the clinic.

Jennifer Doudna, Ph.D.

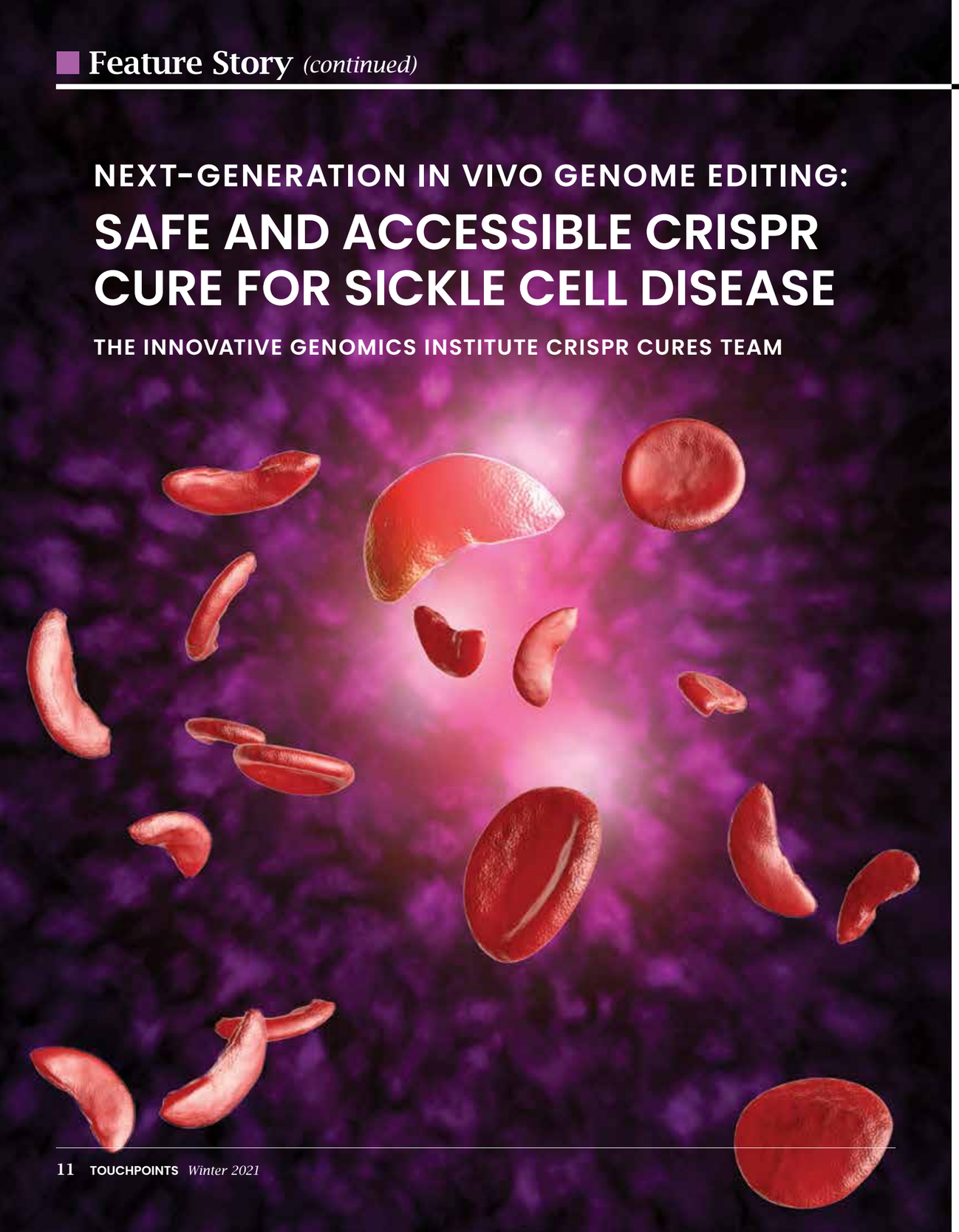
Biochemist at the University of California, Berkeley

Jennifer Doudna is a biochemist at the University of California, Berkeley. Her groundbreaking development of CRISPR-Cas9 — a genome engineering technology that allows researchers to edit DNA — with collaborator Emmanuelle Charpentier earned the two the 2020 Nobel Prize in Chemistry and forever changed the course of human and agricultural genomics research. She is also the founder of the Innovative Genomics Institute, holds the Li Ka Shing chancellor's chair in Biomedical and Health Sciences, and is a member of the Howard Hughes Medical Institute, Lawrence Berkeley National Lab, Gladstone Institutes, the National Academy of Sciences, and the American Academy of Arts and Sciences. She is a leader in the global public debate on the responsible use of CRISPR and has co-founded and serves on the advisory panel of several companies that use the technology in unique ways. Dr. Doudna is the co-author of "A Crack in Creation," a personal account of her research and the societal and ethical implications of gene editing.

NEXT-GENERATION IN VIVO GENOME EDITING:

SAFE AND ACCESSIBLE CRISPR CURE FOR SICKLE CELL DISEASE

THE INNOVATIVE GENOMICS INSTITUTE CRISPR CURES TEAM



In our second in-depth Q&A session, we gain further knowledge into what the IGI CRISPR Cures team have discovered in their research to create a cure for sickle cell disease. Dr. Jennifer Doudna and her team describe the early stages of using CRISPR-Cas9, the challenges they have encountered and what the future holds for expanding this research.

Q: Was the primary purpose of your research targeted specifically to find a cure for sickle cell disease (SCD)?

A: Our work on a CRISPR cure for SCD started shortly after the discovery by Innovative Genomics Institute (IGI) founder Jennifer Doudna and collaborator Emmanuelle Charpentier that CRISPR-Cas9 could be used as a precise, programmable genome editing tool. SCD was a good choice for a disease to go after early on: the genetic basis was well characterized, it affects millions worldwide, and it has a long and unfortunate history of being neglected. Because it's a blood disorder, we had the ability to edit blood-generating stem cells ex vivo, facilitating targeted editing of specific cells. This ex vivo approach simplifies things in some ways, but raises new challenges; requiring chemotherapy, bone marrow transplantation, long hospital stays and cell manufacturing that can only be done in a limited number of facilities around the world.

In partnership with world-leading clinicians at University of California, San Francisco and UCLA, we overcame all these challenges, innovated both on CRISPR engineering and ex vivo delivery, and are proud to be the only all-academic group to have a clinical trial for CRISPR in sickle cell disease (all other such efforts are sponsored by biotechnology companies). The multidisciplinary Sickle Cell Initiative team at the IGI and its clinician partners are equal parts inspired by this achievement and mindful of the urgent need to make CRISPR approaches to SCD scalable and safer for the patients, which is the focus of our Heritage Medical Research Institute-funded effort.

With the IGI's initial ex vivo cure for SCD receiving Food and Drug Administration (FDA) approval to move into the clinic, we are excited to continue advancing the technology and facilitating improved access to CRISPR-based cures for SCD. The most critical hurdle is the delivery challenge: Can we move away from the ex vivo approach — where cells are brought into the lab, and CRISPR is sent into the cells — and enable in vivo administration, with the corrective CRISPR enzyme administered via an intravenous infusion? We are optimistic that this game-changing shift will be made possible by molecular engineering of CRISPR-Cas9 itself. Instead of relying on a viral vector or a nanoparticle — each of which has substantial limitations — we will transform CRISPR-Cas9 into a self-delivering, homing particle that can locate and enter the blood-generating stem cells in need of correction. Such an approach should be amenable to large-scale manufacture and greatly reduce the cost while increasing the accessibility of the treatment, and will provide the same appealing safety and efficacy profile observed with the successful CRISPR cures that have already been transforming patients' lives.

Q: What are some of the major challenges?

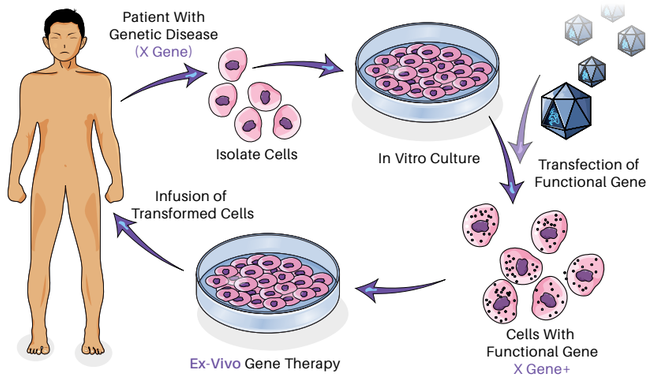
A: In our efforts to create a self-delivering, cell-homing form of CRISPR-Cas9, there is a central balancing act: How can we ensure that our enzyme efficiently enters the targeted cell type rather than getting wastefully soaked up by organs in the body, such as the liver? To strike the correct balance, we will carefully balance two elements: "sticky" targeting molecules that can recognize the specific details on the surface of the cells we want to edit, and "slippery" molecules to prevent unwanted interactions with cell types that need not be edited. Our success in balancing these two elements can be evaluated using cells in research settings (e.g., human blood stem cells

> "Developing a safe and effective CRISPR medicine is a multidisciplinary problem that spans areas of biochemistry, bioengineering, cell biology, molecular genetics, hematology, regulatory and clinical science."

in a dish and in animals), allowing us to compare dozens of variations and find a winning recipe.

Q: Can you describe how the IGI Delivery Collective team and your team work together and the advantages of this collaboration?

A: Developing a safe, scalable and effective CRISPR medicine is a multidisciplinary problem that spans areas of biochemistry, bioengineering, cell biology, molecular genetics, hematology, regulatory and clinical science. The Sickle Cell Initiative team at the IGI and our partners at UCSF and UCLA is precisely such a cross-functional group. We bring together biochemistry and bioengineering experts to design novel CRISPR enzymes and ways to deliver them into the cells along with hematologists who enable testing these modalities in blood stem cells and animal models, as well as molecular geneticists who can test the safety and efficacy of CRISPR for the cells.



> "CRISPR has been revolutionary because it is a bona fide plug-and-play technology."

We are leveraging the IGI Center for Translational Genomics that harbors vertically integrated expertise for FDA-grade human blood stem cell engineering, and the IGI's CAP-accredited CLIA laboratory for high complexity molecular testing, to put together an investigative new drug-grade dataset regarding the safety and efficacy our approach. We have a deep partnership with a world-leading, best-in-class clinical cell manufacturing team for genomic therapy products (led by Dr. Donald Kohn at UCLA), and a world-leading transplant center for genomic therapies in the hemoglobinopathies (led by Dr. Mark Walters, M.D., at UCSF) that enable us to develop methods for clinical trial-grade at-scale manufacturing of such a cell product and then administering it clinically.

Q: What would the successful outcome of this research mean for you personally?

ROSS WILSON: The use of CRISPR to cure sickle cell disease is both breathtaking in its success and saddening due to its current limitations. Merely seven years passed between the initial report that suggested CRISPR-Cas9 as a possible tool for genome editing and its first clinical use to cure sickle cell disease. This blistering pace is a testimony to the power of CRISPR-driven cures, but the complicated route of administration places severe real-world limitations on access to these cures. Current state-of-the-art therapies will not be able to cure all sickle cell disease patients in the U.S., let alone the rest of the world. This gap is what motivates us at the IGI to develop new delivery technology that is better suited to CRISPR enzymes, allowing safe, affordable and convenient access to life-transforming therapies.

FYODOR URNOV: We have learned from 32 years of human genetic engineering in the clinic that only clinical trial data can provide key information about the safety and efficacy of any given approach. Here, the biggest barrier to entry is having all the right expertise — from basic insight into atom-level processes inside the cell all the way to how to safely transplant edited cells into a human being — in one seamless functioning team. We have precisely such a team at the IGI and UCSF, and it is thrilling for me personally to be part of an effort that aims to clinic-test a highly innovative approach for CRISPR in sickle cell disease.

Q: What is next on the horizon for your team to focus on after SCD?

A: CRISPR has been revolutionary because it is a bona fide plug-and-play technology. Finding a way to send CRISPR enzymes to the bone marrow's blood-generating stem cells that enact a cure for sickle cell disease immediately suggests a clear path to treat other diseases that require a corrective edit of the same cell type. The delivery technology we are developing will initially focus on accessible sickle cell disease cures, but can readily be repurposed to treat immunodeficiencies or to enable production of HIV-resistant immune cells.

Fyodor Urnov, Ph.D.

Professor of Genetics, Genomics, and Development in the Molecular and Cell Biology Department at University of California, Berkeley; Scientific Director for Technology and Translation at the Innovative Genomics Institute

Fyodor Urnov directs the Center for Translational Genomics focused on CRISPR cures for N=1 disease. Dr. Urnov trained as an undergraduate in biology at Moscow State University, at Brown University for his Ph.D., and was a postdoctoral fellow at the National Institutes of Health.

In his subsequent work in the biotechnology sector, Dr. Urnov co-led efforts to develop the fundamental toolbox of human genome editing (gene correction, knockout and integration). Dr. Urnov was a key member of the team that developed the first-in-human application of genome editing (2009), and then led a cross-functional team through basic discovery to receive an investigational new drug application of the first-in-human clinical trials for the hemoglobinopathies, beta-thalassemia and sickle cell disease, developing an approach that has yielded measurable clinical benefit for multiple patients.

At the IGI, Dr. Urnov's focus is on establishing turnkey editability of the human genome and epigenome for clinical use, and leading collaborative teams to first-in-human applications of experimental CRISPR-based editing therapeutics for sickle cell disease and genetic disorders of the immune system, as well as epigenome editing therapeutics for radiation injury, neuroinflammation and neurodegeneration.

Niren Murthy, Ph.D.

Professor in the Department of Bioengineering at the University of California, Berkeley

Niren Murthy received his Ph.D. from the University of Washington in Seattle in bioengineering in 2001, and then did postdoctoral research at UC Berkeley in chemistry from 2001-2003. Dr. Murthy leads an interdisciplinary laboratory that focuses on the development of new materials for drug delivery and molecular imaging. The Murthy laboratory has developed several new biomaterials and imaging agents, such as the maltodextrin-based imaging agents, which are focused on improving the treatment and diagnosis of infectious diseases. In addition, the Murthy laboratory has developed numerous reagents for detecting radical oxidants, such as the hydrocyanines.

Caltech Alumnus Ardem Patapoutian Wins

2021 Nobel Prize in Physiology or Medicine

Caltech alumnus Ardem Patapoutian, Ph.D., Presidential Endowed Chair in Neurobiology and Professor at Scripps Research in La Jolla, California, and a Howard Hughes Medical Institute Investigator, has been awarded the 2021 Nobel Prize in Physiology or Medicine, along with David Julius, Ph.D., of University of California, San Francisco. The two were honored for their "discoveries of receptors for temperature and touch," according to the award citation.

Touch is a major sense through which we perceive the world: We are comforted by a gentle hug and our hands are pleasantly warmed by the heat and heft of a cup of coffee, but we pull away in pain from the stinging prick of a thorn or a hot flame. These perceptions are shaped by sensory information related to both temperature — hot or cold — and pressure.

Drs. Patapoutian and Julius were recognized for their major contributions that helped to uncover how these processes work in the body, and for discovering how temperature and pressure stimuli from the external world are converted into electrical impulses in our nervous systems. Their work is now leading to new treatments for chronic pain, including the development of non-opioid painkillers.

For his half of the prize, Dr. Julius was lauded for research that made use of compounds, such as capsaicin (responsible for spiciness in chili peppers) and menthol to identify temperature-sensitive sensors in cells.

Dr. Patapoutian was honored for his discovery of the cellular sensors in the skin and internal organs that respond to mechanical stimuli such as touch.

He and his collaborators first cultured a cell line that gave off a measurable electrical signal when individual cells were poked with a tiny pipette. The team systematically knocked out individual genes in these pressure-sensitive cells, which allowed them to identify the genes that encode for the receptor or receptors that respond to pressure.

Dr. Patapoutian and his team identified two genes that each encode for previously uncharacterized ion channels that open up in response to mechanical pressure; ion channels are a kind of tunnel connecting the inside and outside of a cell. The two channels, which were named Piezo1 and Piezo2 after the Greek word for pressure (píesi), have since been shown to sense body position and motion (known as proprioception), and regulate important physiological processes, such as blood pressure, respiration and urinary bladder control.

As a biology graduate student at Caltech from 1990 to 1996, Dr. Patapoutian worked in the laboratory of Barbara Wold, Ph.D., Bren Professor of Molecular Biology. In the Wold lab, Dr. Patapoutian studied how individual genes specify cell-type identity, specifically the ones that make muscle.

> "I think it's the environment, the people around you, and just to focus on big questions that can be answered. In science, many times we focus on the big questions but you have to ask it at the right place and the right time where the tools are present to answer those questions."
>
> ~ *Ardem Patapoutian, Presidential Endowed Chair in Neurobiology and Professor at Scripps Research in La Jolla, California and a Howard Hughes Medical Institute Investigator*

"This is a joy to see" says Dr. Wold, who also serves as the Allen V. C. Davis and Lenabelle Davis Leadership Chair and director of the Richard N. Merkin Institute for Translational Research. "Ardem was wonderful to work with from the day he arrived at Caltech. He came with a great love of biology, zest for discovery and capacity for fine experimental design. And he was always willing to go an extra mile when it required pure work. The project that led him and his students to the Piezos showed all of that. It was a bold, scientific risk, hitched to a fine design and tons of work, ultimately achieving beautiful biological insights."

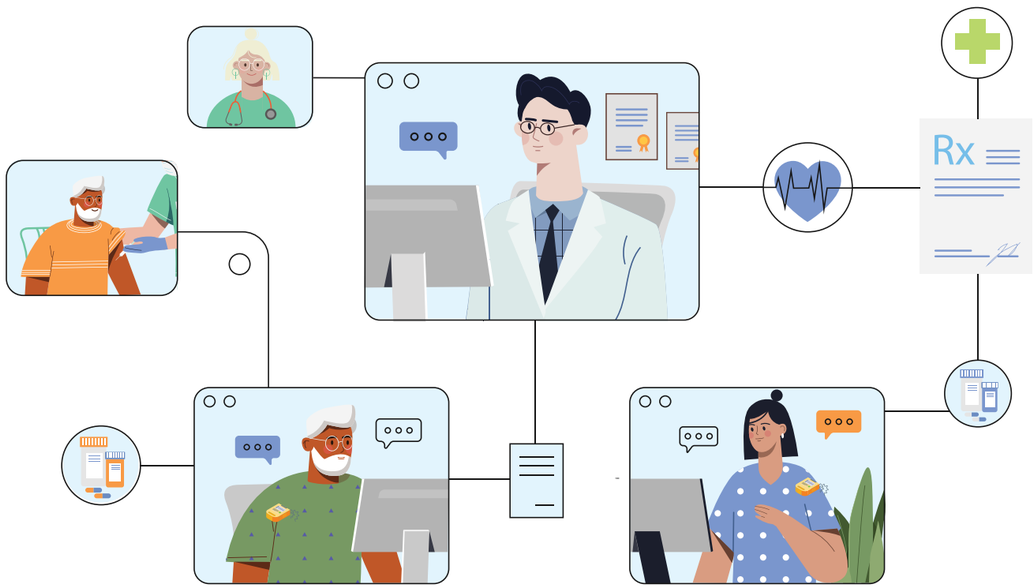
Dr. Patapoutian was born in 1967 in Beirut, Lebanon. He received his B.S. in molecular, cellular and development biology from UCLA. After his Ph.D. research at Caltech, Dr. Patapoutian was a postdoctoral fellow at UC San Francisco from 1996 to 2000, and then joined the faculty of Scripps Research and the staff of the Genomics Institute of the Novartis Research Foundation.

When asked about the secret of his success in his Nobel interview, Dr. Patapoutian noted the importance of nurturing surroundings. "I think it's the environment, the people around you, and just to focus on big questions that can be answered," he said. "In science, many times we focus on the big questions but you have to ask it at the right place and the right time where the tools are present to answer those questions."

In 2020, Drs. Patapoutian and Julius shared the Kavli Award for Neuroscience. Dr. Patapoutian is an elected member of the American Academy of Arts and Sciences, the National Academy of Sciences and the American Association for the Advancement of Science.

To date, 45 Caltech faculty, alumni and former postdoctoral scholars have won a total of 46 Nobel Prizes.

Source: caltech.edu



Caltech Chosen to Join NSF's New Center to Stream Healthcare in Place

$3M Center to Advance At-Home Healthcare Technology

Caltech, the University of Arizona, Baylor College of Medicine and USC have joined together to create a new National Science Foundation (NSF) center that aims to shift healthcare from a model that requires patients to receive care in a hospital or doctor's office to a model in which patients manage their health from home.

Dubbed the Center to Stream Healthcare in Place (C2SHIP) and led by University of Arizona electrical and computer engineering professor Janet Roveda, Ph.D., the collaboration seeks to connect clinicians to patients via wearable, portable and implantable devices; these devices allow doctors to gather patient data and provide care without patients needing to leave their house. C2SHIP has been selected as an NSF Industry–University Cooperative Research Center. It is receiving an initial grant of at least $3 million from the NSF, with this award supplemented by industry funding.

"At Caltech, we will be device oriented, focusing on new wearable, portable or implantable sensor technologies and artificial intelligence tools for data analysis and visualization," says Chiara Daraio, Ph.D., director of the Caltech site of the new center and the G. Bradford Jones Professor of Mechanical Engineering and Applied Physics. "The idea is to go from bench to bedside. In order to accelerate knowledge transfer between academia and the medical field, we are collaborating with medical schools to have direct input in and access to clinical trials."

> "At Caltech, we will be device oriented, focusing on new wearable, portable or implantable sensor technologies and artificial intelligence tools for data analysis and visualization."
>
> ~ *Chiara Daraio, Caltech, G. Bradford Jones Professor of Mechanical Engineering and Applied Physics*

At Caltech, Dr. Daraio is already planning to work with Yu-Chong Tai, Ph.D., Anna L. Rosen Professor of Electrical Engineering and Medical Engineering and Andrew and Peggy Cherng Medical Engineering Leadership Chair; and Azita Emami, Ph.D., Andrew and Peggy Cherng Professor of Electrical Engineering and Medical Engineering and Heritage Medical Research Institute Investigator; both of whom are co-investigators on the project. She will also work with Axel Scherer, Ph.D., Bernard Neches Professor of Electrical Engineering, Applied Physics and Physics; and Wei Gao, assistant professor of medical engineering. Dr. Daraio also hopes to recruit more Caltech researchers across campus to explore questions about medical diagnostics, cybersecurity, data manipulation, and the economic and social impact of remote health care.

"The C2SHIP center is an exciting program well matched to the Caltech engineering tradition of multidisciplinary work connecting fundamental science to translational opportunities" said Harry A. Atwater, Ph.D., Otis Booth Leadership Chair of Caltech's Division of Engineering and Applied Science.

The last two decades have seen an uptick in the numbers of people who have chosen to monitor their own health using wearable technology such as Fitbit and Apple watches. But even though information is being continually collected, these data have not been validated at a clinical level and so are not yet necessarily usable by medical professionals.

Some clinics, Dr. Roveda says, are already working toward in-home health care. For example, her own father recently was provided with a high-end blood pressure cuff for home use for a few months after he was put on a new medication for a heart condition. "His doctors wanted to make sure the new medication was regulating his blood pressure, so the device was continuously sending data to the clinic," she says. "There were a couple of days that he didn't want to wear it, and he got a call from the doctor checking on him. I see huge potential in a device like that. Our vision is that, someday, you could go to CVS and pick up not just a medication but also a home-care-based instrument to gather data about your health."

The COVID-19 pandemic has made it clearer than ever that in-place care, especially of medically fragile patients who should not attend in-person appointments, can make a major difference.

"COVID-19 has disrupted best practices for preventing disease-related complications. In response, many healthcare providers are re-engineering their pathways to promote 'care in place," said Bijan Najafi, Ph.D., co-director of C2SHIP, director of the Baylor College of Medicine site, professor in the Michael E. DeBakey Department of Surgery, and director of clinical research in the division of vascular surgery, in a press release. "Care in place is an increasingly important topic in health care, becoming the foreground in governance practices to decentralize care delivery and reduce care disparities."

The team is moving forward with a commitment to remote care that is stronger than ever.

"The proposal brings together quite a lot of potential research and industry firepower to focus on an area that couldn't be more primed for innovation," said David G. Armstrong, Ph.D., D.P.M., director of the USC site and professor of surgery and director of the Southwestern Academic Limb Salvage Alliance, in a press release. "We really have the potential to develop some of the basic foundations about how we merge consumer electronics and medical devices moving forward. Working with early-stage startups all the way up to the biggest of the big tech is such a spectacular gift. We look forward to paying it forward."

Source: caltech.edu

Richard Merkin, M.D., Renews Support for Transformative Science at the Broad Institute

For more than a decade, Dr. Merkin has supported research at the Broad, enabling scientists to develop new genome-editing technologies, gain insight into how DNA is organized in cancer cells and devise methods for discerning the function of genetic variants. Through the Merkin Institute Fellowship, he has helped nearly 20 promising early career scientists gain experience, drive impact and launch innovative research.

Most recently, he supported the founding of the Merkin Institute for Transformative Technologies in Healthcare at the Broad Institute, an initiative whose mission is to realize the potential for innovations in biomedicine — specifically, technologies meant to have a profound effect on therapeutics, diagnostics and data. He also established the Richard Merkin Professorship, an endowed professorship currently held by Broad Institute Core Member David Liu, Ph.D.

Dr. Merkin is making a new transformative gift to the Broad Institute to further advance the Merkin Institute and the Merkin Fellows, as well as to inaugurate a new international prize: the Merkin Prize in Biomedical Technology. He is also establishing an endowment for the Merkin Fund, which will support the most creative and promising research directions in fundamental science.

In recognition of Dr. Merkin's deep commitment to research and innovation at the Institute, the Broad Institute's building at 415 Main Street in Cambridge, Massachusetts, has been named the Richard N. Merkin Building. The seven-story, 234,000 square-foot building, which is located in the heart of Kendall Square, houses advanced research laboratories to allow scientists to investigate the fundamental biology of, as well as new therapeutic options for, diseases ranging from cancer and diabetes to rare genetic conditions. Researchers are also developing new tools and techniques — available to the global research community — aimed at helping science rapidly progress.

Broad Institute Director Todd Golub, M.D., led the building's dedication ceremony on October 6, 2021. "It is hard to put a value on Dr. Merkin's support for science at the Broad," Dr. Golub said. "Many research projects that he has supported, and continues to support, have been so transformative that year by year we see them continue to change the scientific landscape. I'm convinced that in the future we will look back in awe at how consequential his giving has been."

"I can think of no better way to transform biomedicine, and ultimately improve the lives of patients, than to give full support to the most talented and ambitious scientists, those who aren't afraid to tackle bold ideas and take risks," said Dr. Merkin. "This is clearly the goal of the Broad, and that's why I am so excited to partner with them in this mission."

Dr. Merkin is a physician by training. In 1979, he founded the Heritage Provider Network (HPN), one of the country's largest doctor-owned integrated health care systems. Since HPN's inception, he has led the formation of dozens of independent practice association structures — all designed to make doctors' offices more efficient for both doctors and patients. Through his experience with HPN, Dr. Merkin saw how bold and transformative ideas can lead to paradigm-shifting methods and technologies that can revolutionize healthcare.

Dr. Merkin is one of the Broad's early philanthropic partners, dating back to his first gift in 2009 to fund a program for stem cell research that fueled a landmark study on long noncoding RNAs. At the time, these molecules were largely a mystery, but thanks to Dr. Merkin's generosity, Broad scientists were able to develop a comprehensive toolbox of experimental methods and algorithms that enabled them to explore what happens in embryonic stem cells when more than 100 long noncoding RNAs are knocked out, one at a time. The team subsequently discovered that the RNAs play a central role in embryonic development, not just proteins as previously thought.

In 2012, Dr. Merkin created the Broad's first endowed fellowship, the Merkin Institute Fellowship, which is designed to support promising scientists — especially those developing technologies that could dramatically accelerate progress for an entire field. This program has funded almost 20 Broad researchers, including Feng Zhang, Ph.D., core institute member and a pioneer in developing CRISPR; Beth Stevens, Ph.D., an institute member who has made seminal discoveries in the biology of schizophrenia; Martin Ayree, Ph.D., an institute member who has developed tools that generate high-resolution, 3D models of DNA organization in tumor cells; and Fei Chen, Ph.D., core institute member and a pioneer of molecular and microscopy tools that illuminate biological pathways and functions.

"I am especially grateful to Dr. Merkin for his support, not only to myself and to my own work in neurobiology, but to all the other Merkin Fellows at the Broad who have dedicated their lives to transforming human health," said Stevens. "This kind of generosity will undoubtedly help patients and change people's lives. I'm convinced of that."

In 2017, Dr. Merkin partnered with the Broad to launch the creation of the Merkin Institute for Transformative Technologies in Healthcare to support trailblazing scientists. David Liu, Ph.D., the inaugural Richard Merkin Professor and director of the Merkin Institute, ensures that the Merkin Institute achieves its mission by selecting and funding research efforts that can potentially rapidly accelerate our understanding and treatment of disease.

These projects have included research into new classes of drugs for diabetes and several cancers, new approaches to drug development, and a scalable approach for identifying disease-causing mutations.

"Over the past four years the Merkin Institute for Transformative Technologies in Healthcare has supported innovative, early-stage research opportunities for improving how we detect and treat disease," said Dr. Liu. "Dr. Merkin's continued support to the Broad will be key to helping us turn these projects and future creative ideas into promising realities for patients and their families."

All of these efforts and the new transformative gift epitomize Dr. Merkin's two philanthropic passions: supporting promising researchers and driving discovery through the development of bold new technologies.

DESERT OASIS HEALTHCARE:

Celebrated Its 40-Year Anniversary Donating $40K to Nonprofit Organizations

In July 2021, Desert Oasis Healthcare (DOHC) commemorated its 40-year anniversary by generously donating $40,000 to local nonprofit organizations (NPOs) publicly voted on by members of their community. The "40 for 40" initiative was in addition to the $200,000 DOHC had already awarded throughout the year to various nonprofit organizations.

DOHC chose 10 NPOs that would most benefit from the additional assistance. By visiting the DOHC website, the public voted on their favorite NPOs that they believed would best serve the health and well-being of the community, and thus creating a positive impact in the lives of others. The voting continued until July 1 — the date of DOHC's 40th anniversary.

Reflecting back on its humble beginning as a single primary care office in Palm Springs in 1981, DOHC has evolved into one of the largest medical groups in Southern California to date, serving nearly 60,000 members. Their growth has resulted in further advancing their primary and immediate care, home health and palliative care, clinical research studies and more.

Throughout the years, DOHC has proudly built a reputation of generous giving, and

living up to its legacy of taking care of its communities as it has done for four solid decades. Selected nonprofit organizations are supported via money, personal donations, and time volunteered by their dedicated management and staff.

The nonprofit recipients benefited from receiving extra donations to supplement food shortages, services to seniors, families and youth, chronic illness and terminal health conditions, and much more. The extra support could not have come at a better time with immediate needs and services required by those especially affected by the COVID-19 pandemic.

"As COVID-19 has proven, there is always more work to be done," said Marc Hoffing, M.D., DOHC medical director.

The list of winners that received donations included Palm Springs Animal Shelter: $12, 000, FIND Food Bank: $10,000, Shelter from the Storm: $7,000, and Sanctuary Palm Springs: $5,000. The following NPOs each received $1,000: Cathedral City Senior Center, Coachella Valley Volunteers in Medicine, HARC, Mizzell Center, Senior Advocates of the Desert, and Yucca Valley Senior Center.

Desert Oasis Healthcare is committed to providing the highest quality healthcare to the many communities they serve. We celebrate with them on their tremendous growth and accomplishments in the last 40 years, and with each milestone anniversary, we look forward to the countless lives they will change as they continue to partner with organizations whose mission is to help those in need.

DESERT OASIS HEALTHCARE'S TEAM DOHC:

Promotes Better Health by Participating in the 2021 Heart & Stroke Walk

On Saturday, November 20, 2021, Desert Oasis Healthcare (DOHC) joined 2021 Coachella Valley Heart & Stroke Walk sponsored by the American Heart Association (AHA). Their participation aided AHA's efforts to raise funds and awareness for such an important cause, not to mention the personal health benefits they have gained from some much needed postquarantine exercise.

In addition to raising funds and awareness about the importance of heart health and stroke prevention, the AHA is dedicated to funding scientific research to help prolong life and cure heart disease and stroke. The AHA also supports vital research to save babies and young children with congenital heart defects and teaches CPR to thousands of people each year.

Filled with energy and excitement to get outdoors, Team DOHC's Walk team encouraged their employees to join in on the fun and invite along their family and friends. However, DOHC staff are no strangers to these types of events. Special activities happen here on a weekly basis, including focusing on mental health and reducing stress, such as their "Move More Challenge," healthy eating activities and Wear Red Day.

Gift cards provide an extra incentive to stay active. Gift card raffles are held for every 25 Team DOHC members that sign up. A spa and dinner package is also awarded to the employee raising the most Team DOHC money. A personal donation of $10 or more to the Heart Walk enters the employee into the grand prize of winning either a four-pack of San Diego Zoo tickets or a hot air balloon ride for four.

"However people choose to experience this year's Heart & Stroke Walk, it's all about increasing physical activity, reducing stress and reconnecting with each other because heart disease and stroke affect one in every three adults," said Teresa Hodgkins, Pharm.D., and vice president of clinical quality initiatives at DOHC. "Whether our employees walk with Team DOHC at Palm Desert Civic Center Park or walk, run, skip or dance in their living room or their neighborhood, let's keep moving for the heart health of it."

HERITAGE SIERRA MEDICAL GROUP:
Integrates Technology to Advance Care and Accessibility for Its Members

Heritage Sierra Medical Group invests in state-of-the-art technology to improve care coordination and accessibility for its membership.

In response to the COVID-19 pandemic, Heritage Sierra Medical Group incorporated strategic technology to streamline healthcare services for prescriptions, primary and specialty care, and patient-intake information.

To improve care coordination for prescriptions, SpotRx, a kiosk pharmacy service, was installed within the Valencia, California, office location. This allows members to conveniently access their prescriptions on-site at the end of their appointment.

In addition to on-site pickup, SpotRx offers complimentary home delivery of prescriptions, which can be requested via their smartphone mobile app or phone call. This option eliminated transportation, and COVID-19 exposure concerns while also allowing members same-day access to their prescribed medications.

Care coordination was further enhanced through the utilization of telehealth for primary and specialty care. Telehealth improved care accessibility to members seeking care from the comfort of home, convenience, and those managing work/family schedules.

Heritage Sierra Medical Group also offered telehealth video call and phone visits for primary care and incorporated unique remote care technology to support specialty care telehealth visits in Cardiology and Neurology. This allows members to connect with renowned specialty care providers (cardiologist Roger On, M.D., and neurologist Thomas Kurian, M.D.) from the most convenient Heritage Sierra Medical Group location or from home.

Heritage Sierra Medical Group continues its investments in revolutionary technology with its upcoming adoption of NextPen — a smart pen device that compliantly captures patient intake information and seamlessly uploads it to a member's electronic medical record (EMR).

This device streamlines office operations through digitizing a member's response (on pen and paper) to a digital format within the EMR.

As technologies continue to emerge, Heritage Sierra Medical Group will pursue all advancements to enhance care delivery and accessibility for its membership.

Heritage Provider Network Affiliated Medical Groups

THE LARGEST INTEGRATED PHYSICIAN-LED MEDICAL GROUP NATIONALLY

For more than 30 years, HPN has provided quality, cost-effective healthcare to the communities we serve. Today, HPN and its affiliates manage the healthcare of more than 1 million individuals. Our network has thousands of primary care physicians and specialists and hundreds of hospitals.

ADOC Medical Group
adoc.us
Phone: (800) 747-2362
600 City Parkway West, Suite 400
Orange, CA 92868
Counties Served: Central and North Orange

Arizona Priority Care
azprioritycare.com
Phone: (480) 499-8700
585 N. Juniper Drive, Suite 200
Chandler, AZ 85226
Counties Served: Maricopa and areas of Pinal (Casa Grande Area)

Bakersfield Family Medical Center
bfmc.com
Phone: (661) 327-4411
4580 California Ave.
Bakersfield, CA 93309
Counties Served: Kern

Coastal Communities Physician Network
ccpnhpn.com
Phone: (800) 604-8752
1305 Marsh St.
San Luis Obispo, CA 93401
Counties Served: Arroyo Grande, Atascadero, Los Osos, Morro Bay, Paso Robles, Pismo Beach, San Luis Obispo, Templeton and Tulare

Desert Oasis Healthcare
mydohc.com
Phone: (760) 320-5134
275 N. El Cielo Road
Palm Springs, CA 92262
Counties Served: Riverside and San Bernardino

HealthCare Partners, IPA
hcpipa.com
Phone: (516) 746-2200
501 Franklin Ave.
Garden City, NY 11530
Counties Served: Bronx, Brooklyn, Manhattan, Nassau, Queens, Suffolk and Westchester

Heritage Colorado Care
heritagecolorado.com
Phone: (970) 704-5368
2020 North 12th St.
Grand Junction, CO 81501
Counties Served: Mesa

Heritage New York Medical, P.C.
Phone: (516) 531-2001
1225 Franklin Ave., Suite 100
Garden City, NY 11530
Counties Served: Bronx, Brooklyn, Manhattan, Nassau, Queens, Suffolk and Westchester

Heritage Sierra Medical Group
sierramedicalgroup.com
Phone: (661) 945-9411
44469 N. 10th St.
West Lancaster, CA 93534
Counties Served: Kern, Los Angeles and San Bernardino

Heritage Victor Valley Medical Group
hvvmg.com
Phone: (760) 245-4747
12370 Hesperia Road, Suite 6
Victorville, CA 92395
Counties Served: Los Angeles and San Bernardino

High Desert Medical Group
hdmg.net
Phone: (661) 945-5984
43839 N. 15th St. West
Lancaster, CA 93534
Counties Served: Kern and Los Angeles

Lakeside Community Healthcare
lakesidemed.com
Phone: (818) 637-2000
8510 Balboa Blvd., Suite 150
Northridge, CA 91325
Counties Served: Los Angeles, Riverside, San Bernardino and Ventura

Regal Medical Group
regalmed.com
Phone: (866) 654-3471
8510 Balboa Blvd., Suite 150
Northridge, CA 91325
Counties Served: Los Angeles, Orange, Riverside, San Bernardino, San Diego and Ventura

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Heritage Provider Network
8510 Balboa Blvd., Suite 150
Northridge, CA 91325-5810

Our Awards

Recognition of Commitment and Excellence

The recognition we have received demonstrates our practices in excellence. We're proud to be awarded for our commitment to our members and our community.

- Wellness Excellence Award in Health Education — Southern California Foundation for Health Care
- Top Ten Physician Medical Networks in California by America's Physician Groups
- NCQA Certification for Utilization Management and Credentialing
- Elite Status of Excellence for the Standards of Medical Care by America's Physician Groups
- Recognized by the Integrated Healthcare Association for our diabetic registries

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