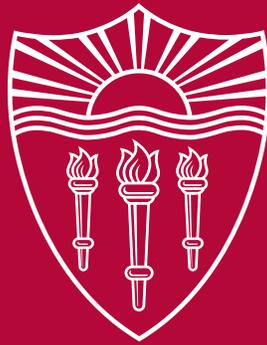




# USC University of Southern California



**The Ming Hsieh Institute**  
for Research on Engineering-Medicine for Cancer



*“Biotechnology is driving the most important advances for the 21st century, and Los Angeles is primed to be a major force. With its commitment to fostering high-risk, high-reward research that will readily translate into pioneering clinical applications, the Ming Hsieh Institute at USC will be a vital engine for this enterprise.”*

C. L. Max Nikias  
President  
University of Southern California

## A Catalyst for Revolutionizing Health

The centerpiece of the Ming Hsieh Institute at USC is the integration of engineering, scientific and medical research that together generates novel thinking, speeds discovery and creates new pathways by which research can be translated into real improvements in human health. While the institute's initial emphasis is on developing new treatments and cures for cancer, it ultimately seeks to fuel new approaches to any human health challenge.

The university's interdisciplinary and entrepreneurial focus, commitment to creating new knowledge to improve our world, and forward-looking approach make it the ideal home for the Ming Hsieh Institute. USC is a global leader in engineering and the biosciences, and is among the world's foremost cancer treatment and research institutes, home to the USC Norris Comprehensive Cancer Center — one of the eight original comprehensive cancer centers funded by the National Cancer Act of 1971.

By bringing together faculty from USC's renowned programs in engineering, medicine, the sciences and pharmacy, the Ming Hsieh Institute cultivates an environment of creativity and collaboration. The breakthroughs developed by the institute's interdisciplinary teams are designed to be translated directly into advances in patient care and catalyzed into inventions that can be licensed and commercialized — with the resulting revenue bolstering further research at the institute.

The Ming Hsieh Institute's pilot grant program plays a unique role in funding early-stage research that has great promise yet limited opportunity to compete for federal funding — which typically only supports longstanding work with proven data. Fostering such high-risk, high-reward research is essential to achieving meaningful advances in improving human health.

*By bringing together faculty from USC's renowned programs in engineering, medicine, the sciences and pharmacy, the Ming Hsieh Institute cultivates an environment of creativity and collaboration.*

**\$150<sub>M</sub>**

total in

**grant funding**

received by MHI  
awardees

**280**

number of  
**grants**  
received by MHI  
awardees

**44**

number of MHI-funded  
**investigators**

**24**

number of MHI-funded  
**research  
projects**

**356**

number of  
**patents pending**  
(MHI investigators)

**92**

**patent  
applications  
awarded**  
to MHI investigators

*“Experts predict cancer can be conquered in the next century, but a great deal of work remains ahead to realize that goal. USC is at the forefront of today’s most exciting biosciences research. That is why I invested in this institute and the innovative, interdisciplinary collaborations that can translate engineering-medicine discoveries into advanced treatments and cures.”*

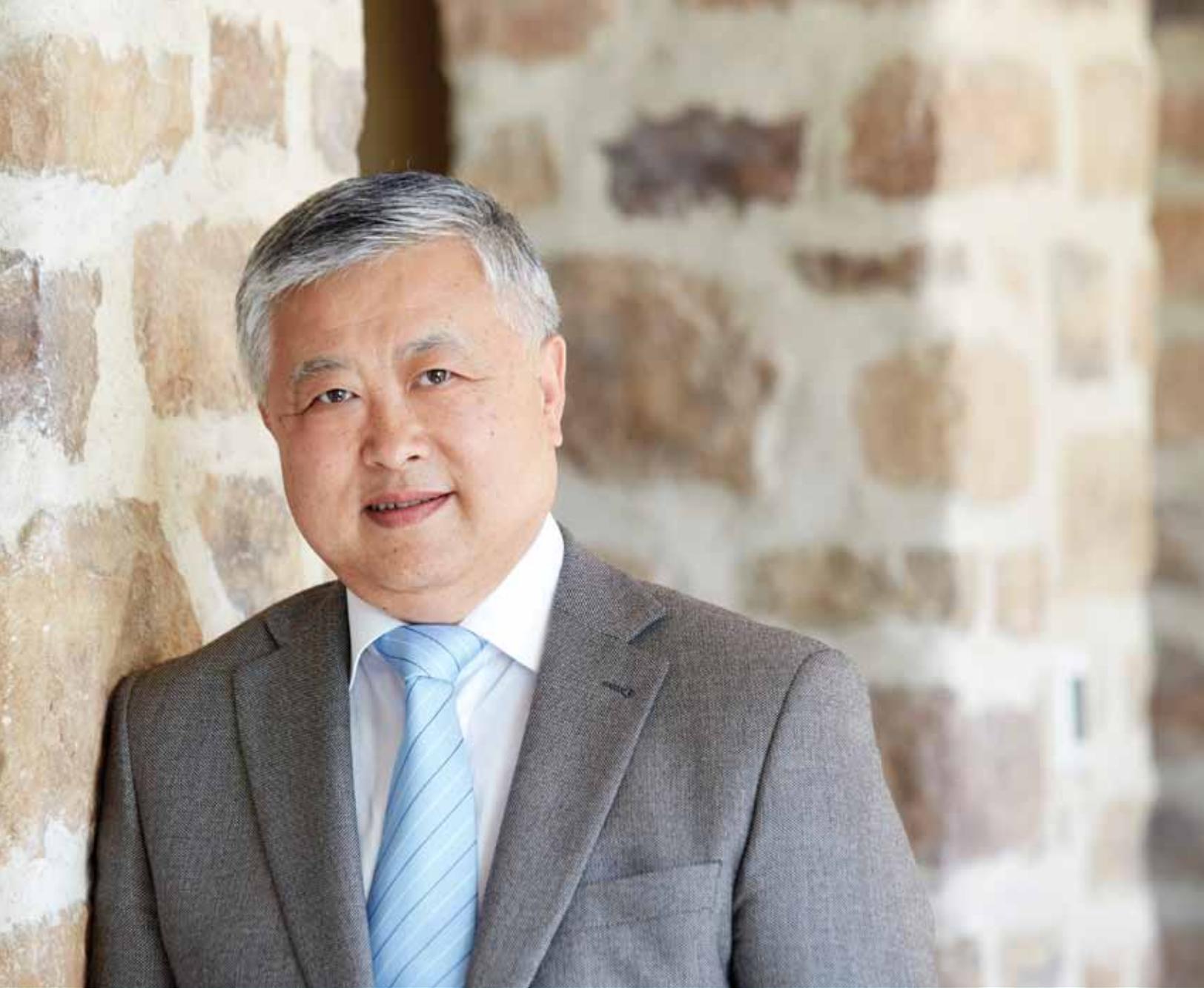
Ming Hsieh B.S. '83, M.S. '84  
Co-founder, Cogent Inc.  
Chairman and CEO, Fulgent Therapeutics Inc.

## Conquering Cancer

By 2030, the incidence of cancer is expected to grow by 45 percent in the United States and by 75 percent globally — surpassing heart disease as the number one killer both here and abroad. While tremendous progress has been made in cancer treatment and patient life expectancy, the death rate has not improved significantly over the past six decades. It is time for a radical new approach to this intractable health challenge.

In the fight against cancer, half the battle is won with early detection. USC researchers are contributing new methods to enable earlier and more accurate diagnosis and treatment monitoring — offering significant improvement over standard cancer therapies, which are currently limited to surgery, radiation and chemotherapy. All three methods risk damage to normal tissue or incomplete eradication of tumors. Ming Hsieh researchers are developing therapies aimed directly and selectively at the cancerous cell that can incorporate both therapeutic and diagnostic actions into a single particle — opening the new field of theranostics.

The Ming Hsieh Institute at USC is harnessing the power of new ideas and approaches by funding promising research that unites scientists, engineers and physicians with the goal of finally defeating cancer and transforming human health.



*“Through the institute, we encourage scientists and engineers to collaborate with clinicians to explore innovative ideas and discover new pathways, new biomarkers and new drugs that can translate to improved treatments and cures.”*

Ming Hsieh

## Titan of Technology

*“From my point of view, donating service or money is part of a citizen’s job.”*

Ming Hsieh

Ming Hsieh developed a keen interest and skill in technology as a young child in northeastern China, learning from his electrical engineer father how to dismantle and reassemble everything from transistor radios to televisions.

Following in the footsteps of an uncle who earned a master’s in mechanical engineering at USC, Hsieh enrolled at USC after two years of college at what is now the South China University of Technology in Guangzhou. He earned his B.S. in electrical engineering in 1983 and his M.S. in electrical engineering just one year later.

Based on what he has called a “heritage of entrepreneurship” instilled at USC, Hsieh founded his first company, AMAX Technology, with several USC classmates in 1987. In 1990, he co-founded Cogent Inc., which revolutionized automated fingerprint and other biometric identification for law enforcement and government agencies around the world. Under his leadership, Cogent became the global leader in such technologies. The company was acquired by 3M in 2010. Today, Hsieh serves as chairman and CEO of Fulgent Therapeutics Inc., a cancer drug research and development company he founded in 2011.

He endowed the USC Ming Hsieh Department of Electrical Engineering at the USC Viterbi School of Engineering in 2006, and then, in 2010, established the Ming Hsieh Institute for Research on Engineering-Medicine for Cancer at USC.

“From my point of view, donating service or money is part of a citizen’s job, to return value back to society, in appreciation for society’s giving us opportunities,” says Hsieh, who serves on the USC Board of Trustees as well as the board of Fudan University in China.

He has received the USC Viterbi School of Engineering’s Mark A. Stevens Distinguished Alumni Award and Ernst and Young’s Young Entrepreneur of the Year Award for Greater Los Angeles in the category of technology and services, and was recently elected to the National Academy of Engineering. He received an honorary doctorate from USC in 2010.





Alan Epstein, M.D., Ph.D.

## Overcoming resistant lymphomas

### Project

Bispecific hybrid nanoworms for immunotherapy of B-cell lymphoma

### Investigators

J. Andrew MacKay, Ph.D.

Peter Conti, M.D., Ph.D.

Alan Epstein, M.D., Ph.D.

Zibo Li, Ph.D.

Nearly 72,000 cases of B-cell or non-Hodgkin's lymphoma (NHL) are diagnosed each year, and almost 20,000 people die from the disease annually.

This project employs protein polymers to develop temperature-responsive nanoparticles that assemble from a fusion between a single-chain antibody and a soluble protein polymer. The team has demonstrated its strategy using the blockbuster drug rituximab — a chimeric antibody that targets CD20, a surface protein present in B cells. Although rituximab is now standard treatment for NHL, nanoworms that bind to CD20 dramatically outperform rituximab in killing tumor cells. Work in animal models has already demonstrated great potential for development of strategies that simultaneously diagnose, treat and monitor outcomes using nanoworm technology.

Next, the team is developing nanoworms that can bind to multiple target receptors, potentially crosslinking normal immune cells with cancer cells. When crosslinked, these immune cells actively kill cancer cells, which has led to the recent approval of biological drugs with a remarkable response rate among patients. This strategy has great potential, and scientists have only scratched the surface of optimizing these materials. The USC team's work could eventually result in new classes of immunotherapies tailored to each patient.

*“Having Ming Hsieh funding saved the day for our research, as NIH funding is simply not available at an early stage. It was essential to demonstrating the potential of our new technology.”*

**Innovation:**  
nanoworm-delivered  
therapeutics that can  
bind to more than one  
target

**Clinical significance:**  
new immunotherapies  
tailored to non-  
Hodgkin's lymphoma  
patients

J. Andrew MacKay, Ph.D.  
USC School of Pharmacy

*“The Ming Hsieh Institute is helping bridge basic and clinical research, which is essential for finding new treatments.”*

Min Yu, M.D., Ph.D.  
Keck School of Medicine of USC

## Finding new hope for breast cancer patients

### Project

Nanoparticle-mediated delivery targeting TAK1 as a metastatic breast cancer therapy

### Investigators

Min Yu, M.D., Ph.D.

Julie Lang, M.D.

Pin Wang, Ph.D.

If breast cancer remains in the breast, it is not fatal. Its worse threat comes from metastasis — when the cancer spreads to other parts of the body, such as bone, liver, lungs and brain. An estimated 155,000 Americans have metastatic breast cancer, which claims some 40,000 lives each year. Up to 30 percent of people initially diagnosed with early-stage disease will eventually develop metastatic breast cancer.

In prior and pioneering research analyzing circulating tumor cells, Min Yu identified the protein kinase TAK1 as a potentially important factor in metastasis. This project focuses on using nanoparticles to deliver oxozeaenol, a TAK1 inhibitor, which could result in a new type of treatment for metastatic breast cancer. The team is testing the treatment in mouse models, using different types of TAK1 constructs and oxozeaenol-containing nanoparticles.

The results to date have shown that nanoparticle-delivered TAK1 inhibitor can suppress metastatic tumor formation. If these promising outcomes continue in future studies, this nanotherapy could provide hope to countless women. It could also help patients with other types of tumors in which TAK1 has been implicated as a factor driving growth, including lymphoma, colon cancer and pancreatic cancer.

**Innovation:**  
delivering a novel nanoparticle/TAK1 inhibitor to halt metastasis

**Clinical significance:**  
a new treatment for metastatic breast cancer



Julie Lang, M.D.



Jennica Zaro, Ph.D.

## Distinguishing tumor cells from healthy ones

### Project

Optimization of pH-sensitive peptide nanoconstructs for use in targeting the mildly acidic tumor microenvironment

### Investigators

Jennica Zaro, Ph.D.

Peter Conti, M.D., Ph.D.

One of biggest challenges in cancer care is differentiating tumor cells from normal ones. This research builds upon the knowledge that areas near tumors are mildly acidic, a fact that has been long known but not yet fully exploited. The approach uses small peptide sequences that become activated in even mildly acidic — low pH — environments.

Using nanotechnology, the USC team has created a specific masking sequence of amino acids that prevents peptides from entering healthy cells, while allowing them to enter or bind to tumor cells. When circulating along normal cells, these peptide sequences travel along without incident. However, lower pH areas activate the peptide carrier, which binds to the tumor cell surface or is internalized by the tumor cells.

The research pursues therapeutic as well as diagnostic objectives. After using the peptide sequences as imaging agents to locate cancer cells, the team aims to optimize the carrier to deliver treatments to the malignancies. The approach solves a problem inherent in current methods that fail to recognize the minute differences in pH levels near cancer cells, causing many tumors to be overlooked.

*“As a new investigator, Ming Hsieh funding is invaluable. The opportunity to directly collaborate with clinicians is crucial to advancing the basic science so it can benefit patients.”*

***Innovation:***  
a method to recognize the minute differences in pH levels near tumor cells

***Clinical significance:***  
enabling more powerful cancer-killing drugs to be used without side effects

Jennica Zaro, Ph.D.  
USC School of Pharmacy

*“We had a promising theory, but no data to confirm our hypotheses. Now we have results that allow us to compete for large external grants. Without the faith and belief from the Ming Hsieh Institute, this work wouldn’t have been possible.”*

Andrea Armani, Ph.D.  
USC Viterbi School of Engineering

## Reaching previously inaccessible tumors

### Project

Nanoparticle-enhanced ultrasound therapy

### Investigators

Andrea Armani, Ph.D.  
David Agus, M.D.

Charles Gomer, Ph.D.  
Qifa Zhou, Ph.D.

Although a promising area of cancer research, photothermal therapy is limited by how far lasers can penetrate into tissue. High-intensity focused ultrasound (HIFU) waves can penetrate deeply, but, used on their own, have failed to completely remove cancerous cells without secondary effects. By combining HIFU with metal nanoparticles, cell death has been demonstrated, but the precise mechanism was unclear.

Using theoretical modeling, the USC team discovered a motion mismatch between the ultrasound waves and the nanometal that seemed to create secondary effects — heat generation and breakdown of the cellular cytoskeleton. Either effect could result in cell death. The group is now on the brink of confirming whether it is the thermal or mechanical mechanism — or a combination of both — that is triggering destruction of the cancer cells.

While the USC researchers initially focused on pancreatic cancer because of how difficult it is to treat with current therapies, their potential breakthrough could be employed against a wide variety of cancers, or even used to change the microenvironment of the cancer and retard its growth. This research could lead to treatments to stop the spread of a broad range of cancers.

**Innovation:**  
combining  
nanotechnology with  
ultrasound waves

**Clinical significance:**  
increasing the  
penetration depth  
of nanoparticle-  
enhanced therapy  
to reach previously  
inaccessible tumors



David Agus, M.D.



Mahta Moghaddam, Ph.D.

**Innovation:**  
a new class of custom-engineered nanoparticles that enhance absorption at microwave frequencies

**Clinical significance:**  
noninvasive, less painful therapy, especially beneficial for patients unable to undergo surgery

## Healing with heat

### Project

Focused microwave cancer therapy using lithographically defined nanoparticles

### Investigators

Wei Wu, Ph.D.  
John Stang, Ph.D.

Mahta Moghaddam, Ph.D.  
Eugene Chung, M.D., Ph.D., J.D.

Heat has been used to treat disease since the dawn of medicine. Current techniques include thermal ablation, which employs extreme temperatures to induce rapid and localized tissue destruction, and hyperthermia, which sensitizes tumor cells to render them more vulnerable to other treatments.

Each method faces the challenge of achieving well-controlled, operator-independent heat that uniformly covers the target without “cooking” the surrounding healthy tissue. The project team set out to invent and test a microwave technology to overcome this barrier by changing the typical nanomaterial involved in thermal therapy.

While infrared radiation to heat gold nanoparticles injected into malignancies has proven successful, the method only works for tumors a few millimeters under the skin. Microwave radiation, however, can penetrate throughout the body. Unfortunately, conventional gold nanoparticles absorb microwaves less effectively than they do infrared radiation.

The USC team’s method employs the technology behind advanced computer chips to generate artificial nanoparticles that better absorb microwaves so the focused energy can selectively “burn” tumors while leaving healthy tissue intact. This noninvasive therapy could potentially reach cancers untouched by infrared-infused gold nanoparticles with significantly less pain to patients.

*“I was able to spend time at the hospital seeing how the physicians treat their patients — something I normally wouldn’t do as an electrical engineer. The opportunity to collaborate with medical doctors is helping us complete research that directly benefits patients.”*

*“The Ming Hsieh Institute funding helped us build an interdisciplinary team. The support was indispensable in refining our project and readying it for commercialization.”*

Chongwu Zhou, Ph.D.  
USC Viterbi School of Engineering

## Detecting disease at the earliest moment

### Project

Metal oxide nanoribbon biosensor chips for point-of-care diagnosis

### Investigators

Mark Thompson, Ph.D.  
Chongwu Zhou, Ph.D.  
Thomas Chen, M.D., Ph.D.

Chongwu Zhou and Mark Thompson have developed a highly scalable biosensor for detecting proteins, enzymes and other biomarkers that indicate a particular form of disease. Built from metal oxide nanoribbons, the technology is so sensitive that illnesses can potentially be diagnosed before the immune system even responds.

The team first used the biosensor chip to detect prostate-specific antigen (PSA), a protein that indicates prostate cancer. They have also published studies on ovarian cancer and brain cancer — with physician Thomas Chen, who specializes in brain tumors — and are working on identifying a marker for pancreatic cancer.

The team has also developed a cardiac biomarker panel that can reveal early signs of a heart attack, a new technique that provides detection levels nearly 1,000 times more sensitive than current conventional methods while also shortening the assay time from more than 10 hours to about an hour.

Ultimately, they are working toward a time when not just cancer but also HIV, SARS, influenza and other infectious diseases and disorders can be caught at the very earliest stages by testing a single drop of blood or saliva.

**Innovation:**  
nanowire biosensors far more advanced for disease diagnosis than anything on the market

**Clinical significance:**  
early detection of cancer, heart attack and infectious diseases



**Innovation:**  
developing a time-  
point-independent  
pharmacokinetic-  
modeling strategy

**Clinical significance:**  
improving  
personalized medicine  
by more accurately  
measuring the  
effects of a particular  
treatment on an  
individual patient



J. Andrew MacKay, Ph.D.

*“We have patented this work through the USC Stevens Center and are investigating licensing and commercialization, as well as federal grants, to push this research further.”*

J. Andrew MacKay, Ph.D.  
USC School of Pharmacy

## Devising smarter theranostic tools

### Project

Diagnostic imaging of smart genetically engineered nanomedicines

### Investigators

J. Andrew MacKay, Ph.D.

Zibo Li, Ph.D.

Peter Conti, M.D., Ph.D.

Nanomedicine candidates typically lack imaging components, which makes it impossible to assess their distribution throughout the body or predict the effectiveness of the drugs they carry. For example, some therapeutic carriers peak at their concentration in a tumor within two hours, while others peak later. Longer accumulation within a tumor might mean better response to a drug, but this hypothesis has been impossible to test in a research setting, much less in a clinical one. Without the ability to quantify distribution in the body, it will remain challenging to determine which patients might benefit from a given nanomedicine.

The team developed a math-based model that measures all time points to form a single parameter to more accurately assess how to target an individual patient's therapy. When combined with such modeling, a diagnostic scan of the nanomedicine may be able to predict the dose, dose frequency and degree of response to theranostic nanomedicines. This precision approach could deliver chemotherapy at much higher doses than would be achieved for patients given unaided drugs.

The project pushes the boundaries of peptide-based drug delivery by developing protein biopharmaceuticals that self-assemble into therapeutic, trackable nanomedicines.

## Providing new hope for metastatic bone cancer

### Project

Therapeutic nanoplatform targeted to bone metastatic cancers

### Investigators

Fabien Pinaud, Ph.D.

Mitchell Gross, M.D., Ph.D.

Charles McKenna, Ph.D.

A common and feared complication of many solid tumors is metastasization to the bone, which can lead to fractures, agonizing pain, spinal instability and decreased mobility. While surgery or radiation therapy can provide relief, such treatments are mainly palliative. Meanwhile, chemotherapy and hormone therapy can help reduce tumor size but generally fail to eliminate the risk of recurrence.

Bisphosphonates (BPs) — a class of drugs that help prevent the loss of bone mass for conditions such as osteoporosis — have an affinity for reaching areas of the bone where metastatic cells are active but are, by themselves, poor anti-cancer agents. Combining BPs with gold nanoparticles holds potential for a novel therapy for metastatic bone cancer, allowing the efficient delivery of various macromolecules — such as DNA, proteins and chemicals — to pathogenic cells. This makes them excellent platforms for deep tissue penetration, specific tumor cell targeting and delivery of tumor-halting agents in vivo.

This project focuses on engineering a compound that will specifically home in on and deliver cancer-killing drugs to tumors at bone metastatic niches, while blocking further malignant cell invasion at these sites, providing new hope for patients.

*“To compete for federal grants, you must have preliminary data, but how do you get that without the grant in the first place? Funding from the Ming Hsieh Institute is of huge importance, especially for young investigators, in obtaining the data essential for obtaining major external support.”*

Charles McKenna, Ph.D.  
Vice Dean, Natural Sciences  
USC Dornsife College of Letters, Arts and Sciences



Fabien Pinaud, Ph.D.

***Innovation:***  
combining drugs that prevent bone loss with gold nanoparticles to treat metastatic bone cancer

***Clinical significance:***  
enhancing the chance of survival for patients with few current options

**Innovation:**  
develop high-affinity peptides for targeted diagnosis and a pipeline for generating other reagents

**Clinical significance:**  
a robust, simple diagnostic test for early detection of head and neck cancers

*“My laboratory has developed a unique skill set in our ability to generate new binding reagents against most cancer targets. The Ming Hsieh Institute has helped us further this work.”*

Richard Roberts, Ph.D.  
USC Viterbi School of Engineering  
USC Dornsife College of Letters, Arts and Sciences

## Building a pipeline for new reagents

### Project

Developing SUPR peptide diagnostics and therapeutics for oral cavity carcinomas

### Investigators

Richard Roberts, Ph.D.  
Uttam Sinha, M.D.

Head and neck cancers account for approximately 350,000 deaths worldwide each year. Risk factors include drinking, tobacco use and human papillomavirus (HPV) infections in the mouth. Early detection is essential for improving outcomes, as two-thirds of patients present with advanced disease, but visual inspection is currently the only screening method. Even successful treatments can carry significant side effects.

To improve patient outcomes, the team developed nanodiagnostics for early detection. Their technique builds upon the messenger RNA (mRNA) display technique developed by Richard Roberts to create nanoparticles and Uttam Sinha's identification of six cytokines that are elevated in patients with squamous cell carcinoma of the tongue.

The results could enable physicians to take a sample of a patient's saliva and detect tiny molecules shed by cancer at a very early stage. The use of these saliva biomarkers unlocks the potential of identifying patients with premalignant lesions. While useful against all head and neck tumors, the method could prove especially valuable in treating those caused by HPV, as such malignancies are easier to cure than other cancers if caught in time.



## Making tumors more sensitive to radiation

### Project

Scintillating nanoparticles for radiosensitization of cancer cells

### Investigators

Stephen Bradforth, Ph.D.

Colin Hill, Ph.D.

Jay Nadeau, Ph.D.

Jonathan (Kin) Ha, Ph.D.

Eric Chang, M.D.

About half of the 11 million people diagnosed with cancer each year undergo radiation therapy. Malignant tumors remain challenging to target, as their lack of well-defined borders risks damage to normal cells during radiation. The side effects can be painful — and in rare cases even give rise to secondary cancers.

To improve the precision of radiation therapy and enhance protection of healthy structures, this project explores cerium doped lanthanum fluoride ( $\text{LaF}_3:\text{Ce}$ ) to make the tumor more sensitive than surrounding tissue to radiation. The nanoparticles are water-soluble, tend to accumulate in tumor cells and can be conjugated with photosensitizing agents already approved for photodynamic therapy.  $\text{LaF}_3:\text{Ce}$  is used because of its high absorption of X-ray and the way it scintillates — that is, emits ultraviolet radiation upon exposure to X-rays. The attached photosensitizer in turn absorbs the ultraviolet to produce an active form of oxygen that destroys malignancies. Scintillating nanoparticles promise a substantial improvement over gold nanoparticles in terms of cost and potential toxicity.

Additional research to confirm the team's promising findings could open up new clinical avenues for treating cancers resistant to radiation therapy.

*“Funding from the Ming Hsieh Institute seeded a fruitful cross-campus collaboration that otherwise would not have happened.”*

Stephen Bradforth, Ph.D.  
USC Dornsife College of Letters, Arts and Sciences



*Eric Chang, M.D.*

***Innovation:***  
exploiting nanoparticle scintillation as a new avenue to cell killing and to compare the effectiveness of scintillating particles with and without photosensitizers

***Clinical significance:***  
potential applicability to all cancer patients receiving ionizing radiation treatment



*“Support from the Ming Hsieh Institute is helping us move one step closer to translating our laboratory work to the clinic for patients in need.”*

Timothy Triche, M.D., Ph.D.  
Children’s Hospital Los Angeles

## **Improving treatment for a deadly childhood cancer**

### **Project**

Targeted nanoparticle therapy for Ewing’s sarcoma

### **Investigators**

Timothy Triche, M.D., Ph.D.

Richard Roberts, Ph.D.

Ewing’s sarcoma is a rare but deadly bone cancer that strikes children and young adults. Its survival rate is only 50 percent.

Efforts to improve outcomes have failed because of limits on the amount of cancer-fighting drugs that can be safely administered without damaging normal tissue like bone marrow, liver and kidney. Existing drugs could be effective, but not at the doses currently used. To address this issue, the team developed a method to deliver drugs at any desired dose to tumor cells while avoiding normal tissues.

The team sought to synthesize hybrid polymerized liposomal nanoparticles (HPLNs) that are biocompatible and better able to deliver drugs to cancer cells to ensure absorption. The HPLNs are coated with proteins that bind to CD99, an antigen overexpressed on the surface of Ewing’s sarcoma cells. The researchers employed a messenger RNA (mRNA) display technique that enables peptide and protein design by directed molecular evolution, using libraries of some 1,013 independent sequences.

While more study is needed, this project could one day improve the lives of those afflicted with Ewing’s sarcoma — as well as patients with other sarcomas and leukemia.

***Innovation:***  
a more precise way of targeting treatment for Ewing’s sarcoma

***Clinical significance:***  
new insights into one of the most challenging childhood cancers

*“The Ming Hsieh Institute fosters high-risk, high-reward science. It takes a chance on bold new ideas that can lead to tomorrow’s advanced therapeutics.”*

Amir Goldkorn, M.D.  
Keck School of Medicine of USC

## Triggering cancer’s self-destruction

### Project

Telomerase reprogramming nanoparticles (TeRN): design and validation of a universal cancer therapeutic

### Investigators

Amir Goldkorn, M.D.  
Nicos Petasis, Ph.D.

The enzyme telomerase builds telomeres, which form protective buffers at the fragile ends of DNA strands and enable chromosomes to keep dividing. As telomerase production stops and the telomeres shorten, cells stop dividing and begin aging — and so do we.

Virtually every type of cancer has high levels of telomerase that allow the cancer cells to maintain their telomere lengths and continue dividing uncontrollably. But this also means the possibilities of telomerase as a therapeutic target are virtually unmatched because it is both universally found in malignant cells and uniquely active within them.

This project aims to rewrite the internal template telomerase follows to keep cancer cells dividing. Such reprogramming could activate a cascade of signals that induce rapid death in cancer cells. To unlock the enzyme’s full potential, Amir Goldkorn and Nicos Petasis have designed and are testing a novel telomerase reprogramming nanoparticle (TeRN), a systemically deliverable small molecule that will reprogram telomerase in cancer cells to induce cell death.

Because this is such a unique approach, the scientists have set a high bar for their proof of principle. But if successful, TeRN could ultimately work against many cancers while being relatively harmless to healthy cells.

**Innovation:**  
creating an utterly novel mechanism for triggering cancer cell death

**Clinical significance:**  
potential for a universal cancer therapeutic



Amir Goldkorn, M.D.



## Creating a versatile platform for cancer therapy

### Project

Engineering nanoparticles for enhanced cancer therapeutics

### Investigators

Pin Wang, Ph.D.

Michael Wong, M.D., Ph.D.

The American Cancer Society estimates there are some 221,000 new cases of prostate cancer and some 28,000 deaths from the disease each year. Pin Wang and Michael Wong are combining oncology with engineering to develop a versatile nanoparticle platform that could potentially revolutionize prostate cancer treatment — and that of other malignancies as well.

This project tests the hypothesis that cross-linked multilamellar liposomal nanoparticles (cMLN) displaying the peptide arginine-arginine-leucine (RRL) — which is specific to tumor blood vessels — can achieve targeted delivery of the anticancer drug doxorubicin to prostate tumors. Results so far have shown that that cMLN formulation can issue sustained releases of doxorubicin while reducing systemic toxicity.

The research also demonstrated that CML nanoparticles could be readily applied to combination therapies, especially for co-delivery of drugs that are both hydrophobic — repelled by water — and hydrophilic — attracted to water. This offers several potential advantages, including synergistic effects and suppressed drug resistance.

As a result, the scientists' liposomal formulation could significantly advance current nanomedicine research and open up new avenues in treating a wide range of diseases in addition to cancer.

*“Support from the Ming Hsieh Institute allows us to explore, develop and discover. It also enables us to do the preclinical work that can lead to human trials.”*

Pin Wang, Ph.D.  
USC Viterbi School of Engineering

***Innovation:***  
a new nanoparticle  
capable of targeting  
tumor blood vessel  
formation

***Clinical significance:***  
creation of a versatile  
platform for targeted  
delivery of therapeutic  
agents to a variety of  
tumor types

*“Our initial project will lead to the first orally available MRI contrast agent.”*

Travis Williams, Ph.D.  
USC Dornsife College of Letters, Arts and Sciences

## Uncovering an unexpected breakthrough

### Project

An ultrasound-activated nanoparticle vehicle for selective imaging and drug delivery

### Investigators

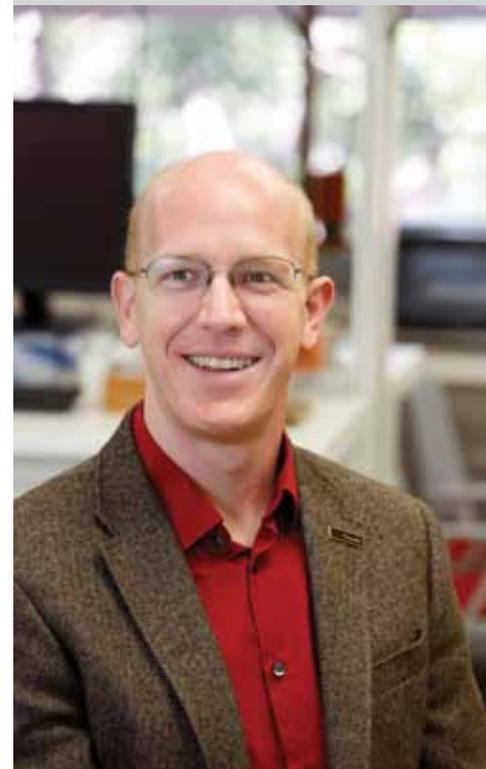
Travis Williams, Ph.D.  
Andy Chang, M.D.

Travis Williams and Andy Chang set out to construct phosphate-covered, variably sized nanoparticles containing a magnetic resonance imaging (MRI) contrast agent, non-covalently load them with lipophilic drugs — those that can dissolve in fats and oils — and then add a shell aimed at masking the MRI agent. In principle, once injected into patients, the construct should have aggregated in tumors. The researchers hoped to activate the particles through ultrasound, simultaneously releasing the drug and enhancing the contrast of the MRI.

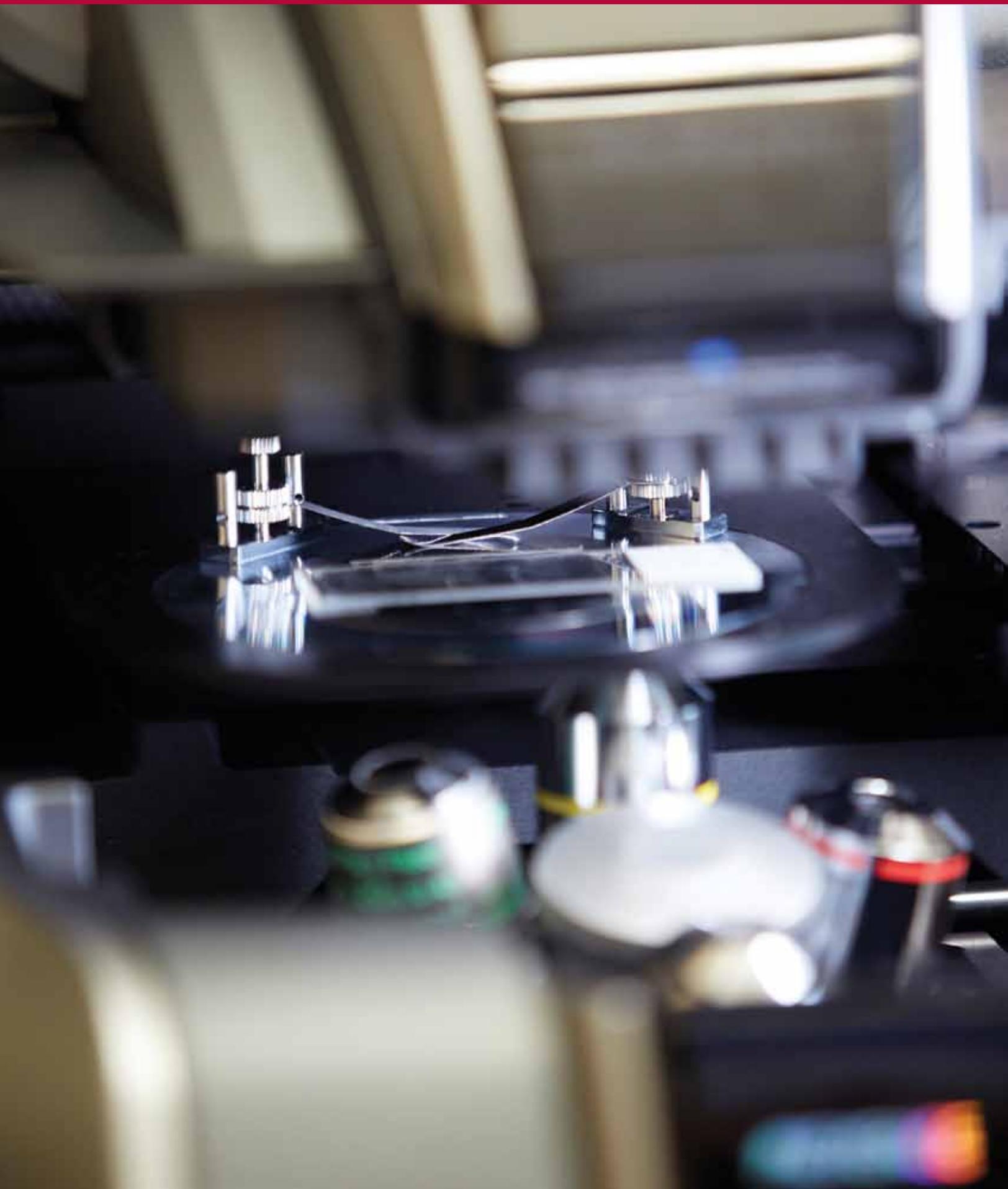
It did not work out that way. However, even when scientific projects funded by the Ming Hsieh Institute fail to prove their desired hypotheses, they contribute valuable basic science that can lead to new advances. The team went on to discover the first example of an ultrasound-activated MRI contrast agent. The pair also are developing an “MRI pill” that can rapidly and selectively release useful doses of an imaging contrast agent in the stomach, leading to unparalleled resolution and greater accuracy diagnosing gastric motility disorders, from gastroesophageal reflux disease (GERD) to gastroparesis (delayed gastric emptying), from which tens of millions of Americans suffer.

***Innovation:***  
an ultrasound-activated MRI contrast agent

***Clinical significance:***  
an “MRI pill” that can improve diagnosis of gastric disease



Travis Williams, Ph.D.



## Supporting Scholarship with Consequence

The Ming Hsieh Institute for Research on Engineering-Medicine for Cancer is helping USC fulfill its vision of “scholarship with consequence” by conducting research that not only advances knowledge but also helps people overcome disease and improve their lives.

In the Office of Research, we support the advancement of research by investing in innovative interdisciplinary teams, through which human needs inform scientists and engineers, and scientific discovery is rapidly translated into therapies and diagnostics for disease. In addition, our technology transfer office — the USC Stevens Center for Innovation — supports the aspirations of our faculty, staff and students to turn their discoveries into impactful products by creating relationships with private companies, licensing technologies, forming start-up companies and building research partnerships with industry.

The Office of Research is proud to support the Ming Hsieh Institute’s efforts to catalyze research that is innovative, interdisciplinary and impactful.



*Randolph Hall, Ph.D.*

*“In the Office of Research, we support the advancement of research by investing in innovative interdisciplinary teams.”*

*Randolph Hall, Ph.D.  
Vice President, Research  
University of Southern California*



Stephen Bradforth, Ph.D.



Wei Wu, Ph.D.

**David B. Agus, M.D.**

Professor of Medicine  
Keck School of Medicine of USC  
Professor of Engineering  
USC Viterbi School of Engineering  
Director, USC Center for Applied  
Molecular Medicine  
Director, USC Norris Westside Cancer  
Center

**Andrea Armani, Ph.D.**

Fluor Early Career Chair of Engineering  
Associate Professor of Chemical  
Engineering and Materials Science  
USC Viterbi School of Engineering

**Stephen Bradforth, Ph.D.**

Professor of Chemistry  
USC Dornsife College of Letters, Arts and  
Sciences

**Andy Chang, M.D.**

Assistant Professor of Urology  
Keck School of Medicine of USC

**Eric Chang, M.D.**

Professor and Chair, Department of  
Radiation Oncology  
Keck School of Medicine of USC  
Medical Director, Radiation Oncology  
Service  
USC Norris Comprehensive Cancer  
Center

**Kai Chen, Ph.D.**

Assistant Professor of Research  
Radiology  
Keck School of Medicine of USC

**Thomas Chen, M.D., Ph.D.**

Professor of Neurological Surgery  
Keck School of Medicine of USC

**Eugene Chung, M.D., Ph.D., J.D.**

Assistant Clinical Professor  
Keck School of Medicine of USC

**Peter Conti, M.D., Ph.D.**

Professor of Radiology  
Keck School of Medicine of USC

**Alan Epstein, M.D., Ph.D.**

Professor of Pathology  
Keck School of Medicine of USC

**Parkash Gill, M.D.**

Renette and Marshall Ezralow Family  
Chair in Cancer Therapeutics  
Professor of Medicine, Pathology and  
Urology  
Keck School of Medicine of USC

**Amir Goldkorn, M.D.**

Assistant Professor of Medicine  
Keck School of Medicine of USC

**Charles Gomer, Ph.D.**

Professor, Cancer Biology  
The Saban Research Institute  
Children's Hospital Los Angeles

**Mitchell Gross, M.D., Ph.D.**

Professor of Medicine and Urology  
Keck School of Medicine of USC  
Research Director, USC Center for  
Applied Molecular Medicine  
Research Director, USC Norris Westside  
Cancer Center

**Jonathan Kin Ha, Ph.D.**

Assistant Professor of Radiation Oncology  
Keck School of Medicine of USC

**Colin Hill, Ph.D.**

Associate Professor of Radiobiology  
Keck School of Medicine of USC

**Kian Kani, Ph.D.**

Assistant Professor of Research Medicine  
Keck School of Medicine of USC

**Julie Lang, M.D.**

Associate Professor of Surgery  
USC Norris Comprehensive Cancer  
Center  
Keck School of Medicine of USC

**Heinz-Josef Lenz, M.D.**

Professor of Medicine  
Co-director, Colorectal Center  
Keck School of Medicine of USC  
Associate Director, Adult Oncology  
Co-leader, Gastrointestinal Cancers  
Program  
USC Norris Comprehensive Cancer Center

**Zibo Li, Ph.D.**

Assistant Professor of Radiology  
Keck School of Medicine of USC

**Stan Louie, PharmD**

Associate Professor  
Director, Clinical Experimental  
Therapeutics Program  
USC School of Pharmacy

**J. Andrew MacKay, Ph.D.**

Assistant Professor  
Pharmacology and Pharmaceutical  
Sciences  
USC School of Pharmacy  
Assistant Professor  
Biomedical Engineering  
USC Viterbi School of Engineering

**Charles McKenna, Ph.D.**

Vice Dean, Natural Sciences  
Professor of Chemistry  
USC Dornsife College of Letters, Arts and  
Sciences  
Professor of Pharmaceutical Sciences  
USC School of Pharmacy

**Mahta Moghaddam, Ph.D.**

Professor  
Ming Hsieh Department of Electrical  
Engineering  
USC Viterbi School of Engineering

**Jay Nadeau, Ph.D.**

Associate Professor of Biomedical  
Engineering  
McGill University

**Nicos Petasis, Ph.D.**

Harold E. and Lillian M. Moulton Chair  
and Professor of Chemistry  
USC Dornsife College of Letters, Arts and  
Sciences

**Fabien Pinaud, Ph.D.**

Assistant Professor  
Biological Sciences and Chemistry  
USC Dornsife College of Letters, Arts and  
Sciences

**Richard Roberts, Ph.D.**

Chair, Chemical Engineering and  
Materials Science  
USC Viterbi School of Engineering  
Professor of Chemistry and Biology  
USC Dornsife College of Letters, Arts and  
Sciences

**Kathleen Rodgers, Ph.D.**

Associate Professor  
Clinical Pharmacy and Pharmaceutical  
Economics & Policy  
USC School of Pharmacy

**Kirk Shung, Ph.D.**

Professor of Biomedical Engineering  
USC Viterbi School of Engineering

**Uttam Sinha, M.D.**

Associate Dean, Surgical Stimulation  
Associate Professor of Otolaryngology  
Medical Director, Head and Neck Surgery  
Keck School of Medicine of USC

**John Stang, Ph.D.**

Research Assistant Professor  
Ming Hsieh Department of Electrical  
Engineering  
USC Viterbi School of Engineering

**Mark Thompson, Ph.D.**

Professor of Chemistry  
USC Dornsife College of Letters, Arts and  
Sciences

**Timothy Triche, M.D., Ph.D.**

Professor, Pathology and Cancer Biology  
The Saban Research Institute  
Children's Hospital Los Angeles

**Pin Wang, Ph.D.**

Professor and Kaprielian Faculty Fellow  
Mork Family Department of Chemical  
Engineering and Materials Science  
USC Viterbi School of Engineering

**Travis Williams, Ph.D.**

Associate Professor of Chemistry  
USC Dornsife College of Letters, Arts and  
Sciences

**Michael Wong, M.D., Ph.D.**

Professor of Medicine  
Keck School of Medicine of USC

**Wei Wu, Ph.D.**

Associate Professor  
Ming Hsieh Department of Electrical  
Engineering  
USC Viterbi School of Engineering

**Min Yu, M.D., Ph.D.**

Assistant Professor  
Stem Cell Biology and Regenerative  
Medicine  
Keck School of Medicine of USC

**Jennica Zaro, Ph.D.**

Research Assistant Professor  
Pharmacology and Pharmaceutical  
Sciences  
USC School of Pharmacy

**Gere di Zerega, M.D.**

Adjunct Professor of Research  
Obstetrics & Gynecology  
Keck School of Medicine of USC

**Yong Zhang, Ph.D.**

Assistant Professor  
USC School of Pharmacy

**Chongwu Zhou, Ph.D.**

Professor  
Ming Hsieh Department of Electrical  
Engineering  
USC Viterbi School of Engineering

**Qifa Zhou, Ph.D.**

Research Professor of Biomedical  
Engineering  
USC Viterbi School of Engineering



*Eugene Chung, M.D., Ph.D., J.D.*



*Charles McKenna, Ph.D.*

*“The Ming Hsieh Institute is one of the great research programs at USC. It brings multidisciplinary groups together to make a difference in fighting cancer. It’s even more important in its emphasis on projects that can be translated to the clinic for those most in need.”*

David B. Agus, M.D.  
Director, USC Center for Applied Molecular Medicine

## *Participants*

### **USC Academic Units**

**Keck School of Medicine of USC**  
[keck.usc.edu](http://keck.usc.edu)

**USC Dornsife College of Letters, Arts and Sciences**  
[dornsife.usc.edu/research](http://dornsife.usc.edu/research)

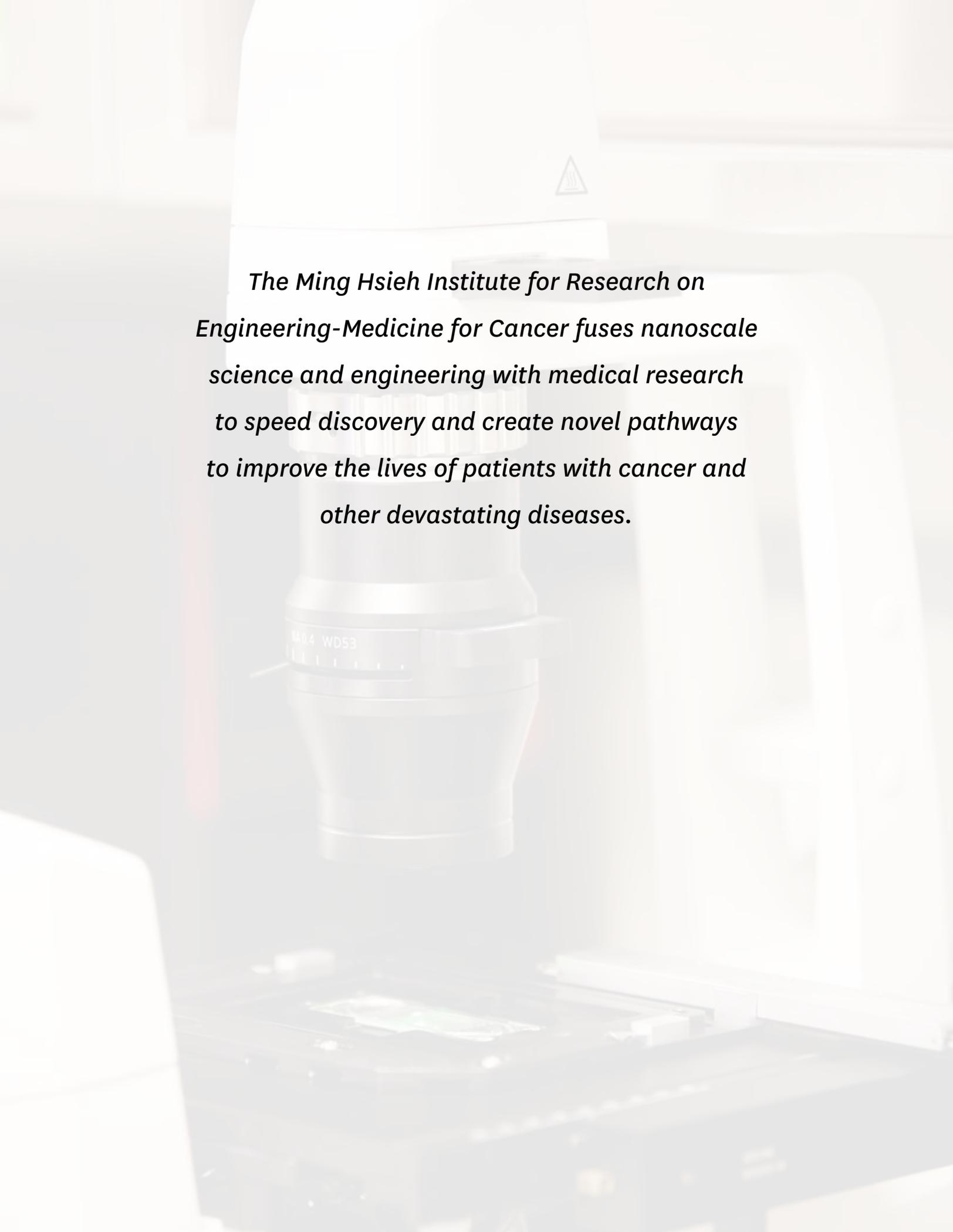
**USC School of Pharmacy**  
[pharmacyschool.usc.edu](http://pharmacyschool.usc.edu)

**USC Viterbi School of Engineering**  
[viterbi.usc.edu](http://viterbi.usc.edu)

**USC Norris Comprehensive Cancer Center**  
[uscnorriscancer.usc.edu](http://uscnorriscancer.usc.edu)

**USC Stevens Center for Innovation**  
[stevens.usc.edu](http://stevens.usc.edu)

**Children’s Hospital Los Angeles**  
[chla.org](http://chla.org)



*The Ming Hsieh Institute for Research on Engineering-Medicine for Cancer fuses nanoscale science and engineering with medical research to speed discovery and create novel pathways to improve the lives of patients with cancer and other devastating diseases.*



# Ming Hsieh Institute

Ming Hsieh Institute  
USC Office of Research  
Credit Union Building, Suite 325  
3720 S. Flower Street  
Los Angeles CA 90089-4019  
(213) 740-6709  
[vice.president.research@usc.edu](mailto:vice.president.research@usc.edu)  
[research.usc.edu/ming-hsieh-institute](http://research.usc.edu/ming-hsieh-institute)