touchpoints

Connecting you to the Heritage Provider Network

FEATURE STORY

Ultrasound Imaging Tools

Use Cellular Agents to Target Disease

PAGE 4

ANNOUNCEMENT

New Warning About Prescribing the Drug Makena for Preterm Labor

PAGE 9

GROUP SPOTLIGHT

Heritage Victor Valley Medical Group Gets a New Look

PAGE 10

Regal, Lakeside, and ADOC Medical Groups Host Drive-Thru Flu Shot Clinics to Combat Influenza

PAGE 11

HERITAGE PROVIDER NETWORK | Winter/Spring 2018, Issue 30

The Editorial

Richard Merkin, M.D.
Healthcare visionary, Dr. Richard Merkin, has spent the last 35 years implementing a successful, workable business model to address the needs and challenges of affordable managed healthcare.

Each year, more than one million people in the United States will be diagnosed with cancer. In 2016, an estimated 1,685,210 received the news from their doctor that they had cancer. Of these cases, 595,690 people will die from the disease[1]. A vital component in the fight against cancer is early detection along with a contingency plan to remove the cancer completely.

There are numerous methods to test for and detect if cancer cells are present in the body. Ultrasound imaging is one of several common methods to diagnose if a patient has cancer by pinpointing the location of tumors and other abnormalities in specific tissues. However, this method is solely limited to using sound waves within the bloodstream.

Once again, Heritage Medical Research Institute (HMRI) collaborates with our engineers and scientists at the California Institute of Technology (Caltech) to deliver solutions that push the boundaries of modern medicine and science forward to bring us closer to winning the war against cancer. Assistant Professor of Chemical Engineering and HMRI Principal Investigator, Mikhail Shapiro and his team at Caltech have discovered a way to use naturally occurring biochemical proteins to enhance ultrasound imaging to capture images at a cellular and molecular level. By applying heat from ultrasound, these modular Lego-like proteins will one day be able to administer medicine and provide noninvasive therapy directly to specific areas to target tumors and cancer cells.

We are optimistic about the possibilities this research will bring to the millions diagnosed with cancer each year and will continue to support the efforts of Caltech engineers. Together, we hope to move forward in delivering better healthcare outcomes and solutions to the millions around the world affected by this disease.

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

*touch*points
WINTER/SPRING 2018
ISSUE 30

Comments? Questions?
Go to "Contact Us" at the bottom of every page on heritageprovidernetwork.com

VIEW THE DIGITAL EDITION

Now you can access the *TouchPoints* and *HealthEd* publications whenever and wherever you want by visiting RegalMed.com/News-Events

[1] *Statistics at a Glance, August 14, 2016, www.cancer.gov/about-cancer/understanding/statistics*

Contents

4

FEATURE STORY

Caltech engineers use cellular nanostructures along with ultrasound imaging tools to define and target disease

CELLULAR AGENTS

USED TO TARGET & FIGHT DISEASE

CALTECH ENGINEERS USE CELLULAR NANOSTRUCTURES ALONG WITH ULTRASOUND IMAGING TOOLS TO DEFINE AND TARGET DISEASE

ULTRASOUND IMAGING AT THE CELULAR LEVEL

Since 1956 when ultrasound was first used for clinical purposes in Glasgow, Ireland by obstetrician Ian Donald and engineer Tom Brown, a significant amount of research has been done with using ultrasound for both imaging and therapy. Whenever we hear about ultrasound imaging, for most of us, it probably resonates with pregnancy and seeing images of babies developing inside the womb, or ultrasound being used to diagnose and isolate various diseases found in different areas of the body. Physical therapists have also used therapeutic ultrasound since the 1940s to treat a variety of conditions, from tissue relaxation, increasing local blood flow, reduce swelling, and promote bone fracture healing[1]. However, ultrasound techniques primarily rely on using sound waves that bounce off the tissues to relay its anatomical shapes and density, thus limiting its ability to penetrate beyond tissue to the cellular level. In many ways, modern medicine is still dependent upon further evolution of science and technology to bring forth revolutionary changes.

The brilliant minds at the California Institute of Technology (Caltech), like Professor Mikhail Shapiro and his team at the Shapiro lab, are diving more deeply to further the value of this discovery to find answers to help bring new therapies. They have discovered a way to use proteins from photosynthetic microbes found in nature to enhance ultrasound-imaging techniques that go beyond tissues to target the molecular and cellular levels. The foundation of their research is geared toward basic biology and cellular therapy with an overall goal to develop ways to image and control the function of cells inside the body.

> Whenever we hear about ultrasound imaging, for most of us, it probably resonates with pregnancy and seeing images of babies ...

During the early stages of research, they found the advantages of using cells as therapeutics, as opposed to molecules, are that cells are more sophisticated and can be programmed to respond and perform very specific tasks. They can also generate more cells and can self-destruct at the appropriate time. Nevertheless, one of the challenges of using

Mikhail Shapiro, Ph.D., Assistant Professor of Chemical Engineering, HMRI Principal Investigator - Biochemistry and Molecular Biophysics, Chemical Engineering

Assistant Professor Mikhail Shapiro completed his B.S. degree at Brown University in 2004 and received his Ph.D. from Massachusetts Institute of Technology (MIT) in 2008. Since joining Caltech in 2013, he and his team have been developing technologies to study biological processes that occur deep inside living organisms. This research involves molecular and cellular engineering, and uses various forms of energy: magnetic, mechanical, thermal and chemical. They utilize multiple biophysical methods that include magnetic resonance, ultrasound, infrared and electro-physiology to enable the imaging and control of biological function.

Professor Shapiro's work has been featured in several publications highlighting his body of work and the progress he has made linking magnetic resonance imaging (MRI) and ultrasound signals to gene expressions in cells, including tumor cells and commensal microbes, found in living tissue. This technique could eventually monitor cells and genes non-invasively, which could ultimately lead to non-surgical biopsies or interventions.

[1]*Source: Dr. John D. Ratcliffe, June 9, 2015, PhysicalTherapyWeb.com/Therapeutic.Ultrasound*

cells is that upon injecting them into the targeted area of the body, it is difficult to verify if the cells have reached their destination and if delivery was successful. It is also difficult for cells to receive instructions from the outside world, for example from a physician, which is why a need to create a cellular "antenna" was required to allow for such imaging and communication.

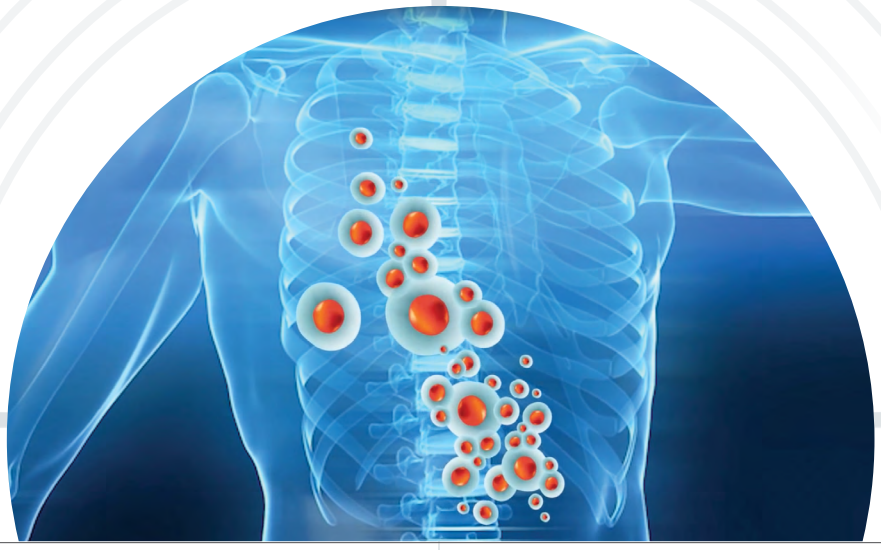
"We're able to engineer sophisticated cellular agents and administer them into the body, but once they are injected we lack the ability to see them or give them commands to perform functions for which they were originally designed," adds Professor Shapiro. "Our goal at the Shapiro lab is to give cells that are engineered the ability to communicate with the outside world from inside the body."

PROTEIN NANOSTRUCTURED GAS VESICLES

In 2014, Professor Shapiro discovered that he could get ultrasound signals from gas-filled structures found inside water-dwelling organisms, which use these proteins to float on top of the water and get ideal exposure to sunlight. During experimentation, he and his team discovered that these gas vesicles, or protein-shelled nanostructures, would be able to reflect sound waves during ultrasound imaging. This protein contains air on the interior that provides the buoyancy mechanism. Since it contains air, it has a different density from tissue (which is mainly water), allowing the ability to scatter sound waves to use with ultrasound.

Gas vesicles would enhance ultrasound methods to capture images of specific cell types. Professor Shapiro and his team work collaboratively on multiple projects with the goal to use this protein to image gene expression and locating cells within the body. The challenge with this approach is that the structure of gas vesicles are much more complicated than a simple fluorescent protein, which is coded by a single gene. Gas vesicles are encoded by a group of genes – at least eight of them to be precise, that have to work together to form this structure. "Transferring this more complex genetic machinery from one domain of life to another, and from one cell to another, presents a difficult challenge," expressed Shapiro. Respectively, the Lego-like proteins would also allow interchangeable pieces of other

We want to understand proteins from both a biological and physical point of view.



Go to **www.caltech.edu/news** to find out more.

proteins to attach to the surface of gas vesicles so that they can be modified to target specific properties, providing enhanced images of the molecules in various colors for greater definition.

Ultimately, gas vesicle proteins can be engineered to target tissues in the body that display specific cellular targets, for example, certain proteins that are overproduced in tumor cells. Gas vesicles can also be designed with longer and stronger nanostructures to prevent them from collapsing. These added functionalities along with a modular, Lego-like system give Professor Shapiro's research some traction.

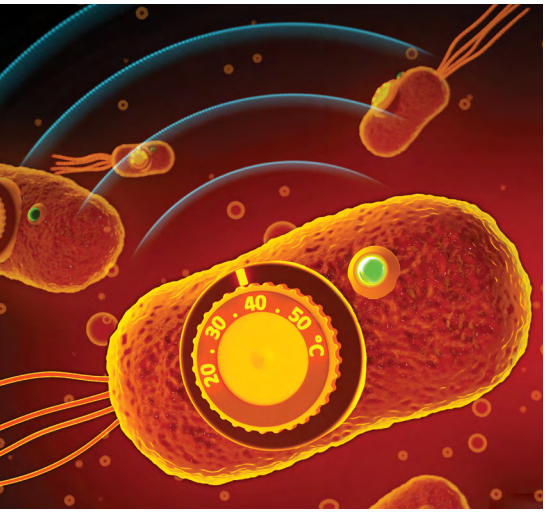
TEMPERATURE GIVES BACTERIAL AND HUMAN CELLS A WAY TO COMMUNICATE

Human cells are not the only cells that can be engineered for specific tasks. A new study conducted by Professor Shapiro's lab involves using genetically altered bacterial cells to release medicine directly into a specific site of a patient who has a tumor or other disease. By using the heat generated from ultrasound, the medicine would be administered at precisely the right time. Controlling the temperature would grant these genetically modified bacterial and human cells the ability to listen and communicate when properly activated.

COMMUNICATING WITH CELLS: LIGHT & SOUND VS. PROTEINS

LIGHT & SOUND	PROTEINS
Most techniques that researchers have available for imaging or controlling cells are designed to work in a dish – with cells grown in a dish, and not inside the body.	The unique proteins used in the Shapiro lab do not rely on light so they would be able to interact with ultrasound or MRI in a manner that enables specific cells to return more clearly defined images.
The majority of current methods use light. Most biology labs around the world are limited to using fluorescent proteins as cell labels and indicators.	Proteins could potentially be engineered to respond to sound waves or magnetic fields as command signals to perform very specific tasks at the cellular or molecular level.
Green fluorescent protein from jellyfish can be introduced into the cell and will light up in green when exposed to blue light. This works well with gene expression but not within the body because light scatters within a millimeter of hitting tissue.	Either an acoustic protein or a magnetic protein would be ideal for imaging the many processes occurring within the cells once administered into the body.
Since light cannot relay images or communicate with cells that are more than a millimeter deep, 99.9% of tools currently developed and being used today to communicate with cells are ineffective.	
Sound waves and magnetic fields are widely used in clinical and medical imaging (Ultrasound and MRI) and can readily permeate through tissue to form images within the body. However, as a standalone, neither is capable of capturing images of cells.	

"We give cells the ability to communicate with the outside world."



"Temperature controlled cells have the ability to break down and self-destruct when necessary."

Many scientists and engineers have shown interest in experimenting with developing cells into therapy, like with immunotherapy. Immunotherapy uses engineered immune cells administered into the body to recognize tumor antigens and to wipe out cancer. Another example of therapy is using engineered probiotics, which are bacteria that can be swallowed and would produce a beneficial activity in the gastrointestinal tract. Once in the GI tract, they can either displace pathogens; prevent pathogens from taking hold on the GI tract, or release molecules, like anti-inflammatory compounds.

His research also showed that medicine administered into the patient would have the ability to break down and self-destruct when necessary, for example, if the patient had a high fever indicating that the bacterial therapy may not be working effectively and it would be in the patient's best interest to terminate the therapy. Using the body's natural temperature as a control mechanism to destroy the cells, it acts as a natural fail-safe kill switch to ensure that the therapy will terminate precisely when required.

THE FUTURE OF ULTRASOUND: NONINVASIVE THERAPY TO TARGET TUMORS AND CANCER CELLS

The future of ultrasound tools and imaging could potentially open a new doorway of possibilities for noninvasive procedures for patients with tumors and other diseases. The idea that cells can be engineered to target a specific area of a patient's body using heat from ultrasound could pave the way to the future of noninvasive surgeries.

"I'm driven by the potential outcome; the ultimate applications and significance of being able to image and communicate with cells inside the body, but I'm equally driven by the challenge of finding and engineering unique proteins, like gas vesicles, that have unusual physical properties. As engineers, we want to understand proteins from both a biological and physical point of view, and engineer them accordingly," Shapiro adds. His busy team at the Shapiro lab consists of students from many different scientific backgrounds from physics, biology, and chemistry. "I enjoy engaging in challenges that include multiple aspects of these various backgrounds to collectively produce promising results and solutions," Shapiro says.

Professor Shapiro and his team at Caltech have every reason to be optimistic about their research and the impact it would have on the health outcomes for millions of people. Their exploration and commitment to creating a new field in biomolecular and cellular ultrasound, and its success, would also create a pathway to help inspire and encourage other engineers and scientists around the world to begin using this technology in various applications to benefit many lives.

NEW WARNING ABOUT PRESCRIBING THE DRUG MAKENA FOR PRETERM LABOR

New evidence shows Makena proven unsuccessful in preventing preterm labor and responsible for causing an increase in gestational diabetes

A recent "real-world" study published in the American Journal of Obstetrics & Gynecology is causing alarming doubts about Makena's effectiveness in preventing preterm labor. This study conducted by physicians from the Department of Obstetrics and Gynecology from the University of Texas Southwestern Medical Center and Women and Infant Studies, also discovered a potential increase in side effects of gestational diabetes among women who are taking Makena versus those with a similar history who were not on the drug. Physicians who are currently prescribing Makena to their patients should consider an alternate prescription method.

As a healthcare community, we consistently strive to make the right decisions pertinent to our patients' health and well-being while delivering on our promise to provide the highest quality of care. It's imperative to keep current on all of the medication available and their potential risks to perform our jobs more effectively. As part of an effort to keep physicians informed, routine email campaigns will be distributed containing relevant information that could significantly affect patients. Additional information about the study on Makena can be found in the American Journal of Obstetrics & Gynecology. To read the full article on the study, visit *tinyurl.com/makenaresearch*.

Source: Nelson DB, McIntire DD, McDonald J, et al. 17-alpha Hydroxyprogesterone caproate did not reduce the rate of recurrent preterm birth in a prospective cohort study. Am J Obstet Gynecol 2017;216:600. e1-9, from www.ajog.org/article/S0002-9378(17)30294-6/fulltext.

The newly renovated Heritage Victor Valley Medical Group Senior Center.

HERITAGE VICTOR VALLEY MEDICAL GROUP GETS A NEW LOOK

By Bryan Kawasaki

Bryan Kawasaki, Public Relations Coordinator, Heritage Victor Valley Medical Group

Heritage Victor Valley Medical Group is in the business of breaking down walls, and our senior center, The Resort, is no exception. As part of a three-year renovation project that spans multiple departments, The Resort recently underwent reconstruction to modernize the 3,200 square-foot facility.

Led by Steeno Design Studio, Inc., the redesign includes open-area seating and a new library with an interactive design that fosters creativity and social interaction. Other upgrades include a new kitchen area and LED lighting.

"Heritage Victor Valley is a very dynamic, cutting-edge company looking to the future of healthcare including their approach to this facility renovation," Tom Steeno said. "They have their finger on the pulse of trends and have been very forward thinking in their approach here to be a state-of-the-art organization."

Renovations to The Resort were completed this summer and it is the second HVVMG department to undergo a makeover. Improvements to HVVMG's Urgent Care Plus finished earlier this year, and upgrades to the Heritage fitness center, that will see the facility quadruple in size, is slated to be completed in September.

With renovations to the four departments that began in 2015, the project is on track to finish in 2018 with the unveiling of a new-look wellness center.

For more information on The Resort, visit hvvmg.com or call (760) 245-4747.

REGAL, LAKESIDE AND ADOC MEDICAL GROUPS HOST DRIVE-THRU FLU SHOT CLINICS TO COMBAT INFLUENZA

Physicians and members alike lined up at the designated drive-thru flu shot clinics. The first to arrive and set the wheels in motion at the Thousand Oaks clinic was Lead Physician, Dr. Fred Lindberg, above. Medical Assistant, Maria Arias helped to administer his flu shot.

Back row left to right: Margie Larson, *Office Manager;* Diedrea Jefferson, *CMA;* Sofia Amezquita-Diaz, *CMA;* Frederick Lindberg, *MD;* Debra D'Angelo, *MEd, RD, CDE;* Sharon Goodenough, *CMA;* Ellyse Lucas, *Receptionist*

Front row left to right: Liza Apodaca, *CMA;* Cathy Chacon, *Back office Lead/ CMA;* Vanessa Herrera, *Front office Lead;* Glynis Hatch, *X-Ray Tech/CMA*

Regal, Lakeside and ADOC Medical Groups, affiliates of Heritage Provider Network (HPN) hosted drive-thru flu shot clinics at Thousand Oaks and West Covina locations. Standard flu shot clinics were also held at various clinic locations across Southern California. The convenient drive-thru flu shot clinics offered members quick and easy access to receiving their seasonal flu vaccines to help prevent the spread of influenza to others.

More than 350 participants were vaccinated at these two locations. The Centers for Disease Control and Prevention (CDC) recommends that everyone 6 months of age and older should receive a flu vaccine every season to prevent contracting or spreading the influenza virus to others. This is particularly important for people who are at high risk of serious complications from influenza. For more information about the influenza virus along with a full list of age and health factors associated with the flu, visit *cdc.gov*.

touchpoints

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

New for 2018!

HealthyWay is now online!

HealthyWayEvents.com

According to our Annual Customer Satisfaction Survey, 93% of our members agree that they feel listened to and respected by their doctor.

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 the California Association of Physician Groups
- NCQA Certification for Credentialing
- Elite Status of Excellence for the Standards of Medical Care by the California Association of Physician Groups
- Recognized by the Integrated Healthcare Association (IHA) for our diabetic registries