touch Oolits Connecting you to Heritage Provider Network

FEATURE STORY

SHERLOCK: COVID-19 **Rapid Testing** Using CRISPR **Diagnostics**

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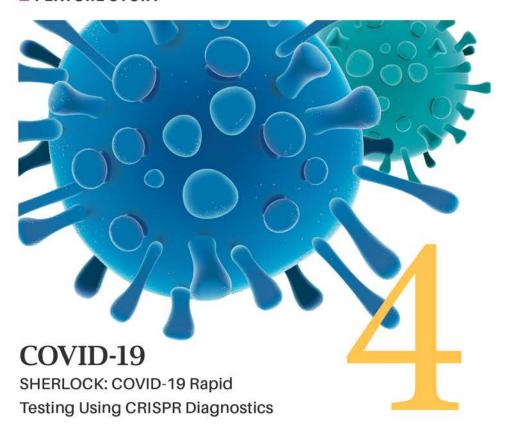
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Crossroads

With Dr. Richard Merkin



Racing Against a Worldwide Pandemic



e are facing one of the most crucial times in our society where our health and lives remain at risk from circumstances beyond our control. As a healthcare organization, our focus continues to be on helping to preserve and protect the well-being and safety of everyone who has placed their trust in us. Finding solutions to alleviate the fear and devastation



resulting from the ongoing COVID-19 crisis remains at the forefront of our priorities as we race against time and limited resources with unwavering dedication and commitment to preserve precious lives.

In our feature article, Professor and CRISPR pioneer Feng Zhang at the Broad Institute of MIT and Harvard unleashed a new discovery in SHERLOCK that rapidly identifies the agent responsible for causing the coronavirus, enabling for quicker and more accurate test results. Using a version of SHERLOCK, the Broad Institute also created CARMEN-Cas13 to increase testing capabilities on a much larger scale further

"The efforts of those whose sacrifice and selfless acts of kindness have made a positive difference in our communities and around the world..."

~ Richard Merkin, M.D.

giving scientists and medical professionals an advantage to test as many people as possible — a crucial factor in staying ahead of this pandemic.

As the world awaits for a proven-effective vaccine in the wake of new technology and methods of testing being introduced almost daily, Heritage Provider Network and its affiliates have never been more proud as I am to support the efforts of those whose sacrifice and selfless acts of kindness have made a positive difference in our communities and around the world as we learn to adjust and embrace an altered way of life.

Richard Merkin, M.D.

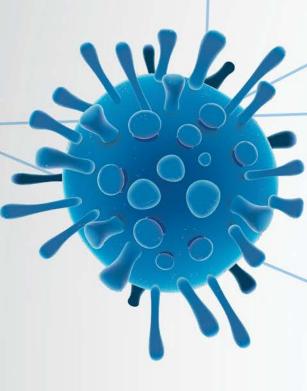
President and CEO of HPN

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.

COVID-19 TESTING

STAYING AHEAD OF THE CURVE

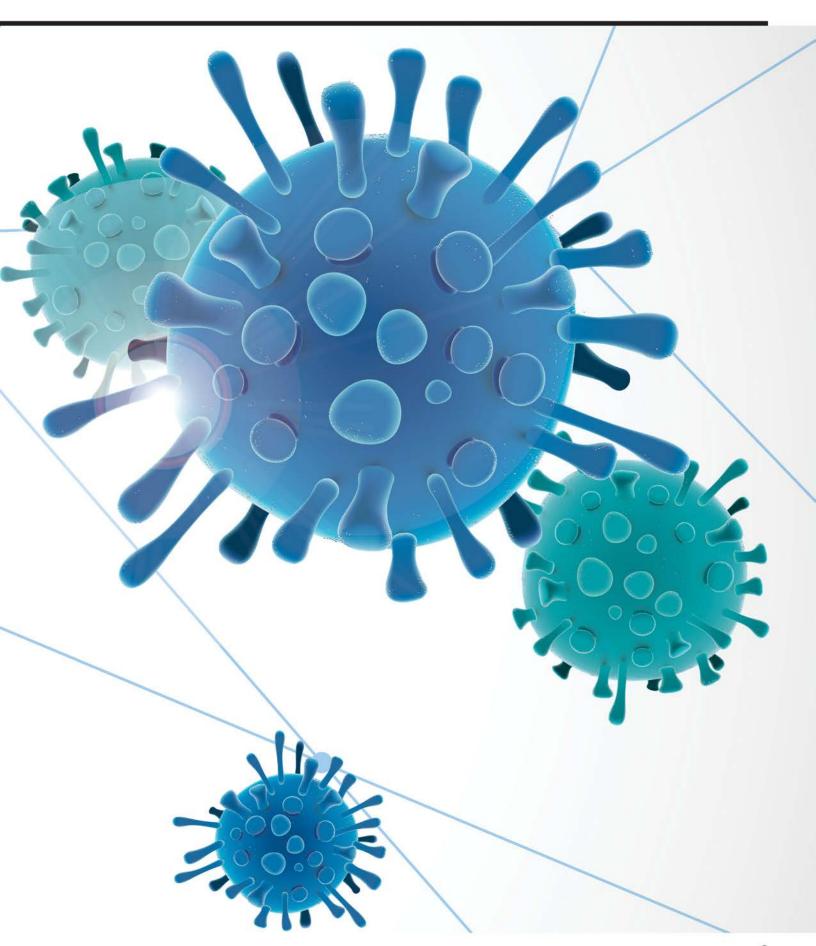


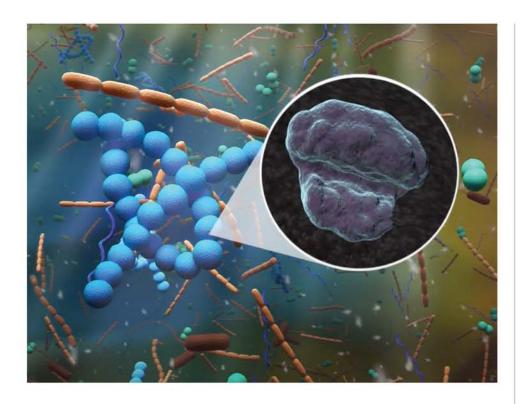
COVID-19 **RAPID TESTING**

USING CRISPR-CAS DIAGNOSTICS IN SHERLOCK

Broad Institute utilizes CRISPR-based SHERLOCK (Specific High Sensitivity Enzymatic Reporter UnLOCKing) for the detection of COVID-19

he current state of the coronavirus pandemic in the United States has resulted in more than one million people testing positive for COVID-19, prompting a more aggressive approach to testing as many people as possible by any means necessary. This enormous threat to our global health has captured the interest of leading scientists and medical professionals around the world to offer their knowledge and experience to assist in finding a cure. According to data provided by the Centers for Disease Control and Prevention (CDC), as of June 2, 2020, approximately 18,908,412 tests have been conducted. Nearly 2,225,186 of these tests have been reported positive, however not all test results are reported to the CDC. As further coronavirus testing continues across the country, scientific data gathered from several resources suggests we are nowhere near having COVID-19 under control.





STAYING AHEAD OF THE CURVE

At the Broad Institute of MIT and Harvard, Professor and CRISPR pioneer Feng Zhang and his team have joined the fight against COVID-19 by presenting the first-ever Food and Drug Administration (FDA) approved, new method for rapid detection of nucleic acids using a CRISPR-based diagnostic platform that combines nucleic acid pre-amplification with CRISPR-Cas enzymology. It is designed specifically to recognize desired DNA or RNA sequences. This platform, called specific high-sensitivity enzymatic reporter unlocking (SHERLOCK), allows for multiplexed, portable, and ultrasensitive detection of RNA or DNA from clinically relevant samples making it an ideal tool for rapidly detecting infectious diseases in humans.1

The average time for most test results takes five to seven days. An additional cause for delay is due to some states being limited in having the necessary coronavirus testing kits available. To stay ahead of the curve, more tests are needed and quickly to accommodate testing as many as possible. SHERLOCK technology will help enable expediting these results to prevent and contain the spread of the virus to the greater population.

THE 3 COMPONENTS OF RAPID TESTING

SHERLOCK allows scientists to detect synthetic COVID-19 virus RNA fragments between 20 and 200 aM (10-100 copies per µl of input) by using purified RNA as input for an RT-RPA before the Cas13 assay. This process

is performed in three steps and can produce results in less than one hour.

Testing begins from extracting nucleic acid to be used for qRT-PCR tests.

Step 1

25 minute incubation isothermal amplification of the extracted nucleic acid sample using a commercially available recombinase polymerase amplification (RPA) kit

Step 2

30 minute incubation detection of pre-amplified viral RNA sequence using Cas13

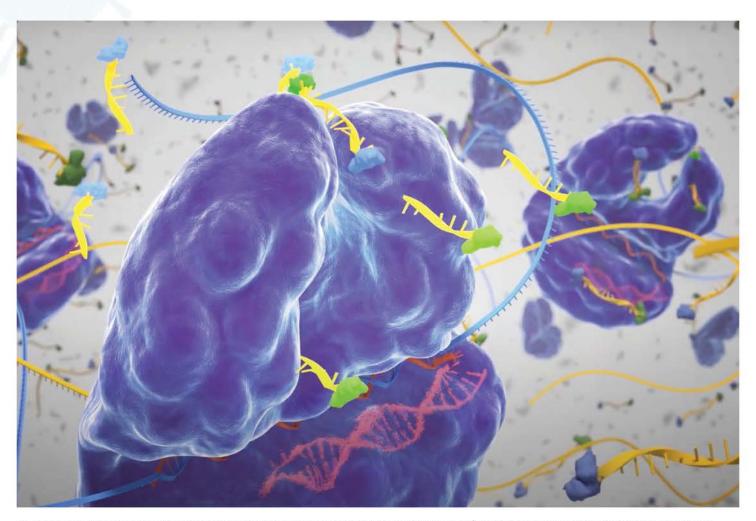
Step 3

2 minute incubation - visual readout of the detection result by eye using a commerciallyavailable paper dipstick

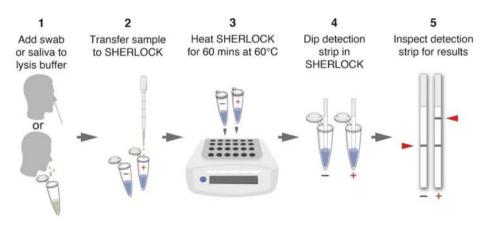
There are many tests authorized by the FDA for emergency use which include molecular tests, serology tests, and most recently, a rapid, proteinbased antigen assay - all methods to help diagnose and track the spread of COVID-19. A handful of companies have also produced at-home testing kits, however due to an influx of potentially unreliable serological antibody tests on the market, the FDA now requires that these tests be authorized.

POSITIVELY ACCURATE

What sets SHERLOCK apart from most well-known therapeutic applications of CRISPR gene editing is that it contains two bases of guide RNA that are complementary to



Cas 13 in its natural environment hunts viral RNA using an RNA guide. Once target is found, it becomes activated to cut the RNA it encounters. This method called collateral cleavage is what scientists have harnessed to create SHERLOCK.



STOPCovid in five steps - from sample to result.

SHERLOCK technology will help enable expediting these results to prevent and contain the spread of the virus to the greater population.

BROAD INSTITUTE INTRODUCES CARMEN-CAS13

Using a version of SHERLOCK, scientists at the Broad Institute have developed a CRISPR-based molecular diagnostics platform using microfluidics chips for the detection of viruses in human samples. This platform, Combinatorial Arrayed Reactions for Multiplexed Evaluation of Nucleic acids (CARMEN), is a chip capable of detecting a single virus in more than 1,000 samples at a time. It can search a smaller number of samples for more than 160 different viruses, including SARS-CoV-2, the virus responsible for the COVID-19 pandemic.2

THE POWER OF CARMEN

What is CARMEN aside from being a platform for scalable, multiplexed pathogen detection? Combined with the Cas13 nuclease (CARMEN-Cas13), it has the power to test more than 4,500 crRNA target pairs on a single assay. It can simultaneously differentiate all 169 human-associated viruses with 10 or more published genome sequences including additional crRNA that can rapidly detect the specific agent causing COVID-19. CARMEN-Cas 13's multiplexing capabilities also make it practical to scale as miniaturization decreases reagent cost per test by more than three-hundredfold. This helps to transform current diagnostic efforts from targeted testing of high-priority samples to more comprehensive testing of large sample sets further increasing the benefits to patients and public health.

The technology used to build CARMEN-Cas13 was first developed in 2018 in the lab of Paul Blainey, Broad Institute core member and MIT associate professor, and co-senior author of the new study. He and his team of researchers created rubber chips that were slightly larger than a smartphone. These chips contained tens of thousands of microwells (flat plate with multiple "wells" used as small test tubes) each designed to hold a pair of nanoliter-sized droplets. One droplet contains the viral genetic material from a sample and the other, reagents to detect a virus. This miniaturized approach proved to be more efficient and easier to implement.

ADAPTABLE & FLEXIBLE BY DESIGN

At a time when rapid testing tools are more crucial than ever, CARMEN-Cas13's CRISPR-based diagnostics make it an ideal tool for the diagnosis, surveillance

sequences of RNA in the virus and are attached to a CRISPR-Cas enzyme. This enables the guide RNA to detect the corresponding sequences in the virus and then combine to activate the CRISPR enzyme to release a detectable signal to produce a positive result. Research has shown that in patient samples these tests have resulted in 100% accuracy.

SHERLOCK continues to have a positive impact on the future of science and medicine as more scientists and physicians take advantage of its

CRISPR-Cas benefits to produce undeniably accurate results, serving as the foundation for expeditious detection of human diseases that are capable of creating a worldwide pandemic such as COVID-19.

"Heritage Provider Network is proud to continue our support of Professor Feng Zhang and the incredible research and discoveries being made at the Broad Institute," adds Dr. Richard Merkin, President and CEO of HPN. "There is no greater time than now when significant threats to

worldwide health is occurring to assist in launching important discoveries such as SHERLOCK to aid in finding ways to prevent and cure a disease that affects so many lives."

and characterization of infectious diseases that will enable clinicians to verify if patients are carrying multiple infections. It is designed to rule out a whole panel of diseases very quickly or test a large population of patients for a serious infection.

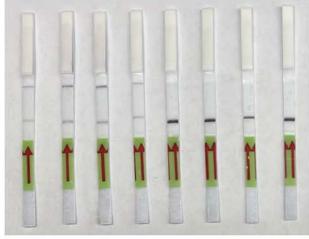
As the COVID-19 outbreak emerged during the study's review process, researchers rapidly incorporated a new test for SARS-CoV-2 into a coronavirus panel for the CARMEN-Cas13 platform. Further analyses found that CARMEN-Cas 13 was sensitive, specific, and statistically robust, demonstrating its remarkable adaptability to real-world challenges. More than 400 samples can be tested in parallel against the coronavirus panel using a single mChip. CARMEN-Cas13 provides specific information eliminating the output of irrelevant data gathered from sequencing from which a significant amount of information can become overwhelming and challenging to work through.

GREAT EXPECTATIONS

Researchers are optimistic about CARMEN-Cas13's future, concluding that it's possible that both region and outbreak specific detection panels could be implemented to eventually test thousands of samples from selected populations. These would include animal vectors, animal reservoirs and symptomatic patients. Blainey stated that while they are working to deploy CARMEN-Cas13 as a generally-available viral diagnostic platform, they are not quite ready to share information about its commercialization strategies. The team did reveal it is seeking Emergency Use Authorization (EUA) from the U.S. Food and Drug Administration to make this possible.

Further refinements are required in order to make CARMEN-Cas13 technology deployable in different contexts since it remains dependent upon using a microscope to read a fluorescent signal from the chip that indicates which virus a patient has. It also requires the preparation of the nanoliter droplets and nucleic acid extraction. This presents a challenging situation when using CARMEN-Cas13 in the field in such places like the airport, in a doctor's office or other clinical settings. Blainey further expressed that the platform's greatest advantages lies within its flexibility and adaptability. CARMEN-Cas13 has the potential to become a huge technological asset with multiple capabilities to be utilized for many test cases.





concentration copies per ul

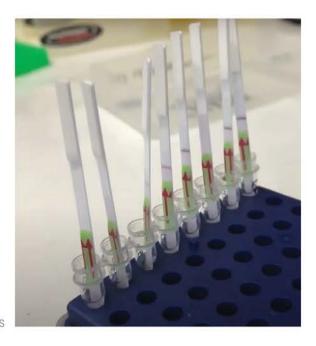
20fM 2fM 10000 1000

200aM 20aM 2aM 100 10

0.2aM 0aM 0.1

(-)

Covid-19 Rapid Test. Detection of the Covid-19 Sigene with Hybri Detect Strips



Merkin Family Foundation contributes to higher education at WGU



estern Governors University (WGU), the largest notfor-profit online university in the U.S. graduates more nurses than any other school in the country. Heritage Provider Network and its affiliates proudly employ many WGU graduates as part of their clinical staff.

Over the past year, Dr. Richard Merkin and the Richard Merkin Family Foundation has provided support for the development of several new certificates in managed care including a new Bachelor of Science in Health Services Coordination (BSHSC) program at WGU. All of these efforts are focused on training new talent for delivery of value-based care healthcare with an emphasis on evidenced-based

population health and care coordination tactics and recognition of the impact of social determinants of health.

"I believe that big things begin with small steps," adds Dr. Merkin. "We hope that this effort will lead to more advanced degree programs and perhaps one day even a medical school."

Annalisa Holcombe, President, WGU Advancement, expressed her gratitude





for the difference the foundation has made in the lives of their students. "Thank you, Dr. Merkin and the Merkin Family Foundation. Your gift to support the founding of this new degree and certificate programs is truly transformational. Not only has your gift changed the lives of more than 250 students enrolled in the program, but you are also creating a ripple effect that will be felt by their children, their families, and the patients they care for, extending the impact of your generosity for generations."



Regal Medical Group responds to their community's needs through CareCalls

Regal Medical Group implemented the CareCalls program in an effort to stay in touch with their members during the coronavirus pandemic. CareCalls is a telephone reassurance service designed to assist homebound and socially isolated older adults, OB/GYN patients and/ or disabled individuals by providing much needed social contact and a check on their safety and welfare. Trained staff responded to questions about coronavirus testing and access to healthcare; members who were identified with needs for food and medication were connected with resources and services.

"Our members are very appreciative of the support and assistance these CareCalls provide."

~ Maarten Lobker, VP, Marketing at Regal Medical Group

The program aims to reduce isolation and help recipients feel safer and more connected to their community by ensuring they have their basic needs met and that they can effectively manage activities of daily living in their own homes. Other anticipated benefits include the promotion of appropriate use of healthcare services, reduction of unnecessary ER visits, and lessening of caregiver burden during extremely stressful times.

"Our members are very appreciative of the support and assistance these CareCalls provide," adds Maarten Lobker, VP, Marketing at Regal Medical Group. "We feel that they will remember we were there for them long after this crisis is over. It also gives us a tremendous feeling of satisfaction to have such a positive impact on our members' lives and make a difference when they need it most."



HIGH DESERT MEDICAL GROUP LAUNCHES First COVID-19 testing site in the Antelope Valley



igh Desert Medical Group (HDMG) was proud to partner with Los Angeles County and the City of Lancaster as one of the first mobile testing sites for the novel coronavirus (COVID-19).

"Our staff was available to assist anyone assessed and determined to be in need of a COVID-19 test," said Rafael Gonzalez, HDMG Administrator. Gonzalez set the groundwork for the partnership after discussions with Dr. Clayton Kazan, Los Angeles County's official coordinator for coronavirus testing.

"Our office collaborated with High Desert Medical Group and the City of Lancaster to implement testing in the Antelope Valley. It was important we reach all portions of Los Angeles



County," said 5th District Supervisor Kathryn Barger, Chair of the Los Angeles County Board of Supervisors.

"We are glad to have partnered with Supervisor Barger, and with our community partner, High Desert Medical Group," stated Lancaster Mayor, R. Rex Parris.

While HDMG does not set the appointments, they can be arranged through Los Angeles County by responding to an online questionnaire. The form can be found at: https:// covid19.lacounty.gov/testing. People without computer access can call the Los Angeles County social services help line, 211 and answer the questionnaire over the phone.

Currently HDMG is partnering with The City of Los Angeles to provide free COVID-19 testing to all Los Angeles County residents, whether or not they are experiencing COVID-19 symptoms.

Tests for residents of Lancaster, Palmdale and surrounding communities are administered at a tented site at HDMG's main clinic located at 43839 N. 15th St. West in Lancaster, about two blocks north of Ave. K. Those calling for test appointments need not be HDMG members or patients. HDMG will continue to do everything that they can to help the Antelope Valley community prevent the spread of COVID-19.

Gonzalez urged that the thousands of HDMG patients who regularly receive care from the organization can arrange to be tested with approval of their primary healthcare provider. It is not necessary to have a face-to-face appointment with a provider or urgent care if you believe you have symptoms, Gonzalez emphasized.

"Telehealth visits are a convenient way to communicate your symptoms with a provider who can then follow up with

"Telehealth visits are a convenient way to communicate your symptoms with a provider who can then follow up with a variety of treatment and diagnostic options, including COVID-19 testing."

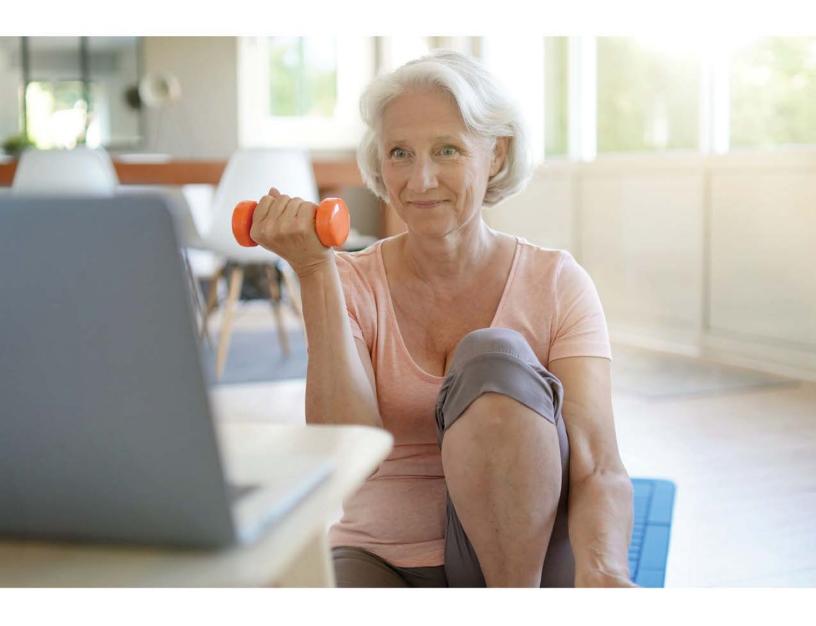
~ Rafael Gonzalez, HDMG Administrator

a variety of treatment and diagnostic options, including COVID-19 testing," Gonzalez said. "Everyone should stay home to limit your exposure, to yourself, and to others."

HDMG and Heritage Health Care members trying to obtain COVID-19 testing should contact the organization directly at (800) 266-4364.

An electronic bulletin board sign, and traffic direction cones provided by the city, will guide people with appointments into the test screening site.

Gonzalez noted that High Desert Medical Group has been screening and testing its own patients since March 15, 2020. Initiation of the parking lot site was an expansion into wider community availability. Since partnering with Los Angeles County, High Desert Medical Group has tested over two thousand and three hundred community members and proud of the valuable service they provide to their community in these uncertain times.



BAKERSFIELD FAMILY MEDICAL GROUP: Staying social when the world shuts down

or many years, Bakersfield Family Medical Center (BFMG) has built a reputation in their community for having a robust selection of free social activities for their senior members. As a result of their dedicated time and effort, senior members have come to rely upon these social activities as an important source of friendship and fellowship and connection to their community.

Before the coronavirus crisis, their weekly calendar was filled with busy activities such as the Coffee Club every Monday morning where the seniors and staff would meet early and the floor would be buzzing with laughter and camaraderie. Attendees are encouraged to introduce themselves and share some information by answering the question of the day. The Coffee Club is also often sponsored by their health plan partners, Aetna and Anthem. Any leftover food from the meeting is given to seniors to take home or donated to other seniors in need.

Wednesdays are reserved for hourly walks at the local mall where it's a hot spot for senior walkers early in the morning. Mall walks are co-sponsored with Aetna, one of their Medicare Advantage partners. The walk begins with a quick set of stretches followed by a one-mile walk that repeats for those interested in extending their cardio workout. Everyone walks at their own pace and in small groups. Afterwards, the members all head to socialize a little more at the nearby "Maccy D's" (what they call McDonald's) for coffee.

Friday is arts and crafts day where it becomes a jewelry-making fest. Homemade cards are crafted and donated to local charities around the holidays to organizations such as Christmas for Seniors and Honor Flight. In partnership with Humana, fleece blankets are also distributed to veterans returning from Honor Flights.

Their senior members have been featured on Christmas floats for several years and often volunteer as a group to assist other charitable activities The long time friendships formed at BFMG through their senior activities have created a valuable support network that is deeply rooted in their community.

within their community. In addition to offering special classes on a variety of subjects, every quarter BFMG hosts a potluck whereby members from all three activity groups gather and share delicious homemade recipes.

How does BFMG help their seniors cope when all of these activities come to a screeching halt due to the COVID-19 quarantine? They encourage their seniors to visit their Facebook group located on the main BFMC Facebook. Here, seniors can find all of the existing activities virtually. The page was implemented back in early 2019, but had been under-utilized. At the beginning of the quarantine, BFMG immediately contacted their senior members and invited them to join their Facebook group so that they could continue their weekly activities in a virtual manner.

Monday mornings are now shared with a virtual greeting along with a cup of coffee. On Wednesdays, they are encouraged to go for a walk around their neighborhood and share something they saw during their walk. Links to online exercise videos are shared to encourage continued physical activities. Arts and crafts on Fridays have become a forum for sharing new ideas to do at home and fun links to virtual art museum tours

at the Metropolitan Museum of Art in New York.

While there are still some technology challenges with some lacking access to a computer, smartphone or the internet, or not wanting to participate in social media, BFMG puts into practice the old fashioned way of communication – by telephone.

The long time friendships formed at BFMG through their senior activities have created a valuable support network that is deeply rooted in their community. Thanks to the BFMG Senior Activity Group, senior members are learning to cope, stay connected, stay active, and independent while being there for each other during such a difficult time.

REGAL MEDICAL GROUP AND REMITA HEALTH Partner to Feed Frontline COVID-19 Healthcare Personnel at Northridge Hospital



Pictured left to right: Brian Hammel, President of Northridge Hospital Foundation, Nelly Leng, Sr. Community Engagement Liaison at Regal Medical Group, and Monnize Sobrinho, Hospice Care Consultant at Remita Health.



Some local heroes dedicated to the COVID-19 unit at Northridge Hospital.



On May 11, 2020, Regal Medical Group partnered with Remita Health to provide lunch to 60 employees working the COVID-19 unit at Northridge Hospital in the San Fernando Valley.

Brian Hammel, President of the Northridge Hospital Foundation welcomed their generosity for helping to take care of the essential workers during this difficult and uncertain time.

"Taking the time to provide lunch to medical staff was meaningful to me and all of us at Remita Health. We were pleased to collaborate with Regal Medical Group as we share the same mission

to bring joy and comfort to frontline workers who are battling this crisis during such uncertain times," added Monnize Sobrinho, Hospice Care Consultant at Remita Health.

Nelly Leng, Sr. Community Engagement Liaison at Regal Medical Group says, "It's a rewarding experience to be a part of an organization like Regal who values generosity in times of adversity.

Supporting a local restaurant while also helping feed the COVID-19 unit at Northridge Hospital is definitely the right gesture to lift up our community."

This event marks the first of many lunch deliveries to local hospitals in recognition of the selfless and tireless efforts frontline healthcare workers make to care for patients across the San Fernando Valley. It also helps to encourage them as they continue the fight against COVID-19.

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*touch*points

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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.



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Recognized by the Integrated Healthcare Association for our diabetic registries