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Caltech Professor Discovers Long Intergenic Non-coding RNA





SPRING 2021 ISSUE 42

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Crossroads With Dr. Richard Merkin



One Step Closer to Curing Some of the Rarest Genetic Diseases



any of us might not fully comprehend the unique structure of our own biology, or the intricate constructs of our DNA. As we embrace new technological advancements in science and medicine that provide further insight into the human genome, we discover just how important a role each genetic material plays in every fiber of our being.



In our feature article, Mitchell Guttman, a professor of biology and biological engineering at Caltech, and Heritage Medical Research Institute investigator, discusses how his discovery of long intergenic non-coding RNAs, or lincRNAs, impacts X chromosome inactivation in early human development. This could mean curtailing the side effects of some of the most severe developmental disabilities in females born with rare genetic diseases. And in light of our ongoing effort to combat COVID-19, Mitch Guttman and his lab continue to drive vital RNA research for SARS-CoV-2 in the fight against the coronavirus.

As we await the increasing availability of COVID-19 vaccines throughout our entire organization, I encourage everyone to continue to adhere to the mandated safety guidelines and regulations to

ensure proper safety measures. Thank you to our employees and affiliates who remain diligent in providing dedicated service and support to ensure the safety of our members and our communities.

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.

Discovery Offers Hope in Treating Rare Disorders

itchell Guttman, Ph.D., professor of biology and biological engineering at California

Institute of Technology (Caltech), Heritage Medical Research Institute investigator and head of Guttman Lab IncRNA Biology, has been uncovering the unique role RNAs play in early human development. HPN's support of Guttman's work began long before his promising career at Caltech. As his research continues to evolve in unlocking some of the mysteries of molecular biology, his determination to one day find a cure to some of the rarest genetic mutations gives hope to many.

Pictured are images of compartments or droplets of an RNAguided regulatory complex in the nucleus. Courtesy of Caltech.

Caltech Professor Discovers Long Intergenic Non-coding RNA to Treat Incurable Neurodevelopmental Disorder

In an in-depth Q&A session, Professor Guttman explains the important connection between long intergenic non-coding RNAs, or lincRNAs, and X chromosome inactivation. A deeper understanding of this unique relationship may provide the gateway to preventing many other genetic diseases.



NSP16 is a SARS-CoV-2 viral protein that acts to block human splicing (gene processing) upon infection. Image shows the locations of this protein within an infected human cell. Courtesy of Caltech.

Q: Heritage Provider Network (HPN) has been a longtime supporter of you and your work predating Caltech. Can you share some of your early experiences while at the Broad Institute of MIT and Harvard, and how your research has evolved since your primary discoveries in genetic mutations?

GUTTMAN: In 2007, I was still a graduate student at the Broad Institute. It was around 2009-2010 that Dr. Merkin started a program funding stem cell research. We had just started to identify a whole new class of genes encoded in human genome. This was incredibly exciting for us and our field since we weren't even a decade since the sequencing of the human genome. One of the biggest surprises of this project was how few protein coding genes the human genome actually encoded. The central dogma of biology of genetics, that we still teach our students today, is this idea that our genetic material encodes messenger RNAs that act as intermediates that then get translated into proteins. These proteins do all of the important work in the body. One of the really big surprises was discovering that only about 1.2% of the human genome encodes proteins. More than 98% does not and this was a big surprise at the time. Many efforts were underway to try and fully understand the remainder of our genome and why it matters.

We began to explore and identify different types of functional elements and came across an entirely new class of genes called long intergenic noncoding RNAs, or lincRNAs. In many ways, they looked just like protein-coded genes but yet they couldn't make a protein. We wanted to further investigate the importance of lincRNAs, such as what role they played in controlling different types of cell behavior or identity functions inside the human body. We wanted to tackle this in the context of early development in embryonic stem cells, and the reason being that embryonic stem cells are a special cell state that is unique in its ability to give rise to virtually any other cell type in the body. We were curious to know if we could systematically dissect what, if any, roles these lincRNAs play and how they connect into the overall circuitry of coded cells, how they interact with proteins, how they mesh into the hierarchy of organization and control what's important in development.

This early funding and support we received from Dr. Merkin was essential for allowing us to dissect the role lincRNAs can play. To this day, I think it's one of the most important things we have done that benefited us and the entire scientific community; to finally understand that there is this whole other class of genes that are more abundant than proteins that play essential roles as organizers and orchestrators of all of the different players in the cell.

This was the very early work we had done that Dr. Merkin supported. I met him while I was transitioning from the Broad to Caltech. Shortly after completing this work, I started my lab at Caltech. When the Heritage program started, it was wonderful to reconnect. In many ways, everything I do today was a direct result of that initial project. When I started my lab, we knew there were tens of thousands of new genes that played essential roles in organizing cellular molecular activity, cellular processes and cellular functions. The next step was to figure out how they do this. What makes these lincRNAs special or unique? Why would the cell utilize an RNA as opposed to a protein? Why create a whole new class of genes whose role cannot be achieved by a protein? These were the types of questions we wanted to answer.



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IncRNAs localizing to precise regions of DNA in the nucleus, where each color represents a different RNA, and a zoomed in example showing various RNA labeled. Courtesy of Caltech.

We then started to dive into the mechanisms and molecular details of how these RNAs orchestrate, creating these different gene expressions and processes. Along the way we were able to uncover whole new principles of what lincRNAs do that proteins cannot. What led our

discovery is that the unique role of RNA is one of spatial organization of the nucleus and quantitative control of molecules. What we found is that these RNAs can effectively act as molecular beacons, or GPS signals, to mark specific territories within the nucleus to guide protein molecules to very specialized places based on signals from these RNAs. That is actually a very unique role because proteins are like an analog signal and made into an RNA. That RNA is then decoded; therefore, there is a gap between the DNA information and the protein information because they are going through these intermediates. These intermediates are not just molecular intermediates but they are also spatially segregated. The RNAs act as a spatial encoder that guides specific proteins to specific places. The focus of my lab is to really dissect this question of how spatial control of molecules drive quantitative behaviors in the cell.

Q: As a Heritage Medical Research Institute (HMRI) investigator and professor at Caltech, how has HPN's support made a difference in your direct field of study with respect to propelling your research forward?

GUTTMAN: I don't think it would have been possible to explore new areas of scientific research or pursue new



direction without Heritage support, and the reason for that is twofold. One of which was Dr. Merkin's message that encouraged us to take risks, follow crazy leads and do transformative work, which became the mantra; the mandate of the program that was incredibly empowering in its own right. This, of course, was different from most traditional funding that typically has the exact opposite mantra, which is that they only fund science that is not as risky, that is very likely to work or the next logical step from something that has already been well established. When you have a transformative idea, it's often very challenging to obtain the necessary resources to tackle it. If I had submitted some of my initial proposals that I had presented to Dr. Merkin when we were first screened to participate in the Heritage Medical Research Institute program to an NIH [National Institutes of Health] study section, it would not have gotten funded. It was a transformative idea that still required a lot of preliminary evidence to demonstrate that the science was true. It was the Heritage program that allowed me to explore



Pictured left, Mitchell Guttman, Ph.D., professor of biology and biological engineering at California Institute of Technology (Caltech), Heritage Medical Research Institute investigator and head of Guttman Lab IncRNA Biology

Above, NSP16 is a SARS-CoV-2 viral protein that acts to block human splicing (gene processing) upon infection. Image shows the locations of this protein within an infected human cell. Images courtesy of Caltech.

these ideas and develop an entirely new class of technologies, methodologies and tools to measure for the first time how molecules moved around and how they come together. The two years it took to develop would have been a struggle in a standard NIH study section.

Since our initial paper in 2009, this field has become such a huge area of study. We have not only led the field since then but I believe we are far ahead because we get to take these really incredible, transformative risks and push the field even further ahead in ways that most in my position would not be able to do. This approach has shaken the scientific community in a positive way that allows other scientists to pick up what we've already created and use that to help propel their own research forward. The Heritage funding has made it possible to accelerate this field. Without the funding, the field would not have moved as quickly as it has.

Q: What led you to focus on genetic diseases, specifically in the areas of X chromosome inactivation?

GUTTMAN: When I started my lab, we were really interested in understanding the "why". Why lincRNAs? To help answer this, one of the things we needed to do was to hone in on the molecular details of how RNAs work and how they brought together molecules and organized space, and so on. We wanted to focus on X inactivation which is an early developmental process in female mammals. Females have two X chromosomes and males have one. Unlike the Y chromosome which does not contribute much other than sex determination, the X chromosome actually contains thousands of genes that are crucial for normal biology and almost nothing to do with sex determination. Every organism that has an X chromosome faces the challenge of having this asymmetry between males and females with the expression of important genes. Placental mammals like humans solve this problem by undergoing a process called X chromosome inactivation. In very early stages of the fertilization

process, females will randomly silence one of the two X chromosomes, and what this effectively does is even though they have two X chromosomes, they will only express one so that it creates a balance; both the female and male have one.

It's a very simple idea, but to carry that out on a molecular level is challenging. It is in itself an incredible process because it's so fundamentally important to development. It's just a great system to dissect, and this entire process is orchestrated by one single gene — the lincRNA. If you turn on that gene in a male, it will silence that chromosome. This gene alone orchestrates the entire program. We were fascinated by how it can orchestrate such an important central program. And that's why we started focusing our attention on the X chromosome.

Subsequently, we quickly developed a new set of new technologies and tools to be able to view and track the progress of this RNA across time in early development; where does it go first, how does it move, what proteins bind to it, and so on. These tools allowed us to uncover the detailed mechanism of how these RNAs were able to move across the chromosomes and silence transcription across all of these genes. One of the things we found was the presence of this new RNA-binding protein that is important for silencing transcription on the chromosome and were able to show that it does so by recruitment of an entire chromatin complex. If we can disrupt this complex, then we can actually affect silencing on the X

chromosome. This is how we initially started to think about targeting genetic diseases. There's a whole family of rare genetic diseases that primarily affect females. One of them being Rett syndrome, which is a genetic, neurological and developmental disorder that affects brain development, causing a progressive loss of coordination, speech and motor skills.

"We are far ahead because we get to take these really incredible, transformative risks and push the field even further ahead in ways that most in my position would not be able to do ... The Heritage funding has made it possible to accelerate this field."

~ Mitchell Guttman, Ph.D.

At 2 years of age, females that have Rett syndrome begin to display severe disabilities. They usually are in wheelchairs most of their lives because they can't walk, talk or perform many basic functions. They also have severe intellectual disabilities and cannot take care of themselves, requiring full-time care. What's special about this case as a genetic disease compared to most genetic diseases that affect both males and females, is that these other diseases don't have a functional copy of the gene in their genome. Here, females have a functional copy that is silenced. Finding a way to turn on this copy would provide a way to compensate for these genetic diseases that would allow those with Rett syndrome, in theory, to live a normal life. Once we knew how this silencing happens and were aware of drugs that could un-silence these genes, we thought about how we'd utilize these strategies to develop effective therapeutics for these female genetic disorders. Our approach is not exclusively tackling rare diseases, but also tumor suppressor genes that would target glioblastomas and other tumors. With this discovery, we hope to treat an entire spectrum of genetic diseases.

Q: A recent publication by Caltech mentions your collaborations with fellow HMRI investigators André Hoelz and Rebecca Voorhees, involving projects to help fight against the current COVID-19 pandemic. These include RNA's role in shaping the nucleus and imaging SARS-CoV-2 protein interactions, and studying the interactions between SARS-CoV-2 and human ribosomes. Can you elaborate on the progress being made in these areas and the impact they will have in the prevention and/or treatment of similar viruses in the future?

Guttman: We have been doing quite a bit of work with SARS-CoV-2 since the pandemic began in March 2020 that uprooted our entire way of life. At the time, one of my students and a former scientist in my lab approached me and pointed out that my lab

Coronavirus structure



had developed all of these tools for studying RNA for nearly a decade. And, SARS-CoV-2 is an RNA virus. That meant that the tools that were uniquely available in our tool kit, that very few other people had available, could become very valuable in understanding the nature of SARS-CoV-2 and when it first infects human cells.

I was approached with a proposal to take two of our technologies to begin cataloging what happens when this virus infects human cells: to understand what it binds to, what it interacts with and what it disrupts. In April 2020, a student of mine sent me a picture mapping the interaction between one of the SARS-CoV-2 proteins. What he found that surprised us was that not only was it binding directly to a human ribosome, but doing so in one specific location. This was so incredibly specific and important that I reached out to Rebecca Voorhees, a fellow HMRI colleague who's an expert on ribosomes, for some answers. After our evaluation, it was evident that where this viral protein sits is right at the region of the ribosome where the messenger RNA comes through. Once we discovered that, we tried to determine how this impacts the translation of human proteins and its ability to shut down an infected cell's call for help. The whole immune response is built upon this idea that the cells are machines that detect viruses and will send out signal molecules asking for help. The virus makes proteins that prevent the cell to trigger a call for help, therefore shutting down any immune response.

We have spent a lot of time with Rebecca, mapping out the exact regions "Our approach is not exclusively tackling rare diseases, but also tumor suppressor genes that would target glioblastomas and other tumors."

~ Mitchell Guttman, Ph.D.

of the viral proteins that bind to the exact regions of the human ribosome, and screening small molecules that can disrupt this interaction with some success. Hopefully that will continue to progress. It might not be the key to unlocking COVID-19, but it could possibly become the gateway to uncovering drugs that would be effective against a whole class of coronavirus in general.

We have also been working with André Hoelz [and his lab] throughout the years. They have identified one of the SARS-CoV-2 proteins that bind to the nuclear pore complex in infected cells. Since we have access to virallyinfected cells, our lab has been assisting them with tracking viral interaction and dynamics, while his team focuses more on the atomic structure.

Q: How do you see your research evolving and what is your hope for the future of lincRNA?

Guttman: As our research continues to progress in the coming years, our goal is to fully understand how small amounts of molecules can trigger such large responses in cellular behavior. I anticipate that we will approach this on a more quantitative level. We've been studying how RNAs can create these exponential responses in the nucleus to control very large programs with just small environmental changes. Exploring this whole paradigm is very exciting for us and we have a unique perspective on tackling it. We have also started doing a lot of work with ALS, or Lou Gehrig's disease, and we expect this research to be transformative. There is a whole class of other genetic diseases we still want to understand.

Q: With human trials potentially scheduled to launch within the next two years, what are some results we can expect to see after attempting to reactivate the X chromosome? What type of data is collected to verify it has been successful?

Guttman: How we measure success would depend upon which diseases we are targeting. Specifically with Rett syndrome, one criteria for measuring success would be in our ability to evaluate improvements in motor functions such as muscle features and seizures that are associated with Rett syndrome. Ideally, our ultimate objective would be to turn these genetic diseases into curable disorders. Of course, we are not going to be able to cure a 20-year-old who has Rett syndrome today, but if we can easily come up with a newborn genetic screen when females are born, we can treat them before they begin to develop symptoms of this disease.

The genetic screening is something we can do already. From a treatment perspective all of the evidence suggests

Mitchell Guttman, Ph.D.

Professor of Biology and Biological Engineering at Caltech

Heritage Medical Research Institute Investigator

HMRI Investigator Appointment: 2015-2021 _____

Mitchell Guttman is a professor in the Division of Biology and Biological Engineering at the California Institute of Technology. He received his Ph.D. from the Department of Biology at MIT. He established his lab as an independent fellow at the Broad Institute of MIT and Harvard prior to joining the faculty at Caltech in June 2013. He is a recipient of the 2012 NIH Director's Early Independence Award and was named one of Forbes magazine's "30 under 30" in science. Guttman also holds two degrees from the University of Pennsylvania: a bachelor's degree in molecular biology and computational biology and a master's degree in computational biology and bioinformatics.

Source: guttmanlab.caltech.edu/guttman.php

that we should be able to get there sooner rather than later, in large part because the initial compounds for utilization have already been tested for safety in patients. At the moment we are really focused on providing efficacy.

Heritage Provider Network Achieves Highest Honors FROM NATION'S LEADING AMERICA'S PHYSICIAN GROUPS





eritage Provider Network (HPN), one of the nation's most experienced and innovative physician-led, valuebased care organizations, and its family of medical groups achieved the highest possible honors from America's Physician Groups (APG) annual Standards of Excellence[™] (SOE[®]) survey. All medical groups in the HPN family earned Elite Status, the top ranking in the nation. "This recognition is a testament to our continued commitment to hard work, delivering quality affordable care to all of our members," said Dr. Richard Merkin, president and CEO of HPN. "I'm very proud of our valued team members at each of our medical groups and share this elite status with them."

The elite 5-star status is the highest possible honor awarded by the nation's leading association for physician organizations practicing coordinated care. Elite 5-star status in all categories of the survey was achieved by all nine of HPN's family of medical groups including:

- Affiliated Doctors of Orange County
- Heritage Sierra Medical Group
- Regal Medical Group
- Lakeside Medical Group
- Heritage Victor Valley Medical Group
- High Desert Medical Group
- Desert Oasis Healthcare
- Coastal Physicians Network
- Bakersfield Family Medical Group



"We commend Heritage Provider Network for earning the coveted Elite status in APG's 2020 Standards of Excellence program," said Don Crane, APG president and CEO. "This recognition demonstrates Heritage Provider Network's commitment to improving patient health outcomes by exceeding the national benchmarks and standards in value-based care."

APG is the country's leading organization representing physician groups practicing coordinated care. APG's Standard of Excellence[™] (SOE*) Elite award for patient care includes care management practices, patient-centered care, information technology, group support of advanced primary care, accountability and transparency, and administrative and financial capability. "This recognition demonstrates Heritage Provider Network's commitment to improving patient health outcomes by exceeding the national benchmarks and standards in value-based care."

~ Don Crane, APG President and CEO

Announcement



Heritage Medical Research Institute Award Supports Efforts at Stanford Medicine Transforming Cartilage Growth Exploration n February 2, 2021, the Heritage Medical Research Institute (HMRI) announced a grant to Stanford University School of Medicine supporting further research that will expand opportunities to explore transformative paths leading to new cartilage growth in the area of skeletal regeneration. HMRI is a nonprofit founded by visionary healthcare executive Richard Merkin, M.D. The award supports investigators at Stanford Medicine working to identify novel approaches to generate new factors in cartilage growth that could lead to alleviating pain suffered by millions as a result of loss of cartilage with degenerative disc diseases, osteoarthritis, osteoporosis aging and cancer.

Dr. Merkin was inspired by the work of Charles KF Chan, Ph.D., assistant professor of surgery, at Stanford Medicine and Michael T. Longaker, M.D., director of regenerative medicine at Stanford Medicine. They were recently able, for the first time, to grow new cartilage that looked normal and lasted for several months in mice suffering from arthritis.

"This work represents critical breakthroughs toward the advancement of treating more than 50 million people who suffer from common knee and hip pain related to osteoarthritis," said Dr. Merkin. "Once I learned about this remarkable step toward growing new cartilage that scientists previously believed could never grow back once lost, I knew I had to jump onboard and encourage this research that is so vitally promising and exciting," he continued.

The award names Dr. Chan as a Heritage Medical Research Institute Investigator, joining a community of over 50 principal science researchers sponsored by HMRI in the U.S. His team will have the opportunity to further their research, expanding it with the goal of preventing and reversing arthritic damage to cartilage tissues in the joints.

"My team, Dr. Longaker and our colleagues in the Division of Plastic and Reconstructive Surgery, Orthopedic Surgery and the Stem Cell Institute, are so grateful to Dr. Merkin, Jeffrey Karish, director, and the Heritage Medical Research Institute for their generous support of our research, which builds on our discovery of mouse and human skeletal stem cells," said Dr. Chan. "Stem cells are the rare 'seed' cells responsible for making and regenerating new tissues. This grant will propel our search for new ways to awaken sleeping stem cells in the body to regenerate diseased, injured or aged skeletal tissues, including bone,

cartilage, blood stem cell-supporting stromal cells, and possibly spinal disc and tendons."

"This work represents critical breakthroughs toward the advancement of treating more than 50 million people who suffer from common knee and hip pain related to osteoarthritis."

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



Bakersfield Family Medical Center and Coastal Communities Physician Network Collaborate TO UNITE THEIR COMMUNITY DURING GLOBAL PANDEMIC

DRIVING THE DISTANCE TO STAY CONNECTED

Like all medical groups caught in the eye of the storm of COVID-19, Bakersfield Family Medical Center (BFMC) and Coastal Communities Physician Network (CCPN) had to adapt from the conventional methods of running their organization to accommodate the changing needs of their community. This is especially so for the senior population who rely on their normal routine of participating in their in-person activities prior to the safer-at-home mandate.

BFMC had successfully launched their Coffee Club and Arts & Crafts events with many regular attendees. In light of the pandemic, and to encourage safety, they proposed to convert these two events as a drive-thru. Fast forward six months and not only are they holding Drive-Thru Coffee Club twice a month in their parking lot, but attendance has blossomed! Drive-Thru Arts & Crafts has been the biggest surprise. Where they previously received an average of 15 attendees they currently average nearly 60 to 80 people attending. Drive-Thru Arts & Crafts is held four times a month at the BFMC main campus in Bakersfield, California. The drive-



thru events have made it possible to keep their connections with their senior members while providing a safer environment to foster and build important friendships.

With the success of drive-thru events at BFMC, they decided to implement the same initiative at CCPN. This type of community engagement was new to CCPN and, therefore, gauging the response was unknown. The events were launched in Templeton/Paso Robles area, reaching approximately 1,000 seniors. After a surprising and overwhelming response, CCPN is currently hosting



between 40 and 50 senior members at two events per month at the Templeton clinic.

EXPANDING OUR REACH

While facing the obvious challenges of reaching their community during the pandemic, both BFMC and CCPN had to get creative in ways of reaching their audience to provide pertinent information that was relevant to maintaining the health and well-being of their members. By adding live studio interviews on local television and using the back of senior Get-A-Lift buses to advertise, they managed to increase focus on the importance of staying healthy during COVID-19. In addition, they also sponsored a large holiday lights event, increased the use of PSAs to encourage new attendance at their drive-thru events and held co-op drive-thru events with two health plans in the parking lots of two of their clinics. Additional collaboration efforts are being discussed to further engage and educate the community while staying connected.

All of the valuable programs and events held by BFMC and CCPN are cosponsored with contracted health plans as they partner to strengthen their relationships while promoting optimal health and wellness throughout the communities they serve.



ARIZONA PRIORITY CARE'S Virtual Socialization Programs Enhance Overall Wellness for Seniors

uring the early days of the pandemic, Arizona Priority Care (AZPC) recognized that it needed to implement new ways of delivering their high quality services and stay connected to their membership. Virtual platforms, including Zoom and other HIPAA compliant programs, were quickly adopted to have the ability of not only providing telehealth services, but to ultimately provide members the opportunity to remain engaged with others in the community.

The clinical team modified their methods of conducting in-home assessments for seniors, providing virtual telehealth visits to their members. However, it was quickly identified that many of their senior population either did not have the technological means to receive telehealth services and/or were not educated on how to use the technology. This barrier was quickly overcome by lending seniors tablets dropped off at their doorstep the day of their telehealth appointment, with a guide on how to use it. This allowed the team to continue providing highquality assessments that are essential to this population.

In addition to meeting the medical needs of members, AZPC viewed the needs of their members holistically, and provided them opportunities to also meet their social needs through their Senior Advantage Club. Prior to COVID-19, they provided members the opportunity to attend events such as



movies, concerts, travel to casinos and more. Unfortunately, the impact of the pandemic has hindered the ability to conduct these face-to-face events. In an effort to overcome social distancing barriers, they automatically enrolled their senior members into virtual programs they developed such as:

- Monthly virtual bingo Bingo cards are sent via email.
- Weekly virtual exercise program "Prolong Mobility"

- Weekly "Virtual Road Trip Through America" — Each week focuses on one of our 50 states.
- **"Family Feud"** Teams are assigned and fun ensues.
- Virtual museum visits All over America

These events continue to provide members the ability to come together once again, as one community, to socialize, engage with one another, share enjoyment and to be distracted from current stresses the pandemic has brought upon them.

These events have also provided an opportunity for the team to engage with members, listen to their health concerns and help AZPC identify important needs senior members may have. Staff are then better able to provide resources for their needs such as meal delivery, pharmacy delivery and pairing them with a community agency that can address their needs. During this effort, AZPC established relationships with many community organizations they rely on to assist their members, including their Area Agency on Aging and the YMCA.

During these challenging times, AZPC exercised their creativity by developing tactics to ensure the health and wellbeing of seniors in their community. The end result is reflected in the improvement of the members' overall health based on the perception of their care. Of course, these higher levels of positive perceptions result in high scores on member satisfaction surveys. What is paramount is the member perception of the care they receive. After all, their perception is their reality.

Heritage Provider Network Affiliated Medical Groups

THE LARGEST INTEGRATED PHYSICIAN-LED MEDICAL GROUP NATIONALLY

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

ADOC Medical Group adoc.us

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Arizona Priority Care azprioritycare.com

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

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Coastal Communities Physician Network ccpnhpn.com

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*touch*points

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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.



AMERICA'S PHYSICIAN GROUPS = Wellness Excellence Award in Health Education — Southern California Foundation for Health Care

Top Ten Physician Medical Networks in California by America's Physician Groups



NCQA Certification for Utilization Management and Credentialing

AMERICA'S PHYSICIAN GROUPS = Elite Status of Excellence for the Standards of Medical Care by America's Physician Groups



Recognized by the Integrated Healthcare Association for our diabetic registries