Prostatepedia[1]

[1]expert insight + advice

Health + Tech Collaborations

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In this issue....

Prostapedia's home office is in the middle of Silicon Valley, which is a great place to be if you want to learn about the application of cutting edge technology to prostate cancer. This issue's focus is on collaborations between clinical researchers and those with applicable technology expertise. The topics range from genome sequencing to telemedicine to phone app development.

Several things stand out. First, prostate cancer has left the era of the solitary genius and entered an era where teams of investigators with diverse skill sets are doing the most exciting work. This is necessary because of the explosion in laboratory science and computer techniques for analyzing large data sets—i.e., big data. Full time clinicians do not have time to keep up with the state of the art in these fields. However, their clinical experience is important in defining the nature of the clinical problems that need to be addressed. Additionally, the clinicians design and execute the clinical studies.

The second major development has been the recent use of machine learning to analyze data. Machine learning, especially deep neural networks, excel at recognizing patterns in large data sets and images. Already, machine learning has had success in reading radiologic images and has matched skilled dermatologists in detecting skin cancers.

This approach has great promise as a means of detecting associations between complex genomic data and clinical outcomes. To give you a sense of the scope of the big data problem we face, comprehensive genome sequencing can easily yield a terabyte of data per patient: this is equivalent to 2,000 hours of music on a CD. Imagine looking for patterns associated with clinical outcome in hundreds or thousands of patients?

Machine learning involves several distinct steps. In the first step, the neural network is trained to recognize patterns. In the second step, the trained network's performance is evaluated on a second data set. I n the third step, the network is used in an ongoing manner to solve problems. The first step can be computationally intensive and with today's technology typically requires expensive hardware. However, once the network has been trained, the actual use of the neural network in problem solving is much less demanding in terms of computer hardware.

Telemedicine represents another potential major advance. In this issue, Dr. Matthew Galsky does an excellent job outlining how telemedicine might improve the conduct of clinical trials. As he points out, many patients live a considerable distance away from clinicians doing clinical trials and this is a factor that limits patient accrual to clinical trials. Telemedicine has the potential to reduce the number of trips a patient must make to the center doing the clinical trials. Other investigators have shown that telemedicine can greatly improve side effect management in patients on chemotherapy.

Finally, nearly all patients have cell phones that contain a variety of sensors that are increasingly being used to monitor patient physiologic function. However, wearables like the Apple watch may have more promise than cell phones. Already, wearables have seen successful use in monitoring patients for cardiovascular disease and Parkinson's disease.

This is an exciting time in the use of technology to improve patient care. However, we are only at the beginning of this revolution.

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Collaborating For Prostate Cancer

This month, *Prostatepedia* explores collaborations between tech and health care in the world of prostate cancer. Long gone are the days in which individual doctors and scientists operate in silos to both treat patients and conduct research. Large multi-institution and multi-disciplinary collaborations that leverage emerging technologies to both collect data and to make sense of that data are the name of the game.

In our first two conversations, we feature two leaders in prostate cancer today—Dr. Felix Feng of the University of California, SF and Dr. Paul Nguyen of the Dana-Farber Cancer Center. Both discuss current projects that exploit emerging technologies and speculate about what the future might—they hope will–hold.

Dr. John Wilbanks of Sage Bionetworks discusses his company's role in the National Institute of Health's newly launched precision medicine initiative All of Us. (Some of you may remember a conversation with another Sage Bionetwork member, Dr. James Costello, in Prostatepedia's May 2017 issue.) Dr. Wilbanks offers a unique perspective; his former role as the executive director of the Science Commons project at Creative Commons placed him at the intersection of tech, health care and patient advocacy arenas. All of Us would love men with prostate cancer to participate in the project.

Ms. Jina Ko and Dr. David Issadore of the University of Pennsylvania discuss using liquid biopsy and machine learning—or artificial intelligence—to diagnose pancreatic cancer. They argue that the technology they've developed should work for any cancer type, including prostate.

Dr. Matthew Galsky of the Tisch Cancer Institute discusses his efforts to incorporate telemedicine into clinical trials. As we learned in our conversations about prostate cancer clinical trials last month, the distance that you have to travel in order to participate in a clinical trial can often be a deal-breaker.

Mr. Dave Furher of Gryt Health introduces us to Stupid Cancer, an app that connects patients. Mr. Fuehrer is keen on getting more prostate cancer patients to lead in-app chatrooms. Those of you who lead support groups may be interested in participating: this is a way for you to reach men outside of your local communities, men perhaps isolated and in need of support.

In his quarterly column, Mr. Jamie Bearse of Zero discusses an astounding increase in federal funding for prostate cancer research. Zero's tireless work on Capital Hill benefits all men. If you haven't yet, take a look at their website to review some of the work they do and the tools they provide for men like yourself.

Finally, Gary tells us about his own prostate cancer experience and offers advice for those of you in a similar situation.

Our conversations this month underscore the tremendous changes happening in the world of prostate cancer The next five years will totally revolutionize the way we diagnose and treat prostate cancer as well as the way in which we conduct research about the disease.

These are exciting times, friends!

Paul Nguyen, MD
Health/Tech Collaborations For Prostate Cancer

Dr. Paul Nguyen is an internationally recognized expert in prostate cancer clinical care and research. He has published over 250 original research articles, has various national leadership roles and is the Dana-Farber Cancer Center Genitourinary Clinical Center Director for Radiation Oncology, Vice-Chair for Clinical Research in the Department of Radiation Oncology, and Associate Professor at Harvard Medical School.

Prostatepedia spoke with him about collaborations between healthcare and tech industries for prostate cancer.

Have you had any particular patients or cases that changed how you view your role as a doctor or how you practice medicine?

Dr. Paul Nguyen: Several years after treating him, I heard from a patient who recounted for me what it was like to meet with me when he had first been diagnosed with recurrent disease. He said he'd had a lot of uncertainty and anxiety about his future. He said that the way I spoke with him had changed it entirely for him. He said I had a plan for him, knew exactly what we were going to need to do, and that we were going to do it.

"That has really shaped how I think about every patient encounter."

I didn't do anything particularly different in that encounter than I normally do, but hearing that made me realize how patients really hang on our every word, our every facial expression, our every cadence, and the emotion that we project when we speak.

This made me so aware and conscious of making sure that, at all times, in every encounter, I have that combination of being sure about what I need to do and maintaining hope and optimism in every part of our discussions.

That was a good learning cycle for me. I hadn't thought of it that way when I was with a patient. You just don't think that every intonation, every gesture has such a huge impact. But it does.

That was a very valuable learning experience for me that has really shaped how I think about every patient encounter before I walk into the room.

What are your current research projects? Which are you most excited about?

Dr. Nguyen: I have spent my entire career using information from the medical record about patients' health status and tumor characteristics to figure out which men should get hormone therapy and for how long.

Now, I'm incredibly excited about the opportunity to unleash the power of genetic testing of tumors. This will help us understand, on a genetic and molecular level, which patients should be given hormone therapy and for exactly how long. This will be a lot more precise than the clinical information by itself. I'm working with Dr. Felix Feng and others, which has been a wonderful collaboration.

How do you see evolving technologies impacting prostate cancer research?

Dr. Nguyen: Technology gives us opportunities to do the kinds of studies we never dreamed possible, which is amazing.

I'll give you an example. Dr. Feng and I are about to take prostate cancer samples from biopsy tissues taken 25 years ago from men who had cancer, samples stored without a clear purpose in mind.

I give a huge amount of credit to the people who designed these studies in the early 1990s. They had no way to analyze this tissue, but they knew that someday, this tissue would be important to humanity. There wasn't a specific test that they were storing these samples for, but they knew some kind of technology could decode what was going on in those tumors, to study how the tumors work, and who should get which treatment.

I feel so fortunate to come along 25 years later, when we do have the technology to analyze this tissue, and research it. This is the research I'm about to do now, which would never have been possible without new technologies.

Do you see technology impacting how we design clinical trials from the get-go?

Dr. Nguyen: Absolutely, because now people are designing trials with technology. There's a trial being led by Dr. Feng from UCSF and Dr. Dan Spratt at the University of Michigan that incorporates genetic technology. All the patients are tested upfront with this new technology to help decide which arm the patient goes into, which is really cool. This new scientific technology is being worked into clinical trial design.

Which innovations or technologies have the biggest impact?

Dr. Nguyen: There are two kinds of impacts. One is the ability to do large-scale genomic studies for a relatively low price. That has been a game-changer because it used to be so expensive to sequence the DNA of patients, but now you can approximate that rather cheaply and then do studies on thousands of patients. This way, we can pick up very small signals, which are very valuable.

The other invaluable impact is the ability to detect very minute amounts of tumor in the blood, very tiny traces that can tell us a lot.

In the circulating tumor cell?

Dr. Nguyen: Exactly.

Do you think artificial intelligence will play a role?

Dr. Nguyen: For sure. I've spent most of my career working on simple, clinical data. You can see the patterns of simple data yourself by doing simple statistical analyses.

But now, the patterns are much more complex. Instead of five datapoints, you might have two million datapoints per patient. So we need AI. We need sophisticated machine learning to help us discern some kind of pattern out of that huge amount of data, to help us make sense of it.

Are there any specific collaborations, other than the ones we've already discussed, that you think look promising?

Dr. Nguyen: We're seeing a lot more collaborations across specialties and disciplines to get research done. So much of what we're seeing now is team science whereas people used to do studies with their own group.

Now, if you look at a paper, it's not just one group or one discipline. At each institution, it's five disciplines, and then you might have ten institutions on a paper, each contributing something different because that's just what it takes now.

Every group has its own, little special expertise that gets put together to get a big paper or a big trial done. That's what has really exploded. We've all recognized that, in order to get good science done, we have to team up.

Is just it easier to collaborate with people now via email and sharing of data? Or is there something about the way cancer research has been funded that has fostered that collaboration?

Dr. Nguyen: Yes. Those factors definitely contribute. It is definitely easier to share data now with the internet. Efforts to fund team science have definitely led teams to be created that might not have been created organically before.

There's something fundamental about the increasing use of technology in studies and trials where only certain groups have this kind of technology expertise. You might have one group that knows a lot about the technology and another group that has a large number of patients and ideas. And you have to reach outside of your little sphere in order to get these kinds of exciting studies done.

It seems like before everything was pretty much siloed: you had tech, you had healthcare, and then, within healthcare, you had prostate cancer versus pancreatic cancer versus breast cancer. But now, the walls are coming down between those silos, with things like increased genetic testing. Would you say that's true?

Dr. Nguyen: Absolutely. For example, some of the cool studies done in prostate cancer genetics were modeled on similar research done in breast cancer genetics several

"We need sophisticated machine learning to help us discern some kind of pattern out of that huge amount of data."

years before. Breast cancer had the Oncotype study, and then prostate cancer developed the Oncotype test many years later. We've seen molecular subtypes of breast cancer (luminal A, luminal B, and basal), and now there's a study led by Dr. Feng suggesting that you've got similar kinds of subtypes in prostate cancer.

We have to be knowledgeable about other fields. You can't just be in your own silo now.

Last week, I spoke with engineers at University of Pennsylvania who are working with microchip-based technologies and machine learning to increase liquid biopsy's usefulness in pancreatic cancer. [See page 18 to read that conversation.] They said this allows them to process much more data than they could before. They hope this has potential in other cancers. I know that's more along the lines of diagnostics than what you're doing, but do you have any thoughts about that?

Dr. Nguyen: We are all trying to take those same kinds of approaches with the folks who do machine learning. We need them desperately now because we've got so much data, and we just can't figure it out on our own. That's exactly where we're all headed.

What else should patients know about collaborations between health and tech?

Dr. Nguyen: Patients should have a lot of optimism about these collaborations. Patients should also know that we're extremely grateful to them for consenting to use this data.

It's really only with the large number of patient samples and teaming up with the folks in technology that we're able to get new answers to questions that we weren't able to get before. All of this starts with patient samples and patients agreeing to participate in these studies. They really are pioneers in the sense that, without patient data, we can't do any of this. Patients should know what an important role they play.

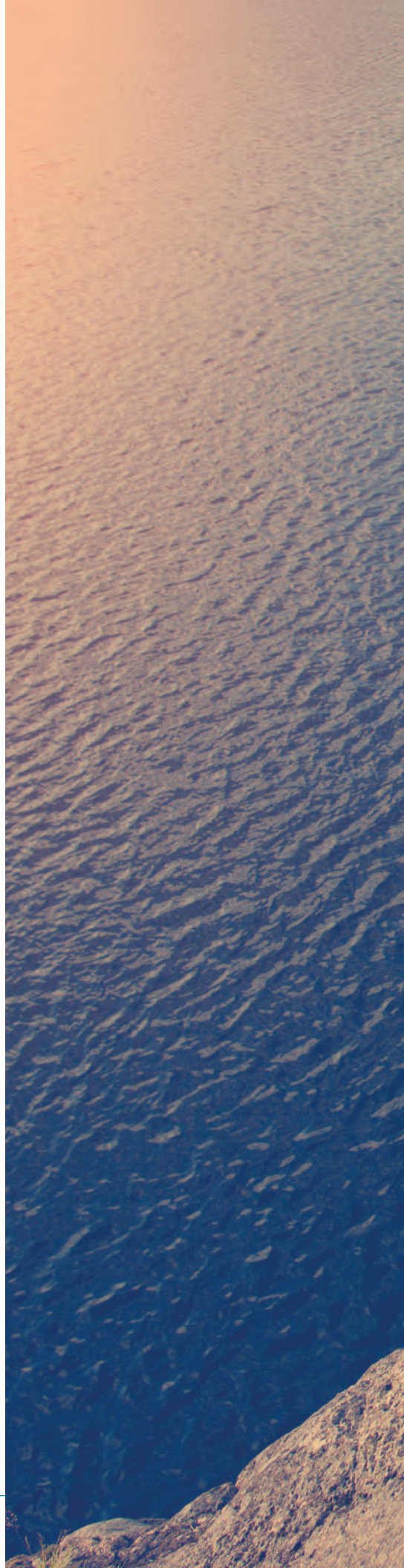
We spoke with Dr. Van Allen about the metastatic prostate cancer projects for our April issue on genomics. Men with metastatic prostate cancer can donate their data to that project. But what about someone who has prostate cancer that has not metastasized? Is there any way that man can participate and donate his information?

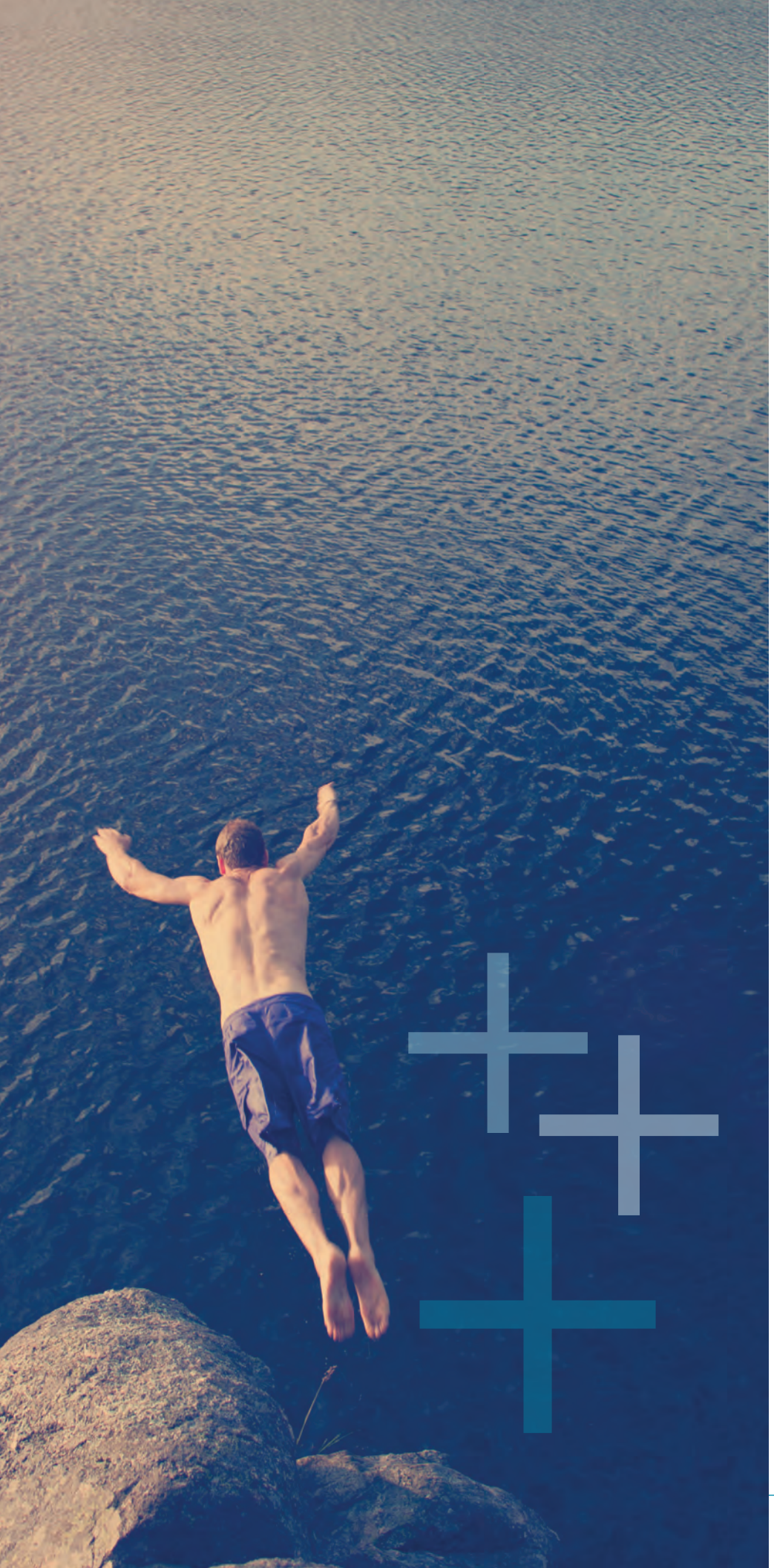
Dr. Nguyen: Almost every major cancer center is now starting up protocols where they just ask patients to allow their data to be analyzed, including their tissue's genetic data. So, patients should ask whether this kind of protocol is available at their institution. They'll find that many institutions have this now. This protocol is really becoming standard.

If you go to a smaller cancer center, maybe they won't advertise it as much, but they will often have these kinds of protocols. You would allow your information to be banked; it might be valuable five years later or it might be *extremely* valuable 20 years later. For sure, your donation will contribute.

Does each institution have their own databank of information? Do they share with each other. Is there some sort of national or international coalition to share all that data?

Dr. Nguyen: Institutions will team up for certain collaborations. For example, many institutions store their own data on prostate cancer patients. Then, Mount Sinai's genomics group and a group in England formed a consortium to analyze genomic data from hundreds of thousands of men with prostate cancer. Each institution then got its own IRB approval to





"It used to be so expensive to sequence the DNA of patients."

share data with this consortium in a totally anonymized fashion to be able to answer bigger questions. Basically, by contributing to your own local institution's database, you gave your local institution the opportunity to collaborate with other institutions and form a really big dataset.

Do health insurance companies participate in that kind of endeavor, or are they just not a part of it?

Dr. Nguyen: That's a good question. Not so much on the tumor genomics level, but we are able to get data from health insurance companies because some make that kind of data available to researchers either for a fee or on a pure research basis. It's totally anonymized data. We never get to see anything that identifies patients, but there are definitely some health insurance plans that share information. For example, Kaiser Permanente in California has a huge patient database, and they will allow researchers access if you're a collaborator.

It's harder to work with private insurance. We have plenty of access to Medicare data, but private insurance doesn't do it as much.

Just imagine if Blue Cross Blue Shield opened up.

Dr. Nguyen: They recently announced that they are sharing some of their data with Harvard and Yale for studying opioid prescribing and cancer screening; this is a big step forward! Pp

Felix Y. Feng, MD

Tech World Helps Prostate Cancer Manage Big Data

Dr. Felix Feng is a physician-scientist at University of California, San Francisco (UCSF) keenly interested in improving outcomes for patients with prostate cancer. His research centers on discovering prognostic/predictive biomarkers in prostate cancer and developing rational approaches to targeted treatment for therapy-resistant prostate cancer. He also sees patients through his prostate cancer clinic at UCSF.

Prostatepedia spoke with him about how technology companies and healthcare organizations are collaborating for prostate cancer research.

Are there any patients or cases that changed how you see your role as a doctor or changed the way you practice medicine?

Dr. Feng: In terms of advanced technology, molecular updates, and imaging, we are at the forefront of medicine. Sometimes we're using new technologies that haven't been validated. At these moments, we have to ask ourselves what we would recommend for our patients, and we also have to ask ourselves, if we were in that patient's shoes, what we would want. So, many different patients have changed the way I think about medicine.

"The beauty of technology is that it allows us to think on a much larger scale than before. Big data has impacted our field tremendously."

Each patient I see changes how I view myself as a physician and how I practice medicine because every case is different. Unique factors play into every patient's case, which always makes me think about things we physicians have yet to consider.

One hopes that each individual would change how you see your role, even if it's just a little bit. Each person is an individual and requires a unique approach, right?

Dr. Feng: Absolutely.

Give us an idea of the work you do. Which current projects are you working on? Which are you most excited about?

Dr. Feng: The scope of my work is quite broad. I run a relatively large laboratory team comprised of molecular biologists looking at the biological drivers of prostate cancer and of computational scientists who interrogate genomic data to identify additional drivers of prostate cancer.

Some of the research we do in studying genomic drivers of metastatic prostate cancer are quite novel and have a potential to change the field. Previous studies looking at the genomic landscape of metastatic prostate cancer have focused on exomes. These are basically the DNA that encode protein. Only about 1-2% of the genome is included in conventional exome sequencing, and right now, we've moved on to whole genome sequencing to look at the other 98% of the genome. Much of our effort is currently focused in this space. This is still unpublished, but there will be interesting findings from our team over the next year.

On the clinical side, I help lead the Genitourinary Cancer Committee of the NRG Oncology Group, a national clinical trials group. In that role, I help shape the next generation of large, national randomized clinical trials, many focused on ways to improve radiation therapy for prostate cancer. These include changes in radiation fields or radiation dose, and more recently, combining radiation with novel drugs. These trials have the potential to change lives, which is exciting.

A third component of my research focuses on developing biomarkers to help individualize therapy for prostate cancer patients. In the last few years, my team has helped develop clinical grade biomarkers to identify which patients should receive radiation after surgery for prostate cancer and which patients should be treated with early androgen deprivation therapy following surgery. We're using these approaches and profiling a number of samples from randomized clinical trials through the NRG Oncology Group in collaboration with people like Dr. Peter Nguyen. We're profiling some samples from these trials to try to develop other classifiers of patients treated with radiation up front. We're trying to determine who should receive hormone therapy, who should receive shorter growth hormone therapy versus longer growth hormone therapy, and who should get radiation of the lymph nodes instead of just to the prostate itself, and so on.

That's a lot. You cover quite a bit.

Dr. Feng: Yes. My scope of research is broadening. We're in a very exciting stage right now in the metastatic setting. We may soon identify new drivers of metastatic prostate cancer and therapeutic targets with new therapies. And within the biomarker state, we're developing trial markers that can be used to prescribe patient therapy. On multiple fronts, there's a lot of exciting potential.

You're at University of California, San Francisco, just north of Silicon Valley, home of the tech revolution. The media talk a lot about how technological advances are changing every aspect of society and healthcare in particular. How will emerging technologies impact prostate cancer research and patients?

Dr. Feng: Certainly, UCSF exposes me to the tech revolution. I also

grew up in Silicon Valley and went to Stanford University during the dot-com boom, so I'm pretty familiar with tech. The beauty of technology is that it allows us to think on a much larger scale than before.

Big data refers to analyzing large amounts of data from multiple sources, from clinical data to genomic data and so forth. Big data has impacted our field tremendously. My research team has had a few very productive collaborations with big data industry partners.

"These CRISPR approaches allow us to broadly study the function of many different genes."

We collaborated with GenomeDX Biosciences, the molecular diagnostics company that makes the Decipher assay. To conduct the Decipher assay and look at the 22 genes that make up the Decipher score, they must analyze the expression of the vast majority of genes within the prostate cancer genome. We've partnered with GenomeDX to analyze samples from around 40,000 patients to generate predictive biomarkers and to identify genes that are associated with bad outcomes in prostate cancer. This provides direction for what we should study in the lab.

Another exciting collaboration is with a sequencing company called Illumina. We recently sequenced the whole genomes of 100 patients with metastatic prostate cancer. The data

from those 100 patients took about 50 terabytes, a very large amount of data. We sequenced these patients, and housed, processed, and analyzed the data using the infrastructure they developed in the Amazon Cloud.

We've also partnered with a number of drug companies that run large clinical trials. These companies provided us access to samples from their clinical trials, recognizing that it costs millions of dollars to run a national clinical trial with many patients. The samples from these trials are an invaluable resource. When utilized in the right manner, these industry partnerships help us accelerate discovery to improve prostate cancer therapy.

Would you say that the greatest impact has been in the arena of genomics just because of the massive amount of data that's generated?

Dr. Feng: That's one of the major areas of advances. But there are so many areas of advancement in prostate cancer therapy right now that it's hard to pick the most exciting.

We're super excited by a technology called CRISPR, a gene editing approach that allows scientists to silence genes, one-by-one in the context of prostate cancer, or in the context of cancer cell line models. These CRISPR approaches allow us to broadly study the function of many different genes and to couple that with what we're finding from sequencing the tumors.

There are other exciting developments in novel therapeutics that target androgen receptor signaling, which is the major diagnosis of prostate cancer, and also in immunotherapy, targeting DNA repair in prostate cancer, and through drugs like PARP inhibitors.

"Partnering with the tech sector has helped us identify the genomic drivers of prostate cancer."

Partnering with the tech sector has helped us identify the genomic drivers of prostate cancer, and that allows for personalized therapy. Interrogating big data from drug companies has also accelerated the pace of drug development.

Are there any collaborations that are not happening that you would like to see?

Dr. Feng: As a radiation oncologist, I am interested in how radiation can modulate immune response. When radiation kills prostate cancer, it might expose the immune system to proteins found in the tumors, proteins called antigens, which the immune system wouldn't have otherwise been exposed to. I wish that more companies would focus on combining systemic drugs with radiation as a way to improve patient outcomes. Whatever the reason, I hope that we recognize the potential of radiation to improve patients' systemic response to immunotherapy.

The field of prostate cancer is advancing rapidly. Academic researchers and industry partners use technological advances, whether big data or improved modeling approaches to identify new therapeutic approaches for patients. Just a decade ago, there was only one FDA-approved drug for patients with metastatic prostate cancer who have become resistant to first time hormone therapy. Now we have six FDA-approved drugs for them. Imagine what the next decade will bring. Pp

John Wilbanks Join A Precision Medicine Study

Mr. John Wilbanks is the Chief Commons Officer at Sage Bionetworks. Previously, Wilbanks worked as a legislative aide to Congressman Fortney "Pete" Stark, served as the first assistant director at Harvard's Berkman Center for Internet & Society, founded and led to acquisition the bioinformatics company Incellico, Inc., and was executive director of the Science Commons project at Creative Commons. In February 2013, in response to a We the People petition that was spearheaded by Wilbanks and signed by 65,000 people, the U.S. government announced a plan to open up taxpayer-funded research data and make it available for free.

Prostatepedia spoke with Mr. Wilbanks about Sage Bionetworks role in All of Us, the National Institute of Health's ambitious precision medicine research program.

How did you come to work at Sage Bionetworks?

Mr. John Wilbanks: I got involved with Sage when it was first beginning. Sage was an informatics unit of Merck, and in 2009, they began to explore what they could get for the unit. But we convinced them to spin it out into a nonprofit organization instead of selling it off.

> *"It is fundamentally an attempt to enroll a million people and to characterize them as completely as we can."*

I got involved then as a board member because I was able to help negotiate what the IP structure would look like, how we would get rid of some of the patent constraints and other kinds of intellectual property so that we could build a nonprofit. I have been involved ever since, at first as a board member, then as a consultant, and then in 2012, as a full-time employee.

I lead the Governance team at Sage, which means that my group works on things like informed consent, clinical protocol design, data-sharing and access policies. We work on strange and weird structures that enable collaboration in a variety of ways, and we have a pretty broad view across the organization as a result.

What is the All of Us program?

Mr. Wilbanks: All of Us is a longitudinal cohort study. It is fundamentally an attempt to enroll a million people and to characterize them as completely as we can. This means we collect and look at their health records, pharmacy records, their environment, biospecimens, metabolic data, their genomes, data that we collect from their devices and smartphones, surveys over a ten-year period—you name it. Then, we make that data liberally available so that we can run all sorts of interesting queries.

We're trying to take the Framingham Heart Study model and reimagine it for the 21st Century. Framingham is a breakthrough study, but it studied one town in Massachusetts, and then its diaspora over time. That means that it's fairly white, and it has all these biases in it. Also, it doesn't study anything besides heart health.

All of Us aims to take the idea and the impact of a study like Framingham and reimagine it using a completely modern, digital approach to everything. What would happen if you made that data liberally available? What would happen if you made a point of including 700,000 out of 1,000,000 being from populations that are underrepresented in biomedical research?

That's one of the reasons it's been hard to talk about; it's not a study of prostate cancer. It's a study that will involve hundreds of thousands of people, some of whom may have

"It's not a study of prostate cancer."

prostate cancer, some of whom may have survived prostate cancer, and some of whom may develop prostate cancer. But that's not the focus. The idea is that we'd be able to subdivide that cohort endlessly in ways that let us think about public health and identify populations for sub-studies as easily as possible.

So then, the goal is to pull in as much data about these people as you can and then make inquiries into the data in various ways?

Mr. Wilbanks: That's right. And we also want to open up who gets access to the data. It's one thing to say the people at Harvard can run analytics; it's very different to say that the community being studied can run analytics. That is also part of the design.

A lot of the questions that will be asked will come from advocates who know what questions need to be asked, questions the scientists don't know need to be asked. We've been trying to design the system to maximize the number of people who are allowed to be data analysts and not just data donors. In many cases, we hope that the donors and analysts are the same people. That level of engagement leads people to start asking questions, not just providing information.

Will people be getting their own information back? Obviously, wearables and devices would feed information to their own electronic records, but I know they're going to be doing some genomic tests. Will people get the results from those kinds of tests?

Mr. Wilbanks: Yes The study is guided by a set of core values and principles, and one is to prioritize the participant's right to their data. All data provided by the participant will be provided back to the participant—nothing about me without me. We're still figuring out how to do that because it's really complicated.

Don't you de-identify data first? Then, how do you re-identify it?

Mr. Wilbanks: That's a little easier. You have to de-identify data before you get it to the data user. But, it's easy to know for a given sample who that sample came from because that's what allows us to connect it to the demographic data.

It's relatively easy to get it back to the individual, but the question of what to return to them is difficult. If it's their genome, do we give them their BAM files, which are massive? Or do we give them a VCF, which is the differences between their genome and the reference genome, which is tiny? Do we give them images? How many times do you let people download data because the cloud transfer cost would be high? How do we get consent for that? It's complicated.

We still have to figure out exactly how we're going to do all of those things, but it is a core principle of the study that nothing about you happens without you, and by the end of the study, you should have as much of your entire electronic health records in one place as possible, in one form. You should have your genome, all of the survey data you offered, all your wearable data, and you should have all the ancillary information we discovered about you. You should be able to take that with you and do what you want with it.

What is Sage's role in all this?

Mr. Wilbanks: We are a sub-awardee of what's called the Participant Center and the Participant Center is led by the Scripps Translational Science Institute in San Diego. We have two different lines of work inside the program, two core jobs. One is governance-based. We work on the clinical protocol, informed consent, and data-sharing systems. The other job is digital health technologies, and that's a different team than mine. They work on building software modules that sit on smartphones and pull data off as measurements. They design them, figure out how to validate them, and how to feed them into the technology system.

You're basically trying to figure out how you can pull data from the apps or wearables that participants already use?

Mr. Wilbanks: That's part of the DHT group, and that's led more by Scripps. We use the features of devices.

For examples, we think we can get a tremor measure for neurodegeneration with a module that measures the accelerometer in a smartphone. We can measure their gait by having them put their phone in their pocket and taking 20 steps forward and 20 steps back. We can measure phonation through a microphone. We can measure memory and tapping through the touchscreen.

We want to design modules like these that are clinically validated to measure those things so that anyone

who wants to measure gait, lung capacity, memory, or what have you can rapidly access that inside the All of Us app or a related app. And they should feel confident that the data is relatively consistent and valid.

Sounds like they'd have applications outside of the study or after the study as well, right?

Mr. Wilbanks: It's certainly part of the long-term plan. In the short-term plan, it'll be part of the study application. For example, the app might say: "You said that you have Parkinson's disease; would you like to try a study module that measures it quantitatively using your phone?" If you choose to, then the modules that we work on would roll out to that person.

That's more of what our team works on in that space. For example, we can determine what a six-minute walk tells us about your VO2 max and your cardiac health. We just did an app with Samsung outside of the study that looks at whether you can detect stress using the camera and the flash. You put your finger over the flash, and the camera flash strobes, and we take a picture during the moment of the strobe. With that, we can make guesses about your stress. It's not clinically valid for blood pressure, but it's the first step on the way

If all this comes up while a participant is in the study, will they be alerted to go to their healthcare provider for follow-up?

Mr. Wilbanks: The only places in the protocol currently where we alert people about clinical care has to do with blood pressure and that sort of thing. If you show up to your physical exam, and your blood pressure is 300/200, that triggers the emergency care process of the clinical system where you went. This is fundamentally a research study; it's not clinical care. It's not healthcare.

Mainly, this study aims to generate data for research and not to feed back to the participants about their clinical care per se.

If you're monitoring cardiac activity, and something comes up, wouldn't you want to let the person know that they're at risk?

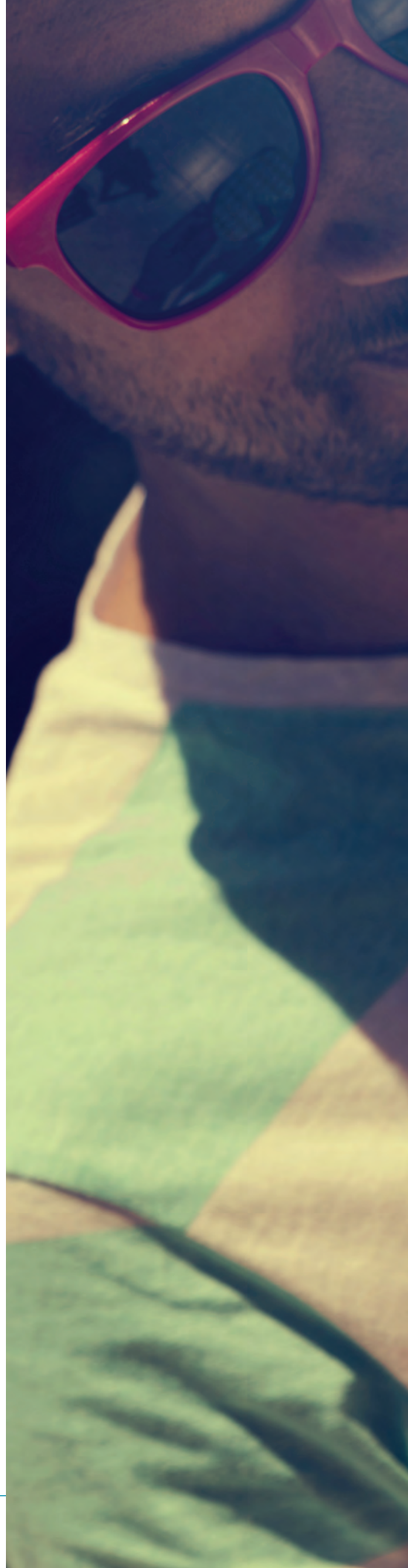
Mr. Wilbanks: How do you do that? Does that create disparities for people who have those concerns versus those who don't? What's the ethical duty, and what if the measures of cardiac activity aren't equally distributed across the cohort because of social determinants? It's complicated.

We spend a lot of time worrying about those things, and those answers aren't simple. Right now, we're enrolling, giving surveys, a physical exam, and collecting biospecimens. So, the only place this has come up is in the physical exam space.

Anything else you think prostate cancer patients should know about enrollment or the ultimate goal?

Mr. Wilbanks: Because Sage is a nonprofit, we try to make everything we do open-source and available. People can contact us if there's something they have questions about.

When it comes to enrollment, I want to encourage people to contemplate participating. Part of what we'll get out of this is the long-term impact of things. We're going to get polygenetic risk scores. We're going to start to understand essential things about the impact of environment, diet, and all this other stuff that you only find when you look at something over a long period of time, especially as compared to a prostate cancer trial where you're



trying to determine if a drug makes you live longer or not. This is a really interesting study that will look at questions like: what does it mean to be a survivor? And what does it mean to be healthy as somebody who's been treated for cancer over time?

This is a really interesting place to get involved. I hope that your readers see All of Us as a place where they want to evaluate participating, and that it's a study at least some of them want to contribute to.

A lot of the anecdotal information around things like diet, environment, and exercise, and how they relate to long-term survival will come from this kind of study. If we don't have diverse, inclusive participation, including people from the prostate cancer world, we won't be able to answer these questions as fully.

It's fairly easy to sign up, right? You just create an online profile, answer some questions, and then provide blood and urine samples, correct?

Mr. Wilbanks: Right. Depending on where someone lives, they may be routed to a local health provider organization for enrollment. That's probably the fastest route.

Eventually, someone who isn't near a health provider organization will be routed to a Walgreens or one of our other community locations to do the physical exam and biospecimen. It's intended to take no more than 20 to 30 minutes to sign up.

Even if you're not near one of the enrollment sites, you can enroll via the internet, via the app. I enrolled myself yesterday this way, so I'm not just selling the Hair Club for Men; I'm also a member. Pp

Cancer Diagnosis With Machine Learning + Liquid Biopsy

Ms. Jina Ko is a PhD student in the Department of Bioengineering at the University of Pennsylvania. She was among 14 PhD candidates from the U.S., Canada, and Germany to be named to the inaugural class of Schmidt Science Fellows. Ms. Ko works in the lab of Professor David Issadore on microfluidics and lab-on-a-chip technologies.

Dr. David Issadore is an Assistant Professor of Bioengineering and Electrical and Systems Engineering at the University of Pennsylvania. Dr. Issadore's research focus is on applying microelectronics, microfluidics, nanomaterials, and molecular targeting to medicine. His lab explores how these new technologies can bring medical diagnostics from expensive, centralized facilities directly to clinical and resource-limited settings.

"We applied machine learning."

Ms. Ko and Dr. Issadore spoke with *Prostatepedia* about a platform for diagnosing pancreatic cancer via liquid biopsy and machine learning, a technology that can be applied to other cancer types, including potentially prostate cancer.

What drew each of you to the world of bioengineering?

Ms. Jina Ko: I did a lot of internships as an undergraduate student working on biomechanics, point-of-care diagnostics, and all things cancer biology. I got interested in diagnostics because, even though there are good current treatment options and emerging treatments, if we don't have good diagnostics to guide patients to the right treatment options, they cannot really benefit. Good diagnostics that guide patients can be a huge bridge to connect patients to treatments.

In terms of pancreatic cancer, everyone's diagnosed really late, when they already have metastases. I saw that as a good chance to develop early stage pancreatic cancer diagnostics: to detect them before metastasis, so that we can increase the survival rate.

Dr. David Issadore: My training is in physics and electrical engineering. I trained to design computer chips and got into diagnostics because I became interested in whether or not the same approaches that reduced costs could be applied to medicine. In the 1960s, electronics were only accessible to big institutions and people with a lot of money, but now, everyone has access to cellphones and laptops. I was interested in whether or not we could do the same thing for medicine, to make ultrasensitive diagnostics that do nearly impossible things and solve intractable problems by miniaturizing and integrating them. That's what we do in my lab here at the University of Pennsylvania.

For her PhD, Jina had a brilliant insight into a new device. She took it all the way from a drawing on the back of an envelope to something we use on patient samples to diagnose disease. She did that in five years, which is rare and pretty incredible.

You've worked on two main projects: integrating microchip-based technologies with machine learning for liquid biopsies and integrating nanofluidic technology with machine learning to diagnose cancer. Can you tell us a bit about that work?

Ms. Ko: Our platform is a combination of those two projects: our approach looked at liquid biopsies to find blood-based biomarkers so that we can minimize invasion for biomarkers rather than doing invasive biopsy. For biomarkers, we focused on exosomes, which are small particles

that circulate in the bloodstream. Exosomes are great as biomarkers, because they have good molecular information of their mother cells.

For example, it's really hard to get at pancreatic cancer cells because of invasive biopsy. But we can derive pancreatic cancer cell exosomes from the blood. The challenge is that they're really small, on the nanoscale at only 100 nanometers in diameter. So, we need a good tool to isolate those exosomes and profile them for the molecular signature.

At first, we developed tools that can isolate specific types of exosomes, so that we can enrich the exosomes and profile them. Even though we profiled the exosomes, we noticed that if we just look at one expression level, with molecular cargo like DNA or RNA inside, we can cover the heterogeneity of different patients.

Also, pancreatic cancer is heterogeneous. That's why we used machine learning rather than profiling individual RNAs from exosomes. We thought we could find a pattern, a combination of biomarkers so that we can find orthogonal information and the signature inside. We applied machine learning to decrease multi-dimensions into a single score. That score can then tell us whether a person has pancreatic cancer.

And how accurate was it?

Ms. Ko: We started with three mouse model groups. One group was healthy, one had tumors, and the third group had lesions in the pancreas, but they did not yet have a tumor, which is considered pre-cancerous.

In the three-way comparison, we got 100% accuracy, but it's a small size sample. There were only about 20 mice, so we definitely need

"We got 100% accuracy."

to increase the number to ensure that it's an accurate representation.

We applied it to clinical patients where we classified metastatic pancreatic cancer patients to healthy controls. In that study of 24 patients, we got 100% accuracy as well.

100%?

Ms. Ko: Yes. Even though it's a small sample size, we got extremely accurate molecular signatures from exosomes. We really want to apply this to early-stage pancreatic cancer patients, to screen some risk groups. We want to be able to predict if people were going to develop pancreatic cancer at a later stage before the disease appears.

Dr. Issadore: The next step of early detection in humans is challenging because we need to measure a lot of people and only some of them are going to get cancer. This study lays the groundwork to take that next step, and we're gearing up to do that.

Do you have any plans to study different types of cancer, or will you just continue looking at pancreatic cancer?

Dr. Issadore: No. We want to branch out. Every cell in the body sheds these exosomes, and the machine learning approach allows us to look for signatures without having to understand the underlying biology. This means that, as long as there is a signature—a difference between cells that are cancerous and cells that are healthy—this technique should work for any type of cancer.

It will be a challenge to find the right animal and clinical models to develop early detection, so we're working with collaborators at the Abramson Cancer Center. Together, we will link this technology with models of breast cancer, leukemia, and many others.

We've also taken the same approach and applied it to different diseases. We've tried it with traumatic brain injury and have had exciting results. It's a pretty general technique.

Ms. Ko: Whenever we talk about 100% accuracy in science, people are a little suspicious because it's pretty rare. To validate that level of accuracy from the pancreatic cancer molecular signatures that we found, rather than some random artifact from machine learning, we trained the algorithm with wrong labels. We shuffled the labels and eliminated the molecular signatures on purpose, and then we trained the algorithm to make sure that it failed.

One hundred percent does sound too good to be true.

Dr. Issadore: You have to do a lot of controls, which we did. It wouldn't be 100% if we had 1,000 or 10,000 samples. But for the members we tested, it was perfect.

You said the obstacles to moving forward are just getting enough people to test? Any other obstacles to the process?

Ms. Ko: Increasing the sample size can be one option, but we want to also find a subgroup classification that can help with clinical decisions. We are looking at short survival versus long survival patients to find signatures there. We are also looking at metastatic patients versus no visible metastases to better understand metastases. Pp1

Matthew Galsky, MD
Telemedicine + Clinical Trials

Dr. Matthew Galsky is the Director of Genitourinary Medical Oncology at the Tisch Cancer Institute. He is keenly interested in developing novel treatments for genitourinary cancers.

Prostatepedia spoke with him about his work exploring the feasibility and safety of using telemedicine to conduct clinical trials.

How did you come to be a clinical trialist?

Dr. Galsky: While going through medical training, I wanted to focus on internal medicine because I was interested in diagnosing and treating disease and the ability to have longitudinal relationships with patients.

"A salvage procedure just means something failed beforehand."

At the time, there was a revolution in our understanding of some of the basic mechanisms that result in the growth and spread of cancer, and a new class of medicines was just being introduced into the clinic. I found that incredibly exciting, and there were some very promising results with some of those initial treatments. That's really what led me to the field of oncology—that and my mentors.

How did you become interested in using the telemedicine platform?

Dr. Galsky: Only a small portion of patients throughout the world, and in particular, the United States, enroll in clinical trials. Yet, this is really the only way that we advance the field in terms of understanding the risks, benefits, and comparative effects of new treatments. We noted that the conduct of clinical trials in the United States had several inefficiencies that could be addressed with technological solutions.

One of our initial studies looked at a large group of clinical trials that had been done in the United States and that had been captured in a large, public database. We looked at thousands of clinical trials done in the United States over a period of about a decade. About 25% of those clinical trials closed early due to poor accrual: not enough patients enrolled in the studies. The studies ultimately closed and didn't answer the questions they set out to answer, which is a huge waste of financial and patient resources. The patients who enroll are altruistic and want to advance the field. But their participation did not accomplish what they had signed up for. This is a big problem.

Our next study was related. We looked at the zip codes of all of the sites that had open trials, we matched those to different cancers in the United States, and then we asked a very simple question. What was the average distance that a patient would need to travel to reach the nearest clinical trial? We focused on trials for some major cancers: prostate, lung, colon, and breast cancer. We found that 40-50% of the population resides greater than one hour driving time, one way to the nearest clinical trial site.

Wow! That's far.

Dr. Galsky: It's far and prohibitive for a large number of patients. It's not surprising, but it's disappointing.

We have one problem, that we don't have enough patients enrolling, and then we have this related problem, that the studies are not geographically accessible to patients. This really hit home.

A study published in the *Institute of Medicine* in 2010 reported that

clinical trial sites are typically opened where the investigators are located rather than where the patients are located.

That makes sense.

Dr. Galsky: Absolutely. But it creates barriers to enrollment.

We thought there might be a technology solution to this, and so we set out to test the feasibility of a prospective clinical trial with an intervention (studying a drug in prostate cancer), enrolling patients who lived at a distance by replacing the on-site study visits with telemedicine study visits.

It was a small study to establish proof-of-concept for this approach. The intervention was a drug called metformin, which is FDA approved for the treatment of diabetes. In various epidemiologic studies, it has been associated with potential anticancer activities and specifically anti-prostate cancer activities. For this pilot study, we had patients come to our site to enroll in the study because we figured that would require the least number of visits and at least one face-to-face interaction.

After that visit, the rest of the study was conducted by telemedicine, so patients took their pills at home. This medicine is oral. It's a pill. We connected with them via telemedicine visits once a month to review their side effects and the numbers of pills that they had taken or missed. The patients had laboratory testing done locally with the results sent into us.

We were ultimately able to show that this is feasible in this specific context. Obviously, the deck was stacked in our favor to ensure we could do this safely, but it was possible.

"The rest of the study was conducted by telemedicine."

Break down what you mean by telemedicine. Was this email contact?

Dr. Galsky: This involved video visits with patients. We had to use a platform that was HIPAA compliant and optimized for security, so we partnered with a company that had developed a technology they were using for purposes outside clinical trials, such as trying to prevent hospital readmissions by having nurses monitor patients remotely. We gave patients a mobile device at that initial visit, a Samsung phone running the software for this platform. On our end, we connected with the software loaded on our desktop computers. With these tools, we were able to conduct video visits once a month.

Did you do any training for the participants?

Dr. Galsky: We did about ten minutes of training at that initial visit, and then we had prepared a pamphlet with troubleshooting questions and answers.

What can you conclude from your results?

Dr. Galsky: The primary endpoint of this study was to show that telemedicine was feasible. We defined feasibility as greater than two-thirds of the enrolled patients completing all of the eligible telemedicine visits. Each patient on the study had six planned telemedicine visits, but if they went off of the study because their cancer progressed, they had less than those six visits. Six visits per patient times 15 patients enrolled, means 90 total visits. We conducted 84 televisits with patients during the course of the study, so we met that primary endpoint of feasibility.

If patients had to go off the trial because their cancer progressed, that's not really a failure as far as the telemedicine element, is it?

Dr. Galsky: Exactly. The primary endpoint was feasibility.

The secondary endpoint was safety and effects of the drug. We saw that seven of the patients had a minor decline in PSA while on the study. So, metformin may have some activity warranting further evaluation of the treatment.

We did questionnaires at the end of the study regarding the patient's rating of their experience with the telemedicine approach. We asked whether they would participate in a similar type of study in the future, and the majority agreed or strongly agreed that they would.

You made it easy for them to participate.

Dr. Galsky: That's the key; absolutely.

What does this mean going forward? Should this kind of approach be integrated into more trials?

Dr. Galsky: There is certainly the ability to integrate telemedicine into existing studies using lower toxicity oral interventions to replace some of the study visits. That's low-hanging fruit.

In terms of expanding to more complicated areas, there is potentially a pathway for investigational sites to partner with local groups to offer trials that are monitored and conducted on a remote basis with local physicians at the bedside. This is similar to what's happened in the intensive care unit field.

There are a huge number of intensive care units within the rural United States that are staffed and monitored by intensivists that are sitting miles away in front of computer screens and interacting with the nurses and the physicians at that hospital just to manage the patients.

If it can be done for some of our sickest patients, then certainly there is a path forward to do this in other contexts. It's just a matter of making sure that the regulatory environment is ready for this and that there is a buy-in from all of the stakeholders involved. We have proof that we can think differently about our entire clinical trials enterprise if we want to.

What do you think about extending that towards prostate cancer care or general cancer care?

Dr. Galsky: We're really focused on clinical trials. That's our main interest. But we're already seeing telemedicine in standard of care applications.

My colleagues here and at other institutions are already doing second opinions appointments via telemedicine. They're doing postoperative visits via telemedicine. For prostate cancer and for other genital urinary malignancies like bladder cancer, where there's been a centralization of surgeries and patients travel a distance for their surgery, then return to the care of their local teams, the ability to do postoperative checks at a distance offers the potential for significant value added. There is a range of applications for this type of technology. Pp1

Dave Fuehrer
Stupid Cancer + Gryt

Dave Fuehrer is the CEO of Gryt Health, creator of the most used app in all of oncology.

Prostatepedia spoke with him about his Stupid Cancer app and about how Gryt partners with pharmaceutical companies, hospitals, and healthcare organizations.

"I was so full of shame."

How is it that you came to create an app for cancer patients?

Mr. Dave Fuehrer: Out of personal agony. I was diagnosed with cancer twice in my twenties. I went through all of the surgeries and radiation, lost my ability to be a biological father. I really struggled with all the side effects.

Ironically, at the time, I managed research projects for Pfizer. You would think that if there were anybody equipped to look for help or find resources, it would have been me. But I was so full of shame, which I wasn't able to overcome.

Three years after my second diagnosis, my father was diagnosed with bladder cancer. He passed away, and I couldn't continue in life being a researcher and unable to help my own family. So, I left my career at that point and have been doing this ever since.

So it's really personal then.

Mr. Fuehrer: Very personal.

Why did you name your company GRYT Health? What does grit mean to you in relation to your own two-time cancer diagnosis, your father's journey, and what you're trying to do?

Mr. Fuehrer: We started out with a different company name—SC Research Ventures—because we believed that we would use research to help improve the experience of cancer. Then, we realized that we're not just researchers, and we don't just do something—we live it.

Our chairwoman, Shelley Nolden, is a young adult APL leukemia survivor who spent 40 days in the hospital fighting for her life. While we were coming up with a new company name, she wrote a blog about having the grit to get through cancer. We all had to find our grit, so we wanted to name our company after that shared experience. One of us looked at the other as said, "We have to spell it with a Y because there is no I in grit. It's a team sport."

I love that. Your first project was the Stupid Cancer app?

Mr. Fuehrer: Yeah, absolutely. We started the Stupid Cancer app more than four years ago. It was a concept to see if we could create something to help people connect.

We built a pilot beta version that we ran from 2013 to 2014. We had a quarter of a million user interactions during that year. It really showed us how significant the demand was, but that we needed to find a business model, a way to make it sustainable.

We founded GRYT to do that. We worked with the National Cancer Institute (NCI). One of my cofounders has a mentor at the Office of Cancer Survivorship, and she told us about this program called the Small Business Innovation Research (SBIR), and how NCI has all these wonderful initiatives. We got some amazing coaching from some of the top researchers in the cancer space.

How does the app work?

Mr. Fuehrer: We spent two years working on building something around our community, not around

a specific goal. When a company does research, they decide to research this type of patient with this type of disease who is experiencing this type of side effect, and they go design the survey to do it. Then, they learn things in a very specific area. We saw that's not how people live.

We wanted to build something around the way people affected by cancer live. We spent two years working with our community. We published a couple of papers. We've been at the Society for Behavioral Medicine conference the last two years presenting our results.

The Stupid Cancer app has been engineered around the way our experience of cancer affects us. We have a proprietary algorithm that looks at what your primary diagnosis is and at the stage you were diagnosed, because somebody with a Stage 1 cancer has a very different experience from somebody with a Stage 4 cancer. We look at the treatments you've been on. We created this platform to help you connect with somebody just like you who knows what you're going through without you having to explain it to them.

So, it's a way to connect with other patients like you?

Mr. Fuehrer: Exactly, right.

Are those interactions one-on-one or are they part of a larger group, like a support group?

Mr. Fuehrer: They are both. We launched The Stupid Cancer app October 1st, and we have had 400,000 interactions since then. A little more than 75% of those are private messages one-to-one.

The other quarter interactions are in chat rooms around specific topics. We have moderators come on who are experts in an area, so the other quarter activity is around dealing with issues like depression or side effects. We have a book club. It's just the experience of being with others.

When you create a profile, the app instantly matches you with others just like you. For me, I'm connected with other two-time testicular cancer survivors who know what that shame is like.

They ask me questions like "I don't know if women are ever going to find me attractive anymore. Am I still a man?" These are things that are too hard to talk through in person or to even admit.

The anonymity of the app allows people to say more than they might in an in-person support group? Can you talk a little bit more about that dynamic?

Mr. Fuehrer: Absolutely. The hardest things to say are the things that need to be said the most.

I'll use myself as an example. I didn't know if I was still a man anymore. I went from being a 20-year-old athlete to my wife leaving me because I couldn't have kids, to not being able to perform sexually. My body parts stopped working. In those trauma moments, the things that we're too embarrassed to say are the most important things to deal with, and they're often not dealt with.

The whole purpose of this anonymous platform is to give you a place to say what you need without worry about being judged or someone knowing you and thinking differently of you.

I'm in awe every day of the types of things people are able to explore, like women in their 30s going through menopause being able to talk to somebody in that situation without being judged. It's life changing.

There's no risk of running into that person later.

Mr. Fuehrer: That's exactly right.

This dynamic comes up a lot in prostate cancer. The attitude can be: "You're 70. Who cares if you have erectile dysfunction? Does it really matter?" To those men, it does, and it's difficult for a lot of them to talk about it, even with their own doctors.

Mr. Fuehrer: I was excited to talk to you because prostate cancer is rare in that there are many treatment options, and the only difference is how each affects your life. You can have the same medical outcome from a couple of different approaches. Are you comfortable with cancer in your body, or do you need to have it removed? That's personal choice, but each makes tremendous differences in your life. Those are the kinds of things that people need help exploring because if you're not thinking about one versus the other, you may make a decision that, six months from now, has turned your life upside down, when you didn't expect that to happen.

Right. For most men, prostate cancer isn't an emergency situation, so the time for them to be talking to other men with prostate cancer is before they even make that treatment decision.

Mr. Fuehrer: Yes.

Do you have many users with prostate cancer on the app?

Mr. Fuehrer: It's not one of our larger populations. Our most active populations are people with rarer or sensitive conditions, including genetic mutations, people with advanced

"We started the Stupid Cancer app more than four years ago."

cancers, and rare cancers because it's hardest for them to find anybody who relates. We find that they are the most active groups on the platform.

I really care about people who aren't in immediate crisis situations because we still have needs. My needs, for example, aren't usually crisis. They're more about how I want to *live* my life.

For people with prostate cancer, this app won't help you make a treatment decision for tomorrow. This is a very different thing, a resource for you to anonymously figure out how this will affect you.

Right, or even the other way around. Thirty percent of our readers are support group leaders, so if each of those support group leaders went on and offered support and advice to other men, they could reach a lot of people they wouldn't normally reach, right?

Mr. Fuehrer: I would love to invite any of those individuals to lead a chat on our app because we have users who don't know they're there. If any readers want to come on and be moderators, I would love to put their expertise in front of our community.

Great, how would they contact you? Directly, or should they just go on the app and mention it in one of the chats?

Mr. Fuehrer: They can contact me. Our program director, Aerial Donavan, works with individuals to set those up, and we help lead it with them.

What other programs do you offer at GRYT?

Mr. Fuehrer: Everything we're doing at the moment is through The Stupid Cancer app, but the organizations that we work with are pharmaceutical companies, health systems, large hospitals, and healthcare organizations. My entire role is to identify resources that address the needs of people on our platform.

For example, someone in Wichita doesn't know about all the treatment options at MD Anderson and Memorial Sloan Kettering. My mission in life is to make sure that wherever you are, you know what's available so that you can make the right decision for you.

Have you thought at all about using it in clinical trial research.

Mr. Fuehrer: Yes. We have a partnership with a pharmaceutical company that's running a Phase III clinical trial on a genetic mutation. We let people on our platform who have those tumor types know about this information.

One of the women with that tumor type wrote back and said she'd been asking her medical team for three years if there was a genetic sequence for her tumor, and they'd been saying there wasn't. She wondered how the trial could be available and her medical team at her hospital say there is nothing for her. We connected her with that company, and they provided no-cost genetic sequence. It changed the whole course of her treatment.

Is there anything else we should know about GRYT and Stupid Cancer?

Mr. Fuehrer: The most important

thing is connection. This is a resource for people to start. Connection is what opens you up to everything else. Whether somebody is looking for someone else who understands them, other treatment options, the people at Dana-Faber, or a way to get that information to patients, connection is what enables all of that to happen.

Also, we believe that caregivers are just as impacted as patients. This platform is not just for those diagnosed. It's for anyone affected by cancer.

We've paid a lot of attention to onboarding, so when you sign up, we don't ask if you are a patient or a caregiver.

My brother looked at our process and said: "I'm neither patient or caregiver. I wasn't diagnosed, and I wasn't yours or dad's caregiver." I realized my brother has gone through cancer alongside two immediate family members, and he doesn't feel welcome. So, we've designed everything to welcome those who've been affected by cancer. We don't use labels to define people.

That's a dynamic at play in the prostate cancer world. We talk about significant others a lot, but often it's adult children doing the research and then providing it to a parent, who then goes and gets treatment. It's a family disease.

Mr. Fuehrer: Totally. In pediatrics, for example, it's the parents. And it's also the 20 and 30 year olds on the platform. And for older generations, it's their kids—me—looking for help. Pp1

Jamie Bearse: Dispatches From The Hill: Research Funding

Mr. Jamie Bearse is the President and CEO of ZERO — The End of Prostate Cancer (www.zerocancer.org). ZERO is a United States-based nonprofit with a mission to end prostate cancer.

Mr. Bearse updates *Prostatepedia* on increased funding for the Prostate Cancer Research Program.

In my last *Dispatches from the Hill* column, I talked about our increase in funding for the Prostate Cancer Research Program (PCRP) to $90M in the 2017 fiscal year and what that meant to prostate cancer patients and their families.

Now, I'm back with even better news: PCRP funding for the 2018 fiscal year was just increased to $100 million, the highest level in the last 18 years!

When the Red Sox won the World Series in 2004, breaking an 86-year championship drought, the Boston Globe covered many heart-filled stories of lifelong fans. They shared stories of how these fans drove hours to visit the graves of fathers and grandfathers who went their whole lives without seeing the team win the big one. Increasing research funding at PCRP to $100M is like that. This achievement is the pinnacle

"I'm back with even better news."

in ZERO's mission—almost like winning the World Series.

Serving the organization for the last 16 years, I've been fortunate to work alongside many of the men who founded this organization and who have fought so hard to increase prostate cancer research funding,

"Funding for the 2018 fiscal year was just increased to $100 million."

men like Ralph Burnett. Ralph served our nation as a Vietnam veteran and Federal Court Judge, as well as Chairman of this organization in the early years. I talked to him almost daily in the last few months of his life, before he succumbed to advanced prostate cancer. Back then, there weren't the many treatment options available now, not as much hope for men diagnosed at a late stage.

Ralph tried talking me into going to law school. He was convinced I should become a judge, but I told him I'd be at ZERO for the long haul. He made me promise to build up our outreach, to never stop fighting for the funding that prostate cancer patients deserve, and to secure $100M for the PCRP. Ralph was a tough old bird, but he loved this organization, and he'd be beaming with pride over this news.

The PCRP is the most successful initiative aimed at ending prostate cancer and has generated three new treatments for prostate cancer and a new tool to determine aggressive from indolent disease. The increase of $10M will give a whole new universe of hope for the far too many men and families today who are hanging on for the help this increase will generate. This is a tremendous victory for patients and families. This historic increase will directly fund a dozen or more life-saving research projects at academic institutions across the country.

Patients Speak
Gary H:
Let's Talk About It

Gary H spoke with Prostatepedia about prostate cancer journey and the choices he's made along the way.

How were you initially diagnosed with prostate cancer?

Gary H: I live in Colorado, and I get a physical every year. I didn't know this, but my doctor started checking my PSA at 40. About five years ago, when I was 54, my doctor said my PSA went up from 2.0 to about 4.4. He said there was a small chance of cancer, but when it gets up to that number, it's important to check it, so he recommended a biopsy. I went in there just for a physical. Next thing you know, I'm going to get a biopsy.

I found a good doc, went in, and did the biopsy. He did about 12 needles. It turned out that I had some cancer in certain parts of my prostate.

He said, "You're a young guy. Just go take it out." But I started researching more and more, and because my PSA wasn't going up very fast, I started the journey looking at what to do.

Where did you go for research? Did you turn to the internet? Friends?

Gary H: Yes. I talked to people I know who knew someone who went through it. I just talked to lots of people who had a friend, brother, or relative, and I just called them. From them, I heard everything from "I had it taken out" to "active surveillance." I was getting calls about the proton or doing brachy. I was amazed by how many different approaches there are. I got a feeling for what I needed to do, and then I talked to four or five top surgeons and in different places, like Sloan Kettering, Johns Hopkins, and MD Anderson.

You did your due diligence.

Gary H: I sure did. I did everything I could possibly do, and from what I understood, if PSA is under 10, it hasn't spread. I had about 8, but it wasn't going very fast. I found a fairly young fellow in Denver that I had a lot of confidence in. After speaking with about seven people who had it removed and told me what to expect, I elected to have it removed. That was a big decision.

How did you find the surgeon that you ended up going with?

Gary H: I felt that someone who had done thousands of prostatectomies was just knocking them out, going right through them and probably pretty fast. I wanted someone who hadn't done so many but who really took his time, someone very serious about it, someone who cared maybe a little more. The surgery may take only an hour, but I wanted a meticulous person.

A friend of mine who sold healthcare products in hospitals all over spoke

"I was amazed by how many different approaches there are."

very highly of this one doctor in Colorado. That's how I found my doctor.

Then I had to decide between the old fashioned or robotic way. While the guys that go in there with their hands can feel what's going on, which can be beneficial, there can be a lot more bleeding. I chose robotic because there would be less bleeding, and I'm glad I did.

Did you have any side effects after the surgery?

Gary H: Not really. Because I was young, they said I should be fine, and I really didn't have any side effects. It took me a little longer to heal than I thought it would. I started exercising maybe before I should've. I should've waited a little bit longer.

Otherwise, everything went the way it was supposed to, and everything was great. That was a little over three years ago. I have been as athletic as ever, and I never had a problem with incontinence.

What kind of monitoring did they do after the surgery?

Gary H: About every three months, for about three years, I had my PSA checked. About five months ago, my PSA showed up as 0.02. Before that, it was 0.01, which is what they call undetectable. It's still undetectable, but it went up to 0.06. I just had another test, and I'm waiting on the results. It's a whole new program now. As far as what I've learned, the doubling time is the big thing, and so it's been doubling every two or three months, which is pretty quick. But the number is very low. I'm starting to ask questions again, but the speed is the concern, not so much the number.

Right: the velocity, they say.

Gary H: Right. Depending on this new test, I may have it radiated.

Is this something your doctor suggested, or is this a result of your previous research and discussions with other men?

Gary H: Probably a combination. My doctor initially told me that if it gets to 0.20, we should look at doing radiation and maybe hormone. Then, it was only 0.02, so I had a long way to go. Because of the speed of it, he advised to just have it radiated, that I didn't need the hormone at this point. Because the doubling time is minimal but going faster, the velocity threw me a curve ball.

Have you had any imaging studies to see what's going on, or is it so far just blood tests that you're getting?

Gary H: No. No imaging. It's because the number is so low. They say they wouldn't be able to detect anything. But I plan to probably do the imaging.

My one doc says it doesn't get in your bones until it goes up to 40 or 50. A PSA of 0.03 or even 0.06 is really just starting to get going, so it's most likely still in the bed.

For right now, you're just in a waiting game, right?

Gary H: Yeah. I'm waiting today, actually. But I'm not concerned or worried. It's a nonissue because of all the information. The more you know, the more comfortable you are. And it's really out of my mind until maybe the day I've got to go and have blood work. Then, I feel like I'm in the electric chair for the next six to eight hours until I find out.

There's that waiting thing, right?

Gary H: That's right. That's the only real negative, I suppose.

They call that PSA anxiety.

Gary H: Yeah. There you go. And now I'm not too worried. There are lots of great technologies and options. It's just the radiation that concerns me, really. I've got to be in one place for two months. That's the thing.

There are many good radiation therapists out there, so I'm sure you'll be in good hands. It's also good to have an action plan for what you would do next if you need to take more action, right?

Gary H: It sure is comforting that way. Now, what I went through with prostate cancer is not the same as other forms of cancers. I guess I could say I'm very fortunate to have found it when I did and to have had a doctor that was checking me all the time.

Right. You didn't even know you were getting your PSA checked.

Gary H: I didn't even know.

Do you have any thoughts for other men who are newly diagnosed or in a similar situation to yours?

Gary H: When you first hear about it, your initial reaction is: okay, what does that mean? Prostate cancer hasn't really changed my life. I still exercise. I feel great. I compete as a golfer. It's not like all of a sudden I've got to go and sit in a chair, and read a book for the rest of my life.

It's just a nuisance more than anything. That's if you stay on top of it.

Now, of course, it could've been a lot worse. I had an uncle who passed away back in 1982 of prostate cancer, so it was in my family. He had waited and waited. He was supposed to have it out, but he was afraid, so he waited an extra year or two. By then, it was too late.

Do what you have to do initially, and learn as much as you can about your disease. There are lots of people to talk to and options out there.

At one point, for example, I was going to do the brachy. Once, I almost did the cryo. I was actually up at 6:00 am getting ready to go to the hospital for the cryo treatment, but I didn't. I just didn't feel right. I went the aggressive route and had it removed.

Just do what you have to do. It's not a painful experience, really. It's more of a nuisance from your daily activities. You have to step back, reevaluate, and take some time. Figure out what approach to take, and go that route.

What about reaching out to other men because it sounds like you really did? You had a lot of discussions with your friends and family. Would you recommend that other men do that as well?

Halberg: Oh, absolutely. Everybody's different. I know people who are not very social and just rely on the internet. Others will talk to every Tom, Dick, and Harry, and that's how I was. I did a little bit of everything. I had three close pals who had it, so I talked to them.

Everybody's an individual and different about what approach they want to take. I have a friend who has a similar situation to mine, but he's chosen active surveillance. He's really staying right around that number, and it's not going anywhere.

"Reaching out and talking with other men is important, even just to sort through conflicting information.."

You do read conflicting things, for example, that PSA is not important, but it is important. If it's on the move, you need to do something about it. So, reaching out and talking with other men is important, even just to sort through conflicting information.

People find it helpful to listen to other men's stories.

Gary H: I like it a lot. I travel all over as a competitive golfer, and I always wanted to hook up with some organization, so while traveling, I could speak in different towns each week. I am competing. I'm out there. I've been through it all. I'd like to share with others.

There's still a bit of a cultural shyness or reticence about speaking about prostate cancer. Perhaps it's a gender thing, but a lot of men are hesitant to talk about it.

Gary H: Yeah. I'm not. I'm not at all.

Any way you can get the dialogue out there is good.

Gary H: I'm very open about it. I don't have a problem. It's a certain age. It's not like an 18-year-old so much. We're older now. Let's talk about it. Pp1

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