

Behind the Breakthrough Podcast - University Health Network

Season 3 - Dr. Gang Zheng

Transcript

BTB

This is behind the breakthrough, the podcast all about groundbreaking medical research and the people behind it at Toronto's University Health Network, Canada's largest research and teaching hospital. I'm your host, Christian Côté, and on the podcast today, Dr Gang Zheng, an award winning senior scientist at the Princess Margaret Cancer Center and one of UHN's inventors of the Year. Dr. Zheng is a research pioneer in the field of nanomedicine. His lab is developing next generation tools to assist imaging in more accurately pinpointing cancer tumors, and he's discovered less toxic, more targeted and effective methods to eradicating cancer. Dr. Gang Zheng, welcome to Behind the Breakthrough.

DR. GANG ZHENG

Thank you for having me.

BTB

Big picture first the field of nanomedicine. It's been dubbed the science of small. And that's because it's predicated on the use of nanoparticles. So let's begin there for the uninitiated, like myself. What is a nanoparticle?

DR. GANG ZHENG

So nanoparticle is about size, a nanoparticle is about 100000 anywhere from a million size smaller than a human hair. Right?

BTB

Than a human hair.

DR. GANG ZHENG

Yeah, in a biological context, if you consider what are the nanoparticle kind of size, you can pick yourself a virus. Right? The most popular virus, the most, the one in our mind is COVID, SARS-COVID 2 and the Covid virus is about 100nm size. Another one, which is in our mind, is a MRNA vaccine for the Covid. And MRNA is about two nanometer size. So if you picture

yourself a nanoparticle, the size is between an mRNA and a Covid virus, right? That's probably the size part. But nanoparticle cannot be a core nanoparticle if you don't make it manmade or intelligently designed to serve a function. If you design a nanoparticle for human medical use, that's called nanomedicine.

BTB

All right. So medical research has spent decades investigating all sorts of uses for nanoparticles, such as contrasting agent in imaging a drug delivery vehicle. What's the advantage here over existing methods?

DR. GANG ZHENG

I think the first thing is nanoparticles and nano size has its unique properties. I can give you a few examples. For example, iron oxide is everywhere, but iron oxide nanoparticle, when it's actually getting smaller as small as like less than 10 nanometer sized, it actually presents itself a unique superpower romantic properties, which you can using for mRNA contrast. Anything above 10 nanometer, the concept property disappears. So the nanoscale property is a very unique. And you can also say, for example, gold, right? Gold is yellow, right? All gold. But once you go to the gold nanoparticle, different size of gold nanoparticle can make up a full spectrum of different colour that can have a potential a lot of application for like optical imaging for different things. So the size of nanoparticle is a number one property because they gave you the unique nanoscale property.

The second, I would say, is the nanoparticle because they are similar to a lot of machinery in the body, like the virus, RNA, DNA. So the nanoparticle is like a biosize, what I would call. So that means they interact seamlessly with like cells within the body. So people are using the nano to take advantage of this size advantage of nanoparticle for the disease detection and treatment in general.

BTB

And when you say the nanoparticle is manmade, if it is used inside the body, does the body see it itself or is it potentially rejecting the nanoparticle?

DR. GANG ZHENG

That's a beautiful question. And just like anything you get into the body, the body will reject it, right? Because otherwise we won't survive. But the intelligent design man-made means you have to find a way to make a nanoparticle get into the body without the human cells recognize as a foreign subject. So you can actually evading the humans, for example, you can what they call the Don't Eat Me signals. If that nanoparticle, reads the don't eat me signal then the macrophage will eat it up and they actually can serve their own function.

BTB

And your field, of course, is cancer research. What is it about the cancer tumor that makes it so attractive to nanoparticles?

DR. GANG ZHENG

Yeah, that's actually a great question. The cancer in the solid tumor particular has two distinct features. One is because of the disorganized rapid growth of the tumor cells. They can always form these kind of tortuous vessels, right? So the vessels a lot of leakage of vessels. Second point of the cancer is you have impaired lymphatic system. So imagine you have a nanoparticle circulating in the bloodstream and they're actually getting to near the tumors, then because of leaky vessel, the nanoparticle, will actually permeate through these vessels getting to the tumors. But because of the drainage that usually the working have drainage, the lymphatic works beautifully to clean up everything else, right. But the lymphatic system is poorly draining. That means you got going through the tumor and the got stuck. So these so-called enhanced permeability retention effect is also one of the key hallmark of nanoparticle nanomedicine because they afford some degree of passive accumulation in the tumor makes a nanoparticle like to be almost like, say, affinity to the tumors.

BTB

So that's interesting. Are you able to again, in layman's terms, explain to me then what is it that the nanoparticle is so attracted to in terms of, say, the leaky vessel or being able to permeate these vessels? What is it about the properties of the nanoparticle that's precise?

DR. GANG ZHENG

It's about size. You know, the nanoparticle actually don't go through vessel using a regular vessel. The nanoparticle, that particular vessel, that particular size match up very well with leaking vessel. So anything a below 150 nanometers, about 200 nanometers you will permeate through the vessel going into the tumor. If you have a particle like micron size, it won't go through. So it is a nanoparticle size, make them go to the tumor through this effect. Obviously, this is a hydrogenous, there is a many different tumors, different tumor type, all different. But most nanoparticle have some degree of a tumor selectivity because of the size advantage.

BTB

All right, let's turn to your groundbreaking work and your lab. You actually developed your own nanoparticle, the porphosome.

DR. GANG ZHENG

Porphosome.

BTB

Porphosome, right, porphosome back in 2011, a discovery that I should pat you on the back been recognized as a top 10 cancer breakthrough. Now, in part because its benefit, I guess, is that it's called the Swiss Army knife of nanoparticles it can be used as a drug delivery vehicle. It helps diagnostic imaging because they light up when exposed to light and when they absorb the light they can heat up, which allows them then to apparently reduce or even eliminate a cancer tumor. So let's start with your discovery how did you come up with the porphosome?

DR. GANG ZHENG

So at the very beginning, we would just try to use lipid nanoparticle, right? Liquid metal. It's a lipid nanoparticle. Lipid nanoparticle is commonly used now. Very famous now because you're the one who actually buy Moderna and Pfizer, which is used in the mRNA vaccine because they're based on the lipid nanoparticle. So now I'm pretty sure everyone knows what's lipid nanoparticle is now. So initially, our idea is very simple. We want to use lipid nanoparticle to deliver a high dose of light active drug for treating the cancer through the laser ablation therapy.

And that light active drug is called porphyrin. And they also actually known these porphyrin, often as known as a color of life. Why we say that because it is everywhere in nature. In your body. Why the blood is red is because blood is having the hemoglobin. Hemoglobin contains a red like porphyrin that makes the blood red. Obviously the most important because the color is because it delivers oxygen, right?

And in nature, also, the grass is green, the leaves are green, spinach is green because they have chlorophyll. Chlorophyll is a green magnesium porphyrin, and that's why the people call the color of life. But for our purpose, the porphyrin molecule we use particularly is literally coming from *Spartina* algae from the Pacific island of Hawaii. For those who are health conscious, you added the *Spartina* algae into your smoothies, and these are the one who consider like a superfood. We basically took this superfood extract, a core of porphyrin out of that using our starting material.

BTB

This is like a food allergy.

DR. GANG ZHENG

Yeah, it's a form of algae. Long story short, we were trying to load in these particular free into lipid nanoparticle. But we failed because the porphyrin is bulky. They just broke up the nanoparticle. So we thought since the lipid nanoparticle is made up with lipid lipids, kind of fat, right fat molecule. And what if we link porphyrin with chlorophyll onto this fat molecule on the lipid so we form porphyrin lipid? Essentially, the chlorophyll fat? And we thought the lipid nanoparticle should have a better chance, recognize this fat molecule analogue, which will have porphyrin on it so they can load more.

But little we know the rest really is the history, because once we made this porphyrin fat molecule porphyrin lipid, they self-assembled into lipid nanoparticle without any help of the regular lipid. That was completely astonishing, and we would never thought of that. And that's where porphosome is actually discovered. But once it's discovered we actually find it so fascinating properties associated with these porphosome nanoparticles.

Imagine each porphosome is made about 100,000 porphyrin lipid molecules by themselves. Each porphyrin lipid has a porphyrin. Porphyrin absorb light. They're dye they're pigment. When you have 100,000 of them, you absorb tons of light. They behave like a black hole. What black hole does absorb everything light energy? The only thing came up is by the heat. So that's why we saw porphosome made a single pigment molecule pigment fat molecule can actually become so much energy, so much heat from the light can destroy the tumor, so can use that to ablate the tumor by the form of thermal therapy.

So right afterwards, we actually figured out, oh, not only you can do photo film ablation, you can use that for fluorescent Sky, a surgery. You can use that for pet and MRI scanning, you know, for imaging detection, tumor detection. Can use that for ultrasound CT. The whole nine yards. And that's where this one stop shopping nanoparticle based on single molecule is makes so excited.

BTB

I want to get into drill down to each of these uses that you talk about, but I'm just curious when you made this discovery, you know, what was your reaction when you realized you had created this all in one nanoparticle?

DR. GANG ZHENG

First is disbelief.

BTB

Disbelief.

DR. GANG ZHENG

because we never thought it can happen. We never saw the molecule can self-assemble. But once it's formed, I was real literally jump upside down if I could, because imagine you have a molecule now from this nanoparticle, 100,000 of them lined together the perfect shape. Then all these new nanoscale property, what I'm talk about, which is associate with the nanoparticle, we creating so many new functions which never existed before. So that's actually from the very, very beginning of the disbelief to the super, super hyped. Then we realized we get back to work. We have to make sure it is useful for cancer patient, but that is a long journey.

BTB

All right, let's start with the potential for advancing imaging. What have you shown that porphyrin can do in your lab when it comes to, I understand this is with animal models, what have you shown so far?

DR. GANG ZHENG

The whole nine yards, to be honest. So we actually proved the porphyrins, many utility. Most importantly, their tumor cell activity in many different model preclinical models and many different cancer type just did not complete, said the cancer type. We actually covered lung, prostate, head and neck, ovarian, endometrial, pancreas, brain, thyroid, **Clairo**, just to name a few. And we actually tested our different models in different species, and we have demonstrated many different utilities. But that's allow us because of intrinsic multi-functional of the porphyrin. It allow us to pick and choose different function for different clinical application. Really, that's what the beauty of the porphyrin is.

BTB

And if you could, then Gang, explain to us how it's advancing imaging?

DR. GANG ZHENG

Let's take the porphyrin's guide to surgery as example. You may consider porphyrins for instance like homing beacon shining and will help a surgeon to easily identify the tumor and to delineate the tumor nodule because they were showing up the tumor differentiate from the surrounding. That will help the surgeon to more accurately, you know, retracting the tumor with the minimally invasive way. So that's one potential imaging application.

But what makes porphyrin really exciting it's not just a homing beak. You may even consider as a killer beacon. Homing beacon is to show where the tumor is, but the because of the function of porphyrin allow us to do the ablation the cancer. Imagine the surgeon cutting the tumors. You don't see anything anymore. The first is clear. You will never know there was a tumor cells left behind. That's where that will cause a tumor recurrence. But because of the porphyrin has therapeutic function, not just a homing beacon, as it has a killer beacon function. If you're shining a light, it actually generating either by the heat or by the chemical reactive oxygen species that will cure the tumor cells left behind. So it's almost like a surgical back cleaning. So the killer beacon is what's differentiate porphyrin from the smart for us and trace it for us and probes.

BTB

How do you deliver the porphyrin nanoparticle into the body?

DR. GANG ZHENG

Circulation through the intravenous administration?

BTB

So it's a simple IV?

DR. GANG ZHENG

Simple IV.

BTB

Travels because it knows to travel towards the cancer tumor. And then you say when you expose it to light to help light up a tumor, how do you light it up?

DR. GANG ZHENG

Light has limited penetration depths, and that's usually is one of the key limitation of any light based therapy. But laser advancement, a combination of the fiber technology nowadays is making the light can be delivered pretty much anywhere in the body through the fiber and the laser. In fact, in one of our work collaborating with casual Yasuo Fukuda, the lung surgeon and a Japanese fiber company, we were able to deliver the light through the bronchoscopy through the fiber almost through the entire lung. Because the fiber is so thin is less than one mm in diameter. We can we can deliver both the light for the imaging light and the treatment light. So technology advancement nowadays can make the light delivery become more practical and useful.

BTB

Is there a danger of when the porphyrin is exposed to light and it heats up, which is positive because it can ablate the tumor? But is there a danger of it heating up too much and damaging a patient?

DR. GANG ZHENG

Oh not, not at all. It is a tissue overheating, which caused the collateral damage is one of the key consideration. In fact, for all thermal therapy ablation therapy, not just a photo, just light, but also radiofrequency high fields high intensity focused ultrasound. Anything to do with a thermal ablation, you have to watch how the temperature goes. Usually you accomplish that by using very precise MRI thermometry, essentially using magnetic resonance imaging as a way to control monitoring the temperature that is actually quite expensive. Because imagine all these therapy, you have to be under the MRI magnet. So we actually came up with the idea to creating this, a new generation of porphyrin with an almost like you will consider like computing thermostat. As soon as reaching the temperature would a desired temperature, it tripped it tell me to stop, this way we're solving the problem of the overheating. We actually have a nice name for this agent. We call the pearl the lady like the pearl, the jewelry, you know, it's time for photo thermal enhancing auto regulated lipid nanoparticles.

BTB

OK? Of course it's an acronym. All right,

DR. GANG ZHENG

That's what the Canadian when I come to Canada, the one thing I learn a lot is about acronyms.

BTB

So talk to us then about to date, what kind of results are you getting with the porphosome in terms of as an agent for help in surgery and or in terms of reducing cancer tumors? What are you seeing?

DR. GANG ZHENG

I think the area it most likely will have, the biggest impact is the imaging guided minimally invasive intervention of early stage cancers. Again, I like to use the lung cancer example because there was a huge success, particularly in Canada, the nationwide, the early lung cancer screening and the risk stratification having achieved amazing result actually reduced the mortality rate of lung cancer. But is also generating a question which is a challenge, I will say that is already so many patients to be diagnosed as early lung cancer. What do you do with them? I especially there is a large small population of these early lung cancer patients are medically inoperable.

So what do you do with them? Right. So really, there is unmet need to come up with a minimally invasive way to intercept these early cancer, which is one of the key goal of our Princess Margaret. Our idea is using what is a minimally invasive way we want using a diagnostic bronchoscope trans broncholly that means through the bronchoscope, usually using for diagnosis, for biopsy, we will feed the fiber into it. We will use this fiber to find the tumor behind the bronchial by the furrows and shining up by the porphosome.

Not only we can detect this tumor behind the bronchial to allow us to do imaging, to do the biopsy. We don't need to do that. We will just stick the fiber in and to ablate it. And this way we can turn a diagnostic procedure into an early cancer intercept procedure. So as same like a similar situation to the prostate, thyroid as the cancer detection, becomes more and more popular and the more successful, we have to find a way to treating these cancer at early stage without impact their daily life. So that's where personally, I see the porphosome may have the biggest impactful.

BTB

It's amazing. So talk to us about the kind of results, though, that you're getting.

DR. GANG ZHENG

Let's say, for example, the endometrial cancer we were in endometrial cancer, we were actually able to achieve a porphosome enabled fluorescence guide surgery, with about 100

percent close to 100 percent sensitivity and 67 percent of specificity. Which is not ideal but is already a major progress over the current way. And that is important because most of these are used to be the endometrial cancer. These early patients not treated by the are competing for lymphadenectomy. You removed all lymph node associated, which is having tons of problems, right?

And now people try to move away from this using the central lymph node mapping try to a less invasive way because if you do the lymphadenectomy, you actually using for taking all the lymph node, imagine you will forever feeling for lymphoedema you rely on a drugs and you can only for the diagnosis purpose. You not have any treatment value that's like such a brutal method. And people trying to moving away from that and sentinel is actually see where the drainage is. But endometrial cancer has a very complex drainage pattern. So if you're using sentinel injecting directly sub Q, you will missing about 15 percent of these patients. So using porphysome giving IV and the porphysome getting into this tumor in the as small as one or two millimeters, we were able to detect by a porphysome able to guiding these lymph node dissection better. So these are the result we are getting right. So there is many different cancers we're working on.

BTB

Let's talk about translation in terms of lab to benefiting patients. When do you see moving out of animal models into clinical trials?

DR. GANG ZHENG

Porphysome was discovered 2011, right, a paper published We are now 2021.

BTB

Correct.

DR. GANG ZHENG

We're not standing still. And this is a long, bumpy journey. We are almost made entirely through. And we were able, fortunately, we don't have any commercial support yet, but we were fortunately supported by academic research grants by the Terry Fox, for example, the program project grant by the C.C.I., I mean the Canadian Cancer Society, but most importantly, by our Princess Margaret Cancer Center Foundation.

And we were able to not just demonstrate all the utility selectivity in all the models I mentioned before we actually able to accomplish the toxicity study. We prove porphysome is safe to use. We were also able to getting the scale up manufacturing done. We are even actually get a clinical formulation ready.

BTB

Wow.

DR. GANG ZHENG

So we are now in the process of discussing with Health Canada, essentially for the clinical trial application. So if all went well and we should see first patient in March 2022 next year?

BTB

Amazing.

DR. GANG ZHENG

Yeah, obviously this is a huge undertaking, right?

BTB

Mm-Hmm.

DR. GANG ZHENG

I'm pretty much have all my best best friends are clinicians covering all specialties, and that's how you can make the work.

BTB

There's actually another use we should touch on for your porphosome discovery, and that's as a drug, the delivery vehicle, what results are you seeing there?

DR. GANG ZHENG

Porphosome, by definition, is a lipid nanoparticle, right. Lipid nanoparticle now is on top of the world because of Covid vaccine, but in fact, lipid nanoparticle been using over many years in some or many of them already in clinical approval stage clinical approval. FDA approved is for the chemotherapy delivery. For the drug delivery, which means is covering from anywhere from small molecule chemotherapy to drug to a protein like antibody to nucleic acid like RNA. So what porphosome does it adding a component of control.

Porphyrin giving its imaging capability help to be a guided delivery porphyrin has a by controlled by the light? It has given, it's like a trigger for controlled release of the drug into more efficient way. So porphosome has drug delivery function as a lipid nanoparticle, but adding something extra flavour.

BTB

It's like an elegance to the delivery of the drug in a way that's way more, I guess better for the body.

DR. GANG ZHENG

In theory.

BTB

Still an investigational stage, yes. I'm curious what's been the reaction to your discovery of the porphysome from the medical research world?

DR. GANG ZHENG

I think that's we were very humbled by the very positive reaction when the porphysome was discovered. Because everybody was excited, not just because this porphysome is a new novel cancer theranostics. Theranostic means therapy and diagnostic right, it can do different functions. The fact is, the intrinsic multi-functional property of the porphysome. It's inspired, a new generation of nanomedicine design, right? Always used to be nanomedicine. You talk about nanoparticle is a legal concept. Having different function come together like a Swiss knife. But porphysome, is different than Swiss knife.

Because it is made with a single component, having all different functions. And that, in theory, should help the clinical translation because it makes it so much simpler. If you based on one component, it would be much easier to track to see how they degrade in vivo, how the fate in vivo so would be more easily to be translated. But this is only the theoretical benefit, but in reality is new chemical entity. You still have to go through very stringent FDA and Health Canada requirement.

But it is our belief when this kind of design concept eventually will help the speed of the translation because imagine the things they are making with a single component. If that component is demonstrated to be safe in patient, then all of a sudden everybody can test all their different function in different cancer. I don't need to getting a next approval, next approval to do all this right. So this concept, one for all cancer has been picking up in the mainstream mainstay of nano medicine research, so I'm very gratified to see that happens.

BTB

You've been quoted as saying nanomedicine big picture is at a tipping point. How so?

DR. GANG ZHENG

I have to say two years ago, very few people in the world know what's nanomedicine is. They may heard about it, but they say they feel it's too far is like a futuristic. But when everyone had a Pfizer or Moderna vaccine in your arms, which is made by lipid nanoparticle, deliver that mRNA vaccine. You have a first experience. You're encountered with the word nanomedicine. That's the best with nanomedicine, a work that change the perception. It also bring almost like gold rush now in everybody trying to deliver nanoparticle nanomedicine for cancer vaccine, for all kind of imaging treatment, and everything.

And when you have the buying of the public and you know, no one should underestimate the human creative nature, our generation and this is that's why I say is a golden age of nanomedicine is reaching very quickly, reaching a tipping point. It was like an order of

magnitude of how many nanoparticles get into a clinical trial. This is the last two years versus, like 20 years ago, 10 years ago or even five years ago. You know, sooner or later, there will be benefit will be realized in patient. Hopefully, we were part of that contributor as well.

BTB

You're listening to Behind the Breakthrough, the podcast all about groundbreaking medical research and the people behind it at Toronto's University Health Network, Canada's largest research and teaching hospital. I'm your host, Christian Coté. Today, we're speaking with Dr. Gang Zheng, an award winning senior scientist at the Princess Margaret Cancer Center. Dr. Zheng's pioneering research in the field of nanomedicine is made possible, in part thanks to generous donor support. If you'd like to contribute to Dr. Zheng's groundbreaking medical research. Please go to www.thepmcf.ca and click on the Donate Now button.

Now Gang, I want to go back in time to examine your origin story. You were born and raised in China. That's one hundred and seventy five kilometers southwest of Shanghai, and you have this amazing family tradition. Your grandfather, your parents were all academics, all in the field of chemistry. You follow the family tradition. You got your degree in chemistry as well in 1988. I'm curious how that family academic tradition has shaped or influenced your career.

DR. GANG ZHENG

First, my grandfather's industrial chemist, one of the first generation of Chinese students, to study abroad in the early 20th centuries. He went to France in Leon. Indeed, the chemistry I have my chemistry blood, so I'm always a chemist. So that's, that's what's the family's contribution. But what's the difference make? How? I'm become a cancer researcher, that's probably a more interesting story to tell.

BTB

Go ahead.

DR. GANG ZHENG

So I'm again a chemist by training undergraduate master degree. In 1994, I get a New York State Fellowship to study Ph.D. at SUNY Buffalo State University in New York at Buffalo. And particularly, that offer came not from the Department of Chemistry is coming from a Roswell Park Cancer Institute. I'm always knowing, you know, being a chemist, you can make the job you can potentially using for patient benefit. But that's very distant. When I'm getting an opportunity to study chemistry in a cancer center got my instantly go up on the first day of my lab visit Professor Tom Dougherty, who is a pioneer. They call him father of PDT photodynamic therapy.

He told me, and about two other student fellow students say, Come with me, I will give you a tool. So I started going to the chemistry lab showing the fume hoods. No, he actually took us

to the surgical suite and we were on top of the glass dome, seeing the surgical cirrhotic surgery operating a patient. We were in the glass dome watching. And he basically told us, this is the photodynamic therapy at work. Essentially, the patient was pre injected with a light activity drug. The porphyrin I mentioned that was invented by Tom Dougherty.

So that drug was infused 24 hours ahead of time, then the patient actually acquiring the tumor because of the porphyrin affinity to the tumor. Then the patients under the operation opened the cirrhotic surgery. Then we see the technician, laser technician at the second floor together with us have feeding the fiber all the way to the patient's cavity. They shine a light, and that's he told Dougherty told me that a combination of the light and the drug and oxygen in the body, we are creating cytotoxic reactive oxygen species to kill the cancer cells.

I mean, imagine the wildness at the first day of your Ph.D. program, you instead of went to a lab, you went to a surgical suite and you see the light going into the patient's body. You see the cancer patient being treated on the spot, That shock, wow. Like, completely overtaking you. It didn't take me like two minutes to say, this is a lab I want to begin. So I joined the myPhD lab is actually called Photodynamic Therapy Center at Roswell Park Cancer Institute, and the lab is made with chemist, biophysicist, biologist, dermatologist, you know, physicians, pathology, the whole thing. And that's kind of like a culture is like a lightning struck, right?

BTB

That's your that's your aha moment.

DR. GANG ZHENG

That's how I got into cancer research 1994. I still remember in September

BTB

I want to just one other thing I want to go back to talk about, in terms of your coming to North America because it speaks to your determination and motivation is you're in a foreign country, no family and limited English. This is early 90s...

DR. GANG ZHENG

Terrible, terrible English and not limited.

BTB

Talk to us about how you overcome those obstacles to get where you are today. What motivated you?

DR. GANG ZHENG

It's the drive, right? It's really as simple as that. Once you have a goal in mind, do you want to make some positive contribution to the society and you have to learn, you have to adapt,

you have to overcome all of these challenges. I'm one of the millions of millions of foreign student and take on the take on the foreign land without even speak. I couldn't even talk to a taxi driver, taxi driver where I'm going right? I show everybody my admission form. You know, just show that this is the way I want to go. You know, I tried to make a phone call by the, you know, coin machine. You know, I never dial into, I don't know how to dial that. So I end up with a two big suitcase on the taxi driver. Drop me on the campus, I don't know where to go. So it was a it was an interesting experience. It was.

BTB

Did you have any fears back then just landing in a new world like that?

DR. GANG ZHENG

You are too busy to fear because you worry about how to survive, how to find a place to stay. How to, how to communicating. At least I found my department. That's the way you know. Then I found my home.

BTB

There's an interview where I read, where you talked about a professor later on at U Penn University of Pennsylvania, who advised you to stay true to, and I'm quoting here the spirit of collegiality always be humble and willing to share and learn from others, unquote. How has that advice served you over the course of your career?

DR. GANG ZHENG

Massively. That, Professor, who actually gave me the first job at Penn?

BTB

Who is it ?

DR. GANG ZHENG

His name is Britton Chance. He is a giant in science, in medicine and in sports. You know, speaking of Britton Chance, I got to say this because Olympics is over only recently. He's not only amazing scientist, he's also Olympic Olympic champion.

BTB

Wow.

DR. GANG ZHENG

He won the 1952 Sailing Gold Medal in Helsinki. He's also the just amazing, amazing scientist. So I treasure that every moment I had with him when I was at Penn and his advice that is literally exactly the advice he gave me and serve me so well because it's almost like you think about it. In a uniquely, I'm a chemist in a cancer center. First, Roswell Park, then U

Penn, then Princess Margaret. I'm a chemist in a cancer center. Ever since my Ph.D. years. This collegiately is how I actually embrace myself and took advantage of the beautiful environment multitude, this multidisciplinary.

The research program research question is viewed on clinical question from the clinicians treating like a frontline clinicians. They're treating patients. They're feedback, this is a clinical question I need addressed. This is unmet clinical need I address. I build a program to essentially focus is to take advantage of that. And that is really the, you know, without the collaboration, without the collegiality, I'm nothing there is literally I got nothing right. So. My goal of developing clinical translatable technology platform is in my blood.

BTB

You are actually mid-career, correct? How do you now mentor students and people in your lab?

DR. GANG ZHENG

This is probably the most, the proudest I'm most proud of, not just I think the, the mentorship is the one which I'm most proud of. You know, my students call themselves gangsters because my name is gang, right? They call them gangsters.

BTB

I get it.

DR. GANG ZHENG

Yeah. But this is actually a interesting story because they used to be a medical by physics. We have these Olympics Department Olympics and the students form a team. My students are so close, so close to each other and also so close to me. And then a student had a one idea, say a very wild idea and said they want to call themselves gangsters. They print a T-shirt with my face on it with my hat, baseball had this way called guns and cheesy lab gangster lab. You know, it was such a hit, and they actually use that for later. How we're using that for the Terry Fox run for the fundraising team. And I remember the Fox family really like the porphysome like this, 'cause the thing so is like, almost like become identity, right?

I really I think what I'm most proud of is I train the next generation of independent thinkers and doers. Because not everyone can become a faculty members, but they were becomes tremendously valuable into the society. I run a very diverse both culturally and the literary group. I have a student over the years from over, like 12 countries. I have all my student, almost half of them are woman, and many of them becomes like a professor like myself. Even just this month, I got like I was tweeting last tweet or like a few days back. I was very happy because even this month, I have a three former student become professors in US, in

Canada and in Chile. And all woman. Is it like my crowning achievement is like my student doing so well? That's, I think, probably is a, I hope they will become my legacy in the future.

BTB

It's a great measure and tribute to gangster Gang Zheng. I'm curious about how you approach failure because we are not taught how to deal with failure in life and that is a part of science.

DR. GANG ZHENG

Yeah.

BTB

How do you navigate that world of failure?

DR. GANG ZHENG

It's really about perception. I treat failure as opportunity. Failure used to be means you are in a dead end. Right? And a dead end is always, often is in the rest of the world where the opportunity and risk coexist. If you can do everything based on exactly what you plan for, that's more like engineering, and I like to use the engineering approach to solve the complex biology problem. If you don't take the failure, if you don't try to find a clue in the field, why you failed, you'll never find something new, right?

Like, for example, let me give you probably the best example is, as we all know, porphyrin. Porphyrin is a failure coming from. We want to load porphyrin into a lipid nanoparticle, we failed. Right then we had one that came up with a find a way to load more right that we came up with the OK lipid is a fat, porphyrin is a pigment, put a pigment together with a fat. The fat will like the pigment fat better. Then the porphyrin discovered. So without the failure, there is no serendipitous discovery of porphyrin.

BTB

And I was just going to ask you in your world, does luck or serendipity play a role in research?

DR. GANG ZHENG

Huge. Right? But not just luck is how you take advantage of your luck.

BTB

I see.

DR. GANG ZHENG

Luck is present itself all the time. It most likely in the failure. It is, you have to identify take advantage of the luck, which is, you know, the lightning struck. If you don't catch it like, frankly, you're out of luck, right? You cannot count on luck you're really hoping the luck will strike, but that's how you, how you have to get ready to catch it.

BTB

You're a pure scientist. You work exclusively in the lab. How do you keep patients top of mind?

DR. GANG ZHENG

For me is an easy answer, right? Because as a chemist in the cancer hospital for like 26-27 years. I have on my mandate, the mandate is make something useful for patient. But. What's really different is when I come to Canada, come to Princess Margaret is not in the environment, just in the cancer hospital, you know, working the silo. You are bombarded with questions, clinical question among many from my all close collaborators, all the clinicians. Right. And let me just give you probably the best example I can think about. One of the urologist, you know, John Trachtenberg, he actually challenged me once. He said, Your porphosome's great, you can do ablation can do all this thing. So as a bunch of other ablation techniques like high fields like IRE. He said, my biggest problem is not just how to ablate a tumor, but how to monitoring the temperature. Right.

Hot or not, overheating it. And right now, I have my dedicate and my magnet for the patient to do it. But you know how long for the regular patient waiting for the waiting time to get to the new exam for MRI? Nobody has a privilege to can treating all the patient in the MRI magnet. So can you take the patient out of Magnet, then your technique will be truly discernible to go everywhere. He said, can you come up with an agent, a new porphosome that can not only have a safety threshold vow, but also can guide itself without MRI? Right. That's what I came up with this thermostat idea using the photoacoustic, a new wave ultrasound, you know, optical way to take the patient out of the magnet, right. So when you are having a research question framed based on the clinical questions, you already have the patient on top of your mind.

BTB

So, you know, full well, the urgency of better treatments, better cures for patients. How do you balance or reconcile that urgency with the fact that science takes time?

DR. GANG ZHENG

I know that so well, patience is a virtue and the science has to run its course. Think about it, porphosome 2011 now it's 2021. If I don't persist, don't work hard and don't let the science run its course, we will not be able to and the knocking on the door of the finally translating to patient right? It's just the, you know, a lot of hard work man and the collaboration and the team. I mean in the end is really the collegiality, the collaboration. You are as good as

your team, right? When I have the best team in the world, we can solve all the problems, right, but it takes time. It just takes time.

BTB

Do you feel pressure?

DR. GANG ZHENG

Yeah, because every year I told everyone next year I will be impatient. I've been speaking, I've been talking that for the last five years now. I'm still the same next year, but this time I think is a, I hope this is a, this is it.

BTB

Why do you do what you do Gang?

DR. GANG ZHENG

Before that light striking moment in Buffalo, I don't know what I'm doing, right, but after the moment, 27 years ago, I know exactly what I want to do, right. I want to do something I want to in my lifetime I can, creating some technology where you can apply and to be, you know, used even as a part of standard of care to actually contributing to the cancer patient, whether for the quality of life or for their for their survival. Right. So now this is a very easy answer because I mean, I consider myself so lucky. I got introducing to the cancer research from so young and I take that is is my, you know, the gift from the above. Know what I'm doing is a gift.

BTB

What does your family think of what you've done, your achievements to date?

DR. GANG ZHENG

Well, they were more urgent than I do. They always said, How can it still not be in patient? Every year they said, I don't want to listen anymore of your discovery. Tell me, when is it going to be in patient? So you have pressure to have a pressure everywhere. Pressure from all sides.

BTB

They must be proud.

DR. GANG ZHENG

Yeah, but they said they were on to, I have been in patient and they will withhold their judgment.

BTB

That is pressure. What should we look for next from you Gang, what would you be, what do you think we'll be reading about next?

DR. GANG ZHENG

I would say signed in maybe two words beyond light. So far, the porphyrins, work at it's best as a light based technology? The light has limited penetration are dimension, even though they can be compensated by the fiber is still a very technology, technology burden is high. So what, I'm actually one of the things we the lab is working on very heavily on is to bring integrating ultrasound X-ray, which are much more deep penetrating technology into the mix together with the porphyrin nanotechnology. And that should be one of the key, interesting frontier, the lab is working.

Second, drug delivery, especially the RNA medicine we want to integrate porphyrin as a control and trigger for more precise, more efficient, RNA medicine. And that is happened to be a hot area, so we are working on that as well. Third is probably a targeted radionuclide therapy. Remember, I mentioned porphyrin chelating metal. Hemoglobin has iron, chlorophyll has magnesium and we show we can do a part by copper 64. We have now a new type of porphyrin can calculate many different kind of ligands, which allow us to creating a new radiopharmaceuticals, which can deliver powerful particle therapy emitter beta electron. Essentially, we can do. We are working on the radio therapeutics. I think that's the probably the three most active area. Hopefully, the early you will hear from me, from from me, probably the the most success in this area we are making.

BTB

And we'll let your parents know. Dr. Gang Zheng, award winning senior scientist at the Princess Margaret Cancer Center. Thanks so much for sharing your groundbreaking research with us and continued success.

DR. GANG ZHENG

Pleasure. Thank you.

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Dr. Zheng's research is made possible, in part thanks to generous donor support. If you'd like to contribute to his pioneering medical research. Please go to www.pmcfc.ca that's the pmcf.ca and click on the Donate Now button. And for more on our podcast, go to the website. www.behindthebreakthrough.ca and let us know what you think. We crave feedback. That's a wrap for this edition of Behind the Breakthrough the podcast, all about groundbreaking medical research and the people behind it at the University Health Network in Toronto, Canada's largest research and teaching hospital. I'm your host, Christian Coté. Thanks for listening.