Season 3 – Episode 1 – Dr. Brad Wouters
Transcript

CHRISTIAN COTÉ:
Welcome to season 3 of behind the breakthrough, the podcast all about groundbreaking medical research and the people behindit at Toronto's University Health Network, Canada's largest research and teaching hospital. I'm your host, Christian cote. And to kick off our third season, a special COVID 19 edition with UHN's executive vice president of science and research, Dr. Brad Wouters. In this special edition, we discuss UHN's leading edge COVID research and treatment discoveries, and the triumphs of basic science to create the COVID 19 vaccines. And how and when does this pandemic end? Dr. Brad Wouters, welcome to season three of behind the breakthrough.

DR. BRAD WOUTERS:

Hi, Christian. Great to be back with you.

CHRISTIAN COTÉ:
First off, I have to say props to you for calling it on vaccinedevelopment. It was a year ago you and I sat down to launch season two ofthe podcast. And at the end of our conversation, you actually predicted we would have vaccines in the arms of the general public early in the year2021. And you were off just by a few weeks. What gave you such certainty back then?

DR. BRAD WOUTERS:

Well, you know, it certainly wasn't just me, Christian. I think the vaccine development has been probably the biggest highlight of all the work that's gone on. And in terms of its effectiveness. And i think we've all been really stunned by how great these vaccines are and how effective they are. And it is a triumph of science. I think you know, perhaps one of the greatest examples of the importance of investing in science is asto how it can bring real impact to society. I think what you know really got me confident around the ability to deliver an effective vaccine was just the extraordinary collective effort and speed and willingness to take risk that was shared amongst science and society and government. You know, it was that joint effort that really helped propel this.

CHRISTIAN COTÉ:

Well, let's unpack that a bit, because, you know, this historic scientific feat unfolded in a way that's really fascinating. It allstarts, I would imagine, and you can correct me if I'm wrong - it all startswith the fact that the genetic sequence of the new coronavirus was published January 11th, 2020, to be specific. So that was available to

Scientists around the world. Talk to us about the significance andprecedent of that first step.

DR. BRAD WOUTERS:

Well, it was very important. And as everyone knows, the outbreak of the coronavirus of COVID started in china, in Wuhan, and it was scientists there that initially isolated this virus very soon after thatoutbreak occurred. They sequenced the virus, now known as sars-cov-2, andthey released that sequence publicly to the world. And they did so at somewhat of their own risk for themselves because of regulations and control that happens in china. But it was essential because it gave everyone in the world that sequence, which did a couple of things. Number one, is it allowed us to test people for being infected. We could develop an assay. These are known as the PCR test. It's kind of amazing, everyone in society knows how these things work now. But a PCR test was developed based on that sequence so that we could tell if people were being infected. But it also became the tool to create the vaccines. And you know, as soon as that virus sequence was released, the vaccine companies and academic groups and many, many people around the world got to work immediately to create vaccines.

CHRISTIAN COTÉ:

And talk to us about the spirit of collaboration, because iimagine that was crucial to anything going forward at that time, right?

DR. BRAD WOUTERS:

Yeah, there were many different avenues of collaboration. There was, you know, academic collaboration. There was open data sharing. You know, I think it's another you know, feature of the pandemic is the degree to which information has been rapidly shared, the use of preprint servers on bio archive and med archive, so that data could get into the hands of decision makers, of colleagues, of governments to use that information in ways that they could make decisions. And the places where we've gotten into trouble during this pandemic are where we've made decisions without scientific evidence and having good evidence. Having good data has not only brought us new treatments, new ways of caring for patients, new ways for testing patients, but also the development of the vaccines themselves. You know, so that collaboration starts among scientists, but it rapidly became collaborations with biotechstartups, with pharma, with manufacturers and with government, who all contributed to the development through risk sharing, through funding and through scientific input and progress.

CHRISTIAN COTÉ:

And I understand initiatives such as, say, ‘warp speed’ in the us decided to spread their vaccine research dollars around it. They didn't want to focus on old school inactivated virus vaccines. What's your senseof what the thinking was there?

DR. BRAD WOUTERS:

Well, I think they hedged their bets. They looked at, you know, a number of different opportunities and i think invested in groups that showed potential promise. And we had really two approaches. You know, I think the classic kinds of vaccines that are based on inactivated virus or viral proteins, which have shown, you know, good efficacy and many, many other kinds of infections and diseases. But we also had these new RNA and DNA encoded vaccines, and especially the RNA vaccines. These are the first effective and clinically approved RNA vaccines to be developed to date. And, you know, they've shown extraordinary effectiveness and safety, and you know, over four billion people have gotten one of these vaccines around the world now. So it really is kind of incredible within a year, that, that has happened. But it was based on data and progress and science that has been achieved over the last three decades, over the last 30 years or even further going back. You know, this includes science in lipid particle nanotechnology contributed here from Canada in Vancouver. It includes the development of modified RNA as a delivery tool. And, you know, that was the real breakthrough that made all of these possible. But that breakthrough happened back in the 90s. And,you know, it's taken this long to move that towards clinical application and clinical development. But we got lucky here because we know, this technology was ready. It's a kind of technology that allows for very rapidresponse because of the nature of the technology itself. Once we had the sequence of the virus, you know, this could be developed quite quickly. And it's proven to be, you know, enormously useful and a great future potential in a number of areas.

CHRISTIAN COTÉ:

Well, let's talk about that origin story of the mRNA basedvaccines. And Katalin Kariko, the Hungarian biochemist who's credited with being the first scientist to actually work with RNA’s going back to the late 80s. If that basic science had not been there to, to begin this, would any of this have been happening?

DR. BRAD WOUTERS:

No, no, it is you know, it's, it's like all great scientific impacts. It starts with a scientific discovery. And Dr. Kariko in particular was extremely passionate and motivated about seeing through this opportunity. She recognized that RNA, mRNA delivery could be an extremelyeffective approach to the treatment of a number of different diseases. But there were huge challenges at the time, and not many people believed that it would be possible to deliver RNA in an effective way. And there was two principal reasons why that was challenging. The first of that is inherent instability of the RNA itself. It's very unstable. It gets degraded very quickly. The idea of sort of injecting it and expecting it to survive long enough to have an impact you know, really seemed impossible. And thesecond part is that the delivery of RNA itself serves a little bit as a danger signal to our immune system. And our immune system recognizes RNAand it sees it as foreign. And as a danger signal, and it mounts an immune response, and will attack and remove cells where RNA may have been delivered. And so those are the two big challenges. And that's what she solved. She figured out a way, you know, with a colleague that she workedclosely with that believed in her at

Penn.

CHRISTIAN COTÉ:

Penn being?

DR. BRAD WOUTERS:
It's the University of Pennsylvania. And what she did is she modified the RNA in such a way to kind of hide it from the immune system so it no longer created this activated danger signal so it could survive. And also that modification also stabilized the RNA. And that was kind of the breakthrough. And that paper was published. But it also didn't get a lot of attention at the time. You know, it didn't even get attention inher home university. She, she struggled with promotion. She struggled with getting funding. She wrote grants, couldn't get grants. You know, there were huge incentives for her to do something else or to leave or to move somewhere else. Huge incentives to do so. But her passion was driven by the scientific opportunity. And it's really you know, it's that part that makes great scientists all over the world. Is that true desire to do something meaningful from a scientific discovery perspective and thank goodness she did, because she really is credited with that.

But there's another Canadian connection here. And when she published that paper, it didn't get a lot of attention, but one of the people that did read that paper and get excited was Derek Rossi. This is a Toronto native who at the time i think was a postdoctoral fellow at Stanford, but started his own lab at Harvard. And he saw this as a potential way to create stem cells. He was interested in stem cell biology. And everyone was trying to, you know, to produce stem cells and reprogram cells into stem cells. And we were worried about introducing DNA because that could modify the genome. And he thought, well, i could use RNA instead anduse that as a way to reprogram and create a stem cell. So this is one potential use of this RNA technology. He got excited about that and talkedto a couple of his Harvard colleagues, Tim Springer and Bob Langer. And both of these individuals at Harvard are both serial entrepreneurs. They're also fantastic scientists.

Bob Langer has a thousand patents, has licensed four hundred of them. Sohas created hundreds of companies. And, what he recognized is that the ability to create stem cells was one opportunity, but there were huge other opportunities if you can successfully deliver RNA. So this sort of brought to attention to you know, to others this idea of what RNA couldbe used for. And so they created a company a month later and they called

It based on modified RNA, and they called it modeRNA. And that's, that's thehistory of modeRNA. So, you know, it's a Canadian that helped create that company. And it's been enormously successful. I was looking at their stock price recently and they capped or had reached almost a market capitalization of 200 billion dollars bigger than Merck. You know, some of the other giant pharmaceutical companies. So incredible run for them over the last couple of years.

CHRISTIAN COTÉ:

What's amazing, i guess, to me is, you know, if Dr. Kariko hadn't persisted over the decades and perhaps if dr. Rossi hadn't seen the potential for it, this might not come about, like how people did back in theearly days, you know, perhaps when the genetic sequence was first published back in January of 2020. How did people know all of a sudden to turn to dr. Kariko's work?

DR. BRAD WOUTERS:

so Dr. Kariko's work didn't end with publishing that paper. She wanted to see that have clinical impact, and she continued to work towards there. And there was a company in Germany that had been started by a husband and wife group that was interested in immunotherapy. And they created a spin out that they've called biontech. And they actually hired Dr. Kariko to come and oversee their RNA platformtechnology. And they saw from the very beginning, unlike modeRNA, when it got started, they saw from the beginning the potential for RNA as a vaccine. And that's what they wanted to use it for. So that company was in place. They had already developed a few different RNA vaccine candidates. They were moving through and looking at different opportunities. And when COVID hit Wuhan in January and that sequence was published, modeRNA and biontech both realized that they had a huge opportunity here to go after it. And that's what they did. There's some other importantscience here that, that is also important to success. And having the sequence is important, but it's not enough. The reason why they could develop these effective vaccines so rapidly was also based on our understanding of coronaviruses.

We knew those sequence and the kinds of proteins that the coronavirus encoded. We knew that a spike protein on the coronavirus was essential for those viruses to enter and infect cells. And we actually knew a lot about the structure of that spike protein. It had been solved. The crystal structure had been solved. You know, we knew a lot about how it got activated and how it works, the functional parts of it. This had been studied for years and years in the structural biology community. And thatunderstanding is what you know, made these companies realize that they knew what part of that virus to go after. They knew the spike protein andin particular the receptor binding domain. The part that binds to the, the

Sticky part on the cell would be the area to go after with a vaccine. And sothey both chose the same target. They both made a very similar vaccine with their RNA technology after that and, you know, both have been extremely effective.

CHRISTIAN COTÉ:

Could you ever have envisioned the vaccines in less than 12months, you know, from development to trial to approval being so effective at reducing the severity of this virus?

DR. BRAD WOUTERS:

You know, I think I was stunned by the progress and the speed at which this was done. So, you know, typically a new vaccine can take five to six years for development. You know, i was reading earlier that modeRNA had its vaccine candidate in vials for human test future human testing. Forty two days after that viral sequence was released andthose clinical trials of phase one started very early. Phase two got ready,phase three got ready. They had to build manufacturing capability, manufacturing plants, hundreds of millions, billions of doses being produced. So, you know, the logistical part of this, you know, they ran terrific trials, both of those companies, phase one trials, phase two trials,very large, phase three trials. They did that in a way that convinced the regulators of the quality of the impact and also on the safety of these vaccines in those studies. And i think it's been important, too, that the scientific community has continued to study the effectiveness of the vaccines once they've been approved and once they're into the general population. And you know, even a phase, a very large, these very large phase three trials - sixty thousand people in those trials - to demonstrate the effectiveness, you know, is still a small number when we talk about inoculating billions of people. And the extremely rare potential side effects of these vaccines that we've heard about, the one in a million, the one in a hundred thousand, you can't detect these in phase three trials. So you need to continue to monitor safety and effectiveness. We've seen the evolution of new variants of the virus. We're not dealing with the same one that caused disease initially in wuhan. It’s a very, very different kind of virus now. And so we need to continue to study that and the effectiveness of the vaccines. And there may be new. New versions of vaccines that are required to, you know, continue to provide protection to people.

CHRISTIAN COTÉ:

and my understanding is that’s sort of the elegance of the mRNA platform, if that's what you want to call it, in that you can continueto tweak its efficacy based on, say, the variants that are emerging?

DR. BRAD WOUTERS:

That’s right. So the variants of the virus are coding changes in their genome. And you know, what happens is that spike protein,there's a change in it that occurs and makes it a little bit more sticky or it

Improves its ability to get into cells or may improve its ability to replicate, whatever that is. And those changes that improve its transmission can also make the virus or the vaccine less effective becauseit's binding to that same region. And so if, if there's a change that's made there, it makes the antibodies our bodies are producing less effective. It means we may need a new vaccine encoding the new version of that spike that's in the variant so that our immune system will make better antibodies against that version of it. But that's what's so, you know, incredible about the RNA platform, is that once you know what that change is, it's a pretty straightforward process to produce a vaccine, you know, a modified vaccine that now produces, you know, a slightly tweakedversion. That's the version carried by the current strain of the virus.

CHRISTIAN COTÉ:

I want to try and take you back to a day, December 14th, 2020. You are part of the first group at the UHN Michener institute when ahealth care worker is the first to get the vaccine in canada. Take us back to that moment. You know, knowing what it took in terms of the medical research and the role of basic science in getting the world to that day, what did that moment and achievement mean to you that morning?

DR. BRAD WOUTERS:

Well, it was very exciting. I, I do remember that day very clearly. We were over there and we were actually waiting for clearance from Pfizer because they had to ensure that the vaccine that traveled to us through the airplanes and through the onto the cargo vans that go out to us, have maintained its cold storage requirements or, you know, a huge amount of careful monitoring happening back then. And we were all in that building waiting for that call to come in, and clear it, and we wereall set up. We had the syringes drawn. We were ready to go. I mean, it was sort of delayed and delayed. We finally got the call. So, you know, a brave long term care worker had stepped up and volunteered to come first. And she got the vaccine. And for us, you know, it was exciting in a number of ways. One was sort of, the sort of the triumph of science and the ability to get a safe vaccine now being administered in Canada before the end of 2020.Really kind of amazing. But it was also exciting because it said to us that, you know, the end of this really, really tough part of the coronavirus might be in sight. And, you know, we've been dealing with it since almost a year at that time, had caused huge disruptions, of course, to society, to many populations, but also to research itself. And we were very much looking forward to being able to get back to a more normal work environment, a more normal society, and get back on the real challenges of dealing with all the other science and research that we were doing. So definitely an inspirational day turned out to be just the first part of a huge logistical challenge of delivering this. The goalposts keep changing, but you know, I think Canada’s done extremely well. And if you look at our

Current vaccination rates, Canada really is either at the top of the worldor leading amongst the world in delivering that. I think it's a reflection of Canadians' belief in science. I think we've managed to quell or dismiss some more of the misinformation that's out there. It's really disappointingto see what's going on in many places. But, you know, upwards of 80, 85 percent of eligible individuals vaccinated, it's great. Here at UHN and at the moment, our staff are about 95 percent vaccinated. We want to get everybody. We hope everyone steps up and does that. But this is creating a much, of course, safer environment for everyone.

CHRISTIAN COTÉ:

That one shadow, i guess you could say, on that light at theend of the tunnel is a safe vaccine for kids under 12. Do you have any sense or insider knowledge on when that might be available for kids under 12?

DR. BRAD WOUTERS:

Well, there's, of course, active work going on. There are clinical trials taking place that have actually been made. Much of that is completed. The FDA is even reviewing some of that data now. They've gone back to the companies and asked for, I think, a bit of extensions and additional other data that they want to make sure these are, of course, extremely safe. Kids are not as at risk as older adults are at getting sick, but they still remain at risk. And they also represent, you know, a large number of people in our population that will continue to support transmission and prevent us from reaching a point where, you know, COVID will go away. So the variants have really changed the game in terms of what's needed to control this. We see in you know, the summer of 2021 cases are higher than they were in the summer of 2020, and they've rebounded quicker, this sort of the fourth wave is happening earlier in 2021. Even with 75, 80 percent of our you know, eligible population vaccinated, and that's the difference in the variants is that they are just far, far more transmissible. People carry much higher viral loads. And my advice to everyone is that, you know, you have sort of two choices to make.You can get vaccinated and get the spike protein or you can get infected and get COVID. And that's you know, i don't think that many people who are unvaccinated will avoid this at some point.

CHRISTIAN COTÉ:

Do you have a sense, though brad, of when the vaccine mightbe in the arms of or available for kids under 12?

DR. BRAD WOUTERS:

Well, I think you know, it could be, it could be relativelysoon. I think there are, you know, there are some that are looking at the data that's available. And it may be enough for the FDA to make a call on that. So that could happen within, within months. And certainly it's the five to 11 year olds that they're looking at, below five is going to be not until next year. But the five to 11 year olds, which are kids in elementary school, you know, that group were hoping that there might be something a

Little bit later on this fall. It's not going to be in time for school. And, youknow, there's going to be a risk associated with that. And everything we can do from a public health measure to continue to slow transmission. Weknow a lot more than we did a year ago. There are lots of tools in the toolbox to help do that. And it's up to the policymakers and governments and so on to, you know, to make sure we create a safe environment as possible for those kids

CHRISTIAN COTÉ:

This miracle of science, the creation of these vaccines to battle COVID 19 - do you care to speculate on whether any of this is Nobel Prize worthy?

DR. BRAD WOUTERS:

well, I think it's going to certainly, they're going to get nominations and the committee is going to be able to make that decision. It's certainly amongst the kinds of discoveries that where, where this prize is awarded that, you know, that could be considered. It's obviously had a huge impact on society so far. It's, it's a vaccine against one virus. Buti think the platform has massive potential for other opportunities. And we're even starting to see some of those come out now.

CHRISTIAN COTÉ:

well, and to that end, the discovery of mRNA in terms of a safe vaccine delivery vehicle and effective - what's your take on what all that means for the future of vaccine development for, for other diseases?

DR. BRAD WOUTERS:

Well, there's lots of work going on already. I mean, the reason modeRNA is worth two hundred billion dollars is not because of COVID, it's because of the other things that they may do. And they're working on flu vaccines, universal flu vaccines. They're working on cancervaccines. And other companies are also using RNA as a platform to deliver, you know, other kinds of RNA encoded drugs they can deliver crispr can be used for gene editing, gene therapy. So, you know, the opportunities and potential for this kind of platform really is, is very big.

CHRISTIAN COTÉ:

Bit of reality check though i guess, is that we still have a pandemic. People are exhausted. Health care workers are burned out. Andit just never seems to end. What's your assessment of the life cycle of thiscoronavirus? Is it going to just keep spinning off new variants that are more dangerous than the last, or will it eventually peter out and die?

DR. BRAD WOUTERS:

Well, it's hard to make predictions on that. I think Christian, you know, we all kind of

thought this is a pretty stable virus. And for the first 10 months, up until October and November, there was a lot of transmission, lots of virus, and we didn't really see any major new variants emerge that, that behaved a lot different than the other ones. There's a kind of always a background change going on because, you know, viruses make mistakes when they replicate. And so they sort of sample opportunities to change. But we didn't see a lot of impact from that. Thosechanges are happening until around November and...

CHRISTIAN COTÉ:

November of?

DR. BRAD WOUTERS:
November of 2020. And it was in December that i kind of really got worried about this. And you know, the potential of variants of emerging that might be more infectious, could pose a danger to the current approaches to public health restrictions. And so we started a program here at UHN, together with colleagues at Mount Sinai and also at oicr to systematically look for new variants you know, in those that were being tested at our facilities, at our joint Mt. Sinai and UHN lab. And it was based actually on a technology that's been developed here in Toronto by Jeff Wrana and ben blencowe and others for a completely different purpose. But it ended up being an opportunity to repurpose this, to allow us to kind of sequence in an efficient and cost effective way every positive case that we found. So we started to do that and in December is actually right around Christmas. We had people in the lab collecting samples from all the positive cases, about a thousand people that had tested positive for COVID over two or three days. And we decided to go and look for those variants. And we sequenced all of those cases.
And we saw, in January, the first variants appear, we saw both the uk variants, what's known as the alpha variant, as well as the variant from brazil and from south Africa. And those are the very first versions of that that had been seen in Ontario. And we continue to track that. And we saw this huge rapid rise of the b1 170 alpha variant come from the UK. And within a few months that became essentially 100 percent of the cases it had a complete replacement of the sort of the Wuhan sars-cov-2 with this new variant. And there was lots of data emerging at the time saying that the variants had about a 40 percent increase in transmission. It created more hospitalization cases. It was certainly worse. And i think at the time, we realized that variants were, you know, going to continue to emerge and were going to be a problem. And we've seen that happen. There's an entire network now across Canada that's funded by the CIHR.

We've got a leadership team that i sit on in the federal level, with the ministry of health at meetings. We meet every week looking at the evidence of the changes in the variants here in Canada and around the world and tracking this. And you know, i think what we still don't know and still worry a lot about is whether or not a variant would emerge that would make our current immunity created by vaccines or previous exposure really ineffective. And, you know, i think to a large extent, and i listen to the immunologists and the virologists discuss around this, i thinkthey're cautiously optimistic that you know, we're even if a sort of a breakthrough kind of virus strain emerged, the kinds of immunity that we

Have, it's you know, both our humoral antibody, our antibody immunity, butalso our t cell immunity and cell-based immunity will continue to provide some protection. And so you may get infected, but you won't sort of suffer a severe disease.

And even in the breakthrough infections we're seeing now, there are people who you know, have had the vaccine, it's fantastic, but it's not perfect. 95 percent sounds great, but five percent of a large number of people is a large number of people. The breakthrough infections, fortunately, are also much less severe, very unlikely to land you in the hospital or make you really sick. So this virus is going to be here for a very,very long time, forever, perhaps. And it's going to cause colds. It's going to cause some disease. It's going to cause some severe disease like the flu does,like other coronaviruses can in certain situations. But what's really important is to get a base level of immunity in everyone against this. And that means going and getting the vaccine now.

CHRISTIAN COTÉ:

Well, that's sobering.

DR. BRAD WOUTERS:
We've lived with viruses since the dawn of time. And, you know, the colds you get every year. That's a coronavirus. And there may have been a time, you know, hundreds or you know, many, many, many years ago where that caused also a lot of severe disease. And you know, eventually it created a level of immunity that that we sort of carry withus now, but you know, i think that...

CHRISTIAN COTÉ:

But really, there's no secret to it. I guess the goal really now has to be the field of downsized dreams where we somehow manipulate this from a pandemic to an endemic situation? Where it's pockets that we can more tightly manage. And really, i guess the pathwayto get there is no different from day one, which is still masking, still physical distancing and getting vaccinated?

DR. BRAD WOUTERS:

Yeah, I think it's you know, it's getting vaccinated. Number one, all the other public health measures are slowing down transmission so that people don't get sick, that we don't create large numbers of cases. It buys us time to get that immunity. But if you look around the world, there are still six hundred seven hundred thousand new cases reported every day around the world. You know, Canada, we'reextremely fortunate to have this vaccine and to be able to deliver it to our, our population. But there are huge numbers of people around the world that don't have that access. And you know, the virus will continueto circulate. It will continue to spread. And, you know, the idea of elimination isn't something anyone's even thinking about at the moment.

CHRISTIAN COTÉ:

Perhaps in scientific circles. But i think in the mainstream,everyone thinks, oh, we're, we're moving towards the end.

DR. BRAD WOUTERS:

Yeah. The infectious disease specialist, you know, they live with, they live with viruses and disease and transmission all the time. Every year we have a flu season. You know, it causes sometimes extreme chaos in the hospital. There are years where, you know, we run out of beds and you know, our icus get really full. And, you know, the public doesn't see this very often and doesn't pay a lot of attention. A lot of people thinkthey don't really need a flu shot, you know. So we do live with endemic viruses all the time, and society gets comfortable with it. It doesn't pose a huge risk. The majority of the population and i think the, you know, we're all just so much more acutely aware of what's going on at the moment. I hope one of the long lessons will be go get vaccinated every year for the vaccines you have an opportunity to protect yourself and protect others. Whether that's a flu vaccine for coronavirus vaccine in the future.

CHRISTIAN COTÉ:

And you keep reading also that really for us to get to endemic stage, this is a world effort because it will continue to spreadand morph unless we get it under control - around the world.

DR. BRAD WOUTERS:

Well, that's right. And also, you know, the more virus outthere, the more opportunity for variants. And so it's in our interest to, andit's in everyone's interest to reduce infection, reduce transmission, get opportunities for vaccination to the entire world. You know, the idea that we can live in a bubble and, and protect ourselves and you know, try and prevent this from coming across the border really is just about impossible.

CHRISTIAN COTÉ:

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, and this is a special COVID 19 edition to launch our third season. And we're speaking with UHN executive vice president of science and research, Dr. Brad Wouters. Brad, the origin of the coronavirus is still highly contentious. There's the Wuhan market theory, the Wuhan lab leak, and Chinese officials are reallypushing a theory of their own that it was a u.s. army lab leak. Needless to say, investigations continue. In the meantime, talk to us, though, about justthe importance of knowing the origin of COVID 19?

DR. BRAD WOUTERS:

Well, that's important. You know, and there are groups that study the origins of viruses.

Expert groups all over the world at themoment there's just not a lot of data or evidence to, you know, to make any sort of firm conclusions around the specific origin of this. I think you know, the experts and the people that i listen to or read about read from,you know, the prevailing opinion in that group is that this has come from azoonotic, traditional kind of approach where it's jumped from one species into the human population. That's, that's the way that virtually all of these kinds of viruses have reached us and without extraordinary evidence of something else. You know, the priors of probability would suggest that that's the most likely explanation, but it needs evidence and you know, it's not there yet. Everyone's looking. And, you know, it's important to understand that because that also serves a potential future route to protection. Obviously, if there was some other source for this, you know, an accident or a leak or something else, we need policies and ways to protect us from, you know, anything like that happening. And there are, of course, lots of those in place. And it's extremely unlikely that these things can happen purely by accident, but it's not impossible. And, you know, it's important to open the books and you know, quell any rumors of that. But, you know, i don't want to get too much into that. You know, there's lots of spin, lots of interpretation and lots of politics is driving a lot of the discussion and writing around this.

CHRISTIAN COTÉ:

Understood. All right. Let's turn to UHN research in the pioneering work of your team over the course of the pandemic. Perhaps.Let's start with a trial spearheaded by Dr. Ewan Goligher and his team. They've just published or recently published, I believe, in the summer of 2021, the potential benefit of blood thinners for hospitalized patients with COVID 19. What can you tell us about that?

DR. BRAD WOUTERS:

Yeah, so it's really terrific work. Ewan Goligher, PatrickLawler, other colleagues here at UHN and some of the team members of theirs across canada and the university of Manitoba and elsewhere. And what they've done is to launch a very large trial, a collaborative trial, you know, interesting trial design, but done extremely great clinical research where they've asked the question around whether or not it would be possible to improve the outcome of patients who are coming intothe hospital with COVID. And this was, was with the use of blood thinners. So traditional kinds of medication that we have on hand all over the world using heparin. You know, lots of people use this as part of a blood thinning strategy for other diseases. And we knew that part of the clinical consequence of getting COVID was developing blood clots. COVID causes blood clots, and this contributes to some of the poor outcomes of the disease.

And so they launched this trial and they actually created a large collaborative network or joined a large collaborative network of other trials across the world and recruited thousands of patients through this

Trial so they could answer this question in a robust and statistically meaningful way. And it's really, you know, I think an example of the power of networks and the power of collaboration and the importance of doingreally strong clinical research to give us that data so that we can make new clinical decisions. There's been lots of examples of the opposite. You know, small trials, underpowered, poorly designed, has created lots of confusion out there. But this is one of the best trials. And it was publishedrecently in the New England jouRNAl of medicine, two papers. And they tested the use of these therapeutic doses of heparin, of blood thinners, both in patients that were critically ill in the ICU. And also patients with more mild disease.

And what they found is a very different response in those two populations. The drugs are really effective and they you know, they help prevent death while those patients are in the hospital they help prevent you know, other kinds of complications in the mild in those with mild disease. And you know that will change practice all over the world. And will now become a part of the treatment opportunity for patients with COVID. It didn't work in the patients that were in the ICU. With more severe disease, which is also important because, you know, every medication also comes with risks. Blood thinners cause a risk of bleeding. And there were patients that, you know, develop complications from heparin itself. And so without this sort of, you know, really good data, knowing who should get it and who shouldn't get it, you now won't place people at risk of getting that of, of heparin if they can't use it. And this is the kind of data we didn'thave, you know, for a lot of the other therapies that were used because we didn't have these strong clinical trials you know, until recently. So this is a real bright spot for Canada. It's a bright spot for UHN and you know, and in this group. And they've changed the way the world will treatCOVID patients. So, you know, hats off to them.

CHRISTIAN COTÉ:

Yeah, amazing. I should make just a quick note. We are interviewing Dr. Wouters from his office downtown at UHN and his office isright outside the UHN emergency and that's why you're hearing sirens periodically. They're not coming for brad.

DR. BRAD WOUTERS:

Let’s hope not.

CHRISTIAN COTÉ:

The other new study, this one from Dr. Deepali Kumar with some welcome news for transplant patients in the COVID vaccine efficacy.Talk to us about that one.

DR. BRAD WOUTERS:

Yeah, Dr. Kumar is a terrific clinician scientist in our, in our Ajmera Transplant Center, you know, the largest transplant center in north America now. But she did some work early on, very early on in the pandemic, we may have even talked about it the last time, you know, to look at the prevalence of infection in health care workers. And so we launched a large, large study. You know it had a lot of impact here lookingat how many of our workers may be

developing asymptomatic infections, something we didn't know at the time. So that was great work. But she's also, you know, been focused on providing proper care and protection for transplant patients. These are very vulnerable groups, because when someone gets a transplant, liver transplant or kidney transplant or other, they often go on immunosuppressive medications. And so they're immune - that's done to prevent rejection of their graft of their organ. But it creates a risk for them of infectious disease.

And it turns out it also makes the vaccine less effective. So these individuals, what they've discovered is that if you are a transplant patient and you're on immunosuppressive medication, you didn't get a very good immune response to getting one dose or two doses, even two doses of the vaccine. They measured this in large numbers of people that they care for and they saw that those patients had low antibody levels, didn't get a good immune response. And so what they did very early on is to, is to start a trial also, again, a terrifically designed, impactful clinical trial, looking at third dose boosters in that population. And what they've seen isthat not in everyone, but in, in a large number of those patients, that third dose is quite effective. It can boost their response and it can provide a protection from them that they otherwise don't have. Unlike the general population. So this will also change practice. And there's already a lot of discussion around booster shots and so on. But again, what you need is good clinical data to make those decisions. There's lots of hand waving. There's countries just doing it already. There's others that say there's no evidence. And so you know, science needs to come with the data so that we can make those recommendations and do, do so in a meaningful way.

CHRISTIAN COTÉ:

another groundbreaking piece of work from UHN researchis that of Dr. Angela Cheung and Dr. Margaret Herridge on the devastatinglong term effects of COVID, which seems to be now emerging as we're goingto, like hospital systems are going to need to respond with new clinics to deal with the long haul patients. Talk to us about their work.

DR. BRAD WOUTERS:

Yeah, also you know, extremely important work. And thisgot started very early on too at the very beginning of the disease. They recognized that it was going to be important to study the consequences ofCOVID long term in people who recove. And the vast majority of people who get COVID recover from that disease, fortunately. But not everyone makes a full recovery as we've learned, and this has been called ‘long COVID’ or COVID-related you know, long term disease. And there's lots of work stillto understand what's causing this and what's happening. There's evidenceof, you know, changes in cognitive function and neurological changes in the brain. In other organs. There is long term immune activation in some individuals. We don't understand much about the risk factors for this, who might be affected, what might drive that, and also importantly, howwe might therapeutically intervene to help those patients. And so that's really, you know, they started with the premise that we're going to needto study this. And so they created a cohort study. Again, this is a network study. They have, they have colleagues across all of Canada.

They're participating in other inteRNAtional approaches to collectively work on studying this, and they've entered a large number of people into this research study, they're collecting samples, they're looking at the virus, they're looking at host factors they're looking at other related comorbidity factors and making samples available to the entire scientificcommunity to be able to study this. Given the number of people that have been infected with COVID, that will be infected with COVID, it's extremely important work you know, on a go forward basis. So it's really been another bright spot for us is that work. They've also created COVID long- term COVID clinics. These are both physician scientists. And so not only are they doing research, but they've actually created clinics for people who are suffering to be able to come in and to be, you know, cared for and treated. And this is, you know, to be rehabilitated. This is something that we'll also be doing for a long time.

CHRISTIAN COTÉ:

Let's touch on one more. And it's not certainly an exhaustive overview of what you have going on at UHN research. But to mymind, this one is really remarkable is the modeling research generated byUHN research's Dr. Beate sander and her team. What's been the impact of her research in shaping government and public health policy in Ontario throughout the pandemic?

DR. BRAD WOUTERS:

Yeah, so it's been terrific work. Dr. Sander sits on the science table that we've heard a lot about here in Ontario. This is an independent table that has advised the government, advised Ontarians and is focused on the science. And you know, as I've talked about here multiple times, when we make decisions and policy that impact you know, millions of people, we want to base that on very solid ideas around what to expect and based on science and data. And that's where she Beate works.That's what she does. She looks at resource utilization, modeling predictions, understanding you know, what those waves look like, how much transmission is happening, and gives us that short term, long term and medium term evidence around what we expect to be coming. And so

That started off you know, around issues around PPE. Was Ontario going torun out of personal protective equipment, was it going to run out of ventilators? Are we going to run out of hospital beds? And a lot of that work stimulated the province, to come together and to work in an extremely coordinated way to make resources available collectively and for and throughout the entire pandemic. You know, over the last six to eight months, we have been operating almost like a single hospital system where, you know, if one hospital was full, patients were being moved to another, it was coordinated and there were patient transfers every day.

We expanded ICU capacity based on that modeling. So we were ready when that third wave hit and when our ICU levels went way up, we were ready inOntario. And we got close to running out, but we didn't. And a lot of that isbased on, you know, that strong scientific modeling that beate and her colleagues contributed to that helped get Ontario ready. And it has helped do that. So it's been, you know, extremely important for functions of hospitals, for the safety of the province, and for us being able to respond collectively to, to deal with the, with the waves as they've come through.

CHRISTIAN COTÉ:

Would it be fair to say part of the legacy of her work isthat it saved lives - Ontarian lives during the pandemic?

DR. BRAD WOUTERS:

Absolutely. And not just lives with COVID. You know, when hospitals get full and icus get full that affects everybody. And thatneeds, that needs to use those resources. So it's undoubtedly saved the lives of countless numbers of individuals in the province.

CHRISTIAN COTÉ:

your team at UHN research has so much going on, especially in terms of COVID trials and investigations. We, of course, can't get to all of them today. Can you help us if we, if our listeners want to find out more,where can they go?

DR. BRAD WOUTERS:

well, they can come and visit us at our website. Uhnresearch.ca our annual report will be there. We're going to highlighta lot of our activity and work that's gone on here over the last year in COVID, as well as the other amazing scientific contributions that we make across all the areas that we're working. And none of this has shut down, you know, over the last year. We've been interrupted. And we've had the labs close and open and trials close and open. But we've got an amazing group of 5000 researchers at UHN that are committed to making impact in the areas that they've dedicated their lives to. And that hasn't stopped. And you know, a lot of great science, even outside of what we're talking about at COVID continues to happen here at UHN.

CHRISTIAN COTÉ:

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, and this is a special COVID 19 edition to kick off our third season of the podcast featuring UHN executive vice president of science and research, Dr. Brad Wouters. We should make mention that UHN's pioneering research, including the COVID 19 initiatives we've been talking about, receive much needed support fromthe UHN foundation and the Princess Margaret Cancer Foundation, which together raise over two hundred and fifty million dollars a year in funding for medical research driven by UHN scientists. And maybe, brad, asa quick example, I know foundation dollars played a role in our recent research discovery over at the Princess Margaret Cancer Center, talk to us about the impact it had on dr. Daniel de Carvalho's work to bring forward a blood test for diagnosing cancer.

DR. BRAD WOUTERS:

Yeah, well, our you know, our foundations and our philanthropic supporters in our community are needed and are responsible for really all of the research that we do. We wouldn't be ableto do any of the research we do without this community and our foundations and our community of supporters really did step up very early and allowed us to get started in new areas of COVID research very quickly. And they fund all areas of research, including what you mentioned at the Margaret. You know, and as I said, we haven't slowed down in terms of research and discovery across all the areas where we're actively working. And Daniel's work, published recently this year, has now been translated through the creation of a startup company you know, to move this into patients. And it's really exciting work. It's work that has allowed for the development of what could become sort of a universal blood test for finding cancer early.

Turns out, you know, when you have cancer, some of that DNA from those cancer cells spills out into your blood. And there are signature markers in that DNA, epigenetic marks - this is the area of work where Daniel spendshis scientific time - and he's developed a way to use that little signature, that epigenetic signature to search in the blood, which is full of DNA fromall over the place. Kind of find that needle in the haystack and the evidence that there might be an early cancer there. And this is a big exciting area overall for Princess Margaret, where earlier detection, earlier diagnosis of disease and earlier identification of those who might not respond to therapy is a very important area to help improve outcomes going forward in the future. So this has been spun out into a company. They've announced an investment of over sixty million dollars into the company. Really exciting team they put together. And so we're, we're really excited to see that now, move quickly to clinical opportunity andimpact on patients.

CHRISTIAN COTÉ:

Let's mention the company name.

DR. BRAD WOUTERS:

Company is called Adela.

CHRISTIAN COTÉ:

Can you spell that?

DR. BRAD WOUTERS:
Adela, Adela, I think and it's a UHN spin out. It's one of youknow, it's an area that we've taken a very active role in over the last five to six years in commercialization. And you know, we recognize we need commercial partners and other investors to, to move our discoveries into clinical impact. And so that's why we do that. And this is, you know, one in aseries of exciting new spin outs and commercial startups that we've been involved with over the past decade and have a big commitment to continueto do this, going forward.

CHRISTIAN COTÉ:

Okay, final theme of the show. I want to broaden the conversation to the profile of medical research in this country. If there's a silver lining in this pandemic, it's that it heightened public, the public awareness of science and research beyond anything I imagine you've experienced in your career. You've actually spoken about how this is likelya once in a generational opportunity. How so?

DR. BRAD WOUTERS:

well, it's I did, and you know, I think the attention that COVID has had in the general press and in media and social media and in conversation circles, I'm sure this is what you talk about when you have a chance to see your friends on the patio or in the backyard. It really has gathered the attention of the world because of the impact it's having. Andthe world has also had the opportunity to see the impact of science in a very overt objective way. And we've seen some of the messiness behind science too. You know, the failures, the starts and stops, you know, how progress gets made. And they've been in, you know, opportunities to, to sortof even see the scientific process play out. Publications and corrections and new publications happen. And you know, what's been very different is that, you know, this isn't so different from the science perspective. This is the way science happens all the time. But it's the media attention on it. Andwhen a preprint paper ends up on the front page of the New York Times, that's not a normal situation. But it happens all the time now.

And so that's I think it's an opportunity for, for us to advocate and to youknow, highlight the importance that investment in research has on solving society's most important problems. Today, it's COVID, but we have alot of them. And science is the, is the engine to address that. It creates economic impact. It creates jobs in Canada, it creates industry, and it

Improves health and wellbeing of our, of our citizens, which is so criticalto all other aspects of society and economic life. And so, you know, it's anopportunity to, I think, double down on that. Canada should be investing more than it is. We have an opportunity to do a lot more than we are. I think we've seen some deficiencies and consequences of underinvestment in Canada. You know, we didn't have manufacturing in Canada. We didn't have the pharma companies to partner with in Canada. We had to rely on buying those vaccines from other countries, even though, you know, as i talked about, some of those important early discoveries were made by Canadians.

So this is an opportunity. And you know, I think it's up to all of society to, to decide to, to want to make that investment you know, for this to be animportant part about who we choose to govern the country and the expectations we have on, on the federal government. I think you know, having scientists develop that relationship with society with individuals to continue to highlight the importance of what we do and the impact it has and keeping that attention on the front page, I think that's a lesson for us and an opportunity for everyone in the future.

CHRISTIAN COTÉ:

well, one thing I remember reading from you a while back isthat what the pandemic has done is, is sort of, brought research out of theshadows and made people understand how integrally intertwined it is with day to day health care. It's - the two are symbiotic, really. But you've also said that you fear that this public profile that's been raised of the role of medical research in society won't last.

DR. BRAD WOUTERS:

Yeah, I think, you know, we all worry about that. And, you know, even around pandemic preparedness in general, the importance of research, the importance of investing. It's got a lot of attention now, but I do worry it will wane once the real you know, risk and impact of disease and so on also wanes. We've seen, we've seen those mistakes happenin the past. When SARS hit many years ago, we had an initial pandemic preparedness and then it, you know, it lost attention. It stopped getting funding. It stopped under investment. And we've seen challenges even in our own public health systems and the coordination and the lack of dataand so on. That has created challenges right now for us. And this has beenalso in large part because of under investment and a lack of recognition of the importance this investment creates when it's needed. So I do worry about that. And it's something that i think it's upon all of us to work towards ensuring that doesn't happen or you know, is at least minimized.

CHRISTIAN COTÉ:

Well, to that end, are your fears perhaps a bit dissipatedafter i guess it was in the spring of 2021 in May, parliament created a Standing committee on science and research. Does that now give medicalresearch a seat at the table, so to speak?

DR. BRAD WOUTERS:

Yeah, that's a positive outcome for sure. We need to becompetitive globally and that takes attention and investment. And certainly that's, that's great to see.

CHRISTIAN COTÉ:

Last word then, brad. How do you and your colleagues in the scientific world across Canada continue this momentum, this profile?

DR. BRAD WOUTERS:

Well, you know, as I talked about, I think a lot of the real discoveries and impact we've had has been through the partnerships and networks. And I think, you know, many of those that have gotten started during COVID will continue. And we'll work hard to do that. We're going to work with our colleagues across Toronto at the University of Toronto on pandemic preparedness and responses. We want to be part of that. The other part you know, and many of the discoveries that we made have come from having in place you know, such a strong scientific team. We didn't have a single COVID researcher before COVID, obviously, but we had cardiologists, we had anesthesiologists, we had cancer biologists, we had infectious disease specialists, we had neurologists, we had public health policy experts. And all of these people contributed to the science and understanding and impact of research that its had on COVID. And that's a reflection of the strength of investment in research in general. It gave anindividual a grant to study how to tune out immune responses to RNA. They never envisaged that they were going to use this to solve a COVID global crisis, so, you can't predict the impact that science will have. It's investing in great people, in smart people, in areas where there's unmet clinical need. That's what we're going to continue to do.

CHRISTIAN COTÉ:

Dr. Brian Wouters, executive vice president of UHN research.Thanks for speaking with us and continued success.

DR. BRAD WOUTERS:

Thank you, Christian.

CHRISTIAN COTÉ:

For more on the podcast, go to our website www.behindthebreakthrough.ca and let us know what you think. We'dlove to hear from you. That's a wrap for this special edition to kick offseason three 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.