Speaker 1:

Welcome to Optimal Neuro Spine podcast, a podcast about optimizing our brain and spine in health and disease. Each episode, leading neuroscientists, neurosurgeons, educators, patients, spine care, and quality improvement experts discuss their research, experience, emerging science, surgical advances, and insights about how to optimize neurological and spine care. Now here's your host, Dr. Max Boakye.

Dr. Max Boakye:

Welcome to the Optimal Neuro Spine podcast. Today, I have a distinguished guest, Dr. Dalton Dietrich, and we're going to talk about traumatic brain injury. Dr. Dietrich is currently a scientific director at the Miami Project to Cure Paralysis and the kinetic concepts distinguished chair in neurosurgery at the University of Miami Miller School of Medicine. He's also the senior associate Dean for Discovery Science, the co-director of the Institute for Neuroengineering and professor of neurological surgery, neurology, biomedical engineering, cell biology there. He received his PhD from Medical College of Virginia, completed a post-doctorate fellowship pharmacology at Washington University. Since 1981, he has been at the University of Miami, where he holds the above titles. He has published over 375 [inaudible 00:01:36] general articles, 75 book chapters, and four books. His published work has been cited over 38,000 times. He's been listed by the Institute of Scientific Information as a highly cited researcher, placing him in the top 0.5% of all scientists.

Dr. Max Boakye:

Dr. Dietrich has been a thesis or dissertation advisor to nine graduate students, has trained over 50 post-doctoral fellows and visiting scholars from all over the world. He has numerous research supports from NIH, Department of Defense, Veterans Administration, state of Florida, Miami Project to Cure Paralysis. He serves on numerous study sections, including the NIH, Department of Defense, Veterans Administration, several editorial boards. He's currently the editor in chief of the Journal of Therapeutic Hypothermia and Temperature Management, and I believe deputy editor or editor of the Journal of Neurotrauma. He can clarify that for us. He's also a founding member of inflammasomes and ACESO Therapeutics, and we want to talk to him about inflammasomes today among other things. Dr. Dietrich, this is a really impressive CV. Welcome to the program.

Dr. Dalton Dietrich:

Thank you very much for the invitations. I'm really looking forward to talking about some of the topics that you're interested in hearing about.

Dr. Max Boakye:

Clarify for me, you're deputy editor Journal of Neurotrauma or you're the editor?

Dr. Dalton Dietrich:

I'm deputy editor of Journal of Neurotrauma and I'm involved specifically in the area of spinal cord injury for the Journal of Neurotrauma.

Dr. Max Boakye:

Oh, I see. Oh, excellent. Maybe we'll bring you back another time to talk about spinal cord injury. [inaudible 00:03:11] some of the things we're going to talk about are applicable to spinal cord injury, although tilting the interview a little bit more on the TBI side. So what is your research on and what have been some of the highlights of your research career?

Dr. Dalton Dietrich:

I think the highlights of my research career have been really the people I've had opportunity to work with. I started out in Richmond, Virginia with my PhD, working with John Povlishock. As you know, John Povlishock is a leader in the area of TBI research and a diffuse axonal injury. I think through John, I got to be introduced to my neurosurgical community and very quickly I learned that multidisciplinary collaborative work could lead to more basic translational and hopefully clinical studies. So I think something that really enlightened me was the ability to work with basic sciences to clinicians and be able to merge those two areas of research. And then I got recruited, as you mentioned, to the University of Miami after the University of Washington, I did my postdoc. And there, I also worked with a group of clinicians. These were neurologists working on cerebral ischemia and stroke, and again, had the opportunity to do good basic research and interact with clinicians to hopefully move things from the bin to the bedside and the bedside back to the bin. So I think it's the people I worked with was really important in my academic career.

Dr. Max Boakye:

So how did you become interested in neurotrauma? Did you set out from the get go to be involved in the area of neurotrauma?

Dr. Dalton Dietrich:

Not at all. I was intrigued about the human body. So I was told that maybe you should either go to medical school or get a PhD in anatomy in cell biology. So I got into a graduate program in anatomy in Richmond at Medical College of Virginia, now Virginia Commonwealth University with Dr. Povlishock, and he introduced me to the trauma field and I didn't realize how important it was clinically at the time, but being a morphologist at heart, Dr. Povlishock taught me light microscopy, fluorescent microscopy, EM, and then I started working with animal models and got really intrigued, especially when we were talking with the neurosurgeons and what they're dealing with, an acute head injury and some of the pathophysiology. So that really initiated my long term studies in the area of TBI.

Dr. Max Boakye:

Your center is known to be one of the best in the world on neurotrauma research. How is TBI and neuro trauma research organized at your center? I do have some follow up questions. For example, how do the clinical departments and the basic science work together? And what is the leadership structure that encourages innovation?

Dr. Dalton Dietrich:

Very good. So the Miami Project to Cure Paralysis is a Center of Excellence at the University of Miami and the members of the project, I think there's about 37 principal investigators. They have academic appointments throughout the basic science and clinical departments. The majority of the faculty in the Miami Project have academic appointments in the department of neurological surgery. So we sit in the department of neurological surgery. So we have the opportunity to go to neurosurgical grand rounds, to hear about the clinical problems. They interact with us at the Miami Project programs. So that's basically why we're so integrated into clinical research. Now, when I took over the scientific director of the Miami Project in 1997, the program was primarily geared to spinal cord injury to cure paralysis. And I was always intrigued about spinal cord injury research. I'd actually done some of that work with Dr. Barth Green at the University of Miami, at the time he was the chairman of neurosurgery.

Dr. Dalton Dietrich:

My vision was that what we can learn from spinal cord injury, we can adopt and transfer to other types of neurological problems, such as traumatic brain injury and stroke and neurogenerative diseases. So we actually expanded the overall goals of the Miami Project, but still focusing on obviously protection and repair. So within the project, now we have a good balance for the people doing different types of science centered around basic, translational, and clinical science. So the way it's formed now, we have basic scientists. We have translational scientists, like myself. I'm a PhD in anatomy, or I'm a neuroscientist. And we also have clinical investigators, some MDs, some MD PhDs, some MDs and neurologists and neurosurgeons. So it's built around the concept of what we can learn from one area of research, we can utilize throughout the domain of different types of neurological disorders. So that's really how it's organized and being the scientific director, and also having some leadership roles at the university of Miami, it gives me the opportunity to enhance collaborations among not only people within the project, not only in colleagues in neurosurgery, but throughout the medical school.

Dr. Max Boakye:

So everybody involved is doing some aspects of neurotrauma research. Do you exclude people studying epilepsy, stroke, and Alzheimer's, and other neuroscience areas?

Dr. Dalton Dietrich:

Well, not at all. I just got a new NIH grant on traumatic brain injury being an important risk factor for Alzheimer's disease, for example. So yes, we are studying the pathogenesis of Alzheimer's disease. We work with the department of genetics and using these new transgenic mouse models. And now trying to figure out how TBI and neurodegenetive diseases fit in. within the project, we have people doing post traumatic epilepsy research. We have people doing multiple sclerosis research and ALS research. So we are kind of doing a lot of... It's really a center for neurological disorders under the umbrella of the Miami Project.

Dr. Max Boakye:

And what is the leadership structure? Is it a single person that leads everything or is it a panel of leaders? How is the leadership structure and how does that encourage innovation?

Dr. Dalton Dietrich:

Yeah, so Dr. Allan Levi is an MD PhD, a spine neurosurgeon. I remember him when he was a graduate student at the University of Miami, did a lot of work with Dr. Richard Bunge and Mary Bunge, and they worked on human schwann cells, which has always been an area of research in the Miami Project. Allan has been very, and before that, Dr. Barth Green, have been very driven about bringing in the best scientists to move new discoveries forward with the ultimate goal of curing these different, very complex neurological problems. So I think, again, it's leadership, that when we're recruiting neurosurgeons, when we're recruiting a scientist, we're all looking for the individual that's going to be highly collaborative, bring in new innovative techniques and be able to advance our programs and make sure that we're doing the best job we can in answering these very complicated problems that we face every day.

Dr. Max Boakye:

So the leadership is both yourself and the neurosurgeon, Dr. Levi, working together to recruit the best collaborative future clinician scientists, and basic scientists.

Dr. Dalton Dietrich:

That's correct. And I'm also co-director of the Neuroengineering Institute. So at the same time, in addition to neuroscientists, we're also recruiting some outstanding engineers, mostly in the area of biomedical engineering. They're coming down and in our building now, and they are helping us think about novel ways, instrumentation, of course, or novel ways in which we can stimulate or activate the brain and spinal cord. So the area that we're really pushing forward right now is the area of neuromodulation. As you know, it's so important in neurosurgery now. So we are doing preclinical studies, looking at vagel nerve stimulation, deep brain stimulation, transcranial magnetic stimulation. Companies from Israel working on electromagnetic stimulation, epidural stimulation, those types of things. So in addition to neuroprotection, growth factors, cell transplantation, rehabilitation, we're now adding the neuromodulation component to pipeline for moving things forward.

Dr. Max Boakye:

Wow. That's really exciting. So just what have you learned works best? And what advice would you give to institutions that are pursuing a neuroscience institute or center that is doing maybe half of what you're doing, for example?

Dr. Dalton Dietrich:

Bring in people that are highly collaborative, don't want to necessarily just work in their laboratory and work on their favorite area of research, but be highly collaborative. Build teams. Together, I think you can do some amazing, amazing things. I think again, you have to have leadership with a vision for doing some cutting edge research. I think that helps a great deal. It certainly has helped me. Be very transparent about the challenges and work together to try to overcome those challenges. Obviously, during COVID we had a lot of challenges in getting into laboratory, in ordering animals, or even bringing in subjects in our clinical studies, but we worked with the university very closely to overcome those and turn them into success stories. So I think it's from the bottom up getting people that like each other, respect each other, want to work together. If you're very fortunate, if you can get the clinicians, neurosurgeons especially are extremely, extremely busy, but at the same time, I've learned that these individuals really want to change medicine as well as we're trying to do. So if you get that right mix of those special people, it can work really well.

Dr. Max Boakye:

You have had a lot of success in philanthropic donations. This seems critical in light of dwindling NIH support for basic and clinical research. What are some of the things institutions interested in advancing scientific care can do to develop this critical arm?

Dr. Dalton Dietrich:

Well, we've been very fortunate. Of course, we live in Miami and there's a lot of interesting people in Miami and they're doing some interesting things. So we try to introduce ourselves to those individuals to get them excited about medical research. I mean, yes, neurological disorders, but cancer, diabetes, eye disorders, all these different types of needs. So the Miami Project has been very fortunate that since 1985 it has always had a strong fundraising arm associated with the project. And it started out when Marc Buoniconti, who was playing football, actually damaged severely his cervical spinal cord. His father, Nick Buoniconti, who had played for the Miami Dolphins middle linebacker, started asking where should Marc go? Who's doing the best research? And it just happened to be that Dr. Barth Green, chair of neurosurgery at that time, was starting a research group, multidisciplinary research group, called The Miami Project to target paralysis.

Dr. Dalton Dietrich:

And with that, they joined forces and started the first fundraising, I think in a dolphin football game, really passing the hat around. Over the years, that's kind of grown and we've put together some special events each year, be it golf tournaments or other great sports legend dinner, where we invite famous sports legends to come and talk about paralysis and we raise money through those programs. So we've been very, very fortunate. I should say that we have a very complex portfolio of income coming into the project. The vast majority is NIH funding, but we also get considerable funds from the Department of Defense, as well as the state of Florida and other foundations that specifically focus on spinal cord injury. So we're very fortunate.

Dr. Dalton Dietrich:

I found out in my many years of doing this, that people want to hear about science. They want to hear what you're doing. They want to hear what's exciting in the field, and these types of people are going to give money to something. So why not give it to medical research? So I really enjoy bringing people into the facility, sitting down for lunch, talking about what their interests are and then showing them what we are doing. Let them talk to some scientists. Many times that turns into some type of gift, large or small, doesn't make any difference, but it's a strategy for both education outreach and hopefully philanthropy.

Dr. Max Boakye:

To improve TBI care, we need to innovate. Now we've talked about the type of institutional structure and leadership that can spur innovation. What is the secret of scientific innovation and success? I'm thinking more of an individual level, like how to create your ideas and be successful as a scientist in TBI to move the field forward?

Dr. Dalton Dietrich:

Well, the first thing that we're really telling our graduate students and post docs and young investigators is that you want your research to be innovative. You want to use the best technology out there. And again, my job is to make sure our scientists have the best technology, have the best confocal microscopes, have the best light sheet microscopes, the best analyzers for biomarkers, for example, and things like that. But at the same time, think about intellectual property and how you can actually do really good science, but at the same time be innovative in terms of getting IP for your ideas, and the university gets this IP. That's really going to help you in terms, of course, doing really good science, and getting funded in IH and all the other funding agencies. But it's also going to allow you to hopefully get industry interested in your discoveries in your research.

Dr. Dalton Dietrich:

And that's going to help, hopefully, to move that research from the bench to IND application, the FDA, or something of this nature. So we're thinking big, that when you really do something research, it should be really innovative. It should be novel. It might be worth getting intellectual property. So we have built that technology transfer unit within the university, and that allows our scientists to move forward. So many of our scientists have intellectual property now. Some of our scientists have companies and things like that. And so I guess to answer your question specifically, do the best research, talk to people that can help you translate it, but maybe also bring in industry to help you advance your research, bringing in new technology that may not be available to you yet in academia.

Dr. Max Boakye:

Thanks. That was awesome. What have been some of the most exciting recent advances in traumatic brain injury treatments or research?

Dr. Dalton Dietrich:

Well, you know as well as I know that we really still do not have any neuroprotective strategies that we can provide the patient that just had a severe traumatic brain injury. We know a lot about the pathophysiology. We're taking blood samples from patients and looking at inflammatory proteins and things of that nature to gauge the evolution of the injury. I've been really excited as you may know about the use of a targeted temperature management in the care of TBI. In 1987, I started with my colleagues. I started working on the importance of mild hypothermia in models of cardiac arrest, and then went into stroke and TBI. I still think that targeted temperature management, inhibiting fevers, possibly a subpopulation of TBI patients that are cooled, you could actually improve outcome and also target ICP elevations, which are critical secondary insults in TBI patients.

Dr. Dalton Dietrich:

So I think targeted temperature management. I know this for a fact, because I just lectured in a podcast last week to 3,500 Chinese neurosurgeons on targeted temperature management in the area of cardiac arrest, stroke, and traumatic brain injury. So there's a big interest in that. So I think we've got to figure out how we use targeted temperature management better, but at the same time we have some new drugs that are coming out that are targeting neuroinflammation that I think are really exciting. And that gets into the inflammasomes signaling cascade that you mentioned previously that maybe we can talk about when you're ready. But I think the combination of targeted management, I mean good neurosurgical care, obviously to neuro protect. Then we're now developing some small molecules that enhance axonal regeneration. Those studies are now hopefully going to clinical trials in the future. So I think a combination of protecting the brain, inducing circuit reorganization and axonal regeneration, and then with rehabilitation and neuromodulation, I think you put those things together and you've got a basis for improving function in people with severe TBI.

Dr. Max Boakye:

Now when you say targeted hypothermia, is that the same thing as therapeutic hypothermia? And where are we with it currently?

Dr. Dalton Dietrich:

Some time ago, single institutional studies on hypothermia targeting severe TBI were positive. I think there was, I got a slide from [inaudible 00:21:42] that shows 22 with single university clinical trials that showed improvement in neurological function. Okay. Then the multicentered trials came out with Guy Clifton. Great trials, but they showed that hypothermia did not work in a larger patient population. There was a lot of reasons for that. They weren't cooling earlier enough, a very heterogeneous patient population maybe did not reach therapeutic temperature fast enough and things of this nature. There's some other papers came out, also showed that it didn't work very well. So right now, maybe cooling all patients when they come in is probably not the answer to this neuroprotective strategies and temperature. But what is, is inhibiting periods of fever. From my own work, we know that if an animal has a TBI and then 24 hours later, you artificially raise the brain temperature to 39.5 degrees, that animal does not do very well.

Dr. Dalton Dietrich:

So I think when I talk about targeted temperature management, I'm thinking about just like blood pressure and all the other PCO2, physiological variables that you have at the bedside, we're now making sure that our patients don't spike fevers, number one, and number two, there are some patients that will benefit from cooling. We're now trying to figure out what that patient population is. As you know, TBI is a very heterogeneous patient population and we think maybe some patients could benefit from cooling. So it's a complicated story. We're not there yet, but we do think targeted temperature management, where you're controlling body and head temperature, more critically may be something that's important to improve outcome.

Dr. Max Boakye:

Before I ask you about inflammasomes work, any research studies and trials that you are anticipating the results of in the next few years? Anything in particular that you're really looking forward to the results? I know we were recently part of the progesterone trial. I think that was about six or seven years ago. That did not really show positive results. Are there any other similar trials that results are going to be available pretty soon that you're heavily anticipating?

Dr. Dalton Dietrich:

Well, just to get back to our work where we're in the middle of a therapeutic hypothermia trial and severe spinal cord injury, and we're working with about seven centers and we're recruiting patients, half of those patients are being cooled to 33 degrees. Half of those patients are normal thermic. I think we're over halfway through and and Dr. Allan Levi, chair of neurosurgery at the University of Miami is the principal investigator. So, he and I, and others are really excited about that study to see number one, is it safe? And number two, does it improve outcomes? Some of the preliminary data suggests a high level of conversion from ASIA As to Bs and C. So that's encouraging. In terms of the traumatic brain injury, there's several big trials going on in China on therapeutic hypothermia. I think those are the type of things that we're going to be looking forward to seeing. There's some other hypothermia trials in Europe that are also ongoing.

Dr. Dalton Dietrich:

In terms of drug trials, I think I'm beginning to feel that the pathophysiology of TBI is so complicated that we're going to have to do combination approaches, a drug that not only targets one particular aspect of the injury cascade, but one like progesterone, for example, little dirty drug that may be more beneficial. Now, the progesterone trial, a lot of reasons people talk about that trial not working well, but one of the major criticisms I understand was that they didn't really reach the therapeutic dose. So people continue to work on dose management and pharmacokinetics of these different types of drugs to make sure they get into the CNS. I'm anticipating a lot of really interesting things coming out, but again, as you know, TBI is such a complicated problem. We may have to think about things like targeted temperature management plus pharmacotherapy.

Dr. Max Boakye:

Thanks. That was great. You're known for your work on the inflammasomes. Now, what is the inflammasomes and its role in TBI and in the implications for how TBI is treated?

Dr. Dalton Dietrich:

Okay. So the inflammasomes is a very interesting topic to talk about. It's a multi protein complex of the innate immune response, this immune response that happens immediately when a cell is stressed and it's responsible for controlling the inflammatory response of the body, of different cells. The inflammasomes was first discovered in inflammatory cells circulating. And our group was the first group to show inflammasomes signaling in brain cells, neurons, and microglia, and astrocytes and things of this nature. So it's a regulator of the activation of caspase-1. Now caspase-1 is the inflammatory caspase. You know, we have caspase involved in apoptotic cell death and things like this. This is an inflammatory caspase and it usually gets activated in response to viruses, bacteria, and other sources of stress to the cell. So, the inflammasomes is really big right now in COVID-19, for example, because we now know it's activated dramatically when that virus comes in.

Dr. Dalton Dietrich:

But getting back to TBI, we were, again, one of the first groups to show that in a pre-clinical model, when you produce TBI, you get activation of inflammasomes signaling. The inflammasomes is composed of different types of proteins, that's sensory protein and adapt to protein and a caspase-1. And these things come together to form a complex that leads to the activation of caspase-1 and the formation of IL-1 beta beta and IL-118. And as you know, these are very important pro-inflammatory cytokines. More importantly, when the inflammasomes signal is activated, it leads to gasdermin activation which forms gaps in cells and the cells die by a process called pyroptosis. And this is another new way in which cells can die. We have so many ways cells can die now. You would think, oh, it's going to be impossible to stop cell death.

Dr. Dalton Dietrich:

But pyroptosis is a new inflammation induced cell death, neurons, other types of cells as well. So what we've done is to develop a series of monoclonal antibodies that actually target the formation of the inflammasomes. It targets this [inaudible 00:28:27] protein that disallows it to form this complex and that therefore decreases dramatically the formation of IL-1 beta. So it's very upstream. It's like the very early steps in inflammatory cascade when a cell's stressed. So we are now giving this to animals and we can block the inflammasomes and we improve TBI outcome and cognitive function. And the other thing I'll just tell you is we can now take blood samples out of TBI patients, and measure different levels of these inflammasomes proteins. And they seem to tell us a lot about the severity of the injury and also the progression of the pro-inflammatory mediators that we think may be associated with more progressive neurodegenerative diseases. So the inflammasomes is very interesting to work with. It reminds me of temperature modification, because it affects so many different types of cells. And now, many of the drugs are targeting neuroinflammation. So this is one that does that as well.

Dr. Max Boakye:

Wow. That's fascinating. Sounds like you might be able to use them on the subject bio biomarkers. Maybe you can provide an update on what you might consider to be the most exciting biomarkers in TBI.

Dr. Dalton Dietrich:

Okay. So yes, we have an inflammasomes protein platform of the biomarkers that are associated with IL-1 beta and one of the proteins ASC caspase-1 and gasdermin. So together that platform kind of tells us about how active the inflammasomes pathway is. So that's one thing that we've been doing, but I think right now most of the biomarker work, which is really exciting by the way, right now track TBI has this large sample basis now that they're doing really outstanding biomark work. But GFAP, glial fibrillary acidic protein is still way up there in terms of the list that seems to be associated with injury severity. I was just reading a paper last night, a new paper just came out on pediatric TBI. It looked like GFAP assessment in the serum was very related to outcome.

Dr. Dalton Dietrich:

And then you have UCHL1, I mean that's ubiquitin terminal hydrolase, which actually is released in the brain when it's damaged or you have misfolded proteins S100 beta is still used in terms of the calcium binding, and that's produced by astrocytes. So that's good. And IL-1 beta is good too. So I think there's a lot of different biomarkers that people are using. They're trying to utilize these again, as I said, we used to take the first 24 hour sample after TBI. Dr. Ross Bullock was my colleague at that time. And we would be taking these blood samples and measuring and very early on, we started at trying to ask the question how we could predict how well the patient did in ICU based on that first biomarker sample. And at that time we were looking very early on at some of the inflammasomes markers and there seemed to be relationship between levels of that at the first 24 hours and how well the patients were doing.

Dr. Dalton Dietrich:

I think in the next time that we looked at neurological outcome and that paper came out in neurosurgery. So I think biomarkers are going to be a big help to help us differentiate different patient populations that should be treated differently. You know, if one particular inflammatory mediator is high, maybe you need to give a drug to target that. If there's evidence of caspase related activity, maybe something else of that nature. So I think the biomarkers as a surrogate marker, as well as imaging, are really powerful ways in which we can assess how well how the brain is doing over time after severe TBI,

Dr. Max Boakye:

Can you provide an update on what we know at the impact of COVID on TBI?

Dr. Dalton Dietrich:

So the impact of COVID on people living with TBI?

Dr. Max Boakye:

Yeah. Is there some sort of association between COVID and TBI outcomes? Do we know enough to be able to make some assessments of that relationship?

Dr. Dalton Dietrich:

I probably do not. I mean, we've been very concerned about COVID-19 and our spinal cord injury population because they're very susceptible to infection, bladder infection, and lung infection, and things of this nature. So we are very concerned about those individuals being highly vulnerable to COVID. And so we really went out in the community and tried to make sure those individuals were finding places to be vaccinated and then doing a lot of virtual zoom meetings to make sure they were engaged and things of this nature. But my gut feeling would be a spinal cord injured patient, as well as a TBI patient, very, very high vulnerability to lung infections. And I think as we know, COVID-19, that was a big thing early on in terms of what it did to the pulmonary system. So it can certainly aggravate their effects in terms of lung function. And now, we know that the virus also affects many other organ systems, be it the heart, be it the brain. So I think again, like any virus, susceptible people, you really have to watch out to protect them from these pathologies.

Dr. Max Boakye:

What about an update on stem cells? Would you classify stem cells as a still promising therapy for TBI?

Dr. Dalton Dietrich:

Well, that's a difficult question. We have transplanted a lot of stem cells into people living with spinal cord injury and we found that they were very safe. We didn't see any tumors of things like that nature, but we really didn't cure anyone with those stem cells. I think the multipotent stem cells, IPS cells, I think that's really what we really now want to think about in terms of more specialized medicine. You can actually produce these from an individual. I think they have the ability to be differentiated and pushed toward even specific neuronal cell types and that's going to be very exciting. I do believe that maybe just putting cell by themselves into the injured nervous system may not be the solution because many times what we've found out when you do cell therapies, the majority of those cells end up dying. They just don't have the right nutrients and things like that, and they don't live long enough to make the circuit.

Dr. Dalton Dietrich:

So what we're doing now is working with some biomedical engineers on biomaterials and developing ways in which we can enhance the survival of those cells, be it stem cell or schwann cell or, or an IPS cell. And maybe through that particular mechanism, those circuits can grow and interact, integrate with the host tissue and produce functional circuits. So I think we have a little way to go, but there's a lot of exciting work being done throughout the world on this particular subject.

Dr. Max Boakye:

I want to circle back on something that you mentioned about a research that you're doing on Alzheimer's and TBI. What have you been finding in your research between the history of TBI and the development of Alzheimer's?

Dr. Dalton Dietrich:

Well, again, on this particular grant, we're specifically focusing on inflammation and what we've done to the studies so far, this is a relatively new program for us, is to use AD transgenic mice and ask the question, what happens when you traumatize one of these transgenic mice and specifically what is happening to inflammasomes signaling? What we're finding out is that inflammasomes signaling is augmented. It's raised compared to a wild type mouse. So we think of the TBI that activates inflammasomes signaling by itself is additive to the effects of the genetic profile of the mouse when it's injured as well. So we think that there is synergy in terms of the inflammasomes signaling that's activated with the TBI and that's happening with the gene susceptibility patterns of that animal. So that's what we're working on, and that just implies that maybe inflammasomes signaling could be involved in accelerating the progressive injury, accelerating the cognitive decline in someone that's living with these AD genetic profiles, and that something like an anti-inflammatory or something that targets the inflammasomes might be something that would be relevant one day in terms of treatments.

Dr. Dalton Dietrich:

So that's where we are right now. We're just starting out these studies, but the data looks intriguing and we're going to follow up on in the future. That's, basically what we're doing in terms of the risk factors. We're also with another laboratory working on phosphodiesterase inhibitors in TBI and AD, and that's another exciting area of research and another target for different type of pharmacological agents. So I think putting together these genetic predisposition to AD with TBI is a fascinating strategy to use, and hopefully we're going to learn something that we can translate to the clinic.

Dr. Max Boakye:

Thanks for that. That's really awesome. So what do you know now that you wish you knew 20 or 30 years ago?

Dr. Dalton Dietrich:

That you can't do everything yourself, so you need to talk to people and learn, and I think I did that very early on. Again, I've emphasized how fortunate I was to talk to really outstanding mentors and scientists and clinicians. But I think that it's really important when you're building multidisciplinary programs to pick out the right people that you want to talk to, you want to collaborate with and make sure that there's a nice synergy between your goals, your visions, and that everyone's going to work together as hard as they can to push this forward. So I think building teams is really important. I think over the years, I've found out that I can build teams. I also think it's extremely important be involved with the university administration. I mean, to make sure that they know how important the work that's going on in basic research departments, centers, institutes, and clinical departments.

Dr. Dalton Dietrich:

And all of this is such an exciting times. We need to do everything we can to support these programs, and the university needs to bring in the support, the infrastructure needed to be successful. So I think all those things together is something that I've picked up over the years. The other thing is just reaching out to people, knocking on doors. If you hear someone has a technique that you think you could use, take the opportunity to talk to this individual. Have some coffee with them or something of this nature and see if you can build some bridges between your research and their research. I think that is always very helpful.

Dr. Max Boakye:

Wow. That's really great. How do you envision treatment of TBI in the next 10 to 20 years? In what ways do you think it would be different from today?

Dr. Dalton Dietrich:

Good question. I think critical care is getting better and better. The ability of severe TBI patients to find the best level one, level two, a trauma center that they can go to immediately so the best surgeons are there to help them in terms of the surgical procedure. The intensive care units, I think you go into one now and they have all this very elaborate technology that we can monitor the patient, be it EEG, be it biomarkers, be it other types of sensors. I think that's going to continue to evolve. I think machine learning and big data. I've got a post doc that's working on that, and I'm finding that's very intriguing in being able to put these large groups of data together, to dissect out why some patients benefit from a particular drug and why another patient population or type of traumatic brain injury doesn't benefit from a drug.

Dr. Dalton Dietrich:

I think those types of things are extremely important. And I think the imaging, I mean imaging has come along just so fast. I think the imaging approaches that we can use to detect molecular imaging, for example, looking at PED, looking at these knee ligands or receptors and changes, I think that's really great. And then, with the MRI, being able to look at fine fibers now, fiber tracks, and finding our evidence for mild demyelination, which leads to dysfunction of circuits, those type of things. I think we'll be able to dissect out to better understand the pathophysiology of the human brain after TBI. Hopefully we will have cellular, pharmacological, neuromodulatory approaches that can enhance, repair, and function.

Dr. Max Boakye:

Oh, that's great. So my last question for you, Dr. Dietrich, is if you had a magic wand, what would you do with it to have the greatest impact on TBI?

Dr. Dalton Dietrich:

Well, I guess prevention is what we really want to do. Correct? So I think some way to prevent TBI in the pediatric, adult populations. I think having a noninvasive surrogate marker for picking up injury severity and the pathobiology of the injury in that particular individual, and of course having a multitude of drugs or strategies to target that specific pathophysiology that we think needs to be targeted, a particular time period after injury. I think those types of things. It's kind of like Star Trek, if you get back to that those types of films where someone can actually use surrogate markers to evaluate less invasively what's actually happening in the brain. I think those types of things are on the horizon, and I think it's again, continuing exciting times in the neurotrauma field.

Dr. Max Boakye:

This brings us to the end of this fascinating update on traumatic brain injury, has been a conversation with Dr. Dalton Dietrich, scientific director of The Miami Project and the Kinetica Concepts, distinguished chair in neurosurgery at the University of Miami. Dr. Dietrich, thank you very much. We're going to bring you back at a later date to talk about spinal cord injury, but thank you for taking the time to speak with us today.

Dr. Dalton Dietrich:

Thank you very much. I really enjoyed it.

Dr. Max Boakye:

Thank you.

Speaker 1:

Thanks for listening to Optimal Neuro Spine Podcast, with Dr. Max Boakye. If you enjoyed this episode, we hope you share it with others. Leave us positive reviews on social media or leave a rating and review on iTunes. Check out our website, Maxwell Boakye.com/podcasts for show transcripts and other information. Join us next time for another edition of Optimal Neuro Spine Show.