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. My distinguished guest today, is Dr. Scott Whittemore. He is the director of our Spinal Cord Injury Center, and it's a real pleasure to talk to him about all things spinal cord injury. Dr. Whittemore needs no introduction. He is a professor of neurosurgery, and is the vice chair of research for the Kentucky Spinal Cord Injury Center. He obtained his bachelor's in biology and his PhD in physiology and biophysics from the University of Vermont in 1981. He subsequently, following some postdoctoral fellowships at UC Irvine and Molecular Biology at Uppsala University in Sweden, he joined the faculty at University of Miami in the Department of Neurological Surgery in 1986, as one of the founding scientists of the newly formed Miami Project to cure paralysis. He was there for 12 years, rose to the rank of full professor and was subsequently recruited to the University of Louisville, where he has held the Henry D. and Marianna Garretson Endowed Professor of Spinal Cord Injury Research, as well as a distinguished university scholar.

Dr. Max Boakye:

Dr. Whittemore is the founding director of the Kentucky Spinal Cord Injury Center, a position he still holds. Over the past 22 years, he has grown Kentucky Spinal Cord Injury Center to 22 faculty members, have successfully raised over $230 million in research support for Spinal Cord Injury Research. His research program has continuously focused on spinal cord injury, and has spanned diverse areas in novel neurotrophic factors stem cells, remyelination and more recently, in novel strategies for neuro protection.

Dr. Max Boakye:

I'm really delighted to have him here. He's at the forefront of emerging technologies over the last 30 years in Spinal Cord Injury Research, with multiple grants from NIH. He has published over 160 manuscripts, 30 book chapters, and has mentored numerous PhD grad-students and fellows, 18 grad-students and 18 postdoctoral fellows. So it's my real pleasure to really speak with such a distinguished researcher and scientist, to talk to him about all things spinal cord injury. He's also, in full disclosure, has been my scientific colleague here at the University of Louisville. It's a pleasure to have you here on board, Dr. Whittemore, welcome.

Dr. Whittemore:

Max, it's nice to speak to you. Thank you for the kind introduction.

Dr. Max Boakye:

Fantastic. Let's delve right into it. So, one thing that I want to talk to you... begin with, is the fascinating history of your collaborative relationships with neurosurgeons. You have had distinguished scientific collaborations with a number of neurosurgeons, can you describe some of these scientific relationships and what is the secret sauce? What makes it work well?

Dr. Whittemore:

Well, it started in Miami when Barth Green, who was the chair of neurosurgery at the University of Miami, was founding the Miami Project. Again, as with many of these centers, they start from very tragic accidents and the circumstances surrounding Nick Bouniconti and his son Mark, who was injured in a football game, had been well chronicled, and they decided to build a center. They recruited Åke Seiger from the Karolinska Institute in Sweden, and I was just finishing a postdoc there in Sweden, as you mentioned, at Uppsala University. And very early in molecular biology, I was in a Rhinovirus Molecular Genetic Center and saw more called viruses than I choose to remember, but learned molecular biology there. And when he came to take over as the first director of the Miami Project, he asked me to join him. And I worked with Barth Green building that center, as many of your listeners are aware.

Dr. Whittemore:

Okie left after three years, and Dick and Mary Bungee were recruited from Washington University, and we continued to work very closely with neurosurgery. Dalton Dietrich took over after Dick Bungee passed away much too early from cancer, and continued to really set the standard for our Translational Research Center. And I think what's important about that is, having a committed neurosurgeon, having a hospital administration that's willing to put resources into the center, recognizing the added value departmentally for having an affiliated research group. Training, we trained residents, medical students, a lot of collaborative work with the faculty, and really, that center evolved to what it is now. It's one of the largest Spinal Cord Injury Centers in the world, and very comprehensive across both basic and clinical. When I was recruited here to Louisville, Dr. Chris Shields was the chair and he had a similar vision.

Dr. Whittemore:

And again, it was a tragic incident of a young woman at college having a good time, no seatbelt and ended up as a spinal cord injured individual. And Dr. Shields knew... I went to see him and one of the cousins... the uncle was the State Senator, Tim Shaughnessy, and they worked together to get a traffic ticket contribution to spinal cord and head injury at the University of Louisville and the University of Kentucky, and that really started building the center. And Chris was incredibly dedicated to the project. His hospital put in significant resources, and again, pretty much we followed the same principle. I tried to take what was good I learned in Miami, and leave what I didn't particularly like. and again, we've been very successful as you highlighted to the extent to which we built the center here.

Dr. Max Boakye:

So the Kentucky Spinal Cord Injury Center, was it fully funded by the traffic accidents or just partially funded? And is this still being funded by traffic?

Dr. Whittemore:

It's still being funded to this day, and it's partial funding. But what they were able to do was, it was at a time when the State budgets across all States in the country, were pretty flush and that were budget surplus. This was back in the late 90s, early 2000s. I came to Louisville in 1998, and they were able to match money with the State to fund endowed chairs. And that's really what... And the university recruited very senior scientists who had a very strong NIH research portfolios, to bring their grants with them on providing endowed chairs. And we used that to recruit very, very senior faculty at first, some junior faculty later. And that was really the impetus to get started building the faculty here. And this could not have started with out that initial contribution of the State.

Dr. Max Boakye:

What typically goes on in a Spinal Cord Injury Center? What is the importance of centers to overall advancement of spinal cord injury treatment?

Dr. Whittemore:

Well, I think what centers do is, they bring scientists and clinicians, as you well know, you yourself have a clinical focus here, as well as a basic science focus, but they bring experienced scientists who collaborate, we kick ideas off, you often talk to your colleagues in the hall. You're all in similar physical space. We have both a basic science component and a rehab component. The clinicians get involved when it's appropriate. Clinicians come to us with problems that they want to model in animals. We talk to the clinicians about problems that we could potentially solve for them.

Dr. Whittemore:

I mean, it's a very fertile environment, there's a lot of cross fertilization. You have to have a mentality to really foster the junior faculty, and the trainees, and the senior individuals have to buy into a group mentality. But when they're willing to do so, it makes for a very productive and very fertile intellectual environment to really do both really cool science, as well as translational work that very definitely helps patients.

Dr. Max Boakye:

So your PhD was in physiology and biophysics, you did postdoctoral fellowships in neurochemistry and molecular biology. How did you become interested in spinal cord injury?

Dr. Whittemore:

Well, many things that happened in life, it really was serendipity. My molecular biology was predominantly in the brain looking... My postdoc was molecular biology, looking at neurotrophic factors, initially nerve growth factor and some novel neurotrophic factors. And when Åke Seiger approached me about coming to Miami, the position was to set up a Spinal Cord Injury Center. And so I switched to spinal cord from the brain, although we still do some work in the brain, but it really was... And I've been with spinal cord ever since. So that was back in 1986.

Dr. Max Boakye:

Looking at your publications, I noticed that they've spanned a few themes. You have a history of working with stem cells, produced stasis, and ER stress and remyelination. Can you kind of touch base on some of your most important contributions in each of these areas?

Dr. Whittemore:

Sure. As I mentioned, I started my second postdoc with whole comparison in Uppsala working with Åke Seiger and Larsh Olson, who really were involved with some of the adrenal gland transplants and subsequent human transplants in Parkinson's disease models, and then ultimately Parkinson's disease. And we started looking at nerve growth factor because of the whole burgeoning field of trophic factors, and neuronal survival and neuronal support. And our work at the time was, we were the first lab to really show nerve growth factor in the central nervous system. I think we were actually five groups that published pretty close to simultaneously, but ours was out first and we continued to work quite a bit with nerve growth factor. At the time, it really was the only well described growth factor. And it was

probably another five or six years before Yves Barde and Hans Thoenen initially isolated brain derived neurotrophic factor, median F, which then started the whole field moving ever increasingly quickly forward.

Dr. Whittemore:

When I moved to Miami, it was another serendipitous interaction I had with somebody, who really started me working in stem cells. This was back in the very, very early days of stem cells. At the time, Miami had a PhD to MD program, and it was a two year program. And one of the students had been a postdoc with Ron McKay, who was one of the early pioneers in stem cells, and came into my office to have lunch and we started talking about some stem cell work that he had just started with Ron, and we started working on it in my lab and it took off to developing our own stem cells. From the CNS, we actually made using temperature sensitive T antigen, so they would proliferate at 33 degrees, and then at body temperature 37, or after engraftment they differentiated.

Dr. Whittemore:

And really, we were able to define some early principles, that the adult central nervous system had the capacity to direct very appropriate differentiation of precursor stem cells. I mean, that was probably the most important finding from some of that early stem cell work. And we moved on to, you could take a Rothe derived stem cell and put it in the hip campus, and you'd get a fully functioning CA1, CA3 pyramidal cell or granule cell in the dente jars. You put them in the spinal cord, we could get motor neurons. It was quite surprising and opened up a whole new avenue of research for us.

Dr. Whittemore:

We then moved on to making other neuronal cell lines, and it was at that time that the Reynolds and Weiss paper came out with neuro spheres. And that really was the takeoff point, when the whole field started realizing that you could get undifferentiated neuro precursor cells that were tri potent, and you could expand them, and we started using them in attempts to repair the injured spinal cord.

Dr. Whittemore:

I think we thought it was going to be quite easy, and we thought we could take cells that were undifferentiated and put them into the spinal cord, and we would get new neurons and be able to reconstruct circuits. But it obviously turned out to be much more complicated than that. And undifferentiated cells at the time, did not do well in differentiating in the cord, and we really started to unravel some of the inhibitors that were involved in preventing the neuro precursor cells from becoming neurons. And I guess it became very clear to me during all that time, I mean, we were successful getting funded and we published quite a bit, but neuronal replacement was really going to be the most difficult aspect of stem cell replacement.

Dr. Whittemore:

Again, this was before IPS cells, ES cells were just starting to be utilized, so it was very early in the whole field. And so we decided to focus on remyelination thinking that, if you just asked a precursor cell to do one thing, to become an oligodendrocyte and remyelinate, and at the time, there was at least a prevailing thought that remyelination was a key aspect to repair in the central nervous system, that we'd be able to facilitate repair. Again, it seemed quite straightforward, there were quite a few hurdles. We ultimately were successful in mouse models and rat models to get glial precursor cells to remyelinate, and show that they had a functional contribution to repair, both ultra structurally and

electro physiologically, but it required a very substantial modification, genetic modification of both the engrafted cells and even the host environment.

Dr. Whittemore:

And every time we made a different molecularly change, adding a growth factor, blocking a signaling pathway that our in vivo studies said should give us more oligodendrocytes, we found we had other consequences in vivo, probably the most dramatic of which was blocking BMP bone morphogenic protein signaling, which would take a real precursor towards oligodendrocytes in the dish and do it very nicely. If you did it in vivo, you got just this robust chronic inflammatory response because the BMPs were pressing the inflammatory responses, and so the lesions were two and three times the size of what we saw with control cells. But I think the contributions that we made there were really, we were one of the main players in remyelination stem cells, and we contributed to the...

Dr. Whittemore:

If you look at the literature entirely, it really didn't support moving forward clinically. If you critically evaluated the preclinical data, and then look... hindsight is always 100%,aAnd then you look at what was done with the clinical trials, none of the optimal approaches that were used pre clinically were used in the clinical trials. And I think that was a combination of some proprietary issues with the companies that controlled them, and also with the fact that the biology was really at odds with the regulatory issues, in the sense that what it required to make that system work and to get remyelination, would not be something likely that the FDA would approve.

Dr. Whittemore:

And really, it was at that point, it was about, oh, maybe 10, 12 years ago that I decided that, that discrepancy between biology and regulatory issues and how soon that would be, I didn't really feel that stem cells is certainly in the glial aspects of it, was going to be an approach that would be translationally relevant. And so we switched the focus of the lab towards new models of neuro protection. That's kind of a long-winded answer, but I think in the early days, the growth factor work with NGF, was I think probably pretty seminal as was the remyelination aspects of it pre clinically. So that's kind of where we stood up until we started working on the proteostasis.

Dr. Max Boakye:

So how many major stem cell trial clinical trials have there been done so far?

Dr. Whittemore:

Well, there's certainly the original... In spinal cord injury, there's been a number of Schwansel trials, the neuro stem cells, neuro stem cells ink trials.

Dr. Max Boakye:

Proneuron, right, was one.

Dr. Whittemore:

There have been a whole host of studies done with various types of mesenchymal stem cells, if you include all the ones that have been done worldwide. I think I had a lecture on this to the graduate

students earlier this year, and I think I came up with 45 or 46 different studies with various cell types. Very few of them replicated each other. There's a lot that's been done.

Dr. Whittemore:

I think you as a neurosurgeon know that, none of them have been successful to the point where it's in routine clinical practice.

Dr. Max Boakye:

So what would be your current view of the potential of stem cells? What do you think the future holds? How do we overcome this barrier of-

Dr. Whittemore:

Well, I'm pretty skeptical. I mean, I think there's some really interesting work, certain Mark Jasinki's work starting in rodents and working into primates with their neuro stem cells that neuronally differentiate, have shown remarkable ability to survive and differentiate, and extend processes. But it's a phenomenal number of cells that are in there. I don't think we understand the full context of the biology enough, to be able to be confidently be moving forward into clinical trials, and most of what is being done right now is, putting cells in and seeing what happens.

Dr. Whittemore:

I mean, most of the clinical trials have all been safety trials. Efficacy has been limited, and in some cases, there have been detrimental outcomes. I think the initial excitement was overoptimistic, and I think proceeding forward from a clinical standpoint based on what we see in the preclinical data, I'm not a clinician, is one has to move very cautiously.

Dr. Max Boakye:

But wasn't there a lot of evidence in rodents, of the success of stem cells, and what does that say about the translational value of studies in rodents? Do you think that could be part of the problem?

Dr. Whittemore:

Well, no rodent model is a really good model of human injury for all the reasons that we all discussed. The mouse particularly, is a really bad model of human spinal cord injury, but we continue to use it because the power of the genetics that we can do with it. The histological outcome of mouse injury, is very different than what you see in a rat and a human. Time courses are different. Very few of the rodent studies have been replicated independently, people report similar levels of success with totally different types of stem cells, modified by various genetic and/or pharmacological or co-transplant approaches.

Dr. Whittemore:

So there's been really no consistency in the preclinical data, that I think if you're truly open and critical, that will give you confidence that there's a defined approach that makes a lot of sense, that has been shown by multiple independent labs that it's one worth pursuing.

Dr. Max Boakye:

So it sounds like you stopped doing stem cell research completely, and you shifted your focus to some of the neuro protective approaches. been known to be an expert on proteostasis, what exactly is proteostasis?

Dr. Whittemore:

Well, proteostasis is, it comes from protein homeostasis. And just to back up a little bit, as I said, I didn't think the stem cells would be clinically translatable within the timeframe I had left in my career, and I wanted to do something that would contribute a little sooner and might be better applicable. And certainly, the history of neuro protection has shown that single factors just don't work, whether you're dealing with spinal cord injury, whether you're dealing with stroke, or traumatic brain injury, or any of the neuro degenerative disease models.

Dr. Whittemore:

And we reasoned that neuro trauma is multifocal, there's lots of distinct sibling pathways that are activated, different cellular systems, and we really wanted to try to get at an approach that would be a little more global than a single factor. And proteostasis is the cellular defense mechanisms that, any time a cell is stressed, the increased misfolded protein load happens in the endoplasmic reticulum, hence ER stress. And if ER stress cannot be aggregated and reversed, and cellular homeostasis is brought back to bear, then the cells initiate a apoptotic response and make the cells basically kill themselves.

Dr. Whittemore:

And so the field of proteostasis 10 years ago, was pretty novel. It was well-established in Cancer and certainly in aging, but really there was very little at the time in the central nervous system.

Dr. Whittemore:

I remember being at a neurochemistry meeting and hearing a proteostasis talk, and I'd never heard the term at the time, and Rick Morimoto from Michigan gave the talk and it was just a remarkable talk. And I went back to my hotel room and typed in CNS, and proteostasis, and ER stress, and just getting in PubMed, and just kept getting no results found.

Dr. Whittemore:

But basically the idea is that, if you can target a process that affects all cells, and that all different types of stressors elicit the same end result, which is apoptotic responses from the proteostasis network, then that may be a more global approach that would be more beneficial to target those secondary events that occur after CNS trauma.

Dr. Whittemore:

Probably the closest thing in the literature at the time targeting that, might be hypothermia, where the Q10 is slowing down all the pathophysiological processes. And there are still ongoing trials on hypothermia now, and a variety of CNS trials that are certainly led by the Miami Group and Al Levy and Don Dietrich in human spinal cord injury.

Dr. Whittemore:

So we have looked at ways to inhibit various components of the proteostasis system, and really trying to define what happens after spinal cord injury. And I think we and others, and in multiple other labs that

are working at this, some in spinal cord injury, some in other models, proteostasis involves, or encompasses, ubiquitin–proteasomal degradation systems, it encompasses autophagy, it encompasses the unfolded protein response, the endoplasmic reticulum stress response, the E-CHOC response, and the integrated stress response.

Dr. Whittemore:

So all of these combined, they interact in ways that we don't fully understand. And even as with single target therapies, you can target one aspect of the proteostasis network, but there's compensation in others. Sometimes it can be beneficial, and other times it's further pathological. So again, we're really trying to understand the system, but I think we and others in the field have made significant progress. A lot of the drugs that we can utilize come out of Cancer, and while they're often trying to do the opposite of what we're doing, there's a lot of tools and a lot of genetic tools that you can really get at that. And I think it's proving to be an appropriate target.

Dr. Whittemore:

What really has emerged over the last five to 10 years that's sort of a confounding variable, is the extent to which secondary injury really is going to restore function. And I think our preclinical work at least, would suggest that there's a ceiling effect above which, no matter what you do, you're not going to be able to restore function. And that really complicates how efficacious this is going to be when it does become... if it were to become translated into clinical practice.

Dr. Max Boakye:

Is that kind of a recenter finding? Because when I was training, the thinking was that NMDA and calcium channel antagonists, were going to be the final solution to all of this. Are we beginning to realize that even by targeting the secondary mechanisms, it's only going to give some partial recovery? Is that kind of where we are?

Dr. Whittemore:

Well, I think Max, if you gave the year in which you trained, you'd probably be dating yourself. And that was quite a while ago, where those single factors were. And those are the types of single factors that I'm talking about, methylprednisolone is another classic example. And so, yeah, it's a much more complicated system. There is no single signaling system that can be individually targeted, that is going to result in significant repair for all the cell types that are affected by a CNS trauma.

Dr. Max Boakye:

So specifically with the proteostasis, any particular drugs that are close to kind of making it into human clinical practice?

Dr. Whittemore:

There certainly are drugs that effect the system, they have been used in Cancer. There are a whole host of natural compounds that people have used. But the problem with all of these drugs that affect proteostasis system, is that in many of them there are off-target effects. There's some really interesting drugs in rodents in preclinical studies that have been used, they have solubility issues, there's toxicity issues, and so the clinical chemistry to move those into clinical trials, a number of them that show great

promise in preclinical studies, affect a signaling pathway through eukaryotic initiation factor 2-Alpha, which is one of the main drivers of global protein synthesis.

Dr. Whittemore:

And when it gets phosphorylated, which just happens in the ER stress, it's just sound protein synthesis to allow the cell induce a synthesis of a very specific effectors of pathways, that synthesize chaperone proteins to refold proteins to degrade those misfolded proteins. And I think those are effective, but the problem is, the ones that are in use in animals, have yet to be approved for clinical trials. And I think they're awaiting some modifications for bioavailability and for much more targeted... specific to knock down some of the secondary effects that some of them may have.

Dr. Whittemore:

And the problem in rodents studies is that, we often don't look at those secondary effects, and so you evaluate what's under the street light looking for your keys. It's often those other signaling pathways that are what's problematic, and that's sort of where the field is right now.

Dr. Max Boakye:

What about the more recent work that you've been doing, I believe you had a nature paper... neuroscience paper on the silencing of the lumbar interneurons. Can you maybe describe that work a little bit?

Dr. Whittemore:

Sure. It's one of the other aspects, and this is collaborative work with David Magnison, and we've been really fortunate to have a number of really talented graduate students working on it. A couple have finished, Amanda Prograski, and Courtney Shepherd and Brandon Brown, they're still working with us.

Dr. Whittemore:

It's a system developed by Tadashi Isa, where you can conditionally silence anatomically defined pathways. So you use a retrogradely transported virus that encodes tetracycline activated, so it's conditionally activated, tetanus toxin fragment, and you inject that into the terminal region and then into the cell body region. We've done L2 to L5 interneurons, we've done long ascending and long descending protein spinal neurons, so C6 to L2, L2 to L5. Through up to C6, the descendings have their cell bodies in C6 and project to L2 to L5, and the ascendings the reverse.

Dr. Whittemore:

And in the cell bodies, you provide a virus that has the Tet activator, so that when you give the animals toxicycline, tetanus toxin fragment is synthesized and it blocks neurotransmission by stopping the cleavage and release of synaptic vesicles. And it's a very efficient system, it's reversible, you can take the toxicycline away and the animals will go back to baseline. What we may be able to show, is just that there's some very previously undiscovered left/right control mechanisms that probably don't fit into the current models of molecular cellular control of locomotive function, and they just need to be...

Dr. Whittemore:

I think that the most of that work has come from genetic models in mice, where you've done deletion studies on specific populations of identified internuerons. These are in adult free-moving rats that we

did these studies. Initial studies that Isa published, were done in non-human primates, and so it's a system that really you can, while you don't know the exact molecular identity of the cells, you can at least pick out anatomically defined pathways. It's probably a mix of multiple cell types, and it's lending itself to the controls of locomotive function. And the contribution of ascending and descending signals, are much more complicated than we currently think.

Dr. Whittemore:

One of the things that came out of that work, which was kind of intriguing, is that if the animal is free-moving on a crippey, a sub-straight with a high coefficient friction with a soft spongy surface for example, versus a piece of plexi glass, most of that control is at the spinal level. But when you start to get on a slippery surface, then the super-spinal control, becomes much more important for regulating locomotion. And silencing those interspinal pathways that connect the two, the cervical and the lumbar central pattern generators, becomes less effective at disrupting locomotion when there's higher control. So it's much more of a top-down system

Dr. Whittemore:

Whereas, if the animals are... And the other time, if they're not just sort of taking a little walk, if they're really focused on feeding behavior and sniffing, then the same thing happens, it becomes a top-down approach. So we're trying to understand locomotion, trying to understand... And the implications of that are... Well, let me back up a little bit.

Dr. Whittemore:

Some of the other data that comes out of that is, if you silence those pathways after spinal cord injury, we hypothesize that the locomotion would get worse, but it actually gets better. And the reason we think that is, is if there's a peripheral component that's been fed into the spinal cord and when the spinal cord is injured that is not functioning properly, and when you silence that communication between those two enlargements, the more intrinsic top-down pathways have much more control. And so you're actually taking away a detrimental signal.

Dr. Whittemore:

And with spinal cord stimulation becoming quite a very promising approach in spinal cord injury, there's some concerns that one has to have in terms of activating some of these pathways. So it's been a very interesting project.

Dr. Max Boakye:

And by spinal cord stimulation, you mean epidural stimulation?

Dr. Whittemore:

Epidural and transcutaneous certainly.

Dr. Max Boakye:

What are your thoughts about those, do you think they hold a lot of promise?

Dr. Whittemore:

Well, we're kind of preaching to the choir. It's a big part of our center, and the work that you and Dr. Harkema and Andrea Berman do, I've seen remarkable results. I don't think we fully understand mechanistically what's going on, but one can't argue with it. And it's not just the center in Kentucky, it's been done by multiple labs, and so I think it holds great promise. It's labor intensive, and it's really tough to think of its widespread use because of the surgical, and then more importantly, all the training that's involved. But yeah, I think it holds great promise.

Dr. Whittemore:

The recovery that we've seen, and you've seen firsthand having implanted those stimulators, is remarkable.

Dr. Max Boakye:

Looking back over your 30, 40 years in the field.. Let me ask you a couple of questions. What do you wish you had known back then? Looking back after 40 years, 30 years in the field, what do you wish would have been great if you knew back then? And the second question is, what has surprised you the most about why we don't have... we haven't made as much progress? What has surprised you most about that?

Dr. Whittemore:

Well, geez, if I had to think about one thing I wish I knew, I wish I'd invented PCR. That would've been a good one. I think that it's been a process, and I think that I wish I had better answers as to how to make stem cells work better. I mean, I think that is becoming pretty clear that in CNS trauma and certainly many neurodegenerative diseases, that tissue loss, or specific cell loss is the critical component. And the only way that that's going to be repaired, is to either graft in exogenous cells, or figure out better how to stimulate endogenous precursor cells. And in the age of brain they're certainly there in the human, but there's not a lot of them, so really you're looking at grafting as the approach for tissue replacement.

Dr. Whittemore:

I wish I better understood how to control that, because certainly the capabilities for the host to respond, are certainly there. But it's still a black box.

Dr. Max Boakye:

And what has surprised you that this has been a more formidable problem than you would've realized?

Dr. Whittemore:

Well, I think any of us who do biology, we have really simple thoughts of how things are going do, and we do things in a dish and they work pretty well, and then try to move in vivo and all of a sudden what you unequivocally thought was going to happen, and based on your in vitro findings this doesn't work. The other thing that I think that will continue to be a difficult problem is, trying to find the right models and trying to translate preclinical data in ways that are meaningful in a patient population.

Dr. Max Boakye:

Let me read back some recent quotes of yours, and this is in our final moments here. Here are three quotes that you said, and I have a question about that. "It is much better for your data to be correct, than to be the first to report it." Second quote, "You can be an honest and compassionate human being,

and still be a successful scientist and administrator." And the last quote is, "Remaining in contact with your mentors and trainees, has unexpected and unbelievably satisfying rewards."

Dr. Max Boakye:

Given that you've trained nearly 40 grad students and postdocs, and what these quotes mean, do you want to say a word or two about what it takes to become a good scientist, and what mentoring trainees and getting future scientists has meant to you, and how do we do it well?

Dr. Whittemore:

Well, first of all, those quotes, while I did present those in a recent talk, which is where you got the, they are not mine originally. They came from my graduate student mentor, a really wonderful scientist named Edi Hentley at the University of Vermont, and I think those quotes just refer to the fact that you do good science, you maintain your ethical principles both in terms of your science and in terms of your interactions with the people that you collaborate, the people that you train. And the third one, really is my personal experience, is that I have stayed in touch with a lot of my mentors and trainees, and those have been probably some of the most rewarding interactions.

Dr. Whittemore:

And I think that we all try to train our students, and postdocs in our image. It's much like children, you expect them to be better than you. And to see their successes as they move forward, you smile and hope that you had a little bit of a contribution towards that success. And I've had some very successful trainees.

Dr. Whittemore:

I think that's a really important aspect of what we do. Trainees do the lion's share of the work. I mean, once you leave early assistant professor levels, you're not allowed as much as you used to be, and you've got to be open to new ideas, and they bring them and it takes a lot of work to train them. You're not always successful with all of them, but it's a really important component and we're not going to sustain our science without training the next generation. And then realistically, they are a collection of your postdocs and graduate students, their contributions collectively are far going to exceed your own. And it's what we can do as scientists, to keep the field moving forward. It's a really important component.

Dr. Max Boakye:

If I gave you a magic wand now, what would you do with it?

Dr. Whittemore:

As I had mentioned, I certainly would like to understand stem cells. I think the one thing that disappoints me the most now that excited me the most two or three decades was... a little more than two decades ago I guess, was the first identification of CNS stem cells. I would love to be able to make them do what you'd like them to do, to replace injured tissue. That's still off in the distance. There's incredible work out there that people are describing new ways in which these cells behave, but to try to understand how to control that and put it in a way that would be therapeutically the most beneficial, is still I think a long way off in the future.

Dr. Max Boakye:

Wow, that's amazing. This brings us to the end of the discussion with Dr. Scott Whittemore, one of the truly distinguished spinal cord injury scientists in the world, who has led the Kentucky Spinal Cord Injury Center for the last 30 years. Scott, I really want to thank you very much for taking the time to speak with us about your experience in the field. Thank you.

Dr. Whittemore:

Well, Max, it's been my pleasure. Thanks for having me.

Speaker 1:

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