Voiceover:

As neuroscientists, our research is at the heart of our everyday lives. From designing experiments to analyzing data, to writing grants and journal articles, this work brings us closer and closer to understanding the most fascinating and mysterious part of our bodies: the brain and nervous system. But for neuroscience to have the greatest possible impact on our world, it must be rooted in a strong foundation of rigorous principles. You're listening to Pathways to Enhance Rigor: A Collection of Conversations, where neuroscientists come together to discuss how to embed rigor into every part of the scientific process. This podcast is a part of the Society for Neuroscience's Foundations of Rigorous Neuroscience Research program, or FRN, supported by the National Institute for Neurological Disorders and Stroke. FRN is designed to inform and empower neuroscientists at all career levels to enhance the rigor in their research and the scientific culture at large.

Voiceover:

In this episode, we hear from Drs. Michael Lehman, Ghazaleh Sadri-Vakili and Tanita Casci. They discuss the critical importance of incentivizing rigorous research to shape modern scientific culture, as well as ways neuroscientists at any career level can advance rigorous research practices to invigorate the field. Without further ado, let's hear about Creating a Culture of Rigor.

Ghazaleh Sadri-Vakili:

Good morning. My name is Ghazaleh Sadri-Vakili and I'm an assistant professor of neurology at Harvard Medical School. I also direct a laboratory at Massachusetts General Hospital, and our work in the lab focuses on neurodegenerative disease where we work to develop new therapies and also, identify viable biomarkers. Therefore, rigor and reproducibility is critical and our work in the lab, given the translational nature of our studies, if there are any mistakes on our end, they will lead to costly and failed future clinical trials.

Tanita Casci:

Hello, I'm Tanita Casci. I'm the head of research policy at the University of Glasgow in the UK. I'm also the institutional core lead for research culture and also, the co-leader of our new lab for academic culture. My background is in genetics. I spent 12 years as a commissioning editor in genetics and genomics. So I have a background in publishing as well. My current role; I oversee the implementation of the research strategy across all the disciplines in the university, and that includes things like recruitment and researcher development and research evaluation. So rigor is fundamental to what I do in research because it means that researchers can succeed in their careers and if they succeed in their careers, we as an institution succeed in our research.

Michael Lehman:

Hi, folks, I'm Mike Lehman. I'm currently director of the Brain Health Research Institute at Kent State University. I'm an active neuroscientist. I studied neuroendocrine systems and in the past, I studied circadian rhythms. Scientific rigor is important to me, not only from the perspective of my own work, but from my experience serving on NIH and NSF study sections for nearly 30 years and also, in my roles as a senior editor at a number of neuroscience related journals. So I think this is a really important topic and I'm looking forward to having this conversation.

Michael Lehman:

I really view rigor as being the core element of how we maintain quality and reproducibility in science in what we do. I think there's lots of reasons, and my colleagues here can expand on the reasons why that's important for us as scientists and important for us as a society to do that, but it really is at the core of what we do and the core of the value of science to all of us.

Ghazaleh Sadri-Vakili:

So, as I mentioned earlier, my lab is focused on neurodegenerative disease, diseases, such as, ALS, Huntington's and a rare disease known as X-linked dystonia-parkinsonism, or XDP. So all of these are devastating and the patients don't have a lot of time. So for our translational projects in the lab, we use a lot of post-mortem human samples, as well as biofluids in order to find new therapies or viable biomarkers. These samples are very precious, they're irreplaceable, and therefore, we have a responsibility to the patients and their families that every experiment that we set up is accurate and reproducible, that we have to put in the extra care and time each time that we want to use these samples.

Ghazaleh Sadri-Vakili:

We also screen FDA approved compounds or novel therapies with the hopes of translating our findings from the bench to the clinic. Therefore, you can imagine how critical it is that our data is accurate and reproducible. As you imagine, know there are millions of dollars and a lot of time that's wasted on failed clinical trials for neurological disease that were based on faulty and non reproducible preclinical data. So we take that very seriously in the lab. Thinking about ALS in particular, which is a very fast progressing disease, it's really important for us to produce the right data, reproducible data that's accurate in order to set up the right clinical trials following up based on what we find in the laboratory. So it's something that we are very conscientious of. Any failures on our parts is going to be very costly.

Tanita Casci:

I think what Ghaz says in the clinical arena is true for the research endeavor more broadly. We have as a duty to advance knowledge and benefit society and develop the next generation of researchers. We have an obligation to do that generally with public funds or with funds from charitable foundations, and also sufficiently to do that is to use those funds wisely to identify the most important questions and address them with the appropriate tools. Let's also not forget that research is a collective endeavor. The rigor that we apply and the rigor we share allows all of us to build on what others have done. So we manage collectively to progress that knowledge and to progress that benefit to society.

Michael Lehman:

I think one other reason that rigor is important to us is that it really, again, reflects the true nature of science, which is not neat and clean all the time. It's messy. For every discovery that we make, there's lots of dead ends and roads that don't lead anywhere, and that negative data and understanding what doesn't work is just as important as understanding what work. Giving the public the full messy story, rather than the selective neat one, I think is really key to basically portraying science the way it is and its value to us.

Tanita Casci:

Yeah, I think that's a very important point too, that there isn't a single linear route to generate results. By not portraying research in that way, w we're actually attracting a greater diversity of people and talent to research, which is exactly what we need. It's built on rigor. The other important factor to put

into research and science is creativity. The more ideas and perspective we attract to research, the better that research will be.

Ghazaleh Sadri-Vakili:

Okay. So I like to go back and just expand on why it's important to publish negative results. I think that we develop many hypotheses in terms of what goes on during a disease process, and it can't be true that all these hypotheses are equally relevant or true. Therefore, it's really important, and I think even more so, in order to be able to cancel some of the noise and to really be able to focus on the real pathways, proteins, or issues that are occurring. So we can't do that without having negative results, and we should pay very close attention to them because they could end up being even more critical and they have huge value, especially in the context of developing therapies.

Ghazaleh Sadri-Vakili:

I think the way that the culture is set up currently in terms of publishing, we do not give credit to negative findings. Unless you have a perfect story wrapped up with a beautiful bow on top, I don't think people care to read these findings. I'd like to advocate that there is room for negative results and that we should pay more attention to them, especially in the realm of drug development because biology is messy. It's not a perfect linear line and there's a lot of variability. So I think we can do better in that sense.

Michael Lehman:

Ghaz, I think this also gets back to the emphasis on the importance of research for again, the treatment of the disease and its impact on patients and particularly in scenarios where that information is also important in terms of getting it rapidly to clinicians and practitioners where we have to be sure about whether we're actually conveying information that is accurate and correct. Sometimes knowing what doesn't work is just as important as knowing what works, but rigor is a key part of being able to basically maintain that confidence and the confidence that we want our patients to have, the confidence that we want each other to have in trying to deal with these sorts of problems.

Tanita Casci:

Yeah. Ghaz mentioned a culture, a research culture of openness and transparency and showing your workings is actually part of a rigorous culture. If you're going to make it open, then you will think much harder about how you've done your research, about your design, about how you've communicated, what you are doing. So by encouraging openness and sharing, we are actually indirectly encouraging rigor, as well as showing our perhaps more junior colleagues that research isn't just about the end point. It's just as much about the process, an openness at all stages of the research process. It gives them more prominence to not just what is done, but how it is done.

Tanita Casci:

One thing we need to do as part of that is to widen our definition of what excellence means. It's currently being equated with a certain type of researcher role, or a certain type of research contribution, or a certain type of output, and that we need to dissolve that. We're going to be doing research much more collaboratively than we ever did before. So if all you're aiming to be is the lead, then I'm afraid the chances are getting ever slimmer. So part of that rigorous and embracing scientific culture is to acknowledge that are different paths to being a researcher and different contributions that

one can make to research, and that each of those contributions needs to be valued as part of the broader endeavor.

Michael Lehman:

It's really, as Tanita was saying, it's really emphasizing the culture of science and how we think about it. That really means that it's part of a key part of the way in which we train our students, that we train the next generation of scientists to think about what they're going to do. And again, what they're going to do in the context of being good for science and research overall, not just individual researchers, not just their individual institution or even their own area of research, but how they're contributing to the overall culture.

Ghazaleh Sadri-Vakili:

I'd like to add that I think in order for it to become part of our culture, we need to start early. So starting with the summer students, even that come to the lab, the undergraduates that come to the lab and just keeping in mind that even if people were trained at another institution or have laboratory experience, it might not be the same way that you want it to be done. So what we do in my lab, for example, is I just make sure that any new person that comes to the lab, I sit down with them, we go over our protocols step-by-step, using the whiteboard even sometimes when we have to, and just really talk about how experiments are done in my lab.

Ghazaleh Sadri-Vakili:

The other thing that we do is I usually ask a new person to replicate some of the older findings, even some of the published findings that we have in the lab and that always makes the new person feel better when they can reproduce them and it definitely makes me feel better knowing that this data was reproducible, that we had done good work and that we put something that was real, a real finding that we shared with the rest of the community. So I think just starting early, training people the right way, and making them realize that everything they're doing has a meaning, asking your research assistants and students, your post docs to really take pride in all the samples they're handling, where they come from, what the bigger goals are, how this could lead to discovery of a biomarker or a new drug going into clinic and just really taking on and sharing the responsibility of doing this together.

Tanita Casci:

Also, one thing you've emphasized is that rigor, you don't come into a lab or a job knowing what it's about. It needs to be taught and it's important. There are costs to learning what rigor is about. You could just be getting on with it in a sloppy fashion, and you'll probably get somewhere quicker. You just wouldn't get anywhere sustainably, and that's what we're doing here, is to elevate importance of rigor and see, "No, we need to stop and think and think this through and discuss it," not assume that people know, but make it a priority for anyone entering a lab or a new environment to see this is the way we do things right here and we value things done properly, and the work will be acknowledged whichever we're ends up in terms of the ultimate outcome because the process was robust.

Michael Lehman:

I think our perspective of rigor being part of scientific culture also means that when we evaluate science, we tend to, and I'm thinking now, again, specifically a NIH study sections where we look at specific projects and are they rigorous projects? But what we really ought to be doing as well as really looking at the careers of scientists, the careers of researchers and asking, are we rigorous in our approach to

science, including our training of others and rigorous in terms of our interactions with colleagues and the way in which we review grants and publications from each other? So really, it's a cultural imperative and it's one that rests with us as individuals and as colleagues and community.

Tanita Casci:

Yeah. One of the things we perhaps should move towards is acknowledging that the core role of a researcher is to communicate their findings, benefit society, but also to develop people. So a researchers track record should be assessed on their success in each of these three domains and we haven't given as much priority to that last one, which is not during developing your growing the next generation of scientists. Maybe when we are reviewing grants in particular or tenure applications or job applications, that should be more prominent and we need to have ways of assessing that.

Michael Lehman:

Yeah. That's great, Tanita. I think the idea of including rigor in portfolios, as one puts it together, is a great way of really emphasizing it and bringing it to the forefront in terms of what's valued. So I think that's a great idea.

Tanita Casci:

And also gets us away from that notion that research is individualistic. It's not. Research is done by communities, and those who know most about how research has done, or what networks can be exploited need to give that back to their communities because that's how we, together, make- [crosstalk 00:17:27]

Michael Lehman:

Absolutely true. It's a team sport.

Tanita Casci:

Yeah. There's no manual of rigor. It's an evolving practice. So the most important thing you can do is acknowledge that perhaps you don't know, and that in dialogue with others, you can reach the correct design or sample size of power calculation, whatever it is it needs doing, and everyone should acknowledge, they don't have the answers. Answers are sometimes developed in dialogue with others.

Michael Lehman:

I would also want to emphasize that rigor really applies to all types of research and to scholarship, and it doesn't matter whether you're doing experimental manipulation studies, whether you're doing data mining or gathering or a case study, whether you're doing scholarship or meta analysis of literature. Rigor is inherent in part of all of those types of activities. I think very often, we have a pretty narrow view of the types of science and projects that rigor that would apply to and that having a bio statistician would be a useful for.

Ghazaleh Sadri-Vakili:

A great example of that is writing a manuscript and getting it ready for publication. The first draft that you have written on your own, if you go back to it, you're going to find many things that you want to change or do better. You ask your coauthors to read through, they'll find some other mistakes or ways of phrasing things that sounds better. So that's also a rigorous process. We know that it usually takes

around 20, 25 drafts before you have that final grant or manuscript that you end up submitting and being happy with. Thinking about on those terms, I think it's those layers and layers and the numerous eyes that are scanning your papers and grants that ends up making it better, and that's a rigorous process. So it's the same type and quality of work that we need to be applying to what we're doing in the lab as well.

Tanita Casci:

And also acknowledging that openness to be critiqued takes time-

Ghazaleh Sadri-Vakili:

Absolutely.

Tanita Casci:

... but we're taking the time to make the product better.

Michael Lehman:

Well, maybe as a transition to starting to talk about ways in which we can bring about a consideration, more consideration of rigor in what we do is to talk about how rigor is involved in our evaluation of science of others in peer review of grants and peer review of publications. I think one of the things that I've come to recognize there is that we, and maybe this is again, part of the issue is that we come to this idea of what is rigor from very different perspectives. I think acknowledging that we have much to learn from each other and that it's really not a black and white area in many respects is part of the challenge. I think that that's something that journals and funders need to recognize that it should be part of an ongoing conversation that individuals have, who are reviewers as to what constitutes the good elements of rigor and reproducibility or...

Tanita Casci:

Yeah, and that alignment between what the institution is evaluating in research and what funders are evaluating and what publishers are looking for. That alignment is absolutely crucial because as institutions or as funders, each of us can do their own thing. We're at liberty, in some ways, to make her own rules, but the research, the whole field advances much more smoothly if it does so in unison so that the researcher, whatever they turn, they see the same values being upheld. It's not so fanciful to imagine that we might be able to achieve that.

Michael Lehman:

Yeah, I think so. I think one of the developments in our scientific world in the last few years has been the increasing emphasis on pre-registration of data and the use of preprint servers, and the expectation that funders have for us to do that. I'm not going to say that all preprints are equal in terms of quality or the review that goes into submitting data and pre-registering data is all the same, but again, it enters that as part of the conversation. It emphasizes that need. I think that that's a really good thing for us to do, both with our colleagues and our institutions and in conversations with our funding agencies.

Tanita Casci:

There are so many platforms that can be used to be open and transparent, whether that be the data repositories, software, the pre-prints, the different journal formats, like preregistered reports.

Ultimately, to acknowledge that different researchers do research in different ways, what we would really like to see in curriculum is a commitment to open practices and then for the individual to outline how they've taken advantage of all the different routes to make their work open, transparent, shareable, and allowing others to build on it. We don't have to be prescriptive about how openness is embraced. It's just, has this thought process run through this person's career? And if so, please describe how.

Michael Lehman:

So I think a core challenge here, for our institutions anyway, is how do we get our senior leaders at those institutions to focus again on what's good for our careers and not just again, the metrics of grant funding or high-impact publications, and again, really see it as a long-term investment in science that benefits society, rather than individual projects or individual income bottom line, that sort of thing? I'll admit to you, that's a real challenge at all. Of the institutions that I've been at, I'm not sure about you guys, having those conversations with our senior leadership is not always easy.

Ghazaleh Sadri-Vakili:

Yeah. I think in general, we need to change our culture and flip the script, as you may say, but it is a difficult thing and that's why starting smaller with labs and training the next generation, I think, is how we have to go about this, right? So if you start small and then you start making change in your own lab and your neighboring labs, then you start to discuss this across the department before it goes up to the institution or the hospital where I work, I think those are the steps that we can take. We all sit on study sections also, perhaps starting these conversations with our program officers and the individual institutions and foundations that we work with. I guess we should start having these conversations as a society because this is...

Ghazaleh Sadri-Vakili:

I don't think that we're on the right track. I think a lot of time, which is even more precious than money and money is wasted, and as I said, in some case, like working on ALS therapy development, I don't have a lot of time and I need to know that whatever I'm reading about, whatever papers published or data I'm looking at, I can trust that data in order to make the next steps and next decisions to do the right thing for the patients.

Michael Lehman:

I can't agree with you more, Ghaz. I think working at a grassroots level is really a great way to be able to really start to change culture. I'll give you an example of that with respect to peer review of grants at NIH. NIH study sections on which I've served and I've chaired, often the reviewers come in without really, again, a very clear idea of what do we mean by rigor. And in fact, what are the good elements of peer review? So having some sessions to essentially help to share thoughts about responsible conduct, the peer review actually turns out to be very important and very effective.

Michael Lehman:

For one of the study sections that I've just finished my term as chair of, we actually started to do things which you might characterize as a school with peer review where we introduced topics, this was outside of the study section, to talk about issues exactly like, what is rigor and how do we measure rigor and what does it mean for us? I think that the more that we do that again, at a grassroots level, we can

basically change the process. My hope would be if we changed at the level of peer review for grants and journals, that for our funders and for our institutions, they will start to pay attention to that as well.

Tanita Casci:

Yeah. They'll pay attention to those drivers that are either coming from national research assessment exercises or from the leading funders or the richer funders, but we can also have that conversation with senior leaders on other grounds as well. We want as much as possible for our researchers to be visible to their communities. So communicating early widely and openly achieves that aim. Visibility is good for one's career. It's good for one's reputation and for the connectivity that they will develop to develop other research, and institutions should be interested in that. Holding on to information, releasing it in a closed manner is not the route by which researchers will be seen, viewed, respected, hopefully, by their peers. So that connectivity is something institutions should be interested in as of now, regardless of the more scientific rigor aspects of the discussion.

Michael Lehman:

Yeah, certainly a rigorous approach to translational and clinical research is really key for academic medical centers to really connect the dots and really show how they're improving public health and society health in their areas. So they have a stake in rigor. I think we have to be more of advocates for that in our individual institutions and be willing to step up and say that this should be an important part of our culture at our university, at our medical center, at our community hospital.

Tanita Casci:

We did this at Glasgow, actually. We revised our professorial, in our case, promotions criteria to do many things, but two that are relevant here. One is to require evidence of collegiality within those promotion application. What that meant in practice was, give us an example of how you have supported others to succeed in each of the various activities that we were evaluating research. Then the second innovation was to require a description of how an individual had embraced the open research agenda. So how have you shown a commitment to open research? We give examples of what they could do. So both of those things, I think, uphold the values that we're talking about here. We're not talking about rigor directly, but indirectly, rigor is what we're rewarding.

Michael Lehman:

Well, I think that Tanita touched on this right now when she talked about how, again, how we evaluate our careers and expectations when we hire people. I think that in an ideal type of scientific research environment, this would be a core expectation that we would have and hold on to, and that we wouldn't just take lightly. We would mentor our students. We would mentor our faculty. We'd provide them with the incentives to be able to incorporate rigor in all aspects of their research.

Ghazaleh Sadri-Vakili:

In an ideal world, I think as scientists, we know that our data needs to be reproducible. However, there are a lot of things that get in the way. So I would say in my ideal world if we had more funding, then you would know that you could be secured that you could set up all the experiments you needed to in order to demonstrate that you have a real finding. So I think in a lot of cases, it's not that people want to cut corners. They just don't have the means to do it. So in that ideal world, people would get paid the right amounts to do the experiments, we would have all the funding we wanted to. That would put people's minds at ease and they could then conduct their experiments with the right type of training. If this

becomes our culture, then I don't see a reason why we couldn't reach this ideal world where everything's reproducible and rigor has been applied across science.

Michael Lehman:

I couldn't agree with Ghaz more about the importance of funding for this, but I would also say that it's really the type of funding. It's funding careers of scientists. I'll draw on part of my past when I was a chairperson at a university in Canada where one of the Canadian funding agencies was committed not to specific projects, but rather to the long-term support of scientific careers. I know that a couple of NIH institutes are supporting the same type of mechanism right now. If in that career support, you emphasize, again, reproducibility, it means that you're giving those investigators the resources to be able to do all the experiments and have a large enough sample size to be able to basically follow and do experiments rigorously with a great deal of confidence.

Tanita Casci:

Yeah. I think back to what we were talking about in terms of bringing in the different types of expertise, I would like an environment in which all contributions are valued and acknowledged because no single individual will know the right thing to do. Many people do pitch in and contribute. And yet, credit is still concentrated in the hands of too few, and that's not a sustainable way to develop a healthy research culture. The only way you get people to collaborate or incentivize them to collaborate is to acknowledge their contribution, and that includes our technical staff, and it includes our students, and it includes perhaps those who are less research intensive in their activities, perhaps those people who comment on your drafts. So to really generate that sense of community where each contribution to research that is important is treated as if it's important and therefore, the conversation away from the quick fixes and the shortcut proxies and more towards the content of what is actually being generated.

Michael Lehman:

Tanita brings up a really important point that I just want to emphasize as well. We've been talking about the team approach to science here. That team doesn't just include the PI, the principal investigator in the lab or the students. It includes the technical staff, in the case of clinical research, it's clinical coordinators, it's the patient groups, it's a whole team of individuals and everyone has to be engaged in that. I think that rigor stretches across all of that throughout all members of the team. So that's a really important element to get forward and really, to make part of how we do this sort of science.

Tanita Casci:

I think just a really important point I'd like to make is that most people listening who'd be nodding their head, go, "Yeah, yeah, we really want that. Of course, we want a better culture and a more rigorous culture," but in the back of their minds, they're thinking, "Trade off." Okay? "There's a trade off here. So either you can be inclusive and team-oriented and rigorous, or you can do, 'excellence.'" I'm going to argue really strongly that is absolutely the wrong mindset. The scientific culture that we put in place is the vehicle by which we will do excellent research and more than that, it will allow more people to access that excellent research. So that is the mindset that we need to change because if we succeed in our ideal culture, what we risk failing at is bringing together the culture with what the culture is enabling. These are not two separate parallel strands, the culture is the environment by which those outputs, that research, that benefit to patients is produced.

Michael Lehman:

Let me just say, amen.

Tanita Casci:

Yeah.

Michael Lehman:

There's no paradox there. It really is part and parcel of the same thing. So thank you, Tanita.

Ghazaleh Sadri-Vakili:

Yeah, that was perfect. I would just add that because we are in the environment of team science, which I really love and thrive in, everyone is an expert in their own area that they're bringing to your project. If each of these people, let's say the biostatistician, they know what the kind of rigor they need to apply to their statistical analysis. So if they come in and they are doing that, and the research assistant in the lab handling the samples needs the kind of rigor they need to apply to what they're doing, if we all know the parts and what we need to bring to it, then I think we can build these very strong teams where we trust each other, we're open with each other and we can communicate and talk about these things openly and really come to some good consensus and get some really important work done.

Ghazaleh Sadri-Vakili:

Now, whether or not it ends up being positive results or negative results, at least that you can trust what's in front of you and that you are still adding to the knowledge base, you're adding to the field, and I think that's the way what we have to work in order to be rigorous and produce reproducible data.

Voiceover:

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