Steve Lewis 00:10
Welcome to Speaking of Mol Bio, a podcast series from Thermo Fisher Scientific about molecular biology and its trending applications in life sciences. I'm Steve Lewis, and today we have a special crossover episode with another podcast at Thermo Fisher. Jordan Ruggieri is the host of the Absolute Gene-ius podcast, and on today's episode he shares what he's learned from interviewing researchers across many disciplines. He also explores the innovation shaping the future of molecular biology, the role of AI, and the grit and curiosity that drive scientific careers. It's a fun, wide-ranging conversation about technologies, the people, and the stories behind modern molecular biology. We start with Jordan telling us a bit about Absolute Gene-ius.

Jordan Ruggieri 01:04
Absolute Gene-ius is really all about the scientists that are doing the science, right. And initially we had set it up to talk about a lot of our dPCR applications and dPCR technologies and really dive into how digital PCR is being used in amazing research around the globe. And from there, it's actually really evolved into talking about the different molecular genetics and genomics techniques that are used by scientists to get answers to their questions. And we talk a lot about the research that's being done, and why it's so impactful, but also around the techniques and technologies that are utilized, and how it helps get from, you know, step one to step two, and how it answers some of the basic questions. We'll talk about the entirety of the toolkit, from PCR to qPCR to digital PCR, to sequencing, to sample prep, and some of the obstacles and challenges that scientists have around going from a sample to getting an answer and what the technologies enable them to accomplish. We also have a career journey section of the podcast to talk about how the scientists got to where they are, their background, and advice for anybody looking to do something similar or, or get into the field. And it's really fun. There's a lot of talk about failures in the lab and challenges that they've had and things they've learned. And we do a lot of laughing on the podcast. It's, it's, it's a ton of fun.

Steve Lewis 02:41
One of the things that we love about your podcast as well is that it really underscores how universal molecular biology methods are in all of your guest's work as well as across the life sciences landscape.

Jordan Ruggieri 02:58
Yeah, it really is universal. I mean, you know, anybody that is, you know, looking at anything molecular is doing some sort of PCR, right. And it's just, it's, it's, it's across a lot of applications, and there's ways to tweak it, and different ways of approaching it to answer the questions that that scientists are looking to answer. But in reality, if you're using DNA or RNA in some way, shape, or form, some sort of PCR technique is and sample prep are going to be utilized in your in your workflow. And so it makes it a lot of fun. We get to see the different ways that they use them and also learn about some incredible research from, you know, cell and gene therapy all the way to microbial studies on the Mariana Trench and expeditions to Antarctica. That was a fun episode, expedition to Antarctica to drill sediment cores from the bottom and ice cores and look at the ancient microbes, actually, was what they were looking to do there. So learned about how they used a toilet brush to try to get samples in an emergency from autonomous vehicles that went down to the bottom.

Steve Lewis 04:07
Like a cell culture tool on a macro scale.

Jordan Ruggieri 04:11
Yes. So that was, that was a fun episode, for sure. And I mean, we talk everything. We talk plant science, we talk microbes, we talk, we have said, AAV cell and gene therapy. You know, we talk infectious disease, the broad spectrum of research. It's a lot of fun. I think you know something for me, I am, I have a science background, right. I spent time in the lab. From there, went into the biotech field in R&D and work to create a sample prep technology that could extract genomic DNA from any sample. Had a really unique opportunity to move into marketing, and I followed my product into marketing. It was actually the first product I launched from a marketing perspective as well, and then from there, I've been in a marketing role ever since. But, you know, just being able to talk and hear about the science that's going on, the ways that different scientists are impacting the globe, and the amazing research that's being done utilizing some of the technologies I was part of designing at some point, right, has been a really fun experience.

Steve Lewis 05:24
Yeah, it's very, very rewarding to be able to highlight the guests and learn about the different ways in which the molecular and scientific and cellular level technologies are enabling just incredible advances at an unbelievable pace. Do you talk a lot about the future of science on your podcast, too?

Jordan Ruggieri 05:50
Yeah, we, I mean, everybody has a different perspective and are working with different, you know, applications in mind, and in different fields. And so we always ask, you know, what does the future look like, and what are they excited about? And it goes from anywhere to, you know, how we approach helping people and helping communities. Anything from, you know, infectious disease research, or, you know, gene therapies for rare diseases that are being researched and promising results there to, hey, I'm super excited about different technologies we can bring in the lab, from what NGS has enabled to what digital PCR has enabled in terms of absolute quantification and allowing, you know more accurate answers and different ways, different, different ways of thinking. And it's just cool to see. You know, the future of science is bright, and we have brilliant minds that are that are looking at things and approaching these different applications.

Steve Lewis 06:53
So far in our conversation, one of the things that I'm struck by is how PCR really does underpin the modern landscape of all of the life sciences, molecular biology, and yet, there are so many flavors of PCR, right. As a core technique, and there's a there's a large set of instruments across different applications and workflows. You mind just jogging my memory about the different flavors and what benefits they provide in different situations?

Jordan Ruggieri 07:29
So talking a little bit about PCR, you know, there are three ways I kind of look at PCR. We have endpoint PCR, kind of the more traditional PCR that we think of you know, with the, with the bands on a gel, right. We have real time PCR, or quantitative PCR, which is adding fluorescence into the different

cycling parameters and taking metrics at the end of each of those cycles to look at different amplification events and help quantify the amount of nucleic acid. And then you have digital PCR, which is all about having and many, many thousands of PCR reactions, kind of a digitization of PCR, where you have thousands of these reactions happening at the same time, which enables really precise and absolute quantification to a whole other scale, right. And each of them have their different use cases and ways that they can be used, kind of together, to help move from point A to point B, or help look at various things, depending on what you're trying to answer. But they're all amazing tools in a toolbox that help scientists look at DNA and RNA and be able to answer questions on anything from genotyping to gene expression right and quantification of mRNA across the board for a variety of these applications.

Steve Lewis 09:00
So it's not like, once you're a qPCR scientist, that's, that's your technique? They have different use cases, and I would assume different costs associated with each approach as well, right?

Jordan Ruggieri 09:16
Yeah, that's very true and accurate to say. I mean things like endpoint PCR, where you're looking at, you know, an amplification event with maybe qualitative quantitation. You're more looking at the size of the bands, or, you know, the thickness of the band. Or did it actually amplify where I thought it would amplify? And that's really good for, you know, you don't necessarily need an actual quantification number, or you're doing things like cloning, and it's definitely less costly, right, to run those. More towards digital PCR, where you need a very accurate and precise quantification number. And in that case, while it is still technically endpoint PCR, you're not looking at an amplification curve, the ability and the addition of fluorescence and the digitization over tens of thousands of PCR reactions happening. You could theoretically get one molecule of your target in the wells there, and it's a straight count, right. They count 1, 2, 3, 4 targets, right, that have been amplified in those wells and can give you a precise copies per microliter metric without the need for a standard curve even, right, that are common for qPCR. And then, obviously, for qPCR, you get the you know, you can actually look at what's happening within the amplification. And while you can still quantify, and you can still create a standard curve to help you quantify, you can actually look at things like melt temps and did you get primer dimers or any other types of things that might indicate some quality issues with your runs to make sure that you're actually looking at the target that you want to amplify.

Steve Lewis 11:01
So in some workflows, I imagine they are complementary. I'm thinking about possibly gene expression analysis?

Jordan Ruggieri 11:11
Yeah. I mean, we see this all the time with gene expression analysis, where these technologies are not used independent of each other, even or even as individual steps of a workflow. There are times where digital PCR might be used for really rare targets or looking at really subtle fold changes in differentially expressed genes, where maybe you're looking at one copy right or a handful of copies, and you're trying to look for that needle in a haystack event. But it's also because it is definitely accurate and absolute way of quantifying, we do see times where it's actually used to quantify the standard curves

that are used for qPCR. So you can get a more accurate standard curve used utilizing digital PCR, you get a better count, which helps your qPCR runs become even more accurate because you have a more accurate standard curve. So you can move between the two technologies to, you know, again, just help, depending on your workflow, your budgets, the questions around, you know, if it's gene expression, if it's maybe something that is more targets you're looking at 50, 60, hundreds of copies, right. And by that, I mean, if you're looking at more copies, hundreds or, you know, 50 or more copies of a gene where qPCR might work and has a broader dynamic range. You know, you can use dPCR for your standard curves to make sure you're getting more accurate qPCR runs. So there's a lot of times they're used interchangeably or used together to help get better answers and a better picture of what's happening within the biological sample that you're looking at.

Steve Lewis 12:58
Speaking of samples, how does sample prep play into each of these technologies?

Jordan Ruggieri 13:05
Sample prep is critical, and again, it depends on exactly what you're looking for, but the general term is garbage in, garbage out, right. If you don't have a good quality source of DNA or RNA, you get things like PCR inhibitors and inhibition that happens that can really impact how you're interpreting your results downstream. Even things like soil, right, have polyphenols and different compounds in them that can impact PCR. But you, even still, you can't necessarily always take a sample of something without liberating the DNA or RNA. And you also know that RNA can be very finicky, sometimes you look at it and you blink and it degrades, and that can impact your answer as well. But even things like FFPE samples, if you're working with FFPE samples, where the nucleic acid is going to be more degraded just because of that formalin fixation, you have to take that into account with your sample prep techniques, the quality that you're getting out of it, and then how that helps enable you and your analysis when using something like a PCR technology. So if you're not thinking about sample prep, it's definitely something you should be thinking about in terms of generating good quality results.

Steve Lewis 14:17
And downstream purification, all the way to, I assume, more like agnostic approaches of maybe size exclusion chromatography plays an impact in that as well?

Jordan Ruggieri 14:28
Oh, 100% Yeah. Or even things like cell free or ctDNA, right, or RNA, where you're looking at very small sizes, or, you know, anything that it might be from an exosome, right. Those are all things that they all have their own considerations, not just for PCR, but, like you said, any type of chromatography, size exclusion, or any other downstream analysis.

Steve Lewis 14:53
What's the most interesting story you've heard about PCR, maybe on your podcast?

Jordan Ruggieri 14:58
Oh, that's a tough question. And, you know, it's, it's funny, it's, it's not, it's not about PCR, per se, it's, it's about the stories of the research that's happening and the broader impact of those techniques, right.

I think those are really where the interesting things happen. I mean, we have things like, we like to talk about lab fails and things that the scientists have messed up in the lab. And, you know, everybody's human, and everybody makes mistakes, you know. PCR interesting stories, or funny stories about maybe not adding the template, or using the wrong Master Mix, or using the wrong assay, and they spend weeks trying to troubleshoot of what happened, and why didn't I get the amplification, or why didn't it work? Why did I have failed runs and they realized it was a pipetting error. Or they pulled from the water source instead of the actual sample. And those are always interesting and funny, and you know, they seem to be very common things that happen in the lab. But the real interesting stories happen from the results that PCR enables, right and that's really where, I think the impact is made is, is that broader answer that the scientist is trying to achieve. Think of some of the stories that we've had, you know, we've talked about transplant research that's happened, and looking at the different markers on transplants, and how that could impact how a an organ is accepted or rejected by a, you know, a transplant subject and recipient, and the research being done there. And you know, while it's PCR And PCR is being used, the broader impact is saving lives, right. And that's the research that's being done, and that's actually where what I find the most interesting.

Steve Lewis 16:50
You touched on both environmental and individual components that the science that we talk about on our podcasts really play a role in. Immunology is one that's so interesting to me. And you alluded to probably graft versus host disease, I would imagine, with that transplant story. Was that a really interesting guest?

Jordan Ruggieri 17:15
Yeah, very interesting guest. It was. It was also an HLA, right. And some of the markers that are there, but depending on the cell type, right of how an organ might be rejected or accepted by a subject. What made that unique is the guest, actually, her husband had, was in need of a transplant, and was on the list for a transplant, and so the research that she had been doing her entire life was coming to play in a very personal family matter, right. And she was able to see the direct result of some of her research on the impact of a direct family member that needed a transplant.

Steve Lewis 17:54
You don't really get to see that kind of direct and like personal impact too often. That's an amazing story.

Jordan Ruggieri 18:00
Yeah, it was incredible.

Steve Lewis 18:01
For your other guests, what are you hearing that excites them behind the scenes?

Jordan Ruggieri 18:08
You know, there's so much. I think it's the excitement happens along the scale of innovation that that is currently happening, and the repertoire of tools that are at their hands. There's a lot of conversation even around AI, and that's a hot topic at the moment as well, is how AI is enabling the next round of

scientific discovery and enabling tools to reach a much broader impact and more significant impact. But it wasn't that long ago that PCR was happening in water baths, right. And you had individual tubes, and you had to move them manually from one water bath to the other. And so when you look at the pace of scientific discovery from 50 years ago, 100 years ago, to where we are now, the discuss, the level, the pace of innovation is incredible. And it's enabling discovery at a level we've never seen in human history. And so there's a lot of excitement around, you know, even digital PCR is newer on the scale of new innovations in the field of PCR.

Steve Lewis 19:21
I can still hear the ice machine from my lab days.

Jordan Ruggieri 19:25
I didn't come from the from the days of water baths. But we've definitely talked to guests that that have vivid stories of standing there for hours at different water bath amounts, and, you know, trying to determine how long it needed to be there, and was it good enough, and did they miss the timing or, you know, and it was not that long ago that that was the way of doing PCR.

Steve Lewis 19:47
Do you have any other themes that are kind of linked throughout the episodes of your series?

Jordan Ruggieri 19:52
Because we talk about career journeys and we talk about advice, a lot of the themes come around being determined, not giving up, knowing that failures happen. Failure is always an answer. It happens all the time in science. And knowing that with time, with determination, with grit and the ability to learn how to think and think through problems and problem solve, there's really nothing that can't be done by scientists nowadays, right. And the ability to lean on mentors and have mentors that came before them and can help point out tips, tricks, different ways of approaching to help, you know, solve the problems they're running into or the frustrations they're having in the lab. That is also another common theme, right, that everybody has had a mentor that has really helped move them to the next level and challenge the way that they thought to really amazing science. But it is around that grit, that determination that's needed to be a good scientist, that your experiment is going to fail, probably more than it succeeds. And you have to be able to understand and how to navigate and troubleshoot those failures in order to get the answers that you want.

Steve Lewis 21:17
Resilience, creativity, critical thinking and the support of those who come before you all sound like really great themes. Now for you, what have you learned throughout this series and maybe in your role and time at Thermo Fisher?

Jordan Ruggieri 21:36
I've learned a ton. One, I never thought I'd be doing this. I went to school to be a dentist. That's what I was determined to do. I took the DATs. I had my letters of recommendation. But, you know, for me, I had to come to terms with I didn't enjoy it. I spent tons of times in dental offices, and, you know, making observations that I don't think I would have enjoyed that pathway. So even looking at that right, and

going into R&D and doing research and then moving into marketing, if somebody would have told me, you know, when I was in college, that I would be doing marketing and I would, I would be the host of a podcast, I would have laughed at them, right. There was no way that was not in my I knew nothing about marketing through school. Never took a marketing class. And ultimately it is the most rewarding thing I think I've ever done, right, in terms of sharing the stories and impact that science has on the globe.

Steve Lewis 22:36
I really love that message overall. Jordan, it's been super cool getting to know you over the course of our crossover episodes. I really appreciate you taking the time with me. We always ask two questions to kind of wrap up our episode. So my first one is, what has been the key to your success?

Jordan Ruggieri 22:58
A great question as well, and I think I talked about that a little before, is trying to figure out what I enjoy, and following that path, right, has been critical for me. Being open to new opportunities, exploring different things. You know, I went from wanting to be a dentist to going into the lab to getting my first marketing role. Never would have thought marketing would be what I love, but just being willing to try, knowing that I could always go back, right. But being willing to try something different and learn new things and be open to other opportunities. Be open to failure, be open to sucking at something at first and having no idea what I'm doing, but being willing to continue to grow and learn, I think, is critical to my success.

Steve Lewis 23:50
Love it, and I think you rolled into that answer. The second question is, what you would advise early career scientists do while they are early in their career, and I think you covered that wonderfully in that answer.

Jordan Ruggieri 24:07
I would also say, you know, for early scientists getting in their career, have a hobby that's not in the lab, right. You don't need to live in the lab. You don't need to sleep on the floor. You don't need to be there till 2am. Mine was photography, right. I love taking pictures. I have a camera. I still take pictures and actually had my own Etsy shop as well you know, for some of those, the photography. But that, I think, in and of itself, open doors to marketing and finding my own path forward. If I would not have had a hobby outside of the lab. I don't know if I would have found something that I would have enjoyed as much as I do today, right. So have a hobby, get out of the lab, talk to people, and go do something outside of the lab that can also help open doors and find you and enable you to enjoy life more and enjoy the work that you do more. That would be my advice.

Steve Lewis 25:04
Love it. Well, Jordan, thank you so much for all of the wonderful conversation and discussion around our favorite topics in molecular biology today. I strongly encourage our listeners to go check out the Absolute Gene-ius podcast. Absolute Gene-ius, love the pun. Jordan, thanks for being here.

Jordan Ruggieri 25:25
Yeah, thank you. And if you love puns, you will love the Absolute Gene-ius. We have puns on every episode, so. Thank you so much, Steve, for having me. Really enjoyed it, and thanks for the opportunity.

Steve Lewis 25:37
That was Jordan Ruggeri, Senior Marketing Manager at Thermo Fisher Scientific and co-host of the Absolute Gene-ius podcast. You can find the show wherever you get your podcasts and there's a direct link to its page on the Thermo Fisher site in the episode notes today. Join us next time for more fascinating discussion about the wide world of molecular biology. Until then, cheers and good science. Speaking of Mol Bio is produced by Matt Ferris, Sarah Briganti and Matthew Stock.