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Steve Lewis 00:09
Welcome to Speaking of Mol Bio, a podcast series about molecular biology and its trending applications in life sciences. I'm Steve Lewis, and today I'm delighted to welcome Dr. Cath Moore to our show. Cath is the chief scientific officer at the Australian Genome Research Facility, commonly referred to as AGRF. There, she uses her 20 years of experience in genomic technologies and biomedical research to help envision a bright future for Australia's healthcare, industry, and more. We hope you enjoy the conversation. We begin by asking Cath to share more about AGRF and how it employs mol bio techniques as part of their genomics services offerings.

Cath Moore, PhD 00:59
AGRF is quite an interesting organization. It's a not for profit, which was actually established over 20 years ago when sequencing technologies were incredibly expensive and we were established by the federal government in Australia to provide the technology platforms to any researcher in Australia who wanted to use DNA sequencing technologies. At that time, it was Sanger sequencing. Since then, obviously, it's moved on to other types of genomic technologies, but my role here as the chief scientific officer is essentially to make sure that the technology platforms that we offer are relevant to the research community today. I've had a number of different roles before getting here. So my path here was probably not a straight one. I did a PhD in molecular genetics, came to Australia to do a postdoc, discovered that academia probably wasn't my calling, and then I actually went into industry. So I was working for an organization, first as an account manager, selling their technologies and all DNA technologies again, and enabling technologies, and then I moved into different roles in that organization, so market development, sales management, traveled around there for quite some time. So I was with that organization for a long time, and eventually, kind of just felt like there were so many different options out there. I didn't really want to just be sprooking [representing or selling] one company's. I wanted to be talking about, you know, the smorgasbord of what was available to people doing molecular biology, and that's what led me to AGRF.

Steve Lewis 02:38
As you've developed in your career across 17 years and through academia during your time there, what have you seen as the biggest change in biotechnology in general?

Cath Moore, PhD 02:51
One of the biggest changes for me is what used to be incredibly difficult information to access has now become really, really simple. My PhD was in molecular genetics, and I was looking at a piece of DNA basically that was 12 kilobases long. And I had conversations with my PhD supervisor, I was like, "You know, I just, can we just, can I just get this sequenced?" And he laughed at me, because at that time, Sanger sequencing was basically the only option. He's like,"This is a PhD. There's no way we're paying for that, that that would be so expensive." And, you know, he was quite right. I mean, it was a bit of a lazy way for me to be thinking as a PhD student to be honest. But now, you know, we can take DNA from a blood sample and within four days have sequenced the entire human gene, the genome of that person. Gathering the information is now really straightforward. It's now the challenge is, how do you interpret it, and how do you understand something meaningful from that information?

Steve Lewis 04:03
As we've, in a way, kind of unlocked more of the puzzle, or kind of, I guess, solved it. You mentioned that it opened more kinds of doors for curiosity. What areas excite you right now?

Cath Moore, PhD 04:19
This is like a puzzle, right. You know, we've got every cell in our body contains DNA, and if you put all of that DNA together, that's our genome. You take one cell, what have we got? 25 billion cells, right? So you take one cell and take the DNA out of the nucleus of that cell and stretch it out. That's like 2, 3, meters long. We can sequence through that in a straight line. We still don't know, though, what happens when we roll that back up into a ball and put it back into the cell? What happens when that DNA is transcribed to RNA? What genes actually are being switched on and switched off, and once those genes have been expressed, what's actually happening to the proteins. And we've got so many pieces of that puzzle to put together. And then you add on top of that, layers of complexity where there are some little things in there that are just slightly changing the way that these things happen. And we don't really understand what's regulating those things either. And there can be environmental factors that can make little changes. And I love the idea of being involved in trying to sort of put all the pieces in place and having proximity to the people that are doing the really incredible research of actually doing that.

Steve Lewis 05:41
I think that's the perfect segue to learn a little bit more about AGRF. Now it spans a few different focus areas, right? Between agriculture conservation and human and animal health. Is that true?

Cath Moore, PhD 05:54
That's exactly right. So I I've mentioned at the start that AGRF was initially established to provide access to these technologies to anybody who wanted to use them. So when we first started out, and probably for our first 10 years, we were providing these technologies to researchers to do academic research, and that's fundamental and crucially important. But as the tools of understanding DNA have developed, and as the researchers that were doing the academic research have published and have learned more, that work has, either by them or by others, inevitably started to be translated. So we started with the human genome. What does that now mean for clinical implication? So what we have at AGRF now is that we've had a key role in helping researchers access technologies that have allowed them to get the basic understanding but now we're moving to the next level, where we're using these technologies to help them translate what's been learned into actual impact, and that might be in animal health, human health. It might be in animal and plant improvement for agriculture. Here in Australia, we have a number of initiatives around threatened species and conservation. You know, understanding what is the genetic diversity out there, and how can we stimulate and ensure that we manage that properly. There's a huge range of different areas now where AGRF is still doing that fundamental academic research, but we're now becoming, you know, partnering with different organizations around specific areas. And if I had sort of segment those, I think that would probably fall into clinical, biotech and pharma, agriculture and aquaculture, and probably conservation and primary industries type work.

Steve Lewis 07:54
And is your organization early adopters of new technologies, oftentimes?

Cath Moore, PhD 07:59
Yeah, yeah, we are. So certainly in Australia, we've been the first to implement a number of different technology platforms. You know, as a large organization where this is our sole focus, rather than on a research question, we want to be able to offer them to the Australian research community as soon as soon as they become available. Sometimes the harder question for us is actually working out which platforms are a good fit for what. And that's some of the work that we do here in terms of our collaborations to just work with researchers who might like to use these sorts of platforms for different applications.

Steve Lewis 08:40
Technologies are so diverse too. It's, it's almost, it's very difficult as a laboratorian to keep up with all of it. So having AGRF as a resource, I'm sure, for many different industries and domains, and just the fact that you focus on the genome is, I imagine, a really valuable resource for the scientific community there.

Cath Moore, PhD 09:03
That's exactly what we're trying to be. So yeah, I hope, I hope we are. And certainly the feedback we've got is pretty good.

Steve Lewis 09:09
You talked a little bit about vetting technology and being really at the forefront of making sure that you are adopting these new technologies. And I'm curious, what does your vetting process look like? Do you have, like, an advisory board, for example, that you explore? And have any Thermo Fisher technologies played a role in really pushing the needle of molecular biology?

Cath Moore, PhD 09:37
Yeah. So we have innovation and development program here at AGRF, and that is sort of overseen by a committee, and it’s that committee that that basically is part of the evaluation and decision making process for any new technologies that we adopt. If you think about where all of this started, when I think about Thermo Fisher and where they're pushing the needle, the Sanger sequencing that we do, the capillary electrophoresis, it's all done on Thermo platforms, of course. But also a lot of the workflow leading into next generation sequencing now is also done on Thermo platforms. There's something that's sort of fundamental and enabling around the Thermo Fisher portfolio. I think the other thing that I'm very excited about in terms of where I see things moving at the moment and where Thermo Fisher is involved is actually now looking at, where do we start to take these technologies, outside of just the analysis of DNA. And an area that we're really excited about at AGRF that is going to be very directly linked now to Thermo is actually looking at a new technology for looking at protein biomarkers, but using a sequencing readout to do that. It is called non-mass spectrometry proteomics, and it allows us to take very small amounts of plasma and look at thousands of proteins that are expressed at really low

abundance. So that then bridges that gap between what's happening in the DNA, what's happening with the gene expression, and what's actually happening in the body and in the cells.

Steve Lewis 11:18
What an incredible capability overall, to be able to simultaneously look at so many different components of biologics.

Cath Moore, PhD 11:28
It's been mind blowing sometimes, I've got to say. But this is where I think, this is where we're going. This is what's this is what's increasingly emerging now is we talked earlier, Steve, about sequencing the human genome and sort of realizing that didn't really give us all of the answers. Now, possibly it was, you know, possibly people never thought that it would, but actually what it did was ask a lot more questions. To be able to answer those questions, we have to think about what's actually happening inside a cell. There are so many interactions, and how do we start to measure those interactions and understand them? That's going to require us to look at, you know, many different aspects of what's going on there. So, like I said, you know, DNA, RNA, the protein expression, but also, you know, in many senses, there are so many what we call omics now. So looking at, you know, metabolomics, what's, you what are the secondary things that are being made in there, and how are they interacting with everything else in the cell? And I think that that's a it's going to be a really fascinating future for people working in molecular biology.

Steve Lewis 12:43
It's really interesting that you brought up the multiomics conversation, because one of the podcast guests who I was speaking to earlier in this season tried to list all of the omics and I do think metabolomics is one that slipped through the cracks. So it just speaks to just how diverse and how emerging these areas and technologies are sometimes even on the month-to-month level.

Cath Moore, PhD 13:13
Yeah. Absolutely. But I think there, there is, there's almost, I think now, a consensus of understanding that, without understanding the multiomic environment, you're not really understanding the true biology of what's happening in a biological organism. And increasingly, in an ecosystem, not just in within one organism, but actually, you know, if you look at what's happening in soils, for example. That's thousands of organisms and how they all interplay, and what that does to soil health and ultimately, what does that soil health do to crop health, for example? Or what does it do to the insect population? I mean, these things then start to play a more significant role in understanding more about the world, about us. And I think that's that that's going to continue to be the case. So we're going to continue to have an approach taken here, where we're looking at systems, not just individual organisms.

Steve Lewis 14:22
On that note, are we at a point where systems biology might be working toward a heyday, or is it a discipline that might be different and undefined at this point?

Cath Moore, PhD 14:34

I think that systems biology, I think, is going to continue to play an increasingly important role. Is it at a heyday yet? I suspect not yet. But I suspect also that we're going to start to see other areas that might not be biology bought into the systems approach. We've been doing some work through one of our research collaborations here, where we've been looking at different soil types all over Australia. Now those soils had already been analyzed and collected. So there was a big Australian microbiome initiative that was funded by an agency called Bioplatforms Australia. They collected all of these different soil types and they studied the microbiome, so they looked at all of the different microbiological organisms that were in those soil types. But along with that information, they collected geographical information about the soil. Where was it from? What altitude? What was the soil type? And all of that information has been stored together. Now, one of the things that we've been trying to work on is we can overlay that with other databases that show you, like all of the vegetation across different areas in Australia. So how can we bring that information together? So we look at what plants have been growing there, what's the soil type, what are the microorganisms that are living there. What are the geographical and environmental factors in those areas? So the temperatures, for example, the salinity. And then we can start to make informed decisions about, okay, if you've got a mine site that's closing down, how do we work out what are the best ways to rehabilitate the land that that mine site was on? What type of plants to put in there? If that mine's been open for 20, 30, years, is it a good idea to plant the same plant species that were there then? Or should we look at trying to be a bit more predictive about it, and saying, well, the soil type has changed significantly, but we can look at soil types from up in this area of Australia, where the temperatures are similar and all the conditions are similar. Maybe we plant those types of plants down here instead. So it gives us a suite of information, but it's not only biology anymore. This systems approach is going to start to mean looking at all sorts of other factors that we haven't previously and combining them.

Steve Lewis 17:21
We're excited to be in season three of Speaking of Mol Bio and we know that we have you our loyal listeners to thank for the growing success of our podcast series. As a thank you, we're offering a free portable wireless speaker so you can listen to the podcast or your music anywhere. I have one on my desk, and I love how easily it connects to my phone. It's nice when I want to break from my headphones or want to share what I'm listening to with others. I hope you'll visit Thermofisher.com/molbiopodcast to request yours today. Please note this item is only available in some regions and only while supplies last. Again, visit Thermofisher.com/molbiopodcast to request yours. And now back to our interview.

Steve Lewis 18:12
You alluded a bit to bioremediation, and that's something that we have not talked about on this podcast before. Since it is a project that you're working on, I'd love to hear more.

Cath Moore, PhD 18:24
The idea is that if we can better understand the dynamics of what's in, in this case soil, but it could be also in mining waste, or it could be in composts. If we can better understand what's present and what's not present, or what might need to be present, and what those organisms produce in terms of how they might help the soil or help the composting or the recycling or whatever it is being applied to, we might be able to start to manipulate that. We could inoculate with different microorganisms that might help

improve the process. Or we can actually think a little bit more about what we actually want to do if we're going to try to do any kind of remediation of land, for example, what can we use that land for? Might not be that we can use it to grow crops, but it might be perfectly good to use as a playing field, for example. And this is, these are the questions that are being answered in this project around mine site rehabilitation. Some of these mine sites are quite close to regional communities which have relied on the mines for their incomes and their regional economy. And it's, you know, a case of, what can we use this land for, and what else can we do there?

Steve Lewis 19:46
Some of the concepts that I've seen come out of the International genetically engineered machines competition, which is iGEM for high school and undergraduate students, I am curious there was a program related to heavy metal or rare earth metal capture from engineering a plant, and I'm blanking on the plant right now, is there a place for some of these new technologies to be applied in, for example, the mining communities that you were discussing?

Cath Moore, PhD 20:21
I think there's always a place for that. The question is, how to do that safely, and how to do that with a strong level of public understanding behind it. I did my PhD in the, well quite some time ago, but when, when there was an effort to launch genetically modified crops in Europe, and there was huge backlash, and I think at that time, probably quite rightly so. There was a lack of understanding of what it means to genetically engineer something. I do think that there's a place for it, Steve. I think that there are lots of things that we can do with small manipulations, whether it's for public health, for individuals health, for bioremediation, but we need to get better at talking about what that means, so that people in the community understand that and understand and trust that it's safe.

Steve Lewis 21:21
Biosecurity is a bit of a theme this season. So thank you for your insights on this. Moving into speaking a bit about the molecular technologies that you used, I'm curious your opinion in the last 30 years, what has been the biggest advancement in molecular biology, and in the last five years?

Cath Moore, PhD 21:45
If I think about the last 30 years, I think that probably the biggest technology advancement has been the ability to sequence DNA. I'm talking about the ability to really, starting with the capillary electrophoresis Sanger sequencing, being able to do that all the way through next generation sequencing. So being able to look at massively paralleled sequencing of short fragments, but then also being able to go to long read sequencing, so being able to take a long molecule of DNA and sequence all the way through it, these continue to be incredibly relevant tools, and we continue to learn a huge amount from how we're applying those. If I think about the last five years, I think for me, in the last five years, probably the most significant advance has been the ability to look at what's happening with protein and RNA expression in a multi-dimensional fashion. So you can take a piece of tissue and basically take a look at specific slices of that tissue and see where in cells and within that tissue particular genes or proteins are being expressed and actually map that and visually see it.

Steve Lewis 23:22

It's incredible to think about the amount of data that can be generated from something like that now.

Cath Moore, PhD 23:29
Well, you know I, and this is going to be the big challenge, right. Because we've undergone this genomic revolution. We're able to sequence all of this DNA, all of this RNA, protein. We just generate so much data, but now we've got so much data, and it's like, so what's going to happen next? That's going to be the digital you know, we're going to need to be able to keep up with that in terms of our digital infrastructure, our ability to reanalyze data, to federate it, and compare one experiment with another. I think that's probably the big challenge to come.

Steve Lewis 24:12
Do you use PCR at your facility at all? And what for?

Cath Moore, PhD 24:17
Ah yes, we use PCR extensively. We use it for a number of different steps and aspects in what we do. There are sometimes when we're sequencing DNA when there's actually not a lot of DNA that's available for sequencing. PCR is a useful tool for being able to target specifically what we want to look at when we've not got enough to sequence everything. So that's one of its applications. But we also use it for producing libraries that are of a consistent yield and concentration that can then go on to sequencing platforms. It's not just used for targeting particular areas of DNA, which is kind of I guess this sort of standard thing that lot of people think of when they think about PCR, but it can also be used to regulate how much of a particular piece of DNA that you actually have and to normalize to the same concentration. We also do a lot of Sanger sequencing that remains a very relevant technology in a laboratory. And the front step to a lot of that is actually to amplify up whatever it is that you want to sequence. That might be to validate a variation in DNA that you see through next generation sequencing, and you want to just target that and just check that that is indeed a true variation, or it might be to look at a specific part of a microorganism, for example, where there's a very conserved area of microorganisms, but there's also variable regions that we can look at to try to classify what a microorganism is. Again, we would use PCR for those sorts of steps.

Steve Lewis 26:06
Throughout our conversation, we've touched on many different topics. Have we missed anything during this conversation that you might want to highlight?

Cath Moore, PhD 26:14
One of the things I think is really important and that I'm quite passionate about, is making sure that genomics remains, or becomes, rather than remains, better understood by the community. Because I think it has a lot of applications that can serve the community and impact community in a positive way. And so I love, for example, that there's this type of podcast where it's being talked about, where molecular biology is being talked about. Because I think there is going to need to be, not just in generations coming forward, I think that they're probably getting a better education than many. But also, there's going to be a need to sort of actually upskill and educate some of the people who could be using genomics now. And that includes, for example, clinicians, general practitioners, general medical

staff. But also, you know, if I think about other areas, I think clinical is an easier descriptor, but if I think of other areas as well, where we've been working quite closely with research and with industry, is looking at, you know, as diverse as people in the farming communities or food production communities, and helping them understand, you know, is there a faster way and a more efficient way that they could be improving the quality of whether it's their crops, their fish, their livestock, by using evidence based on DNA. And I think for the first step to towards getting there is actually helping people in the community understand what genomics is and what molecular biology can do.

Steve Lewis 27:53
What are your favorite resources for spreading the word and additional education?

Cath Moore, PhD 27:58
What I love to see are accessible information being explained when people have a need and an interest. So, for example, during the pandemic here in Australia, and I'm sure that this was probably the case in many places in the world, it was kind of the first time that people weren't just becoming familiar with genomics and DNA sequencing. they were kind of becoming obsessed with it. It was, you know, every time that there was a new variant of the virus, people were talking about how that was sequenced, and so we know that this, that it was this variant or that variant. It was a horrible way for people to learn something that shouldn't be so dire, but it was an immediately accessible form of information for them, because it was being talked about in a non-technical way, by people in the press, by people on TV, by people at supermarket now, by people in GP surgeries, by families just chatting on FaceTime and Zoom, because that's all we could use for quite some time. So I try to take every opportunity I can to talk about what I do, talk about what it means and what the impacts can be. Whether I'm out with friends, out with family, you're always in a situation where somebody's going to say, hey, you know, "Hi, nice to meet you, what do you do?" I try not to bore them, but I give it my best crack.

Steve Lewis 29:35
It's great to have a passion. And as you look back on your career, what have been the keys to your success to get to this point?

Cath Moore, PhD 29:46
One of the things that was key for me was being willing to try new things. Was being willing to say, “Even though this had been my plan and the path that I'd always envisaged for myself, now I'm on it, it's probably not exactly how I imagined it was going to be, and do I want to stick with it?” I'm a great believer in where possible, people should try to get joy from their work, because it takes up so much of our time and our life. I've had a couple of points in my career where I've really had to make a call and say, "This isn't giving me joy anymore, and I'm going to make a change."And I think it takes a little bit of courage to take that step, because it's, it can be a bit scary.

Steve Lewis 30:37
That's a really great answer and an ability for self-reflection too. It's really a fantastic answer. For anybody who wanted to follow in your footsteps, whether it's a student, somebody in an industry or otherwise, what advice would you give them?

Cath Moore, PhD 30:56
Probably the advice I would give is it's always a good idea to keep your interests broad. It doesn't necessarily mean that your focus has to be broad. That's impossible, but your work might lead you down one particular path. You know, it might be a particular research area, or it might be a particular company that you work for, it might be a particular technology that you work on, but I think, make the effort to keep your understanding of what else is happening in the field of molecular biology, try to keep it as broad as you can. You know, one of the things that I sort of joke about often with some of my friends is that throughout my career, I have worked on, you know, I started out in plant molecular biology, I went on to do a molecular genetics degree in plants, and then I went on to do a postdoc in plants. And it was like, you know, that that's I was cut, I was becoming very, very narrow. And one of the things that really sparked my realization that there are so many things that you can do with a science degree was actually starting to talk about what other people were doing with their science and with their research, and what their interests were and what technologies they were using. And you know, just keeping it, keeping it broad, the more strings to your bow you have the better I think, is probably the advice I'd give.

Steve Lewis 32:36
That was Dr Cath Moore, Chief Scientific Officer at AGRF, the Australian Genome Research Facility in Melbourne, Australia. Speaking of Mol Bio is produced by Matt Ferris, Sarah Briganti and Matthew Stock. Join us next time for more fascinating discussion about the wide world of molecular biology. Until then, cheers and good science.