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Steve Lewis 00:10
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 we take a dive into the weird and wonderful world of blood platelets with Dr. Beth Webb. Beth is a post-doctoral researcher at the University of Leeds, where she focuses on platelet biology and cardiovascular disease. She's also a content creator with a passion for science communication, so it's a double treat to have her on the show today. I hope you enjoy our conversation.

Steve Lewis 00:46
Beth, why don't you start today by just telling us a bit about who you are and what you're doing in the lab?

Beth Webb, PhD 00:53
So, I'm a postdoctoral researcher at the University of Leeds, and my research focuses mainly on platelets and specifically looking at how the endothelium and inhibitors that are released from the endothelium control platelet function.

Steve Lewis 01:10
Now, what kind of scientists do you define yourself as? Because I understand that blood platelets, in some circles, may not qualify as cells, traditionally.

Beth Webb, PhD 01:20
Yeah, so I would consider myself a cell biologist. My undergraduate degree was in biochemistry, but since doing my PhD, I've kind of moved into signaling, but it's definitely cell signaling. But I kind of sit at the intersection between vascular biology and platelet biology when it comes to my postdoctoral research, but I would consider it cell biology, but I am a platelet biologist, therefore a little bit biased. Platelets are the small aggregatory cells of the blood. So if you think of when you cut yourself, and it feels a little bit sticky, if you feel the blood that's down to the platelets, they're kind of the glue that helps your blood cells form a blood clot, and they aggregate together and clump together. They've been implicated in the immune system, but also thrombosis, hemostasis, a variety of different things. So, there's a bit more to platelets than I think what people would think. But of course, I'm biased, because I'm a platelet biologist. Your white blood cells are mainly to do the immune system, and then your red blood cells are to do with oxygen. So they kind of make up, that's what kind of makes up the majority of your blood. But there's a there's a lot of platelets, so it kind of makes me think, well, they must be there for a reason.

Steve Lewis 02:34
That's right. And are they smaller or larger than red blood cells?

Beth Webb, PhD 02:39
They're much smaller. So, they're about between two and four microns. So they're really small. And if you look at platelets from other animals, they can vary in size as well.

Steve Lewis 02:51
Must be really difficult to study in the lab.

Beth Webb, PhD 02:55
Yes, they come with their challenges.

Steve Lewis 02:58
How do you isolate?

Beth Webb, PhD 03:00
So platelet isolation, you would, you would take blood, so you'd get fresh whole blood, and then it's essentially a series of centrifugation steps. And you, we tend to, if you isolate platelets, we call that kind of a washed platelet method. So when you first spin them down, you've got your plasma, and then you spin it down again, and then you can isolate the platelets. There's various different methods. You can use different inhibitors, or you can lower the pH of the blood to ensure that the platelets don't activate when you're isolating them, because that is a bit of a risk, because if you've got your if your platelets are already activated, then there's not really much you can do with your experiment, because they've kind of exhausted what they can do. So you need to make sure that they're happy. It's all gentle. Your spins are gentle, and the platelets are willing to cooperate. When it comes to your experiment.

Steve Lewis 03:55
That's interesting. I hadn't thought about, like, the shearing aspect of it.

Beth Webb, PhD 03:59
Yeah, I mean, when you think of how they are in the body, there's, there's different shear of blood flow. So I think if you, if you spin your platelets maybe a little bit too vigorously, then they could, they could potentially activate, and you wouldn't be able to do your experiment. Unless that's what you want, you want them to be completely aggregated and clumped at the bottom of your Falcon tube.

Steve Lewis 04:23
Hmm, and you mentioned that you're focusing more on signal signaling these days. So does that imply that platelets have extra cellular membrane receptors?

Beth Webb, PhD 04:33
Yeah, they have, they have a lot of receptors. That's kind of what my PhD research was looking at a particular trans membrane protein called adenylyl cyclases. So they're present in loads of different cells, but they are actually present in platelets. There's but there's loads of receptors. It's actually kind of amazing, because they're so small, it's a wonder that they all fit on there, that they're all able to be on the surface of one cell.

Steve Lewis 05:01
And is there a component of cell to cell signaling, since they are involved in clotting, for example?

Beth Webb, PhD 05:07
Yeah, so they interact with one another, and they can also interact with neutrophils, monocytes, the surface of platelets, they can express something called phosphatidylserine that can then cause thrombin to activate so it has, they kind of this glue sticky cell that just seems to interact with a lot of different cells.

Steve Lewis 05:29
You kind of joked at the beginning that there must be a reason why we have platelets. What is your theory?

Beth Webb, PhD 05:37
Well, I mean, obvious one, I guess, is, hemostasis and thrombosis. But I think, I don't know, I mean, they just seem to be involved in all sorts of different things. I mean, one of the interesting ones was in COVID, when people were getting blood clots in the lungs, that was to do with hyperactive platelets based on the response to the virus. So, I feel like they're kind of implicated in a lot of diseases, such as cancer, other immune disorders. So, there's more to them than I think we realize.

Steve Lewis 06:11
What drew you to this area of research?

Beth Webb, PhD 06:15
So kind of always really been interested in science as a kid, and I wasn't really sure what I wanted to do. I just kind of followed what was interesting. And when I was doing my undergraduate degree, I had a year in industry, and I worked at a spin out company that was researching or developing small compound drugs for thrombosis, so that kind of was my first snippet into coagulation, and then that was the first time I'd really learned about platelets and what they did. And when it came to applying for PhDs, I applied to a variety of different things, but this particular project was one that I got accepted on, and it was really interesting. And that kind of led me into the world of platelets, which I didn't really know was, was, was a thing.

Steve Lewis 07:03
That's right, and this is an area I know very little about, so I'm excited to learn as a component of today. So, what is one thing you would like everyone to know about platelets in general?

Beth Webb, PhD 07:17
Most people might know this, but they but I don't want to assume. But the interesting thing about platelets is that they don't have a nucleus, which is kind of like, I guess, the brain of a cell, but they behave like a cell. So it's, I find that very interesting. I always kind of liken them to almost like the jellyfish in the sea that they can they, they respond to different stimuli, but they don't necessarily have like the brain that's controlling them.

Steve Lewis 07:46
What does a day in the laboratory look like for you?

Beth Webb, PhD 07:51
So for me, I know it's something that we touched on a little bit earlier. If you want to look at a very specific platelet experiment, so that would be where you use isolated wash platelets, you'd have to get a blood donation and then isolate the platelets. That's not the case for every experiment. Sometimes, and it's something I prefer to do, is to use whole blood, because it's as close as you're going to get to what's inside the body, and it's a bit more physiological. But not every application works for using whole blood. So, so it does depend on what it is you're looking at. We do a variety of different experiments, such as flow cytometry, looking at activation. There's also platelet aggregation experiments as well, which is where you would use wash platelets, or we could do western blots, or PCR, things like that.

Steve Lewis 08:46
I have a really, perhaps, elementary question, without a nucleus, are all platelets in a person considered the same? Are they of the same type?

Beth Webb, PhD 09:01
Oooh, that's an interesting question. I feel like that is, there's a whole area of research that suggests that platelets are not equal. So they're not made equal, and I think some of that comes down to how platelets are produced. So platelets, essentially fragments from megakaryocytes, which are in the bone marrow. So when megakaryocytes mature, they create these pro platelet projections. And platelets kind of bud off into the blood vessel. And if you think about that process, because it's not a traditional cell cycle as such, it's these the megakaryocytes create these projections and the platelets kind of fragment off that they're probably not going to be equal when you when you think about it that way. In terms of mRNA expression, things you can see differences between different clinical cohorts. That could then suggest that this particular cohort could have a difference in their platelets, which means that they are more hyperactive versus the control, for example. So, some of the research that we've done has looked at different platelet sub populations. When you look at the receptors that are expressed on the surface, and you can sub-categorize platelets into pro-aggregatory, pro-coagulatory, or pro-coagulant, and pro-apoptotic as well. That's just within one sample. For example, you can see these different sub populations just based on the receptors that they express in response to different stimuli.

Steve Lewis 10:41
So not all receptors are in all types of platelets. Is that correct?

Beth Webb, PhD 10:47
Um, I think that's a difficult one to answer, because in theory, you'd say yes, but I think it's, it's maybe a lot of these receptors are kind of internalized. So when they become, when the plates become active, it's whether they express them on the surface, sometimes that could be down to the extent of activation. Or if you've taken a sample that's been an inflammatory environment, for example, they're probably more likely to kind of already be a little bit activated or primed for activation. So, when you stimulate those cells, they're going to express more or the amount of antibody that's bound, the binding is stronger, therefore what you would see is brighter when you're looking at it in a flow cytometry experiment, for example.

Steve Lewis 11:34

Is a good analogy, maybe, like in response to sunlight, flowers will bloom or expand?

Beth Webb, PhD 11:42
Yeah. That's a good example actually, yeah.

Steve Lewis 11:46
That's really interesting. And you mentioned our mRNA, tell me how that's involved.

Beth Webb, PhD 11:52
So again, when it comes back to the way that platelets are produced, megakaryocytes have genomic DNA. So they kind of have that start starting process at the central dogma, but when they mature and produce platelets, platelets are so, so small that there's no way that they could ever contain a nucleus. In fact, some platelets are probably smaller than a nucleus of other cells, so there's no way in which that could happen. Instead, it contains the mRNA, which can allow for proteins to be produced. And then also, there's some in there's some research out there that suggests post translational modifications. It's not really my area of expertise, but you do have some machinery in place. You just don't have the DNA.

Steve Lewis 12:39
That is so interesting. So we have these platelets floating around, no nucleus, just have a little bit of mRNA inside, and that's enough to really cause responses to different stimuli in these nucleus-less cell subtypes.

Beth Webb, PhD 13:00
Yeah, pretty much, yes.

Steve Lewis 13:02
That is so fascinating. Tell me a bit about the molecular biology techniques that you might use in your lab.

Beth Webb, PhD 13:08
The main one that we use would be qPCR, and that's generally we use that to look at mRNA expression of different proteins or receptors or anything within the cell. That's kind of one of the main reasons. So for example, if you're looking at a knockout mouse model, for example, using qPCR is one of the ways in which we can assess that we've deleted this particular protein within the cell type that we want. You can do RNA sequencing; that's something that we're in the process of exploring at the moment. We will prepare the samples and then it will be sent off for RNA sequencing, rather than us doing the sequencing ourselves. But it there's a lot in terms of when you use platelets and looking at RNA, either RNA sequencing or qPCR. The preparation of your sample is very, very important, and comes with a little comes with a few challenges when it comes to working with platelets, because platelets are so small, and as we've talked about, the fact that they're maybe not made equal, you can't assume that every single platelet is going to have the exact same amount of RNA. So when it comes to isolating the RNA, there's just not a lot in there, so sensitivity is an issue. And in terms of collecting your, isolating your RNA, getting enough yield to be able to perform the downstream applications is

quite challenging. So you end up either have, there's a fine line between, you have to have a cut off in terms of how much blood you can take. The higher starting material, the more likely you're going to have a higher RNA yield. But that's not always guaranteed. So it can be, it can be quite challenging.

Steve Lewis 15:02
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 15:50
What are some of the challenges that you see with sample preparation of something so small?

Beth Webb, PhD 15:56
I think it's mainly getting enough yield and making sure it's pure enough as well, because if you think about how we isolate the platelets from blood cells, you're probably going to have some contamination of other cells, whether that be red cells, it's mainly white blood cells. So in terms of mitigating that, you can use magnetic beads that can pull out leukocytes that contaminate the platelets. Because you, you don't want to be in a position where you've isolated this RNA and you think, “Okay, I've got enough,” but you can't actually guarantee that it's the platelets specifically, because you're always going to get some contamination of the leukocytes. You do need to have some extra processes in place to mitigate that. But obviously, the more you wash and manipulate your sample you have, you run the risk of having a lower yield yet again. So, it's very much a double-edged sword sometimes, which is doable, but it just, it takes a bit of optimization and finessing.

Steve Lewis 17:04
What, uh, what stage are you at right now for finessing?

Beth Webb, PhD 17:07
For the RNA sequencing, we have just been trying a few different methods of isolation and leukocyte depletion this week. So hopefully by the end of the week, we should, we should have some kind of idea in terms of the yields. But in terms of purity, we need to send them off to the RNA sequencing core unit to see how pure they are, and if they're pure enough to go forward for RNA sequencing. So, fingers crossed.

Steve Lewis 17:40
There's a lot of unique challenges in this application area that I did not fully understand prior to this conversation.

Beth Webb, PhD 17:49
Yeah, I think it's one of those that you don't know until you start with something like this. You'll give it a go. You'll go through a traditional SOP that's, you know, “Yes, you can do suspension cells,” and then you try it, and your yield is pretty much nonexistent. So you definitely have to adapt and amend protocols in order to get something that's somewhat consistent and pure and a high enough yield.

Steve Lewis 18:17
Are there gaps right now that need to be addressed by maybe sample prep suppliers or otherwise?

Beth Webb, PhD 18:28
Potentially. I know, I think within the platelet field and the hemostasis and thrombosis field, there is a lot of communication between research groups and a lot of standardization that goes on to ensure that people are doing the right thing when it comes to platelet RNA isolation, but it's also very niche. So I do understand that from a business point of view, from a company that not everyone's going to be interested in like these little tweaks for using platelets. But it is maybe some, like, sometimes a conversation that platelet researchers could have with companies.

Steve Lewis 19:04
Now, there's a number of factors that you mentioned that are motivating you to stay in this area of research. What are some of the maybe pathologies? You mentioned cancer earlier. Where do you see this research developing over the next five years and maybe having clinical impact?

Beth Webb, PhD 19:21
I can't speak much for cancer, for example, because it's not really my area of expertise. But in terms of cardiovascular research and anti-platelet medication, I think there's some really exciting things happening. I mean, one of the main, one of the main problems with anti-platelet medication is that whilst it protects you from cardiovascular events, you run the risk of bleeding, and you then, once you're on these, your’re kind of on them for life. And that might not necessarily be the case. I think some of the interesting research out there is looking at the aging population and how your body changes once you get over the age of 80, for example. And whether the people that are on anti-platelet medications necessarily need to be on them at that point. So there's some really interesting things out there. And I think my interests lie in personalized medicine. I think that's the same for a lot of scientists. But I think there's some really cool things happening in terms of modulating anti-platelet therapies or tracking the success of current anti-platelet therapies and whether people should still be on them, or whether they could come off them potentially further down the line.

Steve Lewis 20:32
So maybe, like a regular molecular diagnostic, or something, to help with that?

Beth Webb, PhD 20:39
Yeah, because again, coming back to the platelets and the interest of platelets. We talked about that how they're not all made the same, and whilst you have a lot of platelets, it's quality over quantity as well. So someone might have loads of platelets, but they might not necessarily be responding in the way that you'd want them to. So that's also another thing that I find quite interesting is that how can one

person have the upper limit of platelets and another person has the lower limit of platelets but they don't have any phenotype?

Steve Lewis 21:12
Yeah, that's a really fascinating aspect to think of. And earlier in the conversation, I avoided saying “homogenous” because there's no genes in these cell subtypes. So, it's interesting.

Beth Webb, PhD 21:27
They're weird and wonderful.

Steve Lewis 21:29
I love it. Now you do a bit of scientific communication yourself. Is that right?

Beth Webb, PhD 21:35
Yes, I do. I like to use social media as a means of science communication because I feel like science should be accessible, and I feel like social media, at the moment, is free. So, it is more accessible than other platforms. I did used to write blogs as well, because I quite like writing and I like, I do like longer form content, but I know that that seems to be not as trendy these days. But I still like blogs and writing, and it comes down to, I mean, really, it comes down to the fact that a lot of people in my life that are non-scientists, and they would always ask me what I was up to, what I was doing. And I'd kind of give them a very vague answer, because I thought, “Is it worth trying to explain?” But then be like, “No, no, please, please tell me what it is.” And it actually challenged me in a way that I liked, that allowed me to explain science in different ways, and I enjoyed that, and I wanted to do that to different audiences. So that's kind of how I got into it.

Steve Lewis 22:41
That's great. And we, we really champion making accessible scientific communication a big part of everyone's career path. So I think that's fantastic. And I think a bit of what you said absolutely rings true for other laboratorians or otherwise, where sometimes you do have that thought is, “Is it worth going into that level of depth?” And I always think, “Yes, it is”, and because it's an opportunity to challenge yourself to communicate in new ways.

Beth Webb, PhD 23:14
Yeah, definitely.

Steve Lewis 23:15
Now, where do you see the field going over the next let's, let's look far into the future, let's call it 10 to 15 years. You said personalized medicine. What is, what does that look like?

Beth Webb, PhD 23:27
Oh, I mean, the dream would, I guess, be being able to have a bit of just a blood sample and getting that sequenced, and you'd be able to know what medications would respond well to you, or I don’t know, I guess there's things you can do in terms of how diet responds to you. I feel like that would be

the ideal, I guess, yeah, I feel like that's the that's the dream. I believe that one day we'll probably get there, but these things obviously, obviously take time and money.

Steve Lewis 23:59
And probably more researchers into the space?

Beth Webb, PhD 24:03
Yeah, definitely.

Steve Lewis 24:05
As social media continues to grow and be popular and we just discussed the need for more scientific communicators, what advice would you have for maybe younger scientists looking into the field?

Beth Webb, PhD 24:19
So I think the best advice, although it's probably not advice, is that, is to just start. But I understand that that's easier said than done, because I feel like it can be quite daunting. So one of the things I'd say initially is to kind of get used to talking about science to different people, whether that's within your friendship group or family, in a way that you can, you can identify different audiences, or you can think about different analogies to things. That's something that I would say is probably the best way to do it. And then if you want to start communicating on social media, there's so many different means of doing it. That in itself is overwhelming. So I would initially pick one platform and initially one style of content creation, because there's so much out there, right. There's infographics, there's blogs, there's videos, there's podcasts like this. There's so many things that I think starting with one will ease you into it, and then I think you'll become a little bit more comfortable to try other things. And also, like trying new things is, really is useful and seeing what sticks. But I think in the first instance, just make it more simple for yourself, because it can be you can have this feeling of like, “Oh, I need to be on all of these platforms and reach all of these different people.” But it doesn't necessarily have to be that way.

Steve Lewis 25:48
What was the greatest challenge you overcame?

Beth Webb, PhD 25:52
I think the transition that a lot of social media platforms all kind of went through was transferring to video content. I was really nervous about being in front of the camera, because I feel like writing and creating these infographics, I was, I remained hidden. But in a way, it was a good challenge, because it teaches you to communicate in a different way. It's like written content is very different to video content, and it meant that I got to experiment with fun things and make content that was a little bit, I don't know, a bit more exciting and fun. Not saying that the blogs aren't, but it was just a different way of doing it. And I learned a lot through that process about, like, how to edit videos, how to plan and kind of produce and, I guess direct, something that I'd never done before.

Steve Lewis 26:43

Really speaks to kind of the diversity in science right now. You have to do your day-to-day lab work and then you also have the opportunity to communicate and go to the level of depth, like you just said, editing video, which has nothing to do with your day to day, right?

Beth Webb, PhD 27:03
Yeah, but I think it's, I think if you like it, if you enjoy that kind of thing, then absolutely do it. But I know that it's not for everybody, and I wouldn't, I wouldn't sit here and tell everyone that you, “Yeah, you need to set up a TikTok page and do this, this and this,” because it's not for everybody, and it's okay to be a scientist and be in the lab and communicate at conferences and all through publication. But if you do have an interest or a passion, then I think there's so many amazing ways in which you can scratch that itch for science communication.

Steve Lewis 27:37
Well, I think that's really sound advice. As our time comes to a close, I always end the podcast with two questions, the first one being, what have been the keys to your success?

Beth Webb, PhD 27:50
Scientifically or science communication wise? Well, I guess both of them probably a lot of it comes down to resilience, and I guess not quitting when it gets hard, in both aspects. Because science is hard and also communicating science is hard. You deal with people that might necessarily agree with you or might necessarily believe in the things that you're talking about, and that can happen within the science realm and also science communication. But being resilient and just kind of keep going when it gets tough is, is one way. But also prioritizing rest. It's like a fine line, isn't it? You don't, I don't want to say, just never give up. But also, yeah, I think resilience is one.

Steve Lewis 28:46
Would that also be your advice for maybe somebody who wants to follow in your footsteps?

Beth Webb, PhD 28:51
I think resilience isn't something you can teach. It's something I guess you develop with time and experience, and if you go down the academic research path, you will learn that lots of things go wrong and that's okay, and I think it gets you comfortable with that. And I've taken that same approach with the science communication aspect of it, that things go wrong, or something might completely flop, or you might get a negative comment, and that's okay, like it's okay, it's not it's not that you're not doing a good job. It's just that that didn't work out, and that's fine.

Steve Lewis 29:28
That was Dr. Beth Webb, post-doctoral research fellow at the University of Leeds. You can find Beth on Instagram @_bethology. 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.