Shannon Miller: Gene editing, CRISPR, and drawing the line between science and fiction

Lauren Fish (00:08):

This is Science Changing Life, and I'm your host Lauren Fish. Thanks to revolutionary technologies like CRISPR, we're now living in an age where it's becoming possible to rewrite the very building blocks of life itself--our DNA. Today we sit down with Scripps Research fellow and CRISPR expert Shannon Miller, who will walk through the many ways gene editing could reverse an entire slew of different diseases while also easing concerns about anything too dystopian in this area. We start off by hearing about why Shannon chose to pursue a career in science, notably among her many other interests.

Shannon Miller (00:40):

There's a lot of time this notion that really successful scientists have to have this eureka moment in their childhood. You hear these stories of Nobel Laus who got their first chemistry set at 10 years old, and then they knew from there that that was kind of their destiny.

(00:55):

But I really think that this isn't the case for a lot of people, and it wasn't the case for me as a kid. I was smart and I liked science, but I also really liked art and literature and music and video games and reading and everything on the gambit. And so a lot of times throughout my career, I kind of felt that I almost fell into science rather than it was this predetermined thing that I knew since I was a young child. Yeah, this path you had to take, right? Yeah. I think that that is absolutely okay and should be almost talked about more because I think a lot of young scientists feel this pressure that they're like, oh my gosh, I didn't know I wanted to be a scientist until halfway through my undergraduate career, but that was how I ended up. So I think the most interesting story about how this entire career can be also kind of spontaneous was how I got into research.

(01:51):

So I started my undergraduate career as a biologist because I really liked animals as a kid, and I'm like, maybe I should become a veterinarian who wouldn't want to play with animals every day? And as a biologist, you have to take your intro organic chemistry class, which most people despise. I remember that one and I despised myself, but I loved it and I did really well in it. And so in one of the summers between semesters, I just ran into my organic chemistry professor at a cafe and she remembered me because I did well in the class and she offered me a position in her research lab, and I didn't really know what research was. And so I was like, yeah, sure, I'll try it out. But I fell in love instantly. It was something that I felt that I was really good at. It really stimulated me.

(02:39):

It was extremely rewarding, but I didn't change my major to chemistry, and I didn't know that I wanted to do research until halfway through my undergraduate career. So yeah, like I said, I sort of just kind of fell into the science and fell in love with it, and it wasn't a love at first sight sort

of deal. And I really dislike this notion that people kind of have to be these scientific savants as kids and making discoveries before they can drive or drink. Because to be honest, when I was a kid, I think I was more invested in beating the latest Zelda game than actually concentrating on my schoolwork. But that's how you learned how to good problem solving. Right? Exactly. And a lot of the interests that I had as a kid come back as an adult. And so I nurture my creativity through art and reading and even video games.

(03:30):

And I think the fact that I've nurtured my creativity alongside of my scientific prowess really lends to me being a good scientist. It allows you to do these creative problem solving. Absolutely. And I think the best scientists are well-rounded in that sense. Yeah, absolutely. And I think one of the frustrating things about science too, because I was a biology undergrad major, but you have to start it when you are a freshman. If you want to switch over your junior year, it's so much harder because there's so many prerequisites. So that is another issue. What fraction of kids know what they want to do for their living by the time they're what, 18, 19? And that kind of defines a lot of my even current career, the project ideas that come to you after chatting with a colleague at the coffee shop here or at a conference.

(04:20):

I think that if you kind of follow your gut instincts and really just embrace the serendipity of it all, it leads to more interesting science and more interesting project ideas. Yeah, absolutely. So can you tell me what you're working on here at Scripps? My research in general works on genome editing and particularly trying to get it useful enough to the point where we can use it inside of the human body or in vivo and genome editing. What it is is when you have a genetic disease, there is a misspelling in your DNA and genome editing proteins allow you to go in with this microscopic tweezer or pencil and eraser and physically change your genetic code to correct that misspelling. And what that does is it makes your DNA look like healthy DNA, nothing ever went wrong, and it also corrects the phenotype, the symptoms of a genetic disease. And so it's one of the few ways where we can actually get curative therapeutics.

Lauren Fish (05:19):

So crazy that science has evolved to this point in time that we're able to do this.

Shannon Miller (05:23):

Whenever I tell people, it kind of almost bridges on science fiction. It does, absolutely. Which is another testing point where you do need to draw a quite rigorous line in between science and fiction, especially with terms of miscommunication. Things like designer babies are not something that I think are going to be realistic in our future, but genome editing is something that exploded within the past decade due to the invention, the discovery of something called CRISPR Caine. And what CRISPR Caine is is it's a protein that's guided by a small RNA molecule to a region of your DNA in your genome. And I like to kind of put this into perspective because I say this kind of nonchalantly, but it's an incredible feat.

(06:08):

You have 3 billion base pairs in your genome and you're able to just write out a sequence on a small RNA molecule, and this protein can target one out of those 3 billion base pairs to extreme specificity. And so it is a very incredible technology to be able to target and manipulate the genome. And so researchers use this protein to target it, target the genome, and they tether on different DNA manipulating enzymes. And so you're able to make all sorts of DNA manipulations, including you can create indels, which leads to gene disruption. So if you have a disease that has overexpression of a gene, you can tune down that expression to fix the gene.

You can make small point mutations. So a very large majority of genetic diseases are caused by a single base pair misspelling within your 3 billion base pair genome. And this can have extremely devastating disease phenotypes, but we can go in and very precisely fix that one base pair and change it to the healthy base pair.

(07:16):

And so that's kind of in a nutshell what genome editing is. We're starting to really reap the benefits of all of this decade or so of research. So actually quite recently we had a clinical trial that got approval FDA approval, and this is a drug called Cavy where they take patients who have sickle cell anemia, they take cells out of their body, they use CRISPR to engineer them to make them again, similar to a healthy human cells, and they put them back in the body. And this is a curative therapy for sickle cell. Amazing. And so now this is an FDA approved, the first FDA approved CRISPR based therapy, and there are many, many more in the pipeline. And it's extremely rewarding being able to hear stories of people whose lives have been directly impacted with stuff that I work on a daily basis. But I guess in terms of what I want to do to help advance this field is there are a few barriers to advancing it to a general therapeutic.

(08:15):

And so there's this idea specifically of using CRISPR inside of the human body. That's extraordinarily difficult for a variety of reasons. So when you look at the clinical trials that exist now, a majority of them, I think around 70% of them are exvivo therapeutics, which means we take the sickle cell, we take them out of the body. Yeah, exactly. You take them out of the body, you edit them and put them back in, that's a lot safer because you can screen the cells, you edit and make sure nothing's wrong before there's no off target effects. Right, exactly. Slipping some other part of your body that you don't want it to. And so yeah, you have a lot more to worry about when you're using it inside of the human body. Another really big barrier is delivery. It's probably the biggest barrier. And so you need to be able to get your CRISPR machinery into the human body in a very efficient way.

(09:08):

And one of the biggest barriers is something called first pass metabolism. So if you, let's say you want to target your heart or your brain, what you're going to do is you're going to inject it into your bloodstream. And everything in your bloodstream first goes straight to your liver through first pass metabolism. And the liver is a very nonspecific tissue where a lot of these vectors where you use to deliver your genome machinery gets soaked up by the liver. And so in vivo use, we have currently, a majority of them target the liver. There are many diseases that are born in the liver and we're really good at targeting and editing them. It makes sense that they would be our first go, but when you want to target the heart or the brain or the muscle or anything else, having it recirculate and actually get to that organ is extraordinarily difficult.

Lauren Fish (09:54):

And then I can imagine toxicity is such a big issue there, right?

Shannon Miller (09:57):

You have to deliver a ton because so much is going to get metabolized in the liver. It's like, oh, can your body actually handle that? Yeah, you get liver toxicity then as well. Yeah. My lab is currently set up to tackle three big areas of what I feel like are barriers towards clinical translation of crispr. The first is to make current technologies safer. So CRISPR Cass nine is extremely useful, but it does have some issues with immunogenicity and stability. And so if we're able to create highly engineered variants that bypass all of these innate immune responses and these innate degradation responses, we shouldn't make something that is less

immunogenic and more efficient because then your immune system as in like, this is a foreign substance, we need to attack it. Exactly.

(10:47):

It's just much more seamless. And so we're engineering components of the CRISPR machinery to enhance this ability. The second is that we're not currently able to make absolutely every genetic change we can make possible. So like I said, a majority of genetic diseases come from SNPs, but there's also quite a lot that come from very elaborate genomic changes. This can be whole gene deletion, whole gene duplication, chromosomal truncation, chromosomal translocation there. There's quite a wide variety of things that can happen to your genome to create a genetic change. And so the overarching goal of the CRISPR field, specifically on the tool development side, is to be able to make a toolkit of CRISPR genome editors that can theoretically fix all of these anything. And the one thing that we're really struggling with right now is making very large genetic changes. So inserting whole genes, deleting whole genes.

(11:53):

There's a whole subset of repeat expansion disorders that it would be great to very precisely fix. And so this is another area that my lab is exploring is how to develop new tools that are able to make these large genetic changes and deliver large molecules like massive molecules. Which again, circling back to the delivery, that's a really hard problem because the bigger it is,

Lauren Fish (12:17):

I'm sure the more that your immune system wants to attack it and views it as a threat. And just in general, the harder it is to get into a cell the bigger it is. Yeah, it's so specific.

Shannon Miller (12:26):

What makes it across the cell membrane. Exactly. You're trying to get in there. It's not easy. And that's a perfect segue because the third area that I'm embarking on in my lab is delivery. So we have, like I said, there's an issue with liver metabolism, but we have some existing vectors that are at least in mice and somewhat in humans, quite efficient at getting to other tissues.

(12:51):

But these vectors have issues with immunogenicity or longevity leading to off targets. My lab is exploring how to enhance the existing vectors that we have through engineering to make them more specific, more safe and more efficient, and that vector to figure out what the best vector is. It's like an evolutionary process where you iterate, determine the best ones through this evolution and then amplify those ones that are seemingly going to be the best at getting into the cell. Yeah. Yeah. So when I say engineering, a lot of times there are multiple forms of engineering one can use to enhance these molecules. You could use rational engineering or computational engineering, or one of my favorite techniques, which I use very heavily in my lab is directed evolution. And so this is exactly what you're talking about is if you have a biomolecule that you hope to enhance towards some property, you can create a selection very akin to Darwinian survival of the fittest, where you create millions of variants, you ize your whatever you want, whether it be a cast protein or a viral vector, and you subject it to a selection where things that are more fit or more active survive and those that don't die out.

(14:13):

And in this case, this is how we can, instead of screening in a 96, well plate, the bacteria cell or the mammalian cell does it for you. They screen millions of variants all at once so that only the best ones survive, and those are the ones that get presented to you. So it's an extremely powerful method of engineering. But on top of that, I do very much appreciate other forms of

engineering and also the combination of all of these. So using rational engineering as a starting point for directed evolution or using computational engineering to compliment directed evolution, I think that these are the ways where if you really want to engineer extremely novel function or really powerful function, combining all of these techniques is kind of the way to go. So your background is in chemistry and chemical biology. So in terms of the more computational front or the engineering front, how did you gain that skillset?

(15:09):

And like you said, this is such a big problem, you can't just use science to fix it because it's really going to take these multiple disciplines to be able to attack it from all angles. The short story is I didn't ever gain that skillset. This is, again, ties you're teaching yourself. I'm not actually, this is why I think scripts is so wonderful. I don't teach myself computation. It's just that there are many people here who are help out. So willing to collaborate help. And I would be silly not to use the expertise that's in this institute because there are people who are absolutely at the cutting edge of protein design or molecular modeling, the computational engineering that could be really useful for pipelines into directed evolution. And so I don't actually physically know how to code or how to do this modeling, but the people around me do and came to the right place.

(15:58):

Yes, exactly. And it's an amazing, powerful technique to complex with my expertise, which is directed evolution. Yeah, that's amazing. So we talked about you transitioning more to chemistry as an undergrad. What led you more to the gene editing genome engineering field? Like I said, I started college as a biologist. I did and do really biology. I grew to love chemistry. And when I was interested, once I figured out that I really liked research, I had to think long and hard of what I wanted to do with that research long term. And I thought the ideal thing to combine all my interests is why don't I just smush together the biology interests and the chemistry interests, which means that I was interested in chemical biology. So I applied to a variety of graduate schools that had chemical biology programs. I ended up going to Harvard and I ended up joining David Lu's lab at Harvard, who is probably one of the major leaders in crispr, especially on precision genome editing.

(16:58):

And so this was also a little bit of spontaneity because when I started graduate school, I wanted to challenge myself. The only research I did was strict organic chemistry. And the easiest path for me would have been to choose to go directly into an organic chemistry lab for my first rotation. But I challenged myself to do the one thing that was very different from what I did. And I ended up in David Lou's lab. I don't think he knows this, but when I landed in his lab, I didn't know how to do any of the molecular biology. So I didn't know how to do PCR. I didn't know how to run a gel. I had barely held pipettes in my life, but he took me on. And I think this learning curve really kind of enhanced my ability to do science. Absolutely. Because you were diving in then, right?

(17:51):

Yeah. You were committing to learning how to do this. You already had this really rich knowledge otherwise too. So I think that also gave you an advantage there also. Yes, it was hard and I made a lot of stupid mistakes, but I came in with a very fresh perspective towards research. Absolutely.

Lauren Fish (18:09):

That's so cool. So you mentioned some of the diseases like sickle cell is an example of that, just approved medication. What are some of the other diseases that ideally you would be able to tackle with these technologies that you're developing?

Shannon Miller (18:23):

So another one, which is quite advanced in, there's a few that are quite advanced in the clinical pipeline. One of them is using CRISPR to make new CAR T therapies. So this is cell therapies specifically to treat cancers. And there's also been success stories, especially young patients with blood cancers, blood cancer fund.

Lauren Fish (18:43):

Yeah, it's amazing. I was just talking to my friends about that over the weekend, just the great advancements that we're making in hopefully treating metastatic disease eventually.

Shannon Miller (18:52):

And CAR T therapy has already shown a lot of promise, and where CRISPR comes into this is the ability to further engineer CAR T cells or more elaborately engineer CAR T cells to make them more potent or to make them less immunogenic. You could even imagine a future where you don't have to. Right now what people do is you have to take cells from the patient again to edit them and re-engineer them outside and then put them back in. But if you can have an existing pool of any donor and you can engineer them to be non immunogenic when you transfer them to a new patient, so they're just ready to go. You don't have to wait for treatment.

(19:29):

So there's a lot of opportunity here with CRISPR. Another really promising area is eye disease, actually. So the eye is a very privileged organ. It's quite easy to engineer actually, because it's an organ that's right there, you can directly inject into it to deliver your genome editing technology. And so a lot of these barriers with delivery don't exist for that eye. And specifically the eye also lacks a lot of the immune responses for the rest of the body. I mean, it's constantly exposed to foreign. Oh, that's true. So imagine if you constantly had an immune reaction going in your eye because a little bit of dust got into it, but because of that, it's actually quite easy for us to use. And so that's one of the areas where people are pushing forward right now is hereditary blindness disorders. And people have actually, again, been able to see success in this where patients have their color vision restored.

Lauren Fish (20:23):

That's amazing.

Shannon Miller (20:23):

After years of lacking the ability to see color, I can imagine there's so many diseases that there could be hundreds of genes just communicating and we don't necessarily know what the cause is.

Lauren Fish (20:36):

So is that part of, I'm sure there's so many specific genetic diseases that we do know the specific genetic component that leads to its manifestation, but I imagine there's also so much research that's coming out that we're now better able to understand how genes might coordinate to eventually cause the disease. Definitely. And lead to even more application in the future.

Shannon Miller (20:55):

Yeah, that's really tricky because that is true that gene editing really as it exists now requires quite a specific edit to make and people can get creative with it. So for example, in this approved sickle cell drug, you are not actually genome editing the sickle cell allele itself. What you're actually doing is you're disrupting a enhancer that normally turns off fetal hemoglobin.

(21:26):

And when you disrupt this fetal hemoglobin, it gets upregulated again. And so instead of fixing the gene itself, gene itself, they're fixing it by supplementing another gene. And so interesting, if there are diseases that are too complex for us to fix polygenic disorders, et cetera, there might be a workaround where we can supplement another gene. Got it. Like a little bit more downstream maybe it's like, okay, we know the mechanism mechanisms of why this is happening so we can tinker with something else a little bit later down the line. Yeah. I think things like cancer, for example, where it's such a genetic environmental, how everything's interacting. Right, exactly. Like, okay, how can we, what's maybe causing this cancer and how can we disrupt that? Right. Yeah. And another thing which is really tricky, which is something my lab has thought quite a lot about is there are some diseases where a hundred percent of the patients have this one point mutation, and then there are some diseases where it's one gene that's messed up, but within that gene, there are hundreds of known mutations that can lead to the same disease.

(22:41):

And that's a really tricky problem for CRISPR because if you think of one gene that has 100 mutations, you need 100 approved guide RNAs to target each and every single one of those individually. And that's just FDA nightmare, a hundred different therapies for one disease. And so one of the huge overarching pie in the sky dreams I have is how can we make a gene editing technology where we use one treatment to treat all, or at least it takes all of these different components once of the genomes. And so that streamlines the path to approval because you only need one individual drug to treat all of these. I think people are a little bit hesitant when you are trying to push forward a therapeutic that might only treat one 10th of the disease population.

Lauren Fish (23:34):

When you are trying to tackle these huge problems and you are starting to feel a little bit stuck, how do you get unstuck? What do you do to re-inspire yourself or maybe problem solve in a different or see things in a different way?

Shannon Miller (23:46):

Right. Yeah. Honestly, I just love taking a break. I am a huge proponent of mental health. I love my weekend days where I just do nothing or I take a day trip to go outside. I think that on day-to-Day in science, my brain is my biggest asset. And so if my brain isn't up to snuff, then I'm not going to be able to do the research. And so making sure I have those self-care moments are how I relax. And I specifically love and I encourage people to step away from your research when you hit a roadblock, because a lot of times you'll step away and you'll come back after a relaxing weekend and it'll be very clear what either you made a mistake or you overlooked this one area, or it's quite obvious that that direction is the best way to go.

(24:42):

And so I'm a huge proponent of relaxation and just stepping away from it all every once in a while. And I know they even say walking is supposed to, just walking as you're trying to, you're kind of thinking about it, but you're kind of not, and you're just giving your brain a break and you're seeing new things and you're not just focusing on the same thing over again. You're

never going to see anything different at that point. I'm definitely guilty of the shower scientific ideas because same deal I am in the shower, I'm relaxing distracted, and then all of a sudden it just comes to me because I'm, how did I think about this? Exactly it, it's such a good way. Or when I'm half asleep, of course, obviously my brain just activates. It's like, oh my God idea. It's frustrating. But that's, I think, the best way to do it.

Lauren Fish (25:26):

Good. That's great advice, especially for everyone in your lab, to have that perspective, to take care of yourself, and you're going to do your best work when you're able to do that. Definitely. Yeah. I've heard of the people that solve things in their dreams too. I don't know if that's actually, I feel like, yeah, I have a lot of engineers in my family, and my uncle was talking about, he's like, yeah, I was like, I solved the problem in my dream. I'm like, does that actually happen?

Shannon Miller (25:50):

I think for me, it's the opposite. I get scientific anxiety, dreams where in my dream I ran the wrong PCR and it ruined my whole experiment. So I'm not there yet, but maybe one day. So what would you say is the most rewarding aspect of your work and then also the most challenging? Yeah. I think the fact that it's so translational is the most rewarding.

(26:12):

I talked about how now similar science to what I do is in the clinic and even impacting real patients. And so I think having that perspective, it's quite a direct perspective into the significance of what you're doing, is very useful for both me and my students. They can go home and tell their family like, Hey, this thing that you saw on the news, I work on that. And that's rewarding and motivating as well. I've even had people come up to me after talks and I present data on X disease, and they come up to me and they're like, I don't know if you've ever met someone with X disease, but I'm here and I have to take a pill a day and shots every other week. And it's frustrating, and I'm so excited that my children or my children's children might have a cure for this.

(27:02):

And so this is extraordinarily exciting and rewarding.

Lauren Fish (27:07):

Yeah, I can imagine. And especially too, I think you were mentioning how as a biology undergrad, not even really thinking about research or what you could do outside of medicine, or you're talking about veterinary medicine. So the fact that you can be at the lab bench, but still have, you were saying that translational aspect where you can potentially change people's lives even though technically you're on more of the science side, but you're still making such a difference from that medical perspective too.

Shannon Miller (27:34):

And Christopher is super unique example of the bench to bedside translation because of how quickly it's made that transition. Right. So CRISPR was discovered, the technology itself was discovered in 2012, and by 2023, we have an FDA approval. That's insane. And I actually did a little bit of digging into this. Typically the timeline between the discovery of a novel technology and when it gets FDA approved, the average is 35 years.

(28:08):

And so the fact that we've been able to have this extraordinarily impactful technology that was able to create this, do this feed in 10 years is extraordinary. And it underscores the importance of the technology as well, I think, and actually developing it to a point where I can do so well in the clinic. And the clinical trials are more rapid at that point too. Yes. It's insane. And in my PhD, David Lou, one of his biggest inventions is something called base editing, which is a type of genome editing, which is precision very precise. And it can, like I said, target a single base pair and change it into another base pair to target these diseases that arise from SNPs. And even in the span of a single PhD, my PhD, the technology was described my first year as a first year incoming student. And by the time I left, it was already in the clinic.

(29:00):

It had just entered the clinic. And so it's an extremely unique opportunity as a student too, to be able to see technology coming from your same lab, which you've been working on for your entire PhD, and you might've even contributed to make that sort of progress. And I think too, science and medicine has a bad reputation for being slower. Things take time. We want to make sure that they're safe and effective, both we want to figure out things work. So to not be discouraged by that to see, oh, no, things can move as quickly as they can. Once we're living in that time in history, things are moving quickly in a way they, in the past, hopefully it's getting quicker. So this 35 year time mark starts to decrease. And maybe CRISPR and things like the Covid vaccine are things that break down those barriers because I think that there are some very important technologies that need to get out to the human race.

Lauren Fish (29:59):

They need to get to people as soon as possible. So Cool. Well, it's so cool that you're at the forefront of all of this too, and you're getting to invent these new things and build on what's been done in the past, but just make it even better and yeah, change people's lives that way. Wow. Doing science. Changing life. Yeah, changing life. Exactly. So Scripps is celebrating its centennial this year. I know you touched on a couple of things that makes this a unique institution, but what's your favorite thing about Scripps?

Shannon Miller (30:29):

I think Scripps is just such a uniquely curated institute where we're all motivated towards discoveries that change human life, but many different flavors of this. We have people that are working on neurological diseases. I do genome editing. There are people that do small molecule therapeutics. There are people that are trying to save the climate.

(30:54):

It is extraordinarily diverse. But again, when you get diverse people like this in the same room that are all working towards a reasonably common goal, I think it opens the door for collaboration on a scale that's more innovative than traditionally possible. So you come up with extremely unique answers to very hard problems that you probably wouldn't have figured out if these people have not been brought together. If you were just in your department of chemistry or you were just in your department of molecular medicine, it's like to have that cross pollination. And I love that. Even existing in the Beckman building, the auditorium that's in this building hosts lectures from every single department. And so it's unlike many other institutes where a lot of times you have your notes, the grindstone in the chemistry department, the auditorium there only hosts chemistry seminars.

Lauren Fish (31:51):

You are very siloed kind of.

Shannon Miller (31:55):

Yes, yes. And so the ability to walk downstairs and when a lecture is going on, you don't know whether it's going to be hardcore catalysis or some preclinical mouse study of treating a neurological disorder or some basic science X, Y, Z pathway and disease. I really like that. And it really opens up and gives you a refreshing perspective on science. Yeah, I feel like that's consistently what I hear across the board too. It's definitely very unique in how it encourages that kind of collaboration rather than being more siloed or being more closed off. People actually want to work together across, people want to hear about what other people are on and on top of collaboration, just the inspiration as well. I think that there's a lot of things that people don't even think about until you go to these seminars that are not directly within your field, and you're like, oh, I'd never, yeah.

Lauren Fish (32:53):

It's like maybe that's the answer to how to solve a big problem that you're working on. Yeah. That's so cool. So if you were going to give advice to an up and coming scientist, what would it be?

Shannon Miller (33:05):

Yeah. One of the things that has helped me the most throughout my career is not being afraid or embarrassed to ask questions and ask for help. I think that a lot of scientists have this notion of individuality where you have to do everything yourself. You have to do your whole project yourself. But I think it's a waste to not use the resources around you. If I stuck on a particular area of a project, why would I dive deep into a multi-hour literature search of a field that I don't know when someone who is an expert in the field is quite literally next door, and they could just explain it to you probably better than it precisely.

(33:48):

And so I'm never afraid of asking questions or running an idea by a colleague, and I think that that greatly enriches how I do my science. Yeah. Well, and too, I can imagine some people might want to, if they feel like they get help, it's kind of maybe an ownership thing too. I think it diminishes their right. Its like, oh, I haven't, this isn't mine because I've had contributors. But it's like, no, we're all working towards such a big common goal. And when you think of the really impactful science, how often is it that it's those one author papers? It's never, it's the one that has so many collaborators listed, but the actual core science is so incredibly impactful. Absolutely. Yeah.

Lauren Fish (34:32):

I've never really thought about it that way too. Maybe some of the egos involved in not wanting to ask for help, but it's like, no, we're all going to be better. We can just work together on this.

Shannon Miller (34:42):

If we could get rid of scientific egos, I think a lot of scientific discovery would solves go a lot faster.

Lauren Fish (34:48):

Going back to something we were talking about earlier, how things you like to do to unwind reading and getting outside. What are some of your favorite books?

Shannon Miller (34:56):

Oh, I am a very big fantasy lover. So the one thing that I think about my hobbies is I really like hobbies that enhance the creative side of myself. And so that's why when I talked about all of these subjects that I loved as a kid, but never ended up going into professionally, they all became my hobbies. I paint now.

Lauren Fish (35:24):

Oh, so cool. Just I'm not good at it, but it's so fun to do that makes it better. And I think I took a ceramics class a little while ago, and it was so nice to be able to do something creative with my hands, because writing is great, but it's such a heady exercise.

Shannon Miller (35:39):

And so it was so nice and I was terrible. But to literally just do something with your hands and get outside and painting is the same thing. It's so visual. I also recently got into pottery on the wheel, and it's so meditative, it's so meditative and it's wonderful. And then fantasy books have this element of escapism. I'm the same way that I absolutely love. And I also still play video games for the same reason of reading fantasy novels, just like getting out of your head. And again, when you change gears so drastically from everyday, I'm thinking about science quite analytically. And you go home and you indulge in these curiosity driven hobbies. I think it resets and rewires your brain in a very positive way. Yeah, just enriches it more

Lauren Fish (36:28):

To close, we asked Shannon a few rapid fire questions about some of her most beloved things in science. These included, what's your favorite molecule, what's your favorite element? And lastly, if you had to describe your research using only emojis, which ones would you choose?

Shannon Miller (36:44):

My favorite molecule is, the easy answer is definitely Cas nine, but specifically the most popular one, which is a Cas nine from streptococcus ies. And I picked this one for a really unique reason. First of all, I emphasized how amazing it is that it can pick one single base out of 3 billion. And so the activity is just crazy. But the streptococcus IES CA nine is the first CAS nine that people discovered and characterized. And it still to this day is the undefeated best, is the best. That's crazy that it was the first one. And there's all this really cool discussion around maybe it was so evidently out there in the open to be discovered because it's the pest as a bacterial defense mechanism.

(37:31):

Maybe it's because it was more fit. I dunno. But I think that's just really cool. Not often does that happen in a field where your first iteration is just, is actually the best and yeah, 12 years later, like you were saying. Yeah. And so Castine is definitely my favorite molecule. Awesome. Best element I think would have to be magnesium because of how important this is in proteins that have catalytic activity. And so Cas nine uses magnesium to cleave, double stranded, DN. A lot of proteins that function through a TP use magnesium to be able to be molecular machines. So it's just universally a great element in biology that's just prolific arons everything. Yeah. And then in terms of emojis that I would use to describe my research, I spent far too long scrolling through all of the emoji options. There are a lot of science ones. There are so funny story. In my lab slack, we actually use the DNA emoji to react to things. So instead of thumbs up where like emoji, I love that. It's so useful in my field, but I think the easiest answer is a pencil in the DNA emoji, right? Yeah. You're rewriting rewriting. You're rewriting the code. Yeah. That's so cool. That actually is very applicable, right? Yeah. Simple, applicable, obvious.

Lauren Fish (39:00):

Many thanks to Shannon for joining today, providing insight into the many exciting things happening in the gene editing field, and for spending a little extra time studying the emoji keyboard for us. To our listeners, we hope this discussion has sparked curiosity and reflection on the powerful potential and the profound responsibilities of gene editing. Until next time, stay curious and keep questioning the world around you. And please leave us a comment because we love this.