SWW Season 5
Audio Transcript
Episode 1

Raven: (00:06)
Welcome to season five of Science Will Win. I'm Dr. Raven Baxter, also known as Raven, the Science Maven. I'm a molecular biologist and science educator, and I'm joined here by my partner in crime and life

Ron: (00:22)
Dr. Ron Gamble. I am a theoretical astrophysicist STEM educator and science communicator.

Raven: (00:29)
We're taking over as host for this season of Science Will Win. I'm so excited to be a part of this because I'm a lifelong learner and I love to tell people I came out of the womb as a scientist with a pipette in hand, a clipboard, and a lot of questions about the natural world. And ultimately as a biologist, you keep asking why, why, how, how, how until you get down to the molecule.

Ron: (00:59)
I was also interested in the science. I think I came out doing math. But I wanted to know just more of like the mysterious things, like why, why don't we know more about gravity? And I would ask all these questions and my teacher wouldn't know the answer. And I'm like, okay, well why don't you know, I have to go figure this out. So I would read a whole bunch of books I'd read ahead in class, but now I'm like, okay, I know all of this stuff. And I'm like, okay, well there's a lot of stuff to figure out. All this is really cool for me.

Raven: (01:30)
So I think there are so many fields of science where we are just on the tip of the iceberg of discovery. And as a molecular biologist, I know that we know only a fraction of what is possible for molecules to achieve. I mean, there seems to be endless possibilities where medicine can come from and how we can even incorporate technology to further medicine.

Ron: (01:55)
I mean, I think that's like spot on. Even though I'm in astrophysics, my first postdoc was in biomedical engineering education. So I got to design classes around biophysics, like bioenergy interactions through the labs. And so physics is everywhere. It, it's amazing what you can do with physics even in medicine.

Raven: (02:19)
Okay, enough about us. What's this season gonna be about, Ron?

Ron: (02:24)

This season we've done a deep dive on four different topics. We've partnered with Pfizer and a whole production team to learn everything we can about some of the most amazing medical technologies today. These are treatments and preventions that are right on the edge of something big, helping tackle new diseases or tackling old ones in ways we never could before.

Raven: (02:47)
We'll be switching off who leads each of the four episodes and this one is mine. So this all started with me thinking about alternate universes.

Ron: (02:58)
Okay. You know how to get me interested, but we're talking about medicine, right?

Raven: (03:04)
Yes, yes, we are talking about medicine, but here's the twist I've been thinking about. We all have these standard medical practices and policies like how much lead is safe in our water or how antibiotics should be prescribed or which vaccines we get as kids and as adults. And all of that stuff is really easy to take for granted. But one of them might've saved your life and you wouldn't even know it. Like there's no way to go to an alternate universe where some medicine or policy doesn't exist and see if you are still okay. Right?

Ron: (03:44)
That's my area. And no, there isn't like an alternate universe. There's no earth B, there's no earth 6 1 6 or whatever that you can just travel to without a polio vaccine that we could just pop in on. You can't do that, but you're totally right about that. Every standard of care is basically a decision that has to be made. People need to ask questions like, how does this achieve the best outcome? When does the benefit outweigh the risks? These things just don't fall from the sky. So a bunch of people had to figure that out and then convince everyone else through peer review.

Raven: (04:19)
Right? And again, like people don't just discover these things all at once. They sometimes have to build a whole century of research in order to just find the problem and then figure out the best thing to do about it.

Ron: (04:36)
But everything is figureoutable

Raven: (04:38)
True. That's definitely something a theoretical astrophysicist would say

Raven: (04:45)
But I think many scientists can relate. And so today, Ron, I'm gonna tell you about that process when it comes to this specific type of vaccine called a conjugate vaccine. So we're gonna talk about a once

mysterious bacterial disease that affects babies and the chain of events that led to the standard of care changing.

Ron: (05:07)
Okay, this is good. Let's, let's jump into this.

Raven: (05:09)
Let's do it. Okay. So before we get into any of this, I wanna make sure that you're brushed up on how immunity works in the body and what vaccines are doing. So what do you know about that, Dr. Gamble?

Ron:
Well, I know immunity involves something about what happens to bacteria or a virus that comes into your body, how it interacts with your white blood cells. Um, and then of course you have two different like types of white blood cells, your B and t cells, if you get a vaccine, it's basically like a piece of like the bacteria or virus. And then you know, your b and t cells basically turn into like super soldiers and they go and attack it and then your body's gonna remember it next time.

Raven:
I mean, you're not too far off. I often explain to people that vaccines are like sending your immune system superheroes to a superhero bootcamp, right? Where they learn how to fight the bad guy without necessarily encountering the actual bad guy, you know, in the flesh. So there are different types of vaccines. Some of them have only a specific part of a virus or bacteria like a protein or sugar, while some contain a weakened or totally deactivated version of a pathogen. And those things, the things that make your immune system wake up are called antigens. The different types of vaccines rely on different ways to teach your immune system, but the goal is still the same, to teach the immune system how to fight the bad guys. That covers the basics, but we wanna get a little deeper. So we spoke to a scientist at Pfizer for a primer.

Isis: (06:45)
So my full name is Isis Kanevsky. Uh, I've been at Pfizer almost nine years. I'm a senior director and I'm a scientist.

Raven: (06:56)
Isis has been working on vaccines for her whole career. She's part of a team that designs tests and optimizes vaccine candidates. And so we asked her to break down immunity and basic vaccine science and she gave us this analogy to explain how bacteria differ from each other.

Isis: (07:13)
Uh, the bacteria all have a different coat, right? I like to refer to the coat that they're wearing because the coat, what makes up the coat, right? The, the lining of the coat, the outer material of the coat, the color of the coat, that sort of as you said identifies the antigen. And then how we modify the antigen so that the immune system sees it and learns from it. That's the idea. So when we think about a

pneumococcal vaccine, which happens to be the area that I work in now, next generation pneumococcal vaccine. So that first vaccine just took the coat of the bacteria, it took a piece of the coat, used it as the antigen and vaccinated people with it. And that elicited some amount of protection but maybe didn't work as well in younger populations and infants who are very susceptible to this type of pneumococcal infection.

Raven: (08:05)
This is my jam. So let's break it down.

Ron:
Mm-hmm talk to me.

Raven:
So what ISIS just called a coat is actually, it's a real structure on the outside of the bacteria and it's made of these long complex chains of sugars called polysaccharides. And you can think of each of those sugar chains like a little charm. It's unique. They're decorative pieces. They hang off of the surface of the bacteria. It makes everything distinct, unique, fashionable, and that's where cell biology comes in, right? If we zoom weigh in bacterial cells, they don't have all the fancy organelles and compartments. What they do have is this protective outer layer. And those sugar chains are a huge part of it. Not only a part of protection, but also communication between cell to cell and also those sugars are what the body can use to recognize what kind of cell it is. And just like how no two charm bracelets are usually the same. Not every bacterial strain wears the same set of sugar chains, right? That is also why a single vaccine doesn't always cover every version of a bacteria because our bodies are built to recognize certain charms but sometimes not others. And so that's why vaccine science has to be so precise because you wanna make sure you're targeting the right set of charms so your immune system knows exactly what it's looking at.

Ron: (09:34)
So that's like the first edition vaccine, just the coat, right? So what makes a conjugate vaccine different?

Raven: (09:42)
ISIS explained that too.

Isis: (09:45)
A conjugate vaccine takes another protein and attaches it to that coat, right? So you can think of it as a scarf, how you attach the scarf, how you tie the scarf, all of that makes a difference. But then it becomes more beautiful in the analogy of the coat and scarf of course. But in terms of the vaccine, what you're dealing with is something that the immune system recognizes as beautiful or sees at something that teaches it better and then it maybe produces a better response, a better immune response. It lasts longer. You get better durability just by conjugating that antigen that polysaccharide from the bacteria to the protein carrier that we use. And then how you tie those two together makes a difference. And that's what forms the conjugate vaccine. That is a substantial improvement on using the coat or the

polysaccharide or the bacteria alone. You are literally attaching the protein that's gonna help the immune system process the antigen in a way that it drives T-cell responses and provides durability and long-term immunity. Um, because the T cells will then educate the B cells to produce antibodies that will fight the infection.

Ron: (11:01)
Okay? So the coat is like a polysaccharide like your sugar, right? And the scarf is uh, like a protein and they're kind of attached into one unit like an outfit. Is this like fashion week for cells? What difference does a protein make? Like well how does this lead to a better immune response?

Raven: (11:20)
I mean, yeah, it is. It is fashion week for cells, , . But like, let me flip this into like my own favorite analogy. Okay, so we've got coats and scarves. Yes, we love those fashions. We can also think of jewelry. So I like to think of conjugate vaccines as a charm bracelet where the charm is the polysaccharide, that little sugary piece from the bacteria and on its own, it's super cute, right? But it doesn't last. You might lose it. But the bracelet band is the protein carrier and that's what ISIS called the scarf Quick. PSA, we are not talking about the protein in your steak or your protein shake, right? There's no meat involved here in biology, proteins are molecules that do jobs, okay? They are the multitaskers of your cells. And here's the cool part, right? That protein usually comes from another bacteria that your immune system already knows well. So it's like a familiar bracelet that you've worn before. And then the tiny metal loop that snaps the charm onto the bracelet is a linker. So it stays put. And so this is an upgrade from older vaccines where back then we only gave the immune system the charm by itself, just the sugar. And that worked a little, but especially in babies and in young kids, the immune system looked at that single charm and was like, uh, like what am I supposed to do with this

Raven: (13:00)
And the T cells, which are your immune systems hype crew, they basically stayed asleep. They were just like, well, nothing really going on here. So once you connect that charm to a bracelet band, the body can recognize, boom, the immune cells perk up. They're like, oh my gosh, I know that guy, I know that guy. They hype up the B cells. Your whole immune system squad is on the case. You have an immune response, your body's remembering it potentially for the next time. And so conjugate vaccines take what used to be forgettable and turn it into a full bracelet that your immune system can't ignore.

Ron: (13:37)
Okay, I got it. And when were conjugate vaccines first invented?

Raven: (13:41)
Can you guess when these vaccines came out?

Ron: (13:45)
The first vaccine, it's gotta be like

Raven: (13:47)
The first conjugate vaccine.

Ron: (13:49)
I was born in 89, so that's a good year.

Raven: (13:51)
89. Yeah. Okay, well history time, the very first conjugate vaccine hit the scene in 1987.

Ron: (14:00)
I was close.

Raven: (14:01)
So not too far off. And it targeted hemophilus influenza, which can cause several serious infections like pneumonia and meningitis. But it's now part of the typical vaccine schedule. However, scientists first discovered that pairing with a protein can help with the immune response. Guess when Ron?

Ron: (14:24)
It's, I dunno, 18 hundreds.

Raven: (14:26)
The 1920s. So even more recently than that, it took decades of trial and error and scientific progress to actually build on that and create something that was safe and effective for people.

Ron: (14:39)
I have questions. Why would we need an extra strong immune response? Why is it not just use a polysaccharide on its own and then it kind of works?

Raven: (14:48)
I'm sure you have lots of questions. Okay? And this is a great setup because this is actually where the story gets really real. So let me walk you through an example, a case study if you will enter group B streptococcus. Let's talk about what this bacteria is, how it impacts newborns, and why a conjugate vaccine might be the perfect way to fight it.

Ron: (15:09)
We're talking about like strep, like strep throat, .

Raven: (15:12)
Ew, get away from me.

Ron: (15:14)
Sorry.

Raven: (15:15)
No, but close. Okay, so group B strep or GBS hangs out in a totally different neighborhood of the body, although it's in the same family as strep throat. About one in four pregnant people carry it in their vaginal or rectal tract.

Ron: (15:31)
That's a lot of people. One in four is 25%.

Raven: (15:35)
It doesn't cause symptoms in healthy adults. Alright? So someone might have it and never know a, but during birth, as a baby passes through the birth canal, that's when infection can happen. And there's just a small chance of the baby's getting it, but you really don't wanna risk it. This is one of those cases where even a small risk is a big deal because if a newborn does pick it up, GBS can cause sepsis, pneumonia or meningitis. And that's why this is such a high stakes issue.

Ron: (16:10)
Okay, so, so currently like how do we protect the newborns like the level zero humans from threats?

Raven: (16:18)
That's such a great, that is such a great analogy. Level zero humans, right? The way that we protect newborns, it differs around the world, but in the US pregnant women are swabbed as they near their due dates to see if their group B strep positive. And by the way, ISIS was,

Isis: (16:37)
So when I learned during my pregnancy that I was group B strep positive, I was advanced maternal age to begin with. Nobody wants that label, but I had it. And so I knew I had to have a hospital birth, but it put me in a place where I did have to address the birth plan, As an immunologist, I felt it was so, it was very into microbiome at the time and the, and the health of the bacteria from my body to my daughter during birth. And then you go in in your third trimester and you get swabbed and they're your GBS positive. And I'm like, okay, I know what GBS is, could be strep. I'm dealt with bacteria all my life and I really am a little nervous about getting antibiotics. So I said, well, I don't think I want the antibiotics. This is normal for me and my history. And the doctor said, that's great for you, but you don't really have a choice because you want your child to live. And I said, yes, I want my child to live. And they said, okay, you'll be getting the antibiotics. Great.

Raven: (17:43)
Okay, so why even pursue a vaccine for group B strep in the first place? Easy. We need more options. Okay, in the US the current standard of care for group B strep involves giving IV antibiotics during labor, which may not be ideal in all situations. For example, ISIS shared that during her own pregnancy she had concerns about how antibiotics might affect her microbiome. And it's definitely a consideration that deserves discussion. On top of that, we've talked about this before on science will win. Antimicrobial

resistance is a growing global problem. And the more that we use antibiotics, the more chances bacteria have to adapt and fight back and ultimately will make some of our antibiotics become obsolete. We don't want that. The other piece is access. In the us most people are giving birth in hospitals, they can get IV antibiotics, but in many parts of the world that's just not realistic. We're talking places where IV meds might not even be available at all, or where the cost of giving antibiotics to every laboring parent is just too high. And meanwhile the risk to newborns is still there. And so developing a vaccine is more than making things like more convenient. It's also inclusive of giving people around the world a choice and reducing unnecessary antibiotic use and protecting babies in a way that's safer, stronger, and more sustainable. And GBS happens to be a great candidate for a conjugate vaccine.

Isis: (19:27)
Decisions to pursue a vaccine are multifold, right? There's a lot of them for group B strep being a good choice. GBS, the group B strep itself has the components or the coat that it wears, right? You can take advantage of that, you can take pieces of it, you can make a conjugate. It also has multiple variants of the bacteria. So again, you can make a multivalent vaccine, which works really well for the conjugate technology in in the vaccine itself, you can put different components conjugates, multiple conjugates, and it will elicit a strong enough antibody response. And that's really the key, right? Is what kind of immune response you need, what you're teaching the immune system to do. And in the case of conjugate vaccines, you are teaching it to make certain types of antibodies. And we know that those antibodies can help control and kill the group B strep. Again, every mom that's been pregnant, if she's group B strep positive, whatever her plan was, which is very personal to a lot of people, changes when you're told you have to be in the hospital. You have to have antibiotics IV during labor. And for some people that changes their birth plan, as one might say, that's in the US where we have the standard of care outside the US that doesn't exist, babies are dying.

Raven:
A vaccine would be a game changer here. In Sub-Saharan Africa, nearly one in four babies born with group B strep doesn't survive. And it's not just a problem overseas. Babies here in the US still get GBS and die from it too.

Ron:
It's tragic.

Raven:
It is. And for those that survive, there can be long-term effects. Even more complicated. There are cases where moms can test negative before delivery, but still pass GBS onto their babies during birth. So the current system isn't even perfect.

Isis: (21:20)
When we look at developing countries and we think about the medical need, group B strep is a significant medical need. And knowing that we can make the conjugate vaccines that pre-clinically they

do protect against infection and protect the neonate makes it for a lot of scientists an obvious next choice.

Raven: (21:42)
Here's the thing about GBS, the infection happens during the act of birth itself, okay? So as the baby passes through the birth canal, that's when they can pick it up. You can't just vaccinate a newborn afterward. There's not enough time for the immune system to respond. So the question becomes how do you make sure a baby is born with immunity already on board?

Ron: (22:09)
So the mom gets a vaccine, is a baby protected through her?

Raven: (22:13)
That's why maternal vaccination is important because when a pregnant person receives a vaccine, their body can produce antibodies that may be passed to the baby before birth, potentially helping to provide early protection. So to really understand how we got all of the info we've covered so far, conjugate vaccines, group B strep, maternal antibodies, right? These things that we've been talking about, we talked to a few different scientists for background info and over and over again, this one name kept coming up.

Guests:
Carol Baker, Carol Baker, Carol Baker, Carol Baker, Carol Baker, Dr. Carol Baker is the expert in this field.

Raven:
People call Dr. Carol Baker, the godmother of Group B strep and maternal vaccination. You really can't talk about this field without mentioning her. She showed decades ago that it takes a specific approach to make sure that babies are born with enough immunity to actually keep them safe.

Ron: (23:17)
So what she got going on now,

Raven: (23:19)
Lucky me, I got to ask her that myself.

Carol: (23:23)
I'm um, Carol Baker. Um, I'm a pediatric infectious disease specialist and I was head of the division of infectious disease at Texas Children's Hospital for 25 years, but I'm happily retired and looking forward to a group B strep vaccine in my lifetime.

Ron: (23:43)
You got to talk to the Dr. Carol Baker.

Raven: (23:44)
Yes, the godmother of Group B strep and maternal vaccination. I interviewed her now, Carol did way more than just show the world we need a conjugate vaccine for GBS. So let's rewind for a second because it turns out group B strep wasn't always even on the medical community's radar. I'm super excited to speak with you because you've been called the godmother of group B strep prevention. And you with your magic wand, you, your work has changed , your work has changed the way that the world protects newborns. And so I would love to get your origin story. Do you remember perhaps a moment where you realized this infection is something that I will be dedicating a significant part of my life to?

Carol: (24:35)
Well, Raven, I, I never think that far ahead, but I'll tell you the origin story. There is a background. I was the only woman in my medical school class, and that's only relevant because I had to learn to be tenacious and tough and persistent. So my goal was to go to medical school and be a doctor. So during my medical school, um, rotation in neonatology, I fell in love with newborns, started my training in pediatrics, went to Los Angeles, came back to Houston. And during a neonatology rotation, I was called by the paging system of the time to the normal newborn nursery. And I ran and I got there. The baby was blue, not breathing. I tried to resuscitate that baby and was unsuccessful. And the baby died this beautiful, perfectly formed newborn. About a month later, a three week old, I'm now in the big county hospital in a a different building.

Carol: (25:39)
Um, a three week old is admitted critically ill to me. And, um, the spinal tap revealed meningitis. And this baby went on to be more critically ill to have seizures. Um, we did resuscitate the baby and we did, you know, everything we could. And that baby died in the first 24 hours. The first baby died of pneumonia. The autopsy showed severe pneumonia and the second baby died of sepsis and meningitis. So I had been told throughout medical school that a gram negative bacteria e coli, was the major reason for those two scenarios that I'm talking about. But the laboratory identified it as enterococcus. Not gram-negative e coli, I went to my professors, I went to the chief of pathology, the micro lab supervisor, and I said, look, these are newborns in the first month of life. What, what is this? And I don't remember the answer, but I remember the attitude go away. I would never describe this as disrespect because I'm the low man on the totem pole, so to speak, but it was, they didn't take me seriously. Let's say that that's a nice way and that that's how it felt.

Ron: (27:23)
How did she respond to that? Because that's, I would've crashed out.

Raven: (27:26)
She set out to solve this puzzle herself. That's what she does best. She got to researching.

Carol: (27:33)
Long story short, I went to the library and looked up old things from the thirties and forties and fifties and found out that there was this, this streptococcus called group B streptococcus identified by, uh,

Rebecca Lancefield in 1934. She did the classifications and I just knew, so Raven, you'll hear this phrase again. I just knew it was group B strep.

Ron: (28:02)
Okay, so this seems like quite a breakthrough in her spare time, right? Like she signs the heck outta this thing.

Raven: (28:08)
Yeah, she was just talking about how everyone used to think this kind of thing was caused by e coli, but she uncovered the actual cause of these infant deaths and she realized that the lab results indicating enterococcus were not quite accurate. So once Carol discovers Rebecca Lancefield's work on group B strep, things really start to take off.

Carol: (28:29)
So I, I looked up her papers from the thirties and forties and saw at her latest publication, um, was in the late sixties. I'm like, oh, so she's still alive. And her whole career was at the Rockefeller in New York. So I wrote her a letter back when we wrote letters . So she was very excited. She wrote back, she invited me to come to the Rockefeller and study with her for a month.

Raven: (28:58)
By the end of 1973, Dr. Baker managed to accomplish so much in terms of solving this puzzle of those newborn deaths. She was seeing,

Carol: (29:07)
I was able to describe the maternal baby transmission, the colonization rates of healthy pregnant women, the serotype distribution of women who were colonized, uh, babies who were colonized versus babies who were sick. I mean, an incredible amount of, uh, fundamental work was done. And so that's the long beginning. And it takes me to, group B Strep chose me. I did not choose group B strep.

Raven: (29:37)
After her work with Dr. Lancefield, Carol went on to lead another study showing that maternal antibodies would be key to preventing the spread of GBS to infants. And she found that moms who had higher levels of certain protective antibodies were much less likely to have babies who got sick from group B strep.

Ron: (29:55)
So what's the likelihood? Like gimme numbers, what? You know, I'm a numbers guy.

Raven: (29:59)
I do know you're a numbers guy and I've got the numbers for you Dr. Gamble. So in some cases, babies were up to 90% less likely to get the disease if their moms had enough of these antibodies, okay? But

most people with GBS don't naturally make enough of the right kind of antibodies to fully protect their baby.

Ron: (30:19)
So that's like, that's vaccine territory, right? So this is, we're learning.

Raven: (30:23)
Yes. Okay. So once Dr. Baker had this data, the next step seemed obvious, right? Try to make a vaccine. The first thing that she and her team tested was a simple polysaccharide only approach, right? And the bottom line is that she and her team tested three vaccines and none of them produced a strong enough immune response to actually transfer to a baby's immature immune system. And this was right around the same time that the broader medical field was realizing the same thing with other pathogens too. And that set the stage for the very first conjugate vaccine, which was for Haemophilus influenzae, the one we mentioned earlier. So with no vaccine ready yet, Carol didn't stop there. She convened a working group of doctors, nurses, obstetricians, midwives, policymakers, everyone basically to figure out what else could be done. And that effort ended up changing the standard of care and led to the practice that's still used in the US today, which is giving antibiotics during labor.

Ron: (31:35)
So all of this sounds like what we talked about in the very beginning. People are trying to come together, we're trying to have a meeting of the minds, we're trying to make decisions and decide on these standards. And it sounds like Carol, the godmother, a group B strep, she was at the center of these conversations. But even though we have ways to prevent diseases called by GBS, it seems like we still all agree a vaccine would be the ultimate goal,

Raven: (32:03)
Right? So ISIS told us earlier, Pfizer is working right now on a group B strep vaccine. So we wanted to see what that actually looks like in action. The producers on our team visited Pfizer's Pearl River site in New York to meet with one of the team's leaders that's been developing a potentially groundbreaking vaccine candidate.

Ksenia: (32:23)
My name is Kenya Krylova. I'm a senior director in vaccines at Pfizer.

Raven: (32:29)
So Pfizer's current GBS vaccine research kicked off several years ago with the goal being to cover six of the most common serotypes of GBS. Remember, there are about 10 in total, but these six account for the vast majority of cases around the world. We started by asking Ksenia to walk us through the process, how you go from a research concept all the way to a vaccine that's ready for clinical testing. Here's how it works.

Ksenia: (32:58)

We take a strain of bacteria, we identify whether it's the right serotype that we're trying to treat. Um, we grow the bacteria ferment, purify the polysaccharide from the fermentation broth. We take that polysaccharide. It's usually huge, really, really big molecule. It's not a single molecule, it's a mixture of different size molecules.

Raven: (33:23)
As a drug discovery scientist, I would compare growing bacteria and bulk in the lab to cooking because you're using broths of salt and different proteins and they're warm and they're fragrant. Now, I'm sure many people would have opposing opinions about the fragrance, but picture this, right, the bacteria, they're multiplying in a nutrient rich broth that bubbles and churns in a highly controlled environment. And that broth helps them pump out polysaccharides, which are these long sugar molecules that end up floating in a cloudy liquid. And so scientists then harvest it, they filter it, they clean it, and they prep those molecules for the next step in vaccine production.

Ksenia: (34:09)
So we take those molecules and we take carrier protein and we conjugate polysaccharide to carrier protein.

Raven: (34:19)
Let's pause on that word conjugate for a second because this is key. Alright, to conjugate means to connect. They're literally using a chemical connector to attach those sugar molecules to the protein carrier. And without that connector, the system doesn't work. Remember I was talking about that charm bracelet earlier where we have the protein bracelet, the linker, and then the sugar charm. Alright,

Ksenia: (34:44)
Then we purify that again, we test both the polysaccharide, the carrier protein, and then the conjugate. And then we take the conjugate and formulate it into a drug product, which we also test for various quality attributes. And that drug product eventually goes into safety studies. And that process, that whole process, we transfer to our partner lines, including formulation, including purification, fermentation, and analytical tests.

Raven: (35:17)
So speaking of testing, when our producers stepped into the Pearl River lab, they suited up in PPE personal protective equipment, right? Lab coats, safety glasses, gloves,

Speaker 6: (35:27)
Safety glasses.

Speaker 7: (35:29)
Thank you. Thank you. You're

Speaker 8: (35:31)

Welcome. Thank you so much. You're welcome. Now I put these on over my hand

Raven: (35:37)
And the place was spotless and sterile, full of bright lights, a low hum of machines. And every few seconds you might hear some beeps from equipment running diagnostics. And Ksenia and her colleague Abhishek, who works on vaccine production, gave a full tour of where samples are analyzed and vaccines are assembled.

Ksenia: (35:56)
So the samples of the drug comes through the door and it gets distributed to different analysts who have assigned tests. So we test cage, we test appearance, we test concentration of each drug substance in the drug product. We also test certain safety attributes. Analysts are here, uh, they take their samples and they go to their respective benches and do sample preparations.

Raven: (36:30)
One of the most important machines in the lab is called a H-P-L-C, high pressure liquid chromatography. It's basically the lab's truth teller. Alright? If you wanna know exactly what's inside a vaccine, every molecule, every impurity, every peak, this is the machine that spills the tea, basically.

Ksenia: (36:49)
What you're hearing is a pump. It's running liquid that comes through the, the pump. There's a column here in the column compartment and in that column it's packed with resin and there's a needle that comes and injects the sample and it travels to the column. So once the sample is injected onto the column, the mobile faces come and separate the analytes. And so the machine will show us different peaks.

Raven: (37:21)
If you're trying to picture what an HPLC looks like, okay, you can imagine like a tall boxy tower of stacked modules, each with its own screen blinking lights. It looks like a copy machine. There's tubing running between the boxes, there's pumps going, there's a little auto sampler tray where vials of liquid are sitting waiting their turn for processing. It looks like a high-tech espresso machine. All right? But instead of making lattes, it's separating molecules, . Since you can't see molecules, you have to separate them out so you can measure them. And that's how we figure out what's inside of stuff. So think of it like this, right? If your sample is a smoothie, the HBLC is a filter that can take it apart and line up the banana can line up the strawberry, the mango one by one, so that you know exactly how much of each is in there.

Ron: (38:20)
So we've, we use something very similar to that, if not like the exact same thing in physics, especially experimental physics. Biophysics definitely uses chromatography in figuring out the concentrations in things. So those peaks, I mean it's very important science.

Raven: (38:37)

So that's just one of the tests that they use. Ksenia says that they don't just build a process that works once they build it so that it can go from one vial to millions of vials pending regulatory approval. Of course, everything from fermentation to purification to final formulation of the vaccine candidate is designed to scale from small lab equipment to massive bioreactors in industrial sized columns. And at every step they test what happens when you go bigger.

Ksenia: (39:08)
From the very, very beginning. When we develop the process, we develop it with our eye on commercial process. So we never develop just so we can make one vial. So we test what happens if you do a little bit bigger, a little bit bigger. So our team scales it up a little bit, and then when we transfer all the processes to another team, they scale it up a little bit more or bigger. Actually, they scale it up for clinical and commercial.

Raven: (39:39)
Pfizer's team isn't starting from scratch.

Ksenia: (39:42)
I think the totality of our knowledge from the previous vaccines and the willingness to use new processes, new techniques, new analytical methods, that all is coming to fruition now. And obviously calibration, because you don't, you don't have the knowledge sometimes and somebody else does. So you learn, you learn from other teams, from other people. I've been here 19 years and those 19 years were one long vaccine education.

Raven: (40:17)
So Ksenia first got into vaccines 19 years ago, but her superhero origin story actually began many years before that. She was actually really young. Ron.

Ksenia: (40:28)
I was probably five, maybe four. My parents are chemists, used to be chemists. Um, so I feel like I grew up in a chemistry lab. I did my grad school in analytical chemistry, but it feels like I've always been in a lab. To me, it's amazing from when I started when I saw my first chemical setup, which was huge and big and bulky, and everything was done on paper to now when there's pretty much no paper. And everything is so miniaturized and so fast that it is just amazing to see the progress.

Ron: (41:20)
That's crazy.

Raven: (41:21)
Shout out to the parents for that exposure to science at such an early age. And in that time, Ksenia has seen so many things change.

Ksenia: (41:30)

There's a couple of machines upstairs in the analytical lab that didn't exist at PCR, but very advanced PCR machines, they didn't exist, um, probably 20 years ago. Good point.

Speaker 9: (41:44)
Which I don't know about because, you know, I wasn't doing science back then. Yeah.

Ksenia: (41:48)
And no, no.

Raven: (41:50)
She's describing so many steps that used to be done completely by hand, okay? But over the last couple of decades, new tools and technologies have been added that make vaccine development way more effective and efficient.

Ron: (42:04)
One, I can't imagine they've been doing this by hand. I mean, I do math by hand, but like some other stuff we don't do by hand. So that's incredible. That's amazing. Some of these changes show like just how technology has advanced really accelerated in vaccine development and how much more is possible now. So it's all these tools in place. We have all these new techniques, all these methodologies. Bringing it back to our original question, how close are we to seeing the group B strep vaccine in the real world?

Raven: (42:38)
So the vaccine is in phase three clinical trials right now, and there's still a road ahead, but if it's successful and gets approved, it could make a huge difference for so many families. Everyone does their part, right? I think one of the sometimes underappreciated things about these medical breakthroughs is that there are so many things that lead up to a major breakthrough, right? So like for example, in order for us to even have a GBS vaccine, someone had to understand the structure of bacterial cells, right? And then someone had to understand the structure of the walls of bacteria and what's on them and what are the sugars, what do they do? How can we utilize that to make better vaccines? What vaccines are effective? I mean, there's just so many steps to major breakthroughs. And I think the culmination of it is like we get to something like a vaccine that saves lives, right? You go from this fundamental question of how is a cell structured to how are we going to take advantage of that knowledge to save lives? And that is very rewarding.

Ron: (43:53)
So what's next? What's next in the docket for conjugates? Even what's beyond GBS?

Raven: (43:59)
Dude? Okay, what's next? Honestly, a lot. Okay, , we're just getting started. The party just got started. Shout out to Carol Baker and everyone. Um, but we, we've got more work to do, right? We're standing on the shoulders of giants.

Raven: (44:14)
Right now. Scientists are looking at ways to expand coverage by packing in more serotypes, right? More of those bacterial sugar coats into a single vaccine. And the more you can cover, the fewer chances the bacteria can have to slip through. True. And then people in the field are also experimenting with different connectors, different carrier proteins kind of mixing and matching to see what combos would make an immune system sit up and pay the most attention. And then of course, group B strep isn't the finish line conjugates are being looked at for other stubborn bacteria too. Anywhere older vaccine approaches have fallen short conjugates can give us another shot at it, literally and figuratively, I guess . And like that's the point, right? All the machines, the tests, the teamwork, everything is going towards this common goal of getting better protection for people who need it the most. Which is why we went back to Dr. Carol Baker to hear what it would mean if this vaccine finally became real improved, effective. Carol, I did read, you know, you mentioned your dreams and I read that you have a favorite quote from Langston Hughes. Hold fast to dreams for if dreams die, life is a broken winged bird that cannot fly. And I wanna get deeper into your dreams. What do you dream of for the future of group B strep vaccines?

Carol: (45:46)
They're, they may be different countries and different geographies and different skin color, but they're all women who, if they're colonized with group B strep may be at risk of having a baby with group B strep invasive disease. And even in the United States where, you know, when I told you about those first patients, there were several other groups in the early seventies, the mortality rate was 50% in some of our hospitals in our children's hospital. And now we have all, all this intensive care and life saving measures, et cetera. And we're talking three to 10% in the United States remaining. Uh, we, we need to get on the wagon here. And you know, on one hand I've told you I'm very persistent in tenacious and everything, but, but if I'm not optimistic, then I can't hold onto my dream anymore. So my dream is a picture, maybe a painting more than a photo of a group of children of various ages who in our dream would've had group B strep but didn't and look beautiful and healthy and from all countries. That's my dream.

Raven: (47:13)
Carol. That is beautiful. I'm tearing up over here. We surely have lost many, many beautiful children to this and we probably can't even imagine the loss. You know, that we've accumulated all of the impact that these children would've had in their own beautiful ways on the world. And I resonate with your desire to see every child have fulfilling lives and they get the opportunity to participate and enjoy the beautiful world that we have, um, and hopefully will become even more beautiful in the future. , thank you.

Carol: (47:51)
Um, you're very welcome. Uh, thank you for the privilege of sharing some of my stories.

Raven: (47:59)

So that's it for this episode. What did you think, Ron?

Ron: (48:03)
This was a very illuminating conversation. You got to talk to one of the goats in some of this work and like, I'm ready to see what's coming up next. Please.

Raven: (48:12)
Yeah. I'm so glad that we could learn about this together. It's really fascinating and I'm so motivated by all of the scientists working hard to solve these problems.

Ron: (48:20)
Yeah, next week I'm going to share what I learned with you, Raven. So prepare yourself. I think this one is gonna hit home like the rest of the season has a lot more in store, new labs, new stories from researchers and patients. So we get both sides right And then new breakthroughs, right? So we can't get away from the science.

Raven: (48:40)
We can never get away from the science because science will win

Ron: (48:43)
Win.

Raven: (48:44)
I can't wait. See y'all then. Science Will Win is produced by Acast Creative Studios and hosted by me, Dr. Raven Baxter.

Ron: (48:57)
And me, Dr. Ronald Gamble. Please take a minute to rate, review and follow Science Will Win wherever you get your podcasts. It really helps new listeners to find the show, to see more of the labs we mentioned today. Head over to Pfizer’s social media accounts. We'll also drop a link down in the show notes.

Raven: (49:15)
Special thanks to all our guests in the Pfizer research and development teams, and thank you for listening.