WE ARE ETH – Episode 23

With Sonja Billerbeck, ETH Alumni and scientist

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[00:00:00] Sonja Billerbeck: I think many people have heard about the fact that many bacteria pathogens for humans become resistant to antibiotics. But this is actually also the case for fungi. So fungi are like, we know, yeast is our friend. So yeast helps us baking and helps us brewing beer, all the good things. But actually many yeasts are also pathogens to humans, so they can cause really severe infections, especially immunocompromised humans.

[00:00:28] **Susan Kish:** In this episode I'm talking with ETH alumni and scientist, Sonja Billerbeck, who is an assistant professor in molecular microbiology at the Youth University of Groningen in the Netherlands. This is the We Are ETH podcast, and I'm Susan Kish, your host.

Sonja. How did you get interested in these areas around biology and microbiology and microbiomes? What sparked your interest in this field?

[00:01:01] **Sonja Billerbeck:** That's a really good question and I get this question actually right frequently in a wish I had a very inspirational story about it that goes all the way back to my youth or my childhood.

[00:01:11] **Susan Kish:** I know you were two years old and you crawled across the floor and said, oh,

[00:01:14] **Sonja Billerbeck:** I think it just organically grew that during my biology studies, which was where I chose, or where I realized just by attending different lectures that I was very much interested in, like more the biochemical or the molecular details about biology and explicitly about microbiology was what sparked my interest was actually metabolism at the time.

So I found it very intriguing that microbes, do not only breathe oxygen and do not only eat sugars like we do, but they have all these different varieties of metabolism that they use and that, give them the ability to growing in a lot of different environments of the deep sea and the Arctic.

[00:01:55] **Susan Kish:** So is synthetic microbiology, is that sort of where computer science meets microbiology or what is exactly synthetic microbiology?

[00:02:05] **Sonja Billerbeck:** Yeah, great question. So indeed, so I'm not a computational biologist.

[00:02:11] **Susan Kish:** Those are different?

[00:02:13] **Sonja Billerbeck:** They're not necessarily different. It's just I never learned much coding and I hate that fact, but it's true.

[00:02:18] **Susan Kish:** Sonja, I'm shocked!

[00:02:22] **Sonja Billerbeck:** But now I'm in a position where I can hire people who do that for me and it feels great.

[00:02:26] **Susan Kish:** Got it.

[00:02:28] **Sonja Billerbeck:** But it definitely has the feeling of putting engineering into biology. And engineering also, of course, goes along with maybe something that can be simulated and and predicted. So it of course needs computational tools, but computational biology is of course a much bigger field.

But definitely it wasn't like synthetic biology in its origin as at least how I see it was inspired by electrical engineering and more like computer guided computer aided design. Because biotechnology in the 1980s when the first genomes of microbes were sequenced had a huge promise.

So people thought, okay, now we can engineer microbes to boost medicines and make all these revolutions, but the dream didn't become true. So people needed a long time to engineer these microbes, and it was like very difficult. It was a lot of trial and error and people started reinventing the reel.

So I think the idea of synthetic biologists really, how can we make this dream come true that we can really use the variety of different biologically and coded function and put them together in new ways and make them work for us in the way we would like that to address human challenges. But we can only do that if we do it a bit more systematically and maybe also a bit in a predictive way.

[00:03:33] **Susan Kish:** And that's where the engineering comes in?

[00:03:34] **Sonja Billerbeck:** That’s where the engineering comes in. But it's the realization of the discipline is also that biological engineering is really distinct from computational or let's say from electrical engineering or from normal engineering.

How we know it, because we work with a lot of black boxes. And I think that was also the ma, at least to me, the major realization of the field is like, we really have to address biological engineering slightly different than electrical engineering. So I think this comparison was useful in the beginning to transmit the concept.

But it didn't hold true for the practical side to actually get something engineered in biology.

[00:04:15] **Susan Kish:** Fantastic. We're gonna return to this topic however, I just wanted to understand, so it sounds like Groningen sounds like an idyllic university town. Sounds like it was a fabulous experience. What was the catalyst for you to move down to Zurich?

Another idyllic town, but not Groningen?

[00:04:33] **Sonja Billerbeck:** Yeah, actually it was Tübingen, so the two sound very

[00:04:36] **Susan Kish:** Tübingen, oh sorry!

[00:04:39] **Sonja Billerbeck:** No worries. It's two "ing"- towns, coincidentally. Personally I'm a person who likes to travel and live in different places. So for me, science was also a way to just explore different parts of the world. So it was clear to me that after my master, I wanted to move somewhere else. And I think at the time I was with my partner and he had already gotten a position at ETH so I have to admit that I was just triggered because at ETH to me, was this like, very elite institute and I didn't see myself there.

I know it was a rare, and I knew they were also doing all these cool engineering and maybe it would even be the place where I could even participate in what I was becoming interesting in. But at the time it was, it just seemed very yeah, I don't know, A bit out of my league, but then actually which is yeah, interesting looking back.

But then actually when my partner started his PhD there, I started to meet just people, PhD students, maybe one of the other post, his mentor, and I realized it's just people. They are like me. Then I started searching for open positions and I knew that Sven Panke who eventually became my supervisor, he had a position in exactly what I had become interested in this kind of

[00:05:50] **Susan Kish:** Oh, cool. which was...

[00:05:51] **Sonja Billerbeck:** Like just engineering microbiology. During my studies I became interested in microbiology, all these different functions that microbes have. And then when I heard about synthetic biology, also a bit through my history studies, I was like, wow, what if we cannot only understand all these different functions, but really engineer them and put them together in different ways? So this sounded like very intriguing to me, and this was at the time, like the core of synthetic biology and not that many research groups in Europe actually had picked up on that, but Sven was one of them, so he was a bit, like the leading figure in Europe.

So I felt great. I just gonna send my application and then he hired me and yeah.

[00:06:36] **Susan Kish:** What was your next step?

[00:06:38] **Sonja Billerbeck:** Yeah, so my next step I moved to do a postdoc at Columbia University in New York City

[00:06:43] **Susan Kish:** Nice.

[00:06:44] **Sonja Billerbeck:** Yeah, this was more, again, in synthetic biology, but rather so in Sven's lab I had very much focused on metabolism, but in self free system. So it was like very biochemical. Yeah, focused on, on fine chemical production. So very applied, very biochemical metabolism, focused in Victoria and cell-free systems.

And I wanted to also move a bit more into higher organisms, so really try to understand how these engineering would really work in a bit higher organisms. And I chose to do that in yeast

[00:07:12] **Susan Kish:** Yeast?

[00:07:13] **Sonja Billerbeck:** In the bakers yeast. Yeah and...

[00:07:15] **Susan Kish:** oh, cool.

[00:07:17] **Sonja Billerbeck:** I knew one PI, Virginia Cornish, she's a full professor at the chemistry department at Columbia. And I could apply for a fellowship from the Swiss Science Foundation, the postdoctoral fellowship. So I reached out to her if she would be willing to. Like co-write a proposal with me and potentially host me. And then we started emailing and yeah, I, eventually got this fellowship and I moved into her lab. And then there I also applied for an American fellowship, which I then also coincidently got.

So I had like funding for four years of postdoctoral work. And yeah, that's what I pursued over there in New York.

[00:07:51] **Susan Kish:** So yeast is interesting. Is yeast, what is it? Is it an animal? Is it a mush, a fungus? Is it a plant? What is yeast?

[00:07:59] **Sonja Billerbeck:** It is actually a fungus.

[00:08:01] **Susan Kish:** Other than the stuff that's in the little packet that I use when I make bread.

[00:08:05] **Sonja Billerbeck:** Indeed. It's a microorganism, it's a fungus. It's a single cell fungus. And yeast,

[00:08:11] **Susan Kish:** Huh!

[00:08:12] **Sonja Billerbeck:** Yeast is basically just a... because for many people, yeast is really the package powder, the baker's yeast, but for biologists, it's more or less a gross state. So fungi can, of course, have a lot of morphologies. Mushrooms the champignons on our pizza. So this is all like fruiting bodies of Fungi that really make this huge mycelium in the ground. But then there's also other fungi, like for example, yeast and they just grow as single cells. And this single cell fungus is called a yeast. So there's actually a lot of different species that we call yeast.

There's also fungi that sometimes grow in this yeast form, meaning just this like single cell fungi and sometimes grow as mycelium.

[00:08:56] **Susan Kish:** So you're in the Netherlands, where exactly is Groningen in the Netherlands?

[00:09:00] **Sonja Billerbeck:** It's in the northern Netherlands. It's about two hours northeast from Amsterdam. I think Amsterdam is probably the best known city. So the Netherlands is like very populated in the South. That's called the Randstad towards the north, it's very agricultural.

So if you take a train from Amsterdam to Groningen and you drive through a lot of land, like a lot of agriculturally used land, and then at one point you arrive in Groningen.

[00:09:26] **Susan Kish:** Got it. Are those fields of greenhouses that are illuminated at night That I read about?

[00:09:32] **Sonja Billerbeck:** Actually the greenhouses, there must be somewhere different because I don't see them. Or maybe they're just not located next to the train track. So it's mostly actually like small national parks, but it's mostly agricultural land: Potatoes, onions. I don't know what this other green stuff is that grows there, but Yeah. Cows.

[00:09:51] **Susan Kish:** So tell us about what you do as a professor. I know that you have something called the Biller Beck Lab, which has, what I have to point out is the only picture of a lab I have ever seen that features five women on the staff page. I just went that makes me so happy.

Yeah. Although maybe that's not the exception. Maybe that really is the rule in the area you're in, but tell us about what you do.

[00:10:14] **Sonja Billerbeck:** Yeah, no, unfortunately it's not the rule. I'm also very happy about this because I do actually have a lot of women in my lab, which is a bit coincidental. I'm a bit worried about the diversity in my lab.

So I always say I also hire men. I also hire men. But coincidentally all the applications for my PhD positions I got were, I had fantastic women applying. And I really also like and take some pride in kind of mentoring them and seeing them

develop. So that's a lot of fun. But I also hire men. my major goal is still, the driving force is to really engineer yeast and bacteria towards their application in the bioeconomy in human health in agriculture. So this is of course very broad, but it's still the driving force.

And within this bigger topic area I currently work on antifungal proteins that are actually secreted by many yeast. And interestingly they participate in a warfare against each other and against other fungi in the environment.

Or maybe warfare is a bit very negative. But it's maybe like competition. But this leads them this made them evolve. Yeah. Proteins that are toxic for other yeast, so they kill other yeast, which could also be pathogens and filamentous fungi. And in this context of and what I try to do is, understand how they function and how we could use them to develop new, yeah, antifungals.

Because we're currently not only facing an antimicrobial resistance crisis, I think many people have heard about the fact that many bacteria pathogens for humans become resistant to antibiotics. But this is actually also the case for fungi. So fungi are like, we know. Yeast is our friend. So yeast helps us baking and helps us brewing beer, all the good things.

But actually, many yeasts are also pathogens to humans, so they can cause really severe infections, especially immunocompromised humans. But they're also a huge issue in agriculture. So about 30% of our crops are destroyed annually by fungo pests. And also a lot of fruits and other products are destroyed post-harvest by spoilage, which is also due to yeast or fungi.

This is a huge issue in agriculture, which could be controlled over the last decade by using a lot of pesticides. But I think now with the European Green deal, for example, we're trying to move away from these pesticides. There's also a huge issue with. With the fact that many of these antifungals have been co-used in the clinic and in agriculture.

[00:12:46] **Susan Kish:** What does that mean?

[00:12:48] **Sonja Billerbeck:** So that means that the same molecules that we use to control plant pests, so that are really used in agriculture are also used in the clinic. So humans get the same molecules. And that is actually not done with antibiotics because the risk is always. If you develop that, The more antibiotics you use, for example, the higher the risk for resistance buildup because the microbiome of the world gets exposed to these and they learn how to counteract them.

So this is something that is really not done with antibiotics, but with antifungals it's actually done because we have so few of them. And people were not concerned about them that much. So Yeah. What I tried to do in my work is address this challenge by really understanding how fungi themselves, kill each other in this warfare. And if we can find new ways on Achilles heels, how to really target them

and how to really control them in a in a bit more natural way. So that's a bit the idea. And yeah, so that's what we study now with this applied aspect in our mind.

[00:13:53] **Susan Kish:** So I went to Chat GPT and I asked Chat GPT how can generative AI be used to design and optimize synthetic biology?

And CHAT GPT gave me a bunch of questions. So I'm gonna see if any of these actually make sense, becuase you actually know this. And it says how might, so this is the first question. How might generative AI be used to design new biological systems with enhanced functionality? And what are the potential benefits and risks of such systems?

[00:14:23] **Sonja Billerbeck:** That is definitely a good question. That was part of the field. From onset on, because of course when you tinker with DNA, when you tinker with organisms, you might create something very harmful. So I might just take a very recent example. I think it's still unclear, for example, if the coronavirus evolved naturally or if it actually escaped from a laboratory where people were trying to. Maybe even not with a bad purpose in mind, trying to understand how this virus works and how you can make it even more potent or less potent. So whenever you tinker with DNA and then whenever you try to understand systems or purposefully engineer them towards a goal, they might also turn into something that is very harmful for humans. As I said earlier biological engineering has a lot of black boxes in it, so we really don't, fully understand what we're doing. So there is always a risk factor in it.

[00:15:18] **Susan Kish:** And how do you protect against that risk factor? How do you insulate your lab and the people who work in it?

[00:15:24] **Sonja Billerbeck:** So we do of course have so-called GMO regulations. So GMO stands for genetically modified organisms. So many people, not only in synthetic biology, many people work with genetically modified organisms because many disciplines in biology require that we modify d n a of organisms and then understand the effects of these notifications. So we do, of course, have our laboratories, we don't do our work in kitchen at home. We do always make sure that we destroy our biowaste a accordingly before it goes out into the nature. So the DNA cannot escape. We do train our students into properly, discarding and working these genetically modified organisms, such that they cannot escape into the environment. We also have four more risky project, risky in a sense of once we start working with pathogens, for example, we have a second level of safety, which is in the Netherlands it's called ML2 two, in the US it's called biosafety level two. It's a more closed laboratory, so it has kind of like a lower pressure inside. So kind of air would always go in rather than out. You have to really register who goes in, who goes out, you

[00:16:36] **Susan Kish:** Do you wear those bodies things?

[00:16:38] **Sonja Billerbeck:** In the laboratories we work in, this is not required, this would be biosafety level three. So currently we are rather concerned of our

microorganisms getting out, rather than us getting a real infection from them. So the biosafety level three is really the ones where people work with really dangerous pathogens for humans. I'm not doing that type of work.

[00:17:00] **Susan Kish:** That sounds like a relief.

But it does bring up this interesting question, which is around generative AI. Since it can deal with billions and trillions amounts of data, does it have impact on the kind of research and modeling that you do?

[00:17:13] **Sonja Billerbeck:** Yeah, definitely. Let's say in the last three, four years, we had a huge amount of publications coming out that use artificial intelligence to predict for example how proteins can fold that also predict how certain designs might work.

And which designs might work better than others? So this is like machine learning for example, and given these papers came out in the last two, three years, it means that people have been doing this research already for maybe five years earlier. I think the biggest impact is really what I just said about protein falling. So there' s one algorithm that was released. I think it was like almost two years now, which is called AlphaFold. Which helps us predict how proteins fold. So a protein is basically a strain of amino acids that is encoded in a gene that gets translated from Gene.

But until now, even though a decade of research, we were unable to really know how it folds into its test area structure. And this structure, how it folds, is really important for the function of a protein. So usually we use tools like crystallography or electron microscopy to really experimentally determine the structure of these proteins.

But it was really hard. Just from the sequence alone, knowing how it would fold and this usually to get the structure of a protein would take researchers years and years to actually purify and then do crystallography. So it was a very, almost one of the bottlenecks. For some of the engineering we do, because often for engineering you need to know the structure of these biomolecules and this AI is now able to just based on sequence, predict how the structure looks like.

We're still debating how good these predictions are, some of the very good and how much we can really just use them as if they were experimental data. But definitely this was like one breakthrough technology that artificial intelligence delivered. That we can use every day. And it's open and it doesn't require computational knowledge to use these algorithms.

So that's really hugely forward.

[00:19:17] **Susan Kish:** Do you think just in general that generative AI will be... will affect how basic research is done? I can see it for applied research, but I just was.

It, it's an interesting, open question. How does it affect the sort of world of research?

[00:19:35] **Sonja Billerbeck:** Yeah. What I just mentioned. So this protein folding algorithm, it is also very helpful for basic research because we all need this information.

This structural information to better understand how these biomolecules work on the basic level. But I also wanna give another example, which we actually just discussed in, one of our recent staff meetings. That's indeed Chat GPT. So how do you deal with like artificial and general intelligence that actually creates text because a lot of research is based, at least the dissemination of research or how we interact with each other as researchers is based on writing text. Writing our publications, writing discussions. Introducing topics to others, writing reviews, and even writing grant applications. So when we ask for money. And we are wondering how is that used in the good and the bad? And I think we obviously have to embrace it. So currently it's still, I feel Chat GPT delivers very superficial knowledge.

So it doesn't help me a lot and kind of really writing my research papers, although try to find out how I can use it in the best way, but I think it'll definitely change the way we do dissemination and research for the good and the bad, because I think it'll be more and more difficult to distinguish, like really thought through text from experts.

From just someone generating I could see that generating texts. It'll also come to intellectual property and who belongs. So this is a different aspect where science and communication will be affected through artificial intelligence.

[00:21:12] **Susan Kish:** But it is a really interesting questions. It's not like academic papers are written with a really sharp voice that you can say that's a New York Times, or that's The Economist where there's a voice to it. It's always written in a pretty dispassionate standard way. One, a paper about X reads a lot like a paper on Y, which would tend to imply that You could see applications to speed up that process of writing those papers.

[00:21:40] **Sonja Billerbeck:** Yeah, definitely. And I still wonder if that's a good or a bad thing.

I still think certain people have a certain style in writing and I think there is something to the writing process. that includes extracting, condensing your thoughts and I wonder if we...

[00:22:00] **Susan Kish:** If it forces a Christmas!

[00:22:01] **Sonja Billerbeck:** Yeah. It forces a Christmas. And I wonder if we should outsource that to artificial intelligence.

Maybe we're losing this, we are losing this ability to do that ourselves. That's a bit my concern. But on the other hand, given we all work so much under pressure, it's of

course also a great help to speed up certain things. And I think. Why not? If we can speed up dissemination and in the writing process and just get more science done in a shorter time, then well, I see the benefits of that.

[00:22:32] **Susan Kish:** Could you ever see yourself, because my assumption is that there's so many publications on any particular area, that it's almost impossible to read all of them and actually digest them and think through how it applies to what you're doing. Do you think you could develop your own platform and say, I want Chat GPT to read all these 25 papers and tell me the five things that I should remember.

[00:22:56] **Sonja Billerbeck:** I think that would be great. As a scientist, we're of course always doubting it makes a decision process.

the science for us, what are the most important ones? And I wonder if it would decide in a good way, but it is at least a good way to get a first impression about what is out there.

How much has already, how much has the field been researched, What should I know? So I think for at least getting a first impression it's great. Maybe but then again, I think we should also be careful about, which decisions does it make? Does it really deliver neutral information about these are the topics or what type of decision does it actually make? Because I think it's very difficult to understand, or no one can understand these algorithms anymore. They have a mind of their own. So it might over time then maybe bias certain research fields into a certain direction with us even realizing it because Chat GPT just pushed everyone into this direction, coincidentally, because of some line of code that yeah, it was just in there.

[00:23:56] **Susan Kish:** How did your years at the ETH prepare you for what you're doing?

[00:24:01] **Sonja Billerbeck:** So I think the ETH was the first place for me where I realized that research can really be translated into companies.

So this was new to me. So actually, I had done my master thesis at the Max Plank Institute in Tübingen. So this was associated. And Max Plank in Germany is really basic research. So it's almost forbidden to and that's also the purpose of it. So it's really forbidden to think about applications.

You should really answer basic questions. And transitioning from this position into ETH was really where professors were just having startups and were, there was like this whole translational department where people really thinking across these boundaries.

So this really excited me at the time. And I saw this is also academia. Because at the time I somehow thought there are two ways. Either academia or either an industrial career. But I didn't see it overlapping. And this was really something that I very quickly learned at ETH and what I got really excited about. That this can happen in

the same career, and this is also encouraged by a university. That was really exciting.

[00:25:02] **Susan Kish:** So you can use the word AND.

[00:25:03] **Sonja Billerbeck:** Exactly. Yeah.

[00:25:04] **Susan Kish:** Not just OR.

[00:25:05] **Sonja Billerbeck:** Exactly.

[00:25:05] **Susan Kish:** That's fabulous. So Sonja, thank you so much. I've got some closing questions I'd love to ask. What is your favorite place in Zurich or at the ETH? Where do you like to go?

[00:25:18] **Sonja Billerbeck:** At the ETH I always like the poly terrace.

So I especially because during, when I worked at ETH I loved to go to the sports. I think it's called Polysport or something, because I found that really great how much opportunity there was to just stay fit for free and I was just working above it. Then Afterwards coming out and I like the view and just like having my lunch. So I really, whenever I come to Zurich, I just go back to the poly terrace and yeah, enjoy the view.

[00:25:45] **Susan Kish:** Fabulous. And when you were growing up, let's say you were eight years old or nine years old, what did you think you wanted to be at that time?

[00:25:52] **Sonja Billerbeck:** I grew up in a very small town and I had a very lovely childhood. I went basically horseback riding every day, and...

[00:26:05] **Susan Kish:** That sounds fabulous!

[00:26:07] **Sonja Billerbeck:** It was very fabulous. This is a question I get asked. Very often, but I don't think I really had an idea what I wanted to be. I wasn't picturing me in any type of position.

So I think, which maybe speaks to the fact that my parents kept me like very nicely sheltered in my in my childhood. Just have fun and worry about it later indeed.

[00:26:30) **Susan Kish:** And you mentioned curiosity and you mentioned learning. So what are you reading now? What are the books that are on your nightside table? What are the podcasts you listen to?

[00:26:36] **Sonja Billerbeck:** Actually if I just pick the first book that comes up here next to me, it's Kamala Harris' biography. So what I do like reading is actually

biographies of people in leadership positions. Not necessarily to learn, but rather because it really intrigues me where people come from and where they're going and what motivates them. I think when I mentioned that I studied history I like context. I like understanding why we do things and why things happen in our world. And I think before that I read the biography of Barack Obama. Maybe also because I lived in the US I'm also very intrigued and especially like American history and American politics, just because it's also so complex from

[00:27:19] **Susan Kish:** I thought you say it's so dramatic.

[00:27:21] **Sonja Billerbeck:** From the diversity of people that come together in the US Yeah.

[00:27:25] **Susan Kish:** Very cool. Sonja, thank you so much. This was a fabulous conversation. Really enjoyed talking to you.

[00:27:31] **Sonja Billerbeck:** Thank you so much for having me, for inviting me. It's really a pleasure and it was really an honor to be on that podcast.

[00:27:36] **Susan Kish:** Wonderful.

I'm Susan Kish, host of the WE ARE ETH series, telling the story of the alumni and friends of the ETH Zurich, the Swiss Federal Institute of Technology in Zurich. ETH regularly ranks amongst the top universities of the world in terms of cutting edge research science and people. The people who were there, the people who are there and the people who will be there. Please subscribe to this podcast and join us wherever you listen and give us a good rating on Spotify or Apple, if you enjoy today's conversation. I'd like to close by thanking our producers at the ETH Circle and Ellie Media, and to thank you, our listeners for joining us.