Innovating Alternatives

a podcast about AMR in food-animal production and the researchers around the globe who are working to reduce it.

Episode: Bacteriophages

Featuring: Prof Paul Ebner, Dr. Nicholas Svitek, Prof Sylvain Moineau, Prof Zafar Hayat, Prof Nicole Widmar, Dr. Zoe Campbell

Justin Kemp (JK) - If you were to imagine scientists hunting for the next great alternative to antibiotics, I'm guessing you might be picturing lab coats and gleaming white laboratories.

Prof. Paul Ebner
it's a very glamorous process that starts at a wastewater treatment facility, we've had the best luck using wastewater.

Dr. Nicholas Svitek
We went, in fact, in more than 60 Farms, and we collected faeces samples.

Evelyn Baraké (EB) – The hunt may start in some less than gleaming places, but it's definitely back to long hours at the lab bench after that.

Dr. Nicholas Svitek
So the first step was in fact to get our Salmonella isolates. We cultured them in bacterial culture media.
And then we proceeded in isolating the Salmonella from these cultures on selective media and then we confirmed the identity of the bacterial isolates by rounds of plaque identification, once we knew that sample X was pure phages, we also proved by PCR.

JK – In fact the work is so fascinating and engrossing, that some scientists have even lost track of time.

Prof Sylvain Moineau
First of all, I have not been studying phages for 30 years. I think it's more like 20. I started studying phages in 1989, so is it 30 years? Oh my god. Yeah, that's... Oh my god. I thought it was like more 25 anyhow, okay...

EB - I'm Evelyn Baraké

JK - And I'm Justin Kemp and this is Innovating Alternatives – a podcast about antimicrobial resistance and the researchers around the globe who are working to reduce it. In this episode we meet two teams of researchers looking to develop alternatives to antibiotics by harnessing the natural enemy of bacteria.

JK – Take a moment to consider yourself as a physical being. What do you think of? I'm guessing you probably focus on the obvious bits, the bones and muscle that define your form, maybe your skin and hair, perhaps the face you see in the mirror everyday. Turns out that more than anything else, we are mainly blood - 80% of our cells are red blood cells.

EB – So we are essentially big walking bags of blood.

JK – Pretty much, but that's only half the story.

EB - Oh no. here we go.

JK – Well, we're mainly blood if you only count the cells with human DNA.

EB - What do you mean - if we only count the human cells?

JK – Well, if you were to line up all the cells in the average human body, roughly half of them would be bacteria.

EB – Wow! so now we are basically walking apartment buildings for bacteria.

JK – Well yes, and blood of course. Well if you think it's impossible to escape your personal bacterial shadow, bacteria themselves aren't excused from having their own set of microscopic groupies.

EB – Phages?

JK – Exactly! So to help us get a handle on what's what with phages, here's someone who knows their way around a phage.

> Prof Sylvain Moineau
> [*My name is Sylvain Moineau. I'm a professor of microbiology at the University of Laval in Quebec City, Canada…. Essentially, every time you look for a bacteria you should find phages and I joke sometimes saying that if you do not find phages it's because your protocols are wrong, because you should be able to find them, right.*

EB – But phages don't get along with bacteria quite as well as we do with our microbiome. They wouldn't make for great groupies either…. They'd be more like the hungry zombie type.

JK – Yea, the relationship between bacteria and phages is, how would you say, a little less congenial. Bacteriophages, often just referred to as phages, are parasitic viruses of bacteria.

Prof Sylvain Moineau

I don't know if people are aware of this, but viruses are the most [common] biological entities on the planet. We're surrounded by viruses, they're more abundant than bacteria. Bacteriophages are specific viruses that would attack only bacteria, so they will not have any impact whatsoever on humans, on animals on plants, on insects. They really are viruses that are specific to bacteria.

EB – I'm guessing this will come as a relief to some of our listeners who heard you say "parasitic virus". I mean, considering public enemy #1 in 2020 was a virus…

JK – Right. Well there's even more good news: not only are phages harmless to us humans, they also have some very interesting properties that we can harness to our advantage. But to understand those, I'll first let Sylvain explain exactly how phages work.

Prof Sylvain Moineau

Essentially what they'll do is they will bind, again, specifically, to the surface of a bacteria. And then they will inject the genetic materials inside of the bacteria. And at that point, they essentially take control of that bacteria. And the bacteria becomes like a factory of new viruses. The viruses will start amplifying itself, replicate. And after some amount of time, the bacterial cell will burst and new phage will be released into the environment. So that's your typical way a phage will replicate. And of course, because they are so abundant in our ecosystems, they play multiple roles. And one of them is to control the bacterial population in every ecosystem.

EB – Well it's pretty obvious from that explanation why we might have an interest in phages. Something along the lines of my enemy's enemies are my friends.

JK – Exactly. There are a couple of interesting points in there if you are in the business of finding alternatives to antibiotics, in other words, looking for different way to slow down the growth of harmful bacteria or kill them outright.

EB – Yeah, how did Sylvain put it exactly? "The bacterial cell will burst"? Correct me if I'm wrong, but I don't see bacteria surviving being burst open.

JK – Um no. Not coming back from that easily – that's a process called lysis. But the other interesting, and potentially useful, feature of phages is their specificity.

Prof Sylvain Moineau

Even though a phage will bind to a cell surface of bacteria, this interaction is actually highly specific. So, not any phage will bind to any bacteria. It's really something like a lock-and-key system: the phage will have to key into the right lock for the proper binding and start this lytic or replication cycle. And that's why you will have phages that are specific for Salmonella, you will have phages as specific for E. coli. *So there's really a specificity issue. Not only are these phages infecting only bacteria, but they will also infect a subgroup of bacteria in a way.*

EB – Ok, so we have a naturally occurring virus that is both very good at killing bacteria and is also very targeted in that action. AKA it wouldn't wipe out all of the good, friendly bacteria along the way! In terms of therapy for treating bacterial infections, this sounds like a dream come true. So why isn't phage therapy prescribed at the doctor's office already?

JK – Well, to answer that question, we have to go back in time - just over 100 years in fact to 1915.

EB - Here we go again!

JK – 1915: That was when the British bacteriologist Frederick Twort, noticed little spots on the bacterial cultures he was working with. He came to realise that these spots were the result of dead bacteria, that they could be transferred from one culture to another and, that they required bacteria to grow.

EB – So did he grasp exactly what it was that he was that he was looking at?

JK – Well, kind of. He put forward some ideas – one was that it was a natural part of the bacterial lifecycle or perhaps caused by an enzyme secreted by bacteria themselves or maybe some form of ultra microscopic virus. He gave it the rather broad name of "bacteriolytic agent" - there's that idea of lysis again - wrote it up for the Lancet journal and left for the war.

EB – Well that can't be whole story?

JK – Not at all, so a few years later in 1917, Felix D'Herelle, a self-taught Franco Canadian biologist was working at the Institute Pasteur in Paris when he independently described a new microbe.

French accented voice actor

I isolated-an invisible microbe with antagonistic properties against the Shiga bacillus

This microbe, a true immunity microbe, is an obligate bacteriophage; it is a strictly specific parasite

JK - That's where he coined the term "bacteriophage" which literally means 'bacteria eater" This is a bit off the mark given our current knowledge of virus biology, but it was a remarkable discovery none the less. He also immediately recognised the therapeutic possibilities of phages.

EB - And, did he get a chance to test this out?

JK – Oh yeah, it was only a couple of years later when he tried using phages to treat a bacterial infection for the first time in Paris. His first patient was a 12 year-old boy with severe dysentery.

EB - That must have pretty fringe in those days – especially since this is about a decade before the discovery of penicillin.

JK – Well they ran a quick safety study which involved Felix, the hospitals chief of paediatrics and some unsuspecting interns ingesting the as yet untested therapy first.

EB – Ummmm wow! Cheers to advances in the field of medical ethics.

JK – So the boy recovered fully, as did several other patients, and phage therapy was born. Soon several companies, both in Europe and North America, including Felix's own commercial laboratory, had begun producing phage preparations. D'Herelle devoted his scientific life to bacterio-phages. He penned over 100 articles and five books on the subject. He travelled widely on the trail of phages, finally arriving in Tbilisi, Georgia, where, in collaboration with George Eliava, founded a bacterio-phage institute that still exists to this day. He even chalked up a Nobel prize nomination along the way.

EB – Felix d'Herelle had quite the journey and an illustrious career, too! So now I'm even more confused about why phage therapy isn't in common use today, given its very promising start.

JK – Well, it wasn't all plain sailing. Critical review of early phage therapy studies questioned the effectiveness of the treatment, and with the arrival of the new antibiotic wonder drugs such as penicillin in the 1940's, phage therapy ultimately faded into the background of popular Western medicine. It was not entirely abandoned, though. A handful of countries in Eastern Europe have continued therapeutic phage research, production and even use to this day.

EB – OK, but even though phage research for therapeutic purposes was kind of sidelined, that wasn't the end of research on phages per se.

JK – No, absolutely not. In fact phages have played a pivotal role in shaping modern biology.

> Prof Sylvain Moineau
> *Indeed phages have played a key role in life sciences. They have been used early in molecular biology as tools to understand viruses, because they're very small, very simple to study. There's even Nobel prizes that have been won due to research on phages and phage biology. And in 2018, Nobel Prize in Chemistry was awarded to someone that developed a technology called phage display, which is a technology using phages that help you recognize some specific binding. And even more recently, if you look at the technology called CRISPR-Cas9 – which is a genome editing tool that you can use to modify any organism or the genome of an organism – this CRISPR-Cas9 tool was actually discovered or developed following studies on CRISPR-Cas systems that are naturally found in bacteria. Earlier I was mentioning to you that we are surrounded by viruses and bacteria, and viruses called phages. And bacteria need to defend*

themselves against phages. And CRISPR-Cas is actually a defense system that the bacteria will have to combat phages. And when people start studying, or scientists are studying the system, that's when we develop the CRISPR-Cas9 technology. That technology that now we're using, even in some medical fields, is actually based on studies on phages and bacteria interactions.

Before CRISPR-Cas9, all the cloning was done using enzymes called restriction enzymes. And those restriction enzymes will cut the genome and will allow you to cut and paste DNA, back in the 70s and 80s and 90s, even today also. And those restriction enzymes, those enzymes that helps you with cloning, they're also a defense system that bacteria are using against phages. In the 70s, these enzymes were discovered, and it also won a Nobel Prize on restriction enzymes, again, studying phage biology and the interaction with bacteria. So if you go back into history, you'll find a lot of these stories where phages were studied, were analyzed, and great discoveries were made.

EB - Hold up! This interview was recorded before the announcement of the 2020 Nobel Prizes, wasn't it?

JK - It was

EB - And the 2020 Nobel Prize in chemistry was awarded to the researchers who developed the CRISPR-Cas9 tool, Emmanuelle Charpentier and Jennifer A. Doudna.

JK - Yep

EB - So phages gave a major assist here once again! Sylvain's comments seem very prescient… Maybe I should ask him which lotto numbers to play

JK - Careful, I'm not sure how much scientists like to be compared to fortune tellers… But he is also being a bit modest here. He was part of the team of scientists whose foundational research on the CRISPR-Cas mechanism allowed for the development of the tool.

EB - Wow! Good thing we interviewed him when we did… his inbox must be full of interview requests these days… OK back to Sylvain. Where did we leave off?

JK - He was telling us about the different reasons researchers have studied phages over time.

Prof Sylvain Moineau
Groups still studied phage biology, just to try to understand how these viruses because back in those days, we didn't know how to work with human viruses, we didn't know much how to work with plant viruses and so forth. So phages became a nice model to

study because they were simple. You can work with bacteria; they were safe for the lab workers and so they were their first model of viruses. So in one way, people stopped studying them as phage therapy, but in another way, in life sciences they were the perfect model to study biology. We keep studying them and then, I would say that after a while, when we started to have a better grasp of how to grow eukaryotic viruses – viruses that are infecting human cells or animals cells and so forth – phages kind of went into the backstage a little bit. But now because of antibiotic resistance, they're back. They're back for the past decade now. And a lot of groups are studying them again.

EB – So were entering a new "age of phage".

JK – Great band name - noted! Anyway, yes the growing emergence of antimicrobial resistance is driving researchers to look for new alternatives to antibiotics in all sorts of places. As it turns out, we might just have to look to the past to tackle the challenges of the future.

EB – And we'll need a lot of brainpower and collaboration between all types of sectors to tackle an issue as big and far-reaching as antimicrobial resistance, as we learnt about on the last episode.

JK – Exactly. Drug-resistant and multi-drug resistant bacteria don't stay confined to the environments where they emerge. Antimicrobial resistance is a problem that doesn't respect boundaries. It crosses country borders, economic sectors and affects human, animal and environmental health.

EB – There are so many potential entry points to tackle this issue, but food animal production especially is an area of growing concern for antimicrobial misuse, as last episode's guest, Professor Dame Sally Davies, pointed out:

Prof Dame Sally Davies
Clearly, more antibiotics are used in animals than in humans, and many of those are used for growth promotion, or preventing infection. We can find better ways of doing that through research.

EB - Speaking of better ways to prevent infection in food animal production. Could phage therapy be a potential alternative to antimicrobials?

JK – Yes, it definitely holds potential! One area where cutting edge phage-therapy research is happening right now, literally as we speak, involves poultry and the bacterium *Salmonella*. In fact, I interviewed scientists from two separate research groups who are looking to develop phage-based products to reduce or replace antibiotic use within their specific local contexts.

EB – Tell me more!

JK – Yeah, so one group involves a collaboration between researchers at Laval University in Quebec, Canada – led by Sylvain – and the International Livestock Research Institute or ILRI, in Nairobi, Kenya. Together, these teams are looking to develop a phage product targeting *Salmonella* optimised for use in the Kenyan context.

Dr. Nicholas Svitek

My name is Nicholas Svitek. I'm a microbiology biologist by training and I work at the International livestock Research Institute in Kenya.

In fact there are several diseases that affect chicken farming in Kenya. And among those diseases there, a majority of them are caused by bacterial infections, and among them, Salmonella is a big concern in poultry farming. And this affects farmers at two levels. One we have Salmonella that infects and will cause disease in chicken. So Salmonella is still a problem for chickens in the developing world in low- and middle-income countries. And one of these strains is called Salmonella gallinarum that causes fowl typhoid and there's another Salmonella very closely related to Salmonella gallinarum that causes another disease called the Pulorum disease. This is caused by Salmonella pullorum. But Salmonella can be a zoonotic pathogen also. We know that Salmonella can be transmitted to humans and cause gastrointestinal symptoms such as diarrhea or abdominal pain. And an example of such Salmonella is *Salmonella enteritidis. So Salmonella can then affect those families that rear chicken at these levels, so on one side, it can affect the chicken and cause disease and have a impact on the production level. But it can also be a health risk for the farmers as well as the consumers.*

It's not only a problem in Kenya, but in fact it is a widespread problem in Africa. So we have neighboring countries such as Ethiopia which has also problem with Salmonella. We have cases in Tanzania and a lot of reports also from Nigeria.

EB – I did not realize there were so many types of *Salmonella*! Here in Canada we only hear about *Salmonella* as a potential hazard for the consumer, but it makes sense that it also harms the chickens, and poses a risk to the farm workers who come into close contact with them, too!

JK – Right, not to mention the economic impacts on the farmers.

EB - Alright, so if these various forms of *Salmonella* are a major issue for Kenyan poultry farmers, is it common for producers in Kenya to use antibiotics for prevention and for treatment?

JK – Well, like many things in life It depends, not all poultry enterprises are the same, and neither are all poultry farmers.

Dr. Nicholas Svitek

We have visited both very small scale, midsize and then large scale. The large scale,

most of them are like subcontractors of a company in Kenya where they forbid them from using antibiotics. The farms where they were using bio-control measures were the big commercial farms, in fact, but then when we visited the smaller farms where they had a couple of hundreds or 50 birds, where they would use a lot of antibiotics. And we had also families where they were rearing maybe like 10 chickens very, very small scale. So that's mainly where we saw the use of antibiotics, in those small-scale or middle scale chicken farming.

EB - That's interesting! I would have thought the opposite – that it was the larger industrial-scale producers using antibiotics with abandon.

JK - It might seem surprising at first, but like Nicholas said, bigger operations tend to be governed by stricter regulations and monitoring their compliance is probably easier than it would be to monitor smaller, less organized operations.

Dr. Nicholas Svitek
One thing that we need maybe to clarify is that farmers usually are not well trained to diagnose what is the causing pathogen when the chicken is infected and is showing clinical signs. They might not know if it's a bacteria or a virus. So in the majority of farms we have visited, we saw that the farmers were using additives in the feed that they were giving to the chicken. And that was basically to prevent infections or even to use as a feed supplement to increase growth rate of chickens. And most of the feed additives or the feed that they were using had a panel of antibiotics, so they don't use only one antibiotics but the mix to make sure they target all possible bacterial infections. So that can be a problem when we talk about antimicrobial resistance. And maybe I can add that some studies have shown that about 75% of antibiotics used in poultry farming in the feed is released in the environment. So that most probably contributes to the emergence of antimicrobial resistance.

EB – Antibiotics are commonly given to poultry as a food additive AND 75% of them leak out into the environment?! Sounds like these are the perfect conditions for the emergence of antimicrobial resistance. Have the researchers looked to see if *Salmonella* is becoming resistant?

JK – They have, using a method called the Kirby-Bauer disk diffusion assay.

EB – Quite a mouthful, try saying that 5 times fast!

JK – I'm not even going to try. It's quite a cool little test, actually. So how it works is you inoculate an agar plate with bacteria and then place a little wafer disc containing an antibiotic on the surface of the plate and leave it to incubate. If the antibiotic kills the bacteria or at least stops it from growing, there will be a clear area around the wafer that is visible, called the zone of inhibition. The size of the ring tells you how lethal the antibiotic is to the bacteria being tested.

EB – That sounds way more straightforward than I was expecting, with a name like that. So what did they find?

Dr. Nicholas Svitek

Yes, we saw some resistance. We have analyzed some of our Salmonella isolates with a panel of 12 antibiotics and we also included some E. coli *and* Shigella *strains that we also managed to isolate from the field. And our preliminary data indicate that about 40% of these bacterial isolates are multidrug resistant. So, they're resistant to three or more antibiotics. And when we looked at the farm level, if these isolates came from farms where they used antibiotics or not, there was not much difference, in fact, because we saw multidrug resistance or multidrug resistant strains coming from both farms that use antibiotics and farms that do not use antibiotics.*

EB – So in other words, yes, there are multidrug resistant bacteria on the farms that use antibiotics and they've even made their way to farms that don't use them!

JK – Yep, if there was any doubt, now we should be totally clear on the need for alternative ways to prevent and control *Salmonella* on these poultry farms.

EB – Right so that brings us back to the phages… To develop a phage-based product against *Salmonella*, you'd first need to find suitable phages, which could be tricky right, because they need to be specific to the bacteria that you're targeting.

JK – Yes exactly, you need to find ones that are specifically lytic for *Salmonella* bacteria.

EB - And we already know if you are looking for phages, you need to follow the bacteria.

JK – For sure! Phage hunting will take you to all sorts of interesting places.

Dr. Nicholas Svitek

When we went to do our phage hunting, we went in the environment where the bacterial host was believed to be found. So what we did, we went to visit the poultry farms where we collected our bacteria. And we went, in fact, in more than 60 Farms, and we collected faeces samples because we know that Salmonella can colonize the digestive tract of chickens. So we collected chicken faeces from which then Salmonella can be isolated. And that's where also, in those faeces, we also looked for the phages that should infect or be specific for Salmonella because it's where the host is found. That's where you'll find the bacteriophages. So we collected more than six hundred faeces samples, as well as water samples coming from the chicken farm, as well as from slaughterhouses where they slaughter chicken.

JK – So as we heard in the intro to this episode, there are a lot of steps and a lot of hours at the lab bench to get from a sample collected on a chicken farm to a pure culture of phages which you could use as part of a phage-based product.

EB – Care to break it down for us?

JK – I'll do my best! We know that to get phages, you need their associated bacteria. So first up, scientist isolate the target bacteria, in this case *Salmonella*. To do this they create a primary culture of bacteria, let's call it the mothership culture. It's pretty easy really, mix faecal sample with bacteria culture media and incubate to see what grows. The mothership is essentially a sample of all the microorganisms in the chicken faeces.

EB - OK, but we aren't interested in every kind of bacteria in the sample, just the *Salmonella*.

JK - Exactly, that's where selective media comes in. Different bacteria have different requirements – if you provide only what your target bacteria need to grow in the growth media, you can get them to flourish where others can't. So if you use a media optimised for *Salmonella*, for example, you can selectively culture them on plates – nice monocrop lawns of *Salmonella*.

EB – And what if some other bacteria sneak through?

JK – So researchers confirm that what they have is *Salmonella* using genetic methods: PCR and sequencing.

EB – Well is great that we now have the *Salmonella*, but aren't we looking for phages.

JK - We are. So back to the mothership culture, because if there was *Salmonella* in there it's likely there are phages in there too. The next step is to spot little drops of the mothership culture onto your newly grown *Salmonella* lawns. And bingo, if you see a clear spot develop where there is no bacterial growth, called a zone of lysis, you know that you've found phages. Next follows several rounds of purification to ensure you have a pure culture and then a quick check with PCR to confirm that they are indeed phages and that they are unique.

EB – Is collecting and purifying bacterial muck the only way to find phages, then? It sounds like a lot of work!!

JK – Well, there's actually another place to go looking for phages if you are looking for more options. You can visit a phage library.

EB – A phage library?

JK – Yup, exactly that, a collection of phages for those who need them. Turns out Sylvain is actually the curator of one of the most diverse phage collections out there. It's even named after our old friend Felix.

> Prof Sylvain Moineau
> *The Felix D'Herelle Reference Center for Bacterial Viruses was actually founded in 1982 by a professor named Hans Ackerman, he was a professor here at the University Laval, Faculty of Medicine. And since early 2003 his collection has been transferred to our*

group here, and I've been the curator since. The main value of the Felix D'Herelle collection is adding phages infecting over 130 bacterial species. We have a large diversity of phages. There are other collections out there that have more phages. But none of them have the diversity of phages that is conserved here at the Felix D'Herelle. And essentially, the mission of the Felix D'Herelle is to collect and distribute phages for teaching and research purposes. In the last five years, we have sent phages to over 300 research labs around the world in over 35 different countries.

And the person really in charge of shipping those phages is Denise Tremblay. She has been handling all the phages and is an expert on handling and distributing phages around the world.

Phage research has been picking up quite extensively in the past couple of years and Felix D'Herelle have been a supplier of these reference phages for other researchers to start studying them.

EB – Canada is home to the most diverse collection of phages globally and sends them to researchers all around the world. That's pretty cool!

JK – Yeah, so once researchers have selected their candidate phages, whether from field samples or a phage library, or a combination of both as is the case in this project. They begin the process of characterising the phages – you've got to understand how they function against a range of criteria.

EB – Other than which bacteria they infect?

JK – Yeah there are many characteristics you might need your phage to have. Nicholas provided a couple examples

Dr. Nicholas Svitek
We have a list of criteria or guidelines that we're trying to aim for the best phages. For instance, we want phages that can grow to high titers, for instance, because at some point, we will need to produce the phages to high concentration or to high production levels. We want phages that are stable at low pH because we know that the delivery mechanism will probably be either through the water from where chicken drink or in the feed, and they will go through the gastrointestinal tract of chicken where, in the stomach, for instance, it is quite acid. So we want pages that are stable. We want also phages that grow at higher temperature, for instance. The reason is that the body temperature of chicken is around 42. So we want phages that can also grow or are stable at this temperature.

And another thing we'll look at is, we want phages that have a large tropism because we want to target most of the Salmonella strains that are either causing disease to chicken or are a threat to human health, so targeting also the zoonotic Salmonella.

JK –Now that you've narrowed down the phages you want to use, you can either use them individually or combine them into a phage cocktail.

EB – yummy

JK – It's an actual thing. Fun if you're the phage researcher, not so much if you are the target bacteria.

EB – So I guess the real question is: now that you have phage cocktail, how do you get a chicken to drink it?

JK – Hah - sounds like a bad joke: a phage researcher and a chicken walk into a bar… Anyway, It's true, manufacturing sufficient phages and finding an effective delivery system is a major technical hurdle. So this project has looked to a private sector collaborator to help solve that problem.

> Prof Sylvain Moineau
> [*Indeed phage production can be a bottleneck in this project. And that's why we have teamed up with the small biotech company here in Quebec City, a company called SyntBioLab. And that's a start up company that has a technology to produce phages at very high levels in a powder form. You can ship very easily to different countries. And because of the level of bacteriophages in those powders, you can dilute them in feeds for animals, for example, you could dilute them in water, that you could also feed the animals. So we're looking at different ways of how we're going to provide this phage-containing powder to the farms in Kenya. It's really interesting because, for example, here, if you would do these type of studies in Canada, there's chlorine in our water and phages don't like chlorine at all. Whereas in Kenya, there's no chlorine, so you can put phages in water or there and they'll be infectious for a long period of time over there. Whereas here, it would not work properly. So there's these differences between countries that we need to be aware of.*
>
> *There's a lot of biology, great science, you can do: phages; characterizing your phage; studying phages; interactions; to come up with clever cocktails where the bacteria who are resistant will not emerge, but there is this technology that you need to produce the phage, and sometimes I think this is not appreciated as much as it should be. Because the knowhow of producing the phages is really important as well.*

EB - This is turning into quite the product development process: Let me see if I'm up to speed so far. So to develop a phage therapy you need to first put on your hazmat suit or plug your nose and go phage hunting in bacteria-rich environments. Then you isolate the phages in your samples, test and purify them. After, you might want to mix it with a couple of other phages into a tasty phage margarita – I mean cocktail - for maximum effectiveness against the target bacteria. And then you find someone who can manufacture

the phages in big enough quantities and in a format that you can transport and administer to the animals…. How was that?

JK – Bang on! And were not finished yet. You still need to test the new therapy in controlled animal trials and eventually under field conditions, and assuming all that goes well, get the product licenced in the country where you plan to use it.

> Dr. Nicholas Svitek
> *Eventually, to have a product, you need to license the product in the country. We've been discussing with licensing board of the Veterinary Medicines Directorate of Kenya to have a first interaction with them about the novelty of using phages as a treatment or prevention of infection and as an alternative to antibiotics. So, we will need to have a product that meets the requirements for them to license a product in Kenya in their country and that can vary from one country to another. These are the steps that we need to follow.*

EB – Oof product development is no walk in the park! But it sounds like Sylvain, Nicholas and their teams are making really impressive headway.

JK – It's a big challenge for sure. So they're not the only ones working on this type of product. Want to hear about another team developing a phage-based product in a different context?

EB – Of course I do!

JK – Ok, so time to leave Kenya and travel over an ocean to Pakistan to meet our next research team.

EB – Aaaah, travel, remember those days?

JK – They are becoming a dim memory….

[Travel sounds – Airport announcement, airplane landing, street sounds]

JK - Daydreams aside, this project has some really innovative ideas they are working on.

EB – Sounds interesting. So, is chicken farming a big thing in Pakistan?

JK – You'd be surprised, it's now the 8th largest producer of poultry products globally and is increasingly modernizing and intensifying. It is unfortunately not immune from the issues of antibiotic misuse and the emergence of antimicrobial resistance. Professor Zafar Hayat, one of the lead researchers based at the University of Veterinary and Animal Sciences in Lahore, explains.

> Prof Zafar Hayat
> *Starting from 1962, and like 60s, now the industry is very modernized. It started from the backyard poultry and very few buyers, and [the production was] at home for their*

own consumption. Now, it's a really integrated industry and we can compare this industry with that of any industrialized country and any specialized poultry producer of the word. So, the same problems are here for the poultry industry, including the indecent use of antibiotics in poultry feed. And for the farms and all the poultry production cycle and supply chain, there is the issue of antibiotics, which is the worst thing and disturbing the industry as well as the consumer. Because, as you know, there are two main phases of the use of antibiotics, as a growth promoter in the poultry feed and as a therapeutic to check the infection or to check and control the disease at the farm. So both ways. The poultry industry here in Pakistan is using antibiotics. Although the use of antibiotics is decreasing with the knowhow, but overall, Pakistani farmers are not much educated in spite of several campaigns of the government. Antibiotic use here in Pakistan and associated antimicrobial resistance and all the effects are hampering the Pakistan poultry industry, as well as the consumer who consumes poultry, meat and eggs here in Pakistan.

EB – Zafar mentioned something I've heard a few times now from our guests, that antibiotics are included in poultry feed not just to deal with bacterial disease, but also to promote growth.

JK – Yeah so that's one of those unique little challenges when developing alternatives to antibiotics you are dealing with a many-headed beast. Your alternative has to try and cover as many bases as possible if it is going to compete with antibiotics. The trick might just be that teamwork makes the dream work.

Prof. Paul Ebner

I'm Paul Ebner. I'm a professor of Animal Sciences at Purdue University. Yeah, I think I think you're right – that a silver bullet that replaces everything an antibiotic does – finding that is maybe a fool's errand. But our approach is – we know what these antibiotics do to promote growth, there's preventing a subclinical infection; preventing just a metaphylactic trigger; prevention of an entire flock; there's also a metabolic effect; there's a lower lesion scores, things like this. And so what we do is, we know that there's these different properties of antibiotics or different activities of antibiotics that are helping that chicken grow. They're really just aiding that chicken in being more efficient. So what we try and do is put together a group of different compounds, they might be completely unrelated. They each have their own role and together they can replace the total effect of the antibiotic.

EB – If I'm getting this straight, antibiotics help promote growth by basically giving the chicken's immune system a boost? Like it doesn't have to expend unnecessary energy fighting infections etc., so it can more efficiently convert its energy into…. Meat

JK – Yeah that's basically it.

EB - Ok, so what can we include in the antibiotic alternative that will have a similar growth-promotion effect then?

JK – Well, before we find that out, maybe it's best to know who we are playing against...

> Prof. Paul Ebner
> *We chose those two species because we wanted to have the biggest impact we could. We chose Salmonella gallinarum because it's endemic in in Pakistan and it significantly affects the bird's health. Most of the time, when people are targeting Salmonella with phages, it's more of a food safety issue. They're trying to decrease enteritidis or typhimurium. We are going after* gallinarum *because it's a significant health problem in chickens. So the second one is* Clostridium. *And if you look at different places where they've moved to more antibiotic-free or antibiotic-reduced programs, one of the first impacts that you'll see is increases in maybe coxcydiosis. So what that does is allow* Clostridium, *which is an opportunist, to set up shop and cause infections like necrotic enteritis in chickens. So if you looked at the tonnage of antibiotics that are used, a large percentage of that tonnage is really to control clostridial infections, and those animals are growing quicker, more efficiently, because they're less impacted by* Clostridium. *We figured that if we could come up with something that really limited the need to include antibiotics to control* Clostridium *infections, we would make a great impact in terms of the tonnage of antibiotics used.*

EB – Smart move – targeting the bacteria that cause chicken farmers to use the most antibiotics by volume. Alright, so now we know the target. So back to my question – who are we putting on this antibiotic alternative dream team?

JK – Well, phages

EB – Yeah, I got that.... It is an episode on all things phages after all. But what else?

JK – You're not keen for another phage hunting expedition, a second trip down phage isolation and optimisation alley?

EB – Sure, why not. Highlights reel maybe? Then promise you'll answer my question?

JK – I can do that. Fortunately, Paul has a talent for breaking things down in short form.

> Prof. Paul Ebner
> *It's a very glamorous process that starts at a wastewater treatment facility. You can isolate phages wherever the bacteria you're targeting are. We've had the best luck using wastewater, like from human wastewater treatment facilities. We isolate them, it's similar to fishing where we use the bait that is the bacteria that we're targeting. And that allows us to identify those wild type phages, isolate them and then they go through a very long process. It's one thing to get phages, that's not very hard. And it's another thing to identify those phages that you think will be good in a therapy...*

EB – You weren't kidding "a very long process" - four words that likely substitute for hundreds of hours at the lab bench.

JK – Ok - so if you could choose your favourite fruit, what would it be?

EB – Bit of an abrupt subject change there – but ok, I'll bite. I have to say persimmons. They're very underrated.

JK – Me, I personally like mangoes. They taste great and it turns out., they may contain nutraceuticals which can be used to substitute for the growth promotion effect that antibiotics provide.

EB - New word alert! What's a nutraceutical?

JK - I'll let Zafar answer that one

> Prof Zafar Hayat
> *It's just a combination of nutrient and a pharmaceutical. We like to borrow both words and coin a new term, nutraceutical. Basically, it's a broad umbrella term that is used to describe any product derived from the food sources particularly with the extra health benefits in addition to the basic nutritional value found in it. In our project, we are aiming to quantify the phytochemicals and nutraceuticals like phenolic acids, flavonoids and other bioactive compounds derived from that agro base, especially food waste. If we want to talk about which food waste we are very much interested in, it is mango, mango waste.*
>
> *Mango is very important with respect to their bioactive compounds, and there are so many bioactive compounds, like flavonoids, catechins mangifirens, oleic acid, gallic acid and there are a lot of compounds in the peel of the mangoes and in the seed of the mangoes.*

EB - Finally, some answers! So let me guess, the idea is to use phages in combination with nutraceuticals from mangoes to create an alternative to antibiotics that has both the bacteria-fighting AND the growth promoting properties.

JK – Spot on.

> Prof Zafar Hayat
> *So in our project and with our research team and group, we aim to develop alternatives to antibiotics by utilizing the combined effects of bacteriophages and nutraceuticals that limit bacterial infection and improve growth. It means that both advantages of the antibiotics, to limit the bacterial infections with the use of bacteriophages and to improve the growth performance with the use of nutraceuticals.*

JK – As it turns out, there are a few reasons why mangoes are a particularly well-suited source of nutraceuticals for this project.

EB – Because chickens can't resist the delicious flavour of a mango-phage cocktail?

JK – Well that's a given! But apart from that, there's an environmental and economic argument to be made as well.

> Prof Zafar Hayat
> *Mango availability is very great in certain seasons, especially the seasonal fruit. There are a lot of companies which are processing these mango fruits and there is a lot of waste available and there is a concern of the environment, because now they have only one choice to burn this very precious agro-industrial by-product in the brickmaking industry and others where the smoke is there and all environmental pollution is there. So, side by side, it is a very multi-advantageous approach to use that agro-industrial waste from mangoes, to get rid of the environmental pollution, to give some very appreciable financial incentive to the mango processing industry, and the nutraceuticals, which are very important.*

EB – Ok that's pretty neat! So how do the researchers figure out exactly what's in mango waste – so skins and pips – and whether those compounds are any good at promoting growth in chickens?

JK – Well it's much like the process of isolation and characterisation of phages. In this case the isolation process is more of an extraction process - trying figuring out how to get the bioactive compounds out the wastes. It's a tedious line of study that involves assessing different combinations of factors like temperature, type of solvent, ratio's of solvent to sample, extraction time, etc. etc. etc.

Once you have your extracts you want to know what's in them – that's where LCMS or Liquid chromatography–mass spectrometry comes in. Basically the LC part involves separating a mixture into it's multiple components and the MS part identifies what those parts are. Then the real testing begins – do these bioactive compounds have any antimicrobial properties themselves; toxicity studies to see if they are safe; stability studies – can they survive the high temperatures involved in feed making. Finally, the most promising compounds are combined with phages for pilot animal trials, and if these are successful, large scale trials under commercial farming conditions.

> Prof Zafar Hayat
> *This is a model starting from the extraction to the characterization, and to the isolation enrichment in vitro study, and then small in vivo studies, and large in vivo studies. And then we will be able to, like any product, which can be used to replace antibiotics in poultry.*

EB – Ok, so we've covered what a phage is, we've been phage hunting and got the low down on isolating and characterising them for inclusion in phage therapies. We've seen how they can potentially be combined with other bioactive compounds to mimic the

multifaceted action of antibiotics. Basically, we've answered the question "how can phage therapy replace antibiotics in poultry production?" with very impressive technical answers. But the technical side of product development is only half the story. What about farmers in Kenya and Pakistan who stand to benefit from a phage therapy for Salmonella? How are their needs, concerns and capabilities be taken into account? Cause If they aren't, good luck with adoption.

JK – Too true. That's really important for the success of both projects, which is why both the research teams we've met include a "downstream" component, which means they have experts on their teams looking into factors that can influence the adoption of a new technology and to understand how the social aspect of adoption meshes with the upstream discovery science. So Dr Nicole Widmar is an agricultural economist who is part of the team working on the phage/mango extract product for the Pakistani context:

> Prof. Nicole Widmar
> *I'm Nicole Widmar, I am a professor in the Department of Agricultural Economics here at Purdue.*

JK – Here's how she put it when I asked about the relationship between the upstream discovery science and the downstream social aspects of adoption

> Prof. Nicole Widmar
> *A lot of the investigation that goes on in the lab is in response to a need. And then, you really don't know what you need to have that be socially acceptable until you know what's actually possible. So I really see them as sort of parallel activities that need to take place, because I think you will have things that society would love to have that are simply not scientifically feasible, at least not right now, and you'll have the opposite things that are scientifically feasible that society says no, we don't accept that. I really think you need both. And I don't necessarily see that there's a problem with both of those activities happening simultaneously. And some things will fail one test and not the other and some things, the reverse. We need both components. So I think it's a bit of a chicken and an egg problem.*

EB – I really hope that pun was intended! Anyway, Nicole mentioned that societal acceptability can be a challenge when introducing a new technology to the world. Did she say what the potential barriers to the adoption of phage-based products could be?

JK – Well… it's complicated!

> Prof. Nicole Widmar
> *So the regulatory component is one piece. The more complicated, in my mind, component is the actual social/cultural piece. And so, even if the phage works beautifully, will people want that to be used in their food production system? It's a very complicated question. It sounds simple at first glance, but it's not as simple as just*

throwing a label on a food product and calling it good, right? You have to first wonder… So you know, phages can help because of antibiotic resistance, that is resistance that develops from overuse. So you need to back all the way up to: does society think that's a problem? But before you can answer that, you have to ask: does society actually know the consequences of antibiotic resistance?

EB – Right so part of the problem could actually be that some producers might not even be aware of the problem of antimicrobial resistance – you're providing a solution to a problem that your target consumer might not even know about. That's gotta be tricky when there's already a cheap product – antibiotics - that seems to work just fine for promoting growth and preventing infection…. At least, for now…

JK – Right, or they might know that it's a problem, but not grasp the potential magnitude of the issue, which means they may not be willing to change their behaviour and switch to a potentially costlier product.

Prof. Nicole Widmar

A lot of this goes into what's the starting point of understanding this problem? And in general, it's going to be very heterogeneous, right? So I'll have segments of a population that really do think this is a really big problem and they're willing to take steps that are really extreme. And you'll have another segment that doesn't see it as a problem for them, so why would they take steps to change their own behavior? I think understanding people's starting point of knowledge is a challenge. Understanding the heterogeneous viewpoints of different members of society and why – is that coming from a ethical, moral, spiritual, economic obligation standpoint – those are all very different. The one that I think about most often is for people who are struggling to feed the family right now. If economic constraints are such that putting food on the table today is a concern, then they don't have the luxury of thinking about what other attributes they would like to see in the food production system.

EB – Wow, that's an intricate puzzle to try and unpack. Were do you even begin trying to understand that complexity?

JK – You know what they say, when the going get's tough, the tough go shopping….

Prof. Nicole Widmar

There's a couple of ways to go about it. It's a hypothetical product in most marketplaces right now, so it's not as simple as saying, "well, why don't you go on down to the supermarket and see which product people buy." And so, if both products existed, it's a bit simpler. In this case, we were looking towards developing a simulated shopping experiment. You offer people products that were produced in two different ways and you vary what those products are, and what those attributes are. Honestly, you vary it in such a way so that you're trying to elicit people's actual choice.. And so there's a fair amount of survey design and interview design work that goes into how do you get that

question asked in a way where you really get as close as you can. You can't eliminate all bias, but you try to do as well as you can to get people's true opinion.

EB – Hypothetical shopping, fun! I think I know what we're getting at here – how much you're willing to pay for a product will say something about your preferences.

JK – Right, when we crossed over from microbiology to economics, we ventured into your territory, didn't we.

EB –Yeah I definitely feel more at home here.

Prof. Nicole Widmar

We're trying to understand two things: one, what's your viewpoint on this phage idea right now, and two, where are you coming from? If you take the standpoint that the customer's always right, then they're going to pick the product that's right for them. And we're trying to understand why did you feel that was your right product? Is it because of an economic constraint? Is it because you fear to change the system for various reasons? Or is it because your starting point was that antibiotic resistance isn't a problem. So perhaps there's some educational component that comes after that. But right now, we actually don't know any of those pieces, right? So we're kind of in a multi-pronged approach for simulating shopping and measuring perceptions and knowledge.

JK – Understanding the need for that educational component and incorporating this downstream research from the project's outset seems to be a big part of what Nicole finds promising about this project

Prof. Nicole Widmar

What we don't need is a big public debate of things that could have been answered if we just would have put the information out there in the first place. And at the end of the day, you can't force people to believe something, you can't force people to want something, but we can do our best to communicate science in such a way that people can see the consequences, both positive and negative, of introducing it. I think there's value in that effort, and so that's the part that's most exciting to me.

EB – Right, I think in this current environment of disinformation – in the context of human vaccines, for example – where we're all too familiar with the consequences of poor communication, it's great to hear that research teams are proactively taking steps to understand the informational needs of their user base.

JK – Definitely. So that's how one of the research teams is approaching the complex question of adoption. Now, let's go back to our research team working on the phage-based product for poultry production in Kenya. I think this project really illustrates the need to take tradition, culture and economic systems into account when introducing a new product to market.

EB – Sounds exciting!

JK – It is! this project has developed an innovative stream of research to understand the dynamics around disease identification and treatment and the perceptions of phages and how these relate to gender. This work is being led by Dr. Zoë Campbell.

> Dr. Zoë Campbell
> *[My name is Zoë Campbell and I am a gender and socio economist working at ILRI in Nairobi.*

JK – Similarly to what I talked about with Nicole, Zoë mentioned that in her experience, addressing the issue of the adoption of a new technology is often thought of as the last step.

> Dr. Zoë Campbell
> *In my experience, it seems like often a product gets developed and then and then as a researcher looking at adoption, I'm often brought on later and told "oh, we have this great product. Can you help us figure out how to make farmers use it. We want farmers to use it. Help us make them use it."*

EB – Yeah, like we just heard from Nicole, if you consider the needs and concerns of your end-users from the outset, it can reduce the risk of spending years and countless resources into the development of this really sophisticated technology that no one is willing to use.

JK – Right. It makes total sense to do it that way. And the work that Zoë's team's is doing to understand and identify end-user needs and constraints is also informing the product development process itself!

> Dr. Zoë Campbell
> *This project is exciting because essentially, bacteriophages can do a lot of different things. It could prevent disease in chickens, it could possibly treat disease in chickens, it could possibly be used to clean surfaces. It has a lot of applications. And so, I think by thinking very early about what are different groups of farmers going to see as most important, what gaps does this fill for them? That really depends on if you have 20 chickens, if you have 1000 chickens, it might depend on where in the country you're located and what kinds of access you have to competing products that can do similar things, the main ones being antibiotics, but there are also some vaccines that may address some of the some of the diseases that bacteriophages can also address. So essentially, by asking these questions really early, you can change the way that the product works, the way that it's packaged, its delivery system possibly, or focus on certain qualities of the bacteriophage cocktail that might be more important to a specific group*

EB – What I'm hearing is that, basically, depending on who you're serving, you'll tweak the cocktail recipe. Party of 200 people? You need a tasty cocktail that can be made in large

batches in advance. Serving a similar cocktail to two people on a date? Then you might bring out the fancy glasses and add on some decorative flourishes like rosemary sprigs.

JK – Ah the cocktail analogy, the gift that keeps on giving! Just to add on a bit – if you're serving it to a group of vegans, then you might have to hold the egg whites.

EB – Right, I'm guessing you're touching upon the cultural constraints there.

JK – Exactly

EB – Ok but before I totally lose sight of what we're actually talking about here – phages, not fancy drinks – maybe an example would be helpful.

> Dr. Zoë Campbell
> *If we take, for example, a chicken farmer, let's say she has 50 chickens, and she usually sells them around Easter all at once. She might be more concerned about things like chick mortality or things like foul typhoid, which might affect her chickens. There's a vaccine, but it's very expensive and it's an intramuscular injection, so you have to have someone come out, and needles are involved, so it's more and more costly and more labor intensive. She might be interested in a bacteriophage product because it might reduce chick mortality, possibly, by dealing with a whole host of Salmonella based infections, or she may be interested in it because it might be an alternative to vaccinating for foul typhoid, which a lot of smallholder poultry farmers aren't doing. On the flip side If you look at a farmer who's got a commercial establishment with thousands and thousands of chickens, they might be interested or more knowledgeable in cleaning surfaces or more in the food safety component of reducing Salmonella-caused infection*

JK – So there are different ways of segmenting the potential user base for this product. She hinted at two in this example.

EB – The first one is size of the operation, right. And considering Zoë is a gender expert, the second is the gender of the poultry producer?

JK – You got it. In certain contexts, notably in Kenya, there can be very distinct gender roles in livestock production.

> Dr. Zoë Campbell
> *It's fairly common, for example, in East Africa, for some species to be basically earmarked as being for men or for women. Cows are very much for men. There are jokes about chickens, chickens are the women's cows. There are these stereotypes about who's managing and controlling and taking care of certain types of livestock.*
>
> *The research team reached out to the gender team very, very early because this stereotype or trend, I should say, that women are more responsible for chickens, which is true and especially in smallholder households. That's definitely true. As you go up and*

production intensifies, you become more and more and more commercial. It seems like women fall out a little bit and that men tend to be more likely to be controlling these very large commercial farms. So essentially, the research team reached out to us and said, "hey, well, it seems like women and chickens kind of go together. We're not exactly sure how that works. But maybe we need to think about gender when we're designing bacteriophage products."

EB – Alright, so women are generally expected to be managing poultry production, at least in small-scale production systems. But it's not as simple as just developing a product to suit the needs of small-scale women producers and marketing it to them, is it? Gender dynamics are never that cut-and-dried…

JK – They definitely aren't.

Dr. Zoë Campbell
Ownership for example, is a tricky question. Women might be taking care of livestock, they live in their homes, but their fathers, husbands, males in the household are owning those livestock, so they might be limited. In other systems, for example, in West Africa, it may be that vaccines are provided, for example, for sheep and goats. There are mass campaigns, but you have to go and register animals with the government, and that's usually done by men. So if women go and register their animals within their household, then they're seen for sure as being either someone who perhaps doesn't have a husband or is disrespecting the men in her household by going to do that. So as we go in, we see not only just these trends about who does certain tasks, but we also see differences in access and also access to information.

EB – There's a whole decision-making web at play here. It's not just about identifying your target producers, informing her about your product and giving her the tools she needs to administer it to her poultry. You also have to consider who holds the purse strings, who has access to veterinary services and how information is circulated etc. etc.

JK – And that's not to mention other gendered constraints that can make it more difficult to reach these women producers.

Dr. Zoë Campbell
Sometimes training opportunities are perhaps more geared towards men. Maybe it's at a time of day when it's easier for men to join or women have a lot of responsibilities at home and it's more challenging for them to join a training that doesn't have some additional accommodations specifically for women. As people are starting to look more, we're finding and learning more and more about the way that gender interacts with the roles that people have when they're taking care of their livestock.

EB – Those are a lot of considerations!!

JK – Exactly, hence the need for a gender team. So here's how it all comes together:

Dr. Zoë Campbell

Essentially, by looking very closely at both-gender and also production systems, you can have a better understanding of how bacteriophage products would compete with other products that people have access to, what qualities they may have that are most important to people. We're basically feeding information back to the research team about how they might design or test different aspects and attributes of their phage cocktail.

It's really exciting and great that the beginning of the project already incorporates the socio economic and adoption piece very, very early. I think that that pairing of researchers talking about these challenges early really increases the odds of A) having a successful product that can actually be used commercially in East Africa, B) increases the odds of being able to help probably more farmers with the challenges that they're having.

EB – Well we've gotten a taste of the dizzying number of factors that play into the idea of social acceptability and adoption, but there's a few big ones that probably deserve a closer look – safety and cost.

JK – Well, in general phages are considered pretty safe – there is the possibility of them carrying genes that code for toxins or even antimicrobial resistance, which can spread to bacteria, but early screening can pick these up quite easily.

Prof Sylvain Moineau

The vast majority of bacteriophages are actually safe, they don't cause any problems. Of course, these phages again, are very specific to bacteria, so they will not infect human cells or animal cells. But also, when we start selecting a phage, then we'll go deeper into the biology of that particular phage. And one of the first steps will be to sequence its genome. So, we will sequence a genome of the phages of interest, and then we will analyze the genome of that particular phage. In analyzing that genome, normally, we'll look at if there's resistant genes or there are toxin genes that would be present in that particular phage, and if it's the case, then we will simply remove the phage from our from our bank and will no longer be using it.

EB – And cost? The high-profile focus on phage therapy lately has mainly involved bespoke medical treatments for human patients in other words how phages have saved critically ill patients in high-income countries. That obviously is very expensive and unlikely to translate to lower-income contexts or food production.

JK – That's an interesting point. But there are already examples of commercially available phage-based products used in animal production, mainly to control bacteria on products post harvest. That would suggest that phage production technology is already getting to the level where it is becoming financially viable. Both Sylvain and Paul had some interesting thoughts on the problem of cost.

Prof Sylvain Moineau

Yeah, with every new biological product, there's always a question about costs. But I think with phages, we're lucky because we're able to produce them at very high levels. And I think the cost issue will not be such a big deal. Although we are aware that especially for farmers, you really don't want to have a product that will be very costly to them. So that's why the production part is extremely important. We need to have a product of very good quality, a high level of agency that they can even dilute down on farms. And so, cost is an issue has always been an issue, but I think we have ways to reduce that quite a bit.

Prof. Paul Ebner

We get a lot of questions about costs. And that's legitimate. But there's this idea that phage therapy would be very, very expensive. You know, once the technology is developed, the process is not unlike the process of developing antibiotics. People's incentives to use a product or change a behavior, change your production system aren't solely driven by cost. And in drastic cases that can be the law saying that you can't use this, you can't do this production practice anymore. And a lot of cases, it's consumer awareness. We've had huge changes in production systems and livestock production in the US, and in many cases, those were driven by consumer demand, which is obviously fed by consumer awareness. So if you just look at the costs, you're gonna have a tough time selling it, you know, not necessarily, but if it's solely costs – and yes, it's probably going to be more expensive than then antibiotics, at least in the very short term – but if you're looking at all the incentives that go into someone changing a behavior or changing a production practice and you look at the way that regulations are trending in Pakistan and the United States, there are going to be more incentives beyond cost.

JK – I think Paul highlights an interesting trend, where we are perhaps starting to factor in the cost of some of the externalities of doing business. Whether it is cheap antibiotics vs antimicrobial resistance or cheap oil vs climate change.

EB – Right, and like for climate change, a key component of that has to be public awareness. Us consumers can help this trend forward by making some noise about the use of antibiotics in our food.
Well I have to say, I do feel much more hopeful about the issue of antimicrobial resistance after hearing about how these advances in phage technology might start replacing antibiotics in our food system. Plus, it's great to see research teams proactively incorporating social scientists on their teams to make sure that the end-products are actively considering and responding to the needs of their potential users.

JK - Welcome to the future!

EB – So, now that we've basically solved the issue of antimicrobial resistance, what is there even left to talk about?

JK – Oh, we've only just scratched the surface. How about a sneak peek at what's next then?

EB - Sure! On the next episode we get our feet wet, looking at some of the innovative approaches that researchers are using to develop alternatives to antibiotics in aquaculture.

JK - Yes, you can vaccinate a fish and you might even be able to do it using a robot.

[Robot sound]

EB - For everyone wanting to learn more about the podcast, read the transcript or get in touch, visit us on the podcast's home page linked in the show notes. We'd love to hear your thoughts. And don't forget to subscribe.

JK - Until next time, and thanks for listening.

[end]

*Note that some of the quotes throughout this transcript have been lightly edited for readability.

SHOW NOTES

Chickens, mangoes and hypothetical shopping. In this episode we explore phages, the viruses of bacteria. We talk to researchers who are looking to harness the bacteria-killing abilities of phages to tackle the issue of salmonella in poultry farming in Kenya and Pakistan and how this novel technology might be perceived and adopted by farmers.

Innovating Alternatives is a serialized podcast that will delve into the issue of antimicrobial resistance, a slow-moving pandemic that risks erasing the last 80 years of modern medicine's progress. We will take you right to the cutting edge of science, where researchers are developing new and surprising alternatives to antibiotics and innovative solutions to reduce the use of antimicrobials in livestock and aquaculture production.

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