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#357: Germ warfare: Young researchers seeking answers to diverse microbe threats

VOICEOVER
This is Up Close, the research talk show from the University of Melbourne, Australia.

DR ANDI HORVATH
Microbes, bacteria and viruses. They rule the earth. They dictate the condition of soils, plants and animals. I'm Dr Andi Horvath. Thanks for joining us. Our two guests today are PhD scholars who are researching significant microbes. One, a bacterium that can cause serious and even life threatening infections and the other, a virus that affects our cereal crops. In a while, we'll meet Rebecca Vandegeer who is investigating how wheat plants respond to the Barley Yellow Dwarf Virus and how climate change will alter the wheat's defence system. But first, we get to meet PhD scholar Claire Gorrie. She's exploring aspects of the drug resistant bacteria called Klebsiella Pneumoniae. It's responsible for a range of serious infections. Some can even be fatal. Many bacteria have now become drug resistant which is a problem especially for hospitals. Claire is from the Centre of Systems Genomics at the University of Melbourne. Claire, welcome to Up Close.

CLAIRE GORRIE
Hi.

DR ANDI HORVATH
Claire, introduce us to the bacteria Klebsiella Pneumoniae.

CLAIRE GORRIE
Klebsiella Pneumoniae is a bacteria that's found basically in many, many places throughout the environment and that includes crops, water sources and a wide range of animal hosts, one of which is of course humans.

DR ANDI HORVATH
Okay, so what sort of diseases does it cause in humans?

CLAIRE GORRIE

In humans it can course opportunistic diseases including less serious ones such as urinary tract infections, but it can also cause much more serious diseases like blood infections, meningitis and pneumonia.

DR ANDI HORVATH
When you mean opportunistic, do you mean like when our bodies are at a low ebb it jumps and it does its thing?

CLAIRE GORRIE
Yeah, exactly.

DR ANDI HORVATH
So how does it infect certain sites of the body? Is it an increase in number or is it releasing some sort of toxins? What's going on there?

CLAIRE GORRIE
It doesn't particularly release specific toxins. There are many bacteria out there that are much more adapted to deliberately causing infection. With Klebsiella it's much more a case of it accidentally gets into the bloodstream. Perhaps someone's had surgery and Klebsiella gets transmitted in that way and once it's there, it just does its best to survive, which unfortunately causes serious symptoms in the human host.

DR ANDI HORVATH
That means it increases in number as well does it?

CLAIRE GORRIE
Yes.

DR ANDI HORVATH
So, where does it normally live right now in our bodies?

CLAIRE GORRIE
That's actually something we don't know an awful lot about. There have been a number of studies looking at highly resistant pneumoniae and looking at where they live in the body and generally, we suspect that they live in the gut but also in the nose and the throat. But we don't know really how often that occurs or how persistent it is.

DR ANDI HORVATH
How is it transmitted then from, say, the nose? Does it travel in the air or does someone have to touch something? How does it work?

CLAIRE GORRIE
The typical transmission route, from what we understand, is faecal-oral so not the most pleasant of transmission routes but it is often linked to maybe contaminated food or water or coming from the environment and ingesting it somehow.

DR ANDI HORVATH
This is why washing hands is so important.

CLAIRE GORRIE
Yes, definitely.

DR ANDI HORVATH
Claire, how deadly is it really?

CLAIRE GORRIE
Typically Klebsiella by itself isn't particularly deadly. It doesn't make very strong toxins and it's not out to deliberately cause disease. It can survive very well in the environment. It's more a case of when it does get into somebody whose immune system isn't up to combating a bacterial infection, then it can worsen and potentially kill the host. I guess the other side of that is Klebsiella, if it's not resistant, is very easily treatable with antibiotics, but as it becomes more and more drug resistant we're starting to lose our capacity to effectively treat those infections.

DR ANDI HORVATH
Now we've heard all about drug resistance in germs so how does this happen with Klebsiella? I mean, we are facing a bit of a crisis with drug resistance. Tell us about that.

CLAIRE GORRIE
Yes, absolutely. Klebsiella is very, very good at evolving rapidly and it can do this through just natural mutation, with each generation of Klebsiella, but it's also very good at picking up DNA from the environment around the cell. That can be in a number of ways. It can pick up loose DNA. It can exchange DNA with other bacteria and not just Klebsiella. It can exchange DNA with other species of bacteria and it can even get infected with bacteria-specific viruses that can introduce novel DNA.

DR ANDI HORVATH
Wow. So it meets other bacteria along its journey and says, hey I'll swap you some of this resistance for that resistance?

CLAIRE GORRIE
Yeah, absolutely.

DR ANDI HORVATH
Hospitals are an environment where there's a lot of sick people and a lot of infections. What's specific about hospitals for Klebsiella?

CLAIRE GORRIE
I think it's more the fact that Klebsiella is opportunistic, like we said earlier, and that means that if somebody's immune system is compromised it's much easier for Klebsiella to become a problem. Maybe somebody already Klebsiella but it's not causing an issue because they're healthy. Then they go into hospital because they

get sick - maybe something like influenza, or cancer, or AIDS, something like that that compromises their immune system - and suddenly there's a much easier pathway for Klebsiella to multiply and to take over the system.

DR ANDI HORVATH
Are there different strains of Klebsiella?

CLAIRE GORRIE
There are different species and subspecies. Interestingly, Klebsiella when it was first discovered they thought it was just one species and then they found out that it was much more diverse and there were different lineages or groups of Klebsiella. Now they've decided that those different lineages are actually individual species. That's just an indication of how quickly it is evolving. There are different species and even within those we're getting more and more differentiation. What we're looking into now is - are those different groups or lineages capable of causing different levels of disease or different levels of resistance?

DR ANDI HORVATH
You've just started that work right now, is that right?

CLAIRE GORRIE
Yes, yeah that's true.

DR ANDI HORVATH
How do you go about monitoring the activities of this bacterium in a hospital environment because that's where we find you doing your PhD?

CLAIRE GORRIE
Yes. It's a very big collaborative project that I'm working on. I'm doing much more data analysis and bioinformatics. So that's looking at bacterial genomes and gene sequences. In order to do that, I obviously need a lot of samples of the bacteria. There's a Melbourne hospital that's been co-operating with us and screening people coming into the hospital and monitoring infection rates and factors like that. I get all of those samples in looking at how often Klebsiella pops up in people coming into the hospital and how frequently it turns into disease, what sort of antibiotic resistance is present.

DR ANDI HORVATH
You're dealing with genome samples from the actual microbes that come to you. You analyse their gene sequences and have a look at which ones are causing infections and which ones are being transmitted, is that right?

CLAIRE GORRIE
Yeah, so one of the things we're trying to determine is is there actually transmission occurring into the hospital between patients or something like that, or whether people are bringing it in and it's only turning into infection once something changes in the patient themselves?

DR ANDI HORVATH
That's the question that we need to hit on the head.

CLAIRE GORRIE
That's the million dollar question.

DR ANDI HORVATH
It is and what are the patterns so far that you've observed at this stage of research? I know it's early days but have you seen any patterns where you've gone, look at that?

CLAIRE GORRIE
We have seen some very interesting things in the preliminary results. We do still have one of the best data sets out there for this sort of work but of course you can always get better data sets. But we are seeing some indication of carriage turning into infection after things have changed in the patient and this is not limited to Klebsiella. It's been published in other bacteria which is one of the reasons we're starting to look for it in Klebsiella.

DR ANDI HORVATH
Carriage meaning it's just around but then all of a sudden causing infection in the individual?

CLAIRE GORRIE
Yes and something we've got to look into further is what's causing that transition between carriage and infection and how frequently it's happening.

DR ANDI HORVATH
I know hospitals do their best to try and prevent cross-transmission or cross-infection but what do you do as a PhD student? How does that work?

CLAIRE GORRIE
It's particularly important given that I am working with known resistant samples, so that is not something you want to pick up while you're working in the lab. There's a lot of personal protective equipment - lab coats, goggles, gloves - but we also are very, very careful with actually handling the samples. If there are any spills you immediately deal with that spill. You wipe it up. You use ethanol to disinfect all of the benches and all of the equipment and it's just really a matter of being very, very careful with what you're doing in the lab.
I'm quite lucky because I don't have to spend too much time in the lab, mainly doing DNA extractions, but for other people who work much more in the lab with the samples they have to be very, very vigilant.

DR ANDI HORVATH
Now if I gave you two PhD students what would you get them doing?

CLAIRE GORRIE
My work focus is predominantly on just Klebsiella and how it moves and how it

develops resistance but I think, as we mentioned earlier, Klebsiella can pick up resistance from other bacterial species. I would be very, very interested to have a student working on that and looking into how frequently Klebsiella and other species exchange antibiotic resistance genes and what sort of impact that could be having on the treatments we're choosing in hospitals. Because if you choose to treat Klebsiella that's maybe not resistant, but it's residing alongside an E. coli that is, what's the chances they're going to exchange those genes and suddenly you've got a whole range of a bacteria living there that are all resistant?

DR ANDI HORVATH
Claire, what's your message to the public?

CLAIRE GORRIE
I guess, at risk of being a bit over-zealous, antibiotic resistance is a really big problem and there's a lot of research going on but it's not just the researchers who can really make a difference. Things that increase antibiotic resistance include taking antibiotics when you don't need it, or taking antibiotics but not actually finishing the course, because often those last few survivors that are really hanging on they'll just come back and cause infection again. We're working really hard on our side but we also need the community to really understand the problem with antibiotic resistance.

DR ANDI HORVATH
This is Up Close and we're chatting to two University of Melbourne PhD scholars, Claire Gorrie who's studying the drug resistant bacterium Klebsiella Pneumoniae and, next up, Rebecca Vandegeer who is studying the wheat plant's defence system against a virus called Barley Yellow Dwarf.
Now food security is a pressing problem so insight into viral infection of crops and how crops are going to fare under climate change is critical to our future. Rebecca Vandegeer is from the University of Melbourne and the Victorian Department of Economic Development, Jobs, Transport and Resources. Rebecca, welcome.

REBECCA VANDEGEER
Hi Andi.

DR ANDI HORVATH
Rebecca, what does the Barley Yellow Dwarf Virus actually do to crops?

REBECCA VANDEGEER
Well Barley Yellow Dwarf Virus infects a wide range of crop species including wheat, barley, oats, rice and maze and by the name we know that the Barley Yellow Dwarf Virus, it's a very literal name for a virus, it causes a yellowing in the leaves of the plant and a dwarfing of the plant, so it stunts growth. In terms of crop species, this is reflected by reductions in yield of the crop. For example, in wheat it can be quite devastating to the yield of the crop. You can get crop losses of up to 80 per cent. In addition to this it can cause reductions in the quality of the crop grain. For example, in wheat that can cause grains to be smaller, more shrivelled, which is bad for the growers. The main way that this virus reduces growth is by inhibiting photosynthesis.

This causes a reduction in the growth.

DR ANDI HORVATH
Okay so how's the virus transmitted from plant to plant?

REBECCA VANDEGEER
Yeah, so this virus is spread between plants by an insect. You can probably liken it to how malaria is spread between humans. Malaria exists in the bloodstream of humans in the same way the Barley Yellow Dwarf Virus exists in what is essentially the bloodstream of the plant, which is known as the phloem. The phloem transmits molecules and sugars within the plant.

DR ANDI HORVATH
The Barley Yellow Dwarf Virus goes up and down the phloem. Which insect comes to suck on the plant?

REBECCA VANDEGEER
The main insect that spreads this virus between plants is an aphid, which you may have seen on your rose bushes at home. Aphids feed on the plant by sucking up the sugars from the phloem. That causes the virus to go inside the body of the aphid and so when that flies onto a new plant and feeds on another plant that will spread the virus into that plant.

DR ANDI HORVATH
This is really like the malaria of the plant world. What's happening at the cellular level when the virus infects the wheat? You said it was inhibiting its photosynthesis, but what's really going on?

REBECCA VANDEGEER
Many things occur when the Barley Yellow Dwarf Virus infects a host plant. The main thing the virus does is it takes over the machinery of the plant and disrupts a lot of the metabolism of the cell. When a plant cell is exposed to a virus, a range of things happen. One of the first responses of the plant is the production of a large amount of reactive oxygen species. These molecules, which are actually produced by the plant, can be potentially harmful. On one hand, the reactive oxygen species may be a direct response of the plant to the virus. It may be a way of the plant trying to actively kill the virus. They can also play a role in signalling downstream defence responses in the plant to try and fight the virus. Although they play certain roles, they need to be regulated by the plant so they do this by using the plant's antioxidant defence system which helps regulate them to be used in the way that they want them to be used.

DR ANDI HORVATH
This is like our immune system. We get a bite and then we scratch it. It turns red. It's like an over-reaction?

REBECCA VANDEGEER
Yeah, that's right.

DR ANDI HORVATH
Then finally our body sort of calms down and just deals with what's there?

REBECCA VANDEGEER
Yeah, that's right. It's called a hyper-sensitive response where it tries to control and keep that in one place. If the plant can't control the molecules efficiently, you get what's known as oxidative stress, which can be harmful to the plant.

DR ANDI HORVATH
This poor plant is trying to fight off these reactive oxidative species and this is all part of the oxidative stress that's happening and it needs to draw on antioxidants?

REBECCA VANDEGEER
This is an area that I'm particularly focusing on in my research.

DR ANDI HORVATH
Currently can we control this virus? As a farmer can I do something about it?

REBECCA VANDEGEER
The way that it's most generally controlled is by controlling the insect. Growers or farmers generally will spray pesticides to kill the insect or use seed dressings that protect the plant. However this has its own environmental or economic costs. In addition, it may not be as effective because the insect can transmit the virus quite quickly, so even if a grower can spray a pesticide it may be too late in terms of virus infection.
Another way that they can try and control the virus and the insect is to control the amount of weeds on the farm in the times of the year where crops aren't grown. Because these weeds can harbour high populations of the insect and also the virus, enabling it to be more easily spread into the new crop that's grown in the following year.

DR ANDI HORVATH
Right, so there are various techniques to manage this virus. Now on top of this, our planet is experiencing climate change and atmospheric levels of CO2 are rising. I believe they're expected to rise from 400 parts per million to 550 parts per million by 2050. Now that puts extra stress on plants doesn't it? I mean what happens to plants under elevated CO2 levels? Does it get more stressed?

REBECCA VANDEGEER
We know from research already that because CO2 is a major substrate used in photosynthesis, that elevated CO2 can actually stimulate the photosynthesis in the plant making that more active and that results in more growth of the plant. In terms of crops this can be reflected in higher yields. For example, in wheat you might have more grain. On the flip side of this, increases in yields of crops can often be associated also with reductions in the nutritional quality of the plant. For example, in wheat grains you might see reductions in protein micronutrients which are important for human nutrition.

DR ANDI HORVATH
Now you grow some of your wheat crops in elevated CO2 levels. How do you do that?

REBECCA VANDEGEER
One way you can do it is by growing plants in pots in chambers under elevated CO2. However, a more realistic way of perhaps doing this is to grow crops actually out in the field under elevated CO2. The way we do this is by using state of the art facilities. For example, in Horsham in South Eastern Australia, we have a facility called AGFACE which stands for the Australian Grains Free Air Carbon Dioxide Enrichment facility.

DR ANDI HORVATH
Wow.

REBECCA VANDEGEER
This is a really cool facility. There's only a few of them actually in Australia. With this facility we can grow crops in its natural outdoor environment under elevated CO2. You could picture it as a 12 metre wide ring of stainless steel tubing. It's raised to the level of the crop and there are small holes in it that blow CO2 out onto the crop.

DR ANDI HORVATH
That's quite a sophisticated facility.

REBECCA VANDEGEER
Yeah.

DR ANDI HORVATH
Now you're actually putting the two concepts together. You are studying the wheat's viral defence response under elevated CO2. Tell us about that. What's the pattern so far in your research project?

REBECCA VANDEGEER
Yeah so, as I said, I'm looking at this antioxidant defence system and trying to understand how the plant responds to the stress of viral infection and also whether this will change under elevated CO2.

DR ANDI HORVATH
And does it?

REBECCA VANDEGEER
I'm seeing some really quite interesting changes where you might get a weakening of the antioxidant system with virus infection, which may be associated with these changes in the physiology of the plant that I'm seeing, like reductions in photosynthesis. It's possible that the weakening of the antioxidant system is necessary for the virus to successfully infect the plant. In terms of elevated CO2 there may be some changes as well. I'm still trying to dissect the data there.

DR ANDI HORVATH
Can we actually breed resistant crops?

REBECCA VANDEGEER
In terms of wheat there are only very few varieties that show some resistance or tolerance, so plant breeders and scientists are working on trying to develop new varieties that show some resistance or tolerance. They do this by breeding different varieties together with resistance and tolerance, or by breeding with wild relatives that may have a resistance gene to the virus.

DR ANDI HORVATH
Rebecca, I'm going to wave the magic wand for you too, give you a PhD student or maybe two. What would you like them doing?

REBECCA VANDEGEER
Well, I would probably get them to start working on investigating the insect because I'm particularly looking in the plant virus interactions. To be able to incorporate the insect and how the insect behaves in these environments and with this virus would be really interesting, something that definitely needs to be addressed.

DR ANDI HORVATH
Thank you for being our PhD scholars for 2015. Claire Gorrie and Rebecca Vandegeer, all the very best of luck to both of you.

CLAIRE GORRIE
Thank you

REBECCA VANDEGEER
Thanks Andi.

DR ANDI HORVATH
You'll find a full transcript and more information on this and all of our episodes on the Up Close website. Up Close is a production of the University of Melbourne, Australia. This episode was recorded on 11 November 2015. The producer was Peter Clarke and Andi Horvath, audio engineering by Gavin Nebauer. Up Close was created by Eric van Bemmel and Kelvin Param. I'm Dr Andi Horvath. Cheers.

VOICEOVER
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