Published on *Up Close* (http://www.upclose.unimelb.edu.au)

#254: Vanquishing the vectors: Enlisting bacteria to fight mosquito-borne disease

VOICEOVER
Welcome to Up Close, the research talk show from the University of Melbourne, Australia.

DYANI LEWIS
I'm Dyani Lewis, thanks for joining us. From antibiotics to insecticides to chemotherapy drugs, the 20th Century saw the development of extensive chemical weaponry to keep disease at bay. We've seen how our efforts in the laboratory have paid dividends in terms of longer and arguably healthier lives, and these efforts continue today. In fighting the biological agents that cause disease, be it bacteria or worms or our own cells when they turn cancerous, we've often turned to chemistry. But sometimes the best way to fight biology is with biology. In this episode of Up Close I'm joined in the studio by professor Ary Hoffmann to look at how biological control can be used to prevent dengue fever, a disease that is prone to rapid and pandemic scale outbreaks in tropical regions around the world.
Ary is an insect geneticist and ecologist from the departments of Genetics and Zoology at the University of Melbourne. Welcome to Up Close, Ary.

ARY HOFFMANN
Thanks Dyani.

DYANI LEWIS
Ary when it comes to tropical diseases, there are some that get a reasonable amount of attention from the research community, for example malaria, and then there are others that the World Health Organisation has classified as neglected, and dengue fever is one of these neglected tropical diseases. So how common and how important is dengue fever?

ARY HOFFMANN
Look it's incredibly wide spread and economically the cost can certainly be quite substantial for a country. So for instance in Brazil alone, dengue has been estimated to cause an economic loss of about $1 billion a year. You can get small outbreaks in

some countries. In Australia we tend to have outbreaks in North Queensland that might involve a few hundred people, up to one thousand, say. But of course in other countries it can be much larger than that. So certainly in some South East Asian countries you can have outbreaks that affect tens -- or even hundreds of thousands of people. It might only cause a few thousand deaths per year, it does cause a major economic cost for a country and that's why of course it's not really a disease that should be neglected. I mean it certainly is on the radar for a lot of countries to eradicate if at all possible.

DYANI LEWIS
And by the sounds of it it's affecting mostly countries that wouldn't be able to bear that economic burden.

ARY HOFFMANN
Yeah that is correct. Although dengue is interesting in the sense that it can affect first world countries as well as third world countries. So for instance Singapore has a major issue with dengue, and they can again get tens of thousands of cases in a bad year. So it's one that sort of falls across the board, and it's one of those situations that as long as you've got the right vector presence, then potentially you will have dengue.

DYANI LEWIS
And what actually causes dengue fever?

ARY HOFFMANN
Dengue fever is actually transmitted by mosquitoes. There are two species of mosquito that transmit dengue. I mean dengue itself is of course a virus. But it's the transmission vector that's particularly important here, and there are two species. One's called Aedes aegypti that's the most common vector, and then there's another vector called Aedes albopictus which is a less common vector of dengue.

DYANI LEWIS
You've mentioned that insects or mosquitoes are the vector for the dengue virus, which means that they are the culprits that transmit the virus from one person to the next. Can we simply control dengue fever by controlling the insect vectors using things like insecticides?

ARY HOFFMANN
Yeah and that's actually the most common approach that people use to decrease the incidence of dengue. I mean you can't do too much about the viruses unfortunately. I mean obviously there's been a huge investment in vaccines to try and develop a vaccine for dengue, and there has been success. But unfortunately the efficacy of the vaccine is simply too low at this stage to provide protection. That may change in the future, we hope it does. But at this stage it's simply too low. Now on the other hand of course, if you can suppress the vector then potentially you can suppress the transmission of the dengue virus and that seems to be the most common approach at the moment. Unfortunately that tends to involve chemicals most of the time. So

what people do is they obviously spray chemicals on breeding sites and also around environments to try and decrease the population of adult mosquitoes flying around, and also larval mosquito stages and breeding sites.

DYANI LEWIS
And that hasn't been working?

ARY HOFFMANN
It certainly can suppress the transmission of dengue. But unfortunately, mosquitoes have an incredibly high reproductive potential. So you might suppress the populations for a very short period of time, but they just bounce back incredibly quickly. And you know, that's typically the case of many insects of course. A single female might be able to lay several hundred eggs. In that particular case you do get this very rapid bounce back. So sure, it can suppress it for a short period of time, but you'd have to be putting an awful lot of chemical onto an environment to suppress it long term, and mosquitoes can of course bite back. So in the sense that many mosquito species have evolved resistance to chemicals, and the dengue vector is no exception in that. So Aedes aegypti one of the main vectors is resistant to quite a lot of chemicals which are currently used and resistance levels tend to build up, unfortunately, in the environment quite quickly.
So what formerly was effective in terms of chemical control can very quickly not become effective.

DYANI LEWIS
So quickly lose that arms race against the insecticides?
ARY HOFFMANNYeah look as long as you don't put the chemicals on too often it's fine, but typically of course what you're trying to do when you're suppressing these vector populations is to really put it on repeatedly. It's a bit like when you go to resorts sometimes in South East Asia. You'll often find a situation where there's almost no bugs present in the environment at all, and that's because there is so much chemical going out, there's so much fogging with chemicals going on that simply you're removing the entire insects and invertebrates fauna in that particular situation, which of course is not particularly healthy either.
DYANI LEWISNo, no. Ary you've been looking at a type of biological control that targets the mosquitoes that carry the dengue virus, and it makes use of a bacterium called Wolbachia. Can you explain what Wolbachia is?

ARY HOFFMANN
Yes Wolbachia was first discovered in mosquitoes quite a long time ago, and was really worked on in a group of mosquitoes called Culex mosquitoes, back in the 1950s. And what Wolbachia does is something really interesting. So when a female carries the Wolbachia and the male carries the Wolbachia, then when they mate the embryos are normally produced. But if a female doesn't carry Wolbachia and mates with a male that carries Wolbachia then the embryos actually die. So the Wolbachia seems to be able to kill the embryos in that situation. Now Wolbachia is a bacterium that lives inside cells, and we call that an endosymbiont. So it doesn't actually kill the host cells, but it just lives inside the cells in a symbiotic relationship, or at least a

partially symbiotic relationship.
Wolbachia is an unusual bacterium in that it can't live outside the actual insect vectors. So what it does it lives inside a cell and it's transmitted through the host through the ovaries. So basically it shows a pattern of what we call maternal transmission. It's transmitted through the mother. So if a sperm carries Wolbachia and fertilizes an egg, or tries to fertilize an egg, that doesn't carry Wolbachia, the embryo dies. If a sperm carries Wolbachia and fertilizes an egg with Wolbachia, then the egg is okay and develops. Just like if you had a situation where an uninfected sperm fertilizes an uninfected egg. So we have this situation that's set up where, if you like, the bacteria manipulates the host in such a way that it actually allows certain types of eggs to survive and other eggs to die and the bacteria in that process actually advances its own transmission through the particular lineage.

DYANI LEWIS
Now in symbiotic relationships there's often something to be gained by both parties. But does the mosquito gain anything from allowing the Wolbachia cells to reside within its own cells or is it just a case that it can't actually get rid of them?

ARY HOFFMANN
That's a really good question Dyani. There are different Wolbachia strains out there, and they probably do different things. So there is certainly Wolbachia strains that seem to be absolutely essential for the survival of the host insects or host other invertebrate. So for instance there are some Wolbachia strains that live inside nematodes and those nematodes, or those worms if you like, need the Wolbachia to survive. If you killed Wolbachia you actually kill the worms. That's a truly symbiotic relationship. Another case is probably a partial symbiotic relationship, and that's the insects gain something from having the Wolbachia. So for instance, there's some evidence that Wolbachia can provide nutritional resources for some species of insects which potentially can include mosquitoes. So that's a second advantage that you can get from the Wolbachia. There's also an interesting third advantage, and this is obviously what we're going to be talking about a bit later, and that's that the Wolbachia seem to be potentially virus blockers.
So they seem to be natural virus blockers. That can of course then benefit the insects by stopping the infestation of insect tissue by the viruses and also by other bacteria potentially as well. That seems to be quite effective even against such things as plasmodium, which is responsible for malaria.

DYANI LEWIS
So do we know anything about how the Wolbachia prevent this infection by viruses?

ARY HOFFMANN
There have been a number of different mechanisms that have been postulated. So, on the one hand it seems to be that when you actually have the Wolbachia then you can cause up-regulation of the immune system of the insects. So that's one possible pathway. Another possible pathway is that there seems to be direct competition between the viruses and these bacteria living inside the cell for resources that are needed for reproduction. So if a virus doesn't have the resources available, then it's

going to be able to multiply much less effectively. So that's a second mechanism. Antd it's also possible that there are actually direct interactions between compounds, proteins for instance, produced by the viruses and the bacteria that interacts in a certain way to stop the replication of the viruses. So, you know, we feel that there are a range of mechanisms responsible and it probably depends on the nature of the virus and the Wolbachia strain that you're talking about.

DYANI LEWIS
So you mentioned before that Wolbachia affects the reproduction of the insects. Does this mean that Wolbachia is in the reproductive tissue, or is it more widespread in the insect?

ARY HOFFMANN
Yet again, there's no simple answer to that question. It really does depend on the Wolbachia strain. So some Wolbachia seem to be really quite restricted to the gonadal tissue, the tissue that's involved in reproduction. So you find those Wolbachia at a very high density in ovaries. You also find those Wolbachia at a very high density in sperm tissue, and of course you want to be at a high density there, because if you're being transmitted through the mother that's where you need to be. So in a sense you can understand it makes sense from a Wolbachia point of view. There are Wolbachia strains that are actually much more widespread that occur in a range of tissues. In fact there are some that occur in almost all the tissues of an insect vector. In those particular cases we suspect that there are probably larger effects on the host but probably also better virus blocking in terms of beneficial effects for the host.

DYANI LEWIS
I'm Dyani Lewis and you're listening to Up Close. In this episode we're talking about dengue fever and its insect vector the mosquito with professor Ary Hoffmann. Ary you've spoken about some of the beneficial effects, potentially nutritional effects or effects on the immune system. But what about the costs to the mosquitoes? Do they mosquitoes become unwell when they have Wolbachia?

ARY HOFFMANN
Look they can do and again it depends on the Wolbachia strain. If you can imagine a strain of Wolbachia that only lives inside these gonadal tissues, then there probably aren't too many deleterious effects, too many bad effects resulting from that particular Wolbachia strain. On the other hand of course, if you have a Wolbachia that occurs very widespread in the host species, you can imagine some bad effects happening. You're obviously sucking away resources from the cell that it can use for other purposes. So it's strain dependent. We do find some deleterious effects. We do find that certain Wolbachia strains for instance reduce the lifespan of their vectors. We find that some reduce the reproductive potential of the vectors, and obviously those are going to have an impact on the population of the vector

DYANI LEWIS
The transmission from mother to child in the insects, this is called vertical

transmission. Is there any evidence of horizontal transmission where you might get one mosquito passing it on to another mosquito not through sex?

ARY HOFFMANN
That's an interesting question, and again it's one that's been debated a lot. So we suspect that can be the case but very, very rarely. It might only happen one in a million years or something like this. So I'll give you an example. So there are parasitoids little wasps that parasitise eggs in the mature stages of insects, and what they do is they often undergo unsuccessful paroxysms, so they try and lay their eggs inside say a larva of an insect and that particular process is not successful. Now in that process of actually trying to lay their egg, they might pick up a bit of a tissue of the insect host. They then try and parasitise another egg, and let's say they're unsuccessful again, but they might then transfer that tissue to another larva, and if that's a different species then potentially you could get a transfer of Wolbachia from one type of insect to another type of insect. So that of course would be horizontal transmission, not vertical transmission.
But like I say, that's going to be very unlikely to occur. So yes it does occur, we have got evidence for that. But it's probably a very rare, rare event, one in a million years, one in a 100,000 years or something like that. Very difficult to detect in fact.

DYANI LEWIS
[It's] certainly a very fascinating relationship that's evolved.

ARY HOFFMANN
Yeah, and when you sort of think about the fact that up to half of the insects and mites for that matter that we know about actually carry Wolbachia, it's quite successful from a Wolbachia point of view.

DYANI LEWIS
Ary, getting into the way that Wolbachia can control dengue spread, how many mosquitoes do you need carrying this Wolbachia to release into an environment that has dengue fever around in order to get some kind of transmission prevention?

ARY HOFFMANN
Yeah, so Dyani, the exercise here is to actually completely change the nature of the mosquito population. So what we discovered back in the 1980s, and I have to go back a little bit in time here - but what we discovered back in the 1980s - and this is actually work that wasn't carried out in mosquitoes, it was carried out in fruit flies, and this when I was a post doc back in California - we discovered that Wolbachia could actually spread through a population very quickly. The way it does that is quite simple. So if you think back to what we were talking about, you've got a bacterium that's transmitted vertically, and then of course you've got a situation where this incompatibility in the embryos occurs that's caused by this bacteria. So effectively it means notwithstanding those deleterious effects that we just talked about, the bacterium is actually at an advantage.
It can basically spread very quickly through a lineage because it's transmitted by all the females, and all those females are capable of mating with all types of males. It

doesn't matter whether the male's infected or uninfected. On the other hand, if your lineage doesn't have the bacteria, then you can only really mate with males that don't have the bacteria. So this automatically means that a female that carries the Wolbachia is at an advantage, and Wolbachia of course then spreads because it's passed on to all the offspring of that female. So what we discovered back in the 1980s is this particular process allowed the Wolbachia to spread through a population very quickly. So we started with a situation where we had a large population of vinegar flies in Central California which didn't have Wolbachia, and then what happened was that the Wolbachia was present in a different population around the Los Angeles area, and they then jumped into the Central Valley and the entire Central Valley became infected by Wolbachia over a period of about three or four years.
So Wolbachia was moving at a rate of 100 kilometres per year or more -- very quickly throughout that valley. So that's to give you an indication of how quickly Wolbachia can spread.

DYANI LEWIS
It always seems amazing to me that there are populations that don't have Wolbachia then.

ARY HOFFMANN
We have found some cases where Wolbachia doesn't spread as quickly. But we have found other cases where it's very effective in terms of spreading. If it's not spreading really quickly it suggests that there's something about the effects of Wolbachia on the host that's stopping that spread occurring. So we have had a situation for instance in Australia where we have a different Wolbachia strain that also occurs in vinegar flies and it seems to be quite stable in terms of its frequency. So this particular Wolbachia strain has had a very high frequency in the tropics and a very low frequency in Tasmania, and on the rest of the East Coast it seems to be in intermediate frequencies, and that's a situation that's been stable now for about 20 years. Now in that particular case, the Wolbachia certainly is capable of spreading and it's obviously done that in the tropics.
But it seems to cause some sort of deleterious effects on its hosts that stops it spreading elsewhere. So I think it's these deleterious effects that really drive the ability of Wolbachia to persist.

DYANI LEWIS
So there's kind of an equilibrium point that's reached based on - well, I guess just like any other gene in a population that would be not present in everyone, but present in a few people?

ARY HOFFMANN
That's right, yeah. So we call this equilibrium point the unstable equilibrium. So if you're above the unstable equilibrium point you'll spread, and if you're below the unstable equilibrium you'll actually disappear from a population. That unstable equilibrium depends on the size of the deleterious effects on the host. So in other words, if your Wolbachia strain that causes many, many deleterious effects on the

host, then your unstable equilibrium is going to be quite high. If you don't cause these effects your unstable point could be very, very low, it might even be close to zero.

DYANI LEWIS
So if we go back to the situation of an area that has dengue fever and we want to know how much it would take for us to get a Wolbachia population of mosquitoes replacing the resident population, how do you determine that point?

ARY HOFFMANN
Yeah so what you have to do is you have to go out and you have to measure to what extent this Wolbachia strain that you're interested in introducing causes these deleterious effects. So in that way you can actually estimate the unstable point. There is also another complication and that's not all females transfer with 100 per cent efficiency the bacteria to their offspring. So there's a bit of leakage. We talk about maternal leakage, and that can also affect the unstable point. But it's mostly we think dictated by this host effect, this deleterious host effect. So it effectively means that some Wolbachia strains will spread easily and some won't spread as easily.

DYANI LEWIS
You're listening to Up Close and my guest today is insect geneticist and ecologist Ary Hoffmann. We're talking about using Wolbachia bacterium to control dengue fever. I'm Dyani Lewis. Now you've been using insecticide resistance genes to I guess stack the odds in your favour in terms of getting these Wolbachia strains invading in a population. Can you explain how this works?

ARY HOFFMANN
Yeah. Let me just take one step back before I do that. So we have a situation where we have Wolbachia introduced into a mosquito population, and this is a mosquito vector that actually transmits dengue. Okay, so that's the situation we're facing, and we have different Wolbachia strains that have been introduced in a population, and this has been a large collaboration that we've had with Monash University and James Cook University, and the Monash people were successful in that transfer. So what we've been trying to do is to look at ways of introducing different Wolbachia strains into populations. So you can artificially generate new Wolbachia strains into insect vectors, including the dengue vectors, and what you then want to do is to introduce that Wolbachia into the natural populations of your mosquitoes. Okay, so that's the situation we face. So we have different Wolbachia strains, and some have large deleterious effects on their host and some have small deleterious effects on their host.
The small ones are easy. You can get them in quite easily. But the ones that are difficult are going to be quite challenging. So what we've been doing is to explore ways of trying to get those particular strains in through your population, and as you said Dyani, one of those ways of doing that is to potentially use insecticide resistance. So what you can do is take advantage of the fact that you can hook up insecticide resistance genes to the Wolbachia strain you're releasing and that will

allow you to actually spread the Wolbachia more easily. Effectively if you come back to the unstable point, it lowers the unstable point, so the introductions become much simpler. So let's take two situations. On the one hand, you might not have insecticide resistance present, and in that particular case, to get the Wolbachia through a population your unstable point might sit at something like 60 per cent.
So that means that you actually have to introduce Wolbachia at a frequency of 60 per cent, or greater than 60 per cent, for that Wolbachia to spread in that population. On the other hand what we've shown is that if you actually have insecticide resistance tied up with the Wolbachia, then you can halve that point. So instead of having to beat 60 per cent, you then might only have to beat 30 per cent, which is much easier if you're doing releases of mosquitoes.

DYANI LEWIS
Because in the 60 per cent situation, you're effectively having to more than double the population with your release number?

ARY HOFFMANN
That's right yeah. So you can imagine a situation where you go to an area and there might be 6,000 mosquitoes present, and to get invasion you probably need about 15,000 mosquitoes. So you're boosting a population quite substantially, and of course that might not be acceptable to people living in those environments, because they're going to get more mosquito bites. I mean once the invasion is complete it's quite straight forward, the mosquito population will fall back to its former level, so it's only a temporary increase in the mosquito population we're looking at. But nevertheless, that may be undesirable.

DYANI LEWIS
So how do you go about orchestrating these kind of releases and insecticide applications if you're combining the two?

ARY HOFFMANN
So as I said, chemical control is one of the main ways that people currently use to suppress dengue vectors and to suppress the incidence of dengue in populations. So in a sense people are already doing it. So what you have to do is then go about finding out what chemicals people are using, generate resistance strains to those chemicals, add those resistance genes to the Wolbachia strain that you're releasing, and then make sure that people are actually fogging areas while those releases are going on. So it's part of the process if you like that's being followed to suppress the transmission of dengue. So in that sense we feel this is a control strategy that is actually quite nicely lined up with what's already happening in a lot of countries and we feel that's the advantage.

DYANI LEWIS
And you've done a pilot study of this type of release?

ARY HOFFMANN
So we have been doing releases, and again this is a part of a larger project in

collaboration with our partners at James Cook University and at Monash University, so those are actually going on and that's work that was initially funded by the Gates Foundation. Those initial releases in Cairns did not involve resistance. There's not a lot of chemical that goes on in the Cairns area, so we don't really have resistance issues and we don't really have the situation where fogging is happening all the time, as is the situation in most third world countries. But we have shown, and this is we're going back a couple of years now, that you can certainly get the successful invasion of Wolbachia. That particular case, we released a strain of Wolbachia that was reasonably easy to introduce, so in other words that unstable point was not set high, it was probably around 20 per cent or so.
In that case, we didn't really have to bump up the population too much. But we deal with another strain of Wolbachia that again we have tried to release in Cairns, that one wasn't successful because the unstable point for that particular strain is much higher, it's probably in the order of 50 per cent or 60 per cent in some situations. In that particular case, what we've been doing is developing resistance genes attached to that strain for future release. So we haven't actually quite done that release yet. Combined with the insecticide resistance, we've certainly showed the feasibility of that approach and we are currently developing the strain that will allow us to explore that approach in the future.

DYANI LEWIS
And so how long would you expect, in terms of both insect generations and also in real time, that the replacement would take place in the environment?

ARY HOFFMANN
Yeah so again, that depends on the unstable point and it depends on whether you're putting on insecticides or not. So in the initial releases that we did in 2011 it only took about 10 weeks of releases to exceed the unstable point and watch the invasion process occur. So effectively we released Wolbachia for 10 weeks, we bumped up the population by about one and half to twofold, so in some situations we actually doubled the population size. But it was only for a short period of 10 weeks, and that was enough to get invasion in that particular case. Now if you're releasing a more difficult strain - and let me just explain that when you have these difficult strains, they're often quite desirable because they are probably better blockers a lot of the time of the dengue. So dengue for instance has four serotypes. One of the strains that we have, and this is a strain called wMelPop or popcorn as we like to call it, is an incredibly effective blocker of dengue, of all those serotypes of dengue.
It really is an absolute blocker of dengue. So if you can get that through your population that's going to be really desirable. This is the situation we face, the best viral blockers we have are probably the ones that have these deleterious effects, and that's where you really need this extra boost, because their unstable point is going to go quite high in the population. So you've got to exceed that unstable point to get it through and that's going to be a tougher strain to introduce, and that's why you need these strategies like insecticide resistance to make that happen.

DYANI LEWIS
Now in Cairns in Northern Australia where you did these trials, presumably there's no

dengue virus to look at, and the real test for the system would be whether or not you can decrease the amount of people being infected by the virus. Is that the next step?

ARY HOFFMANN
You're absolutely right Dyani, so in Cairns we do get some dengue. But what typically happens is that the dengue is not endemic. So it's picked up by someone going overseas, bringing the virus back in their system. That person then gets bitten by a mosquito, the mosquito transfers the dengue to another person, and then a cycle is set up of transmission obviously over quite a local area. So dengue is not endemic. In other words, it's not persistent throughout the whole year, even though it can persist for a few months through those sorts of cycles. Now of course, when you go to overseas countries, and for instance we've been working a lot in Indonesia, then you do have dengue being endemic. You have many, many more cases, and if you try to demonstrate suppression of dengue by Wolbachia, you're absolutely right, you do need to go to those environments and then carry out trials where you show that the dengue is definitely being suppressed by the Wolbachia.
DYANI LEWIS
Biological control isn't a new concept at all and in some cases releasing a biological agent to control another has had some very unintended consequences for the ecosystem. Is this a risk for Wolbachia and also I guess with the insecticide resistance genes that you're introducing?

ARY HOFFMANN
Yeah so it's kind of interesting. When we first release Wolbachia, we released Wolbachia at a place called Gordonvale, and Gordonvale is a town in far North Queensland, and it's actually the place where [the] cane toad was first introduced [laughs].

DYANI LEWIS
The infamous cane toad in Australia.

ARY HOFFMANN
That's right, and clearly cane toad is an excellent example of a situation where things went very wrong. But of course cane toad was introduced at a time when biological control basically meant communicating with someone overseas saying, hey I'd like to try this thing because I've heard that it might suppress cane beetle or something like that, let's bring it on and see what it does. Of course these days we're much more rigorous than that and certainly in the case of Wolbachia once we introduced it into mosquitoes, a very rigorous process was undergone in terms of risk assessment. The advantage of Wolbachia, and this really came out in the risk assessment as well, is that Wolbachia is a natural viral blocker. So it's not like you're introducing or creating something artificial. You're taking something that's present in a very large number of insect species. As I mentioned before, over 50 per cent of insect species are probably infected by Wolbachia. So you've got millions of species actually out there in the environment already infected by Wolbachia. That bacterium is then producing natural blockage of these viral agents already.
So you're then transferring that particular Wolbachia into the mosquito that lacks that

Wolbachia strain, and as I said that's something that already occurs at a very low frequency in natural populations. So you're really sort of speeding that process up, and that's the advantage of Wolbachia, you're really taking advantage of a natural situation that already occurs, that already is blocking viruses and other microorganisms inside the insect and taking advantage of that. And that's why it's much more akin to bio-control than creating some sort of potential new agent through genetic modification, that's certainly not what this is. With respect to the resistant alleles, again, we already have resistant alleles present in natural populations. Mosquitoes are very effective at evolving resistance. So all you're really doing is for a short period of time, you're taking resistance and using that to your advantage.
So normally we see resistance as being bad, but here's a situation where resistance is actually good because it allows you to spread the Wolbachia in a population. So yes, I'm not underestimating the issues involved in thinking about this very carefully. But given that you're just using resistant alleles for a short period of time to introduce the Wolbachia, I think it's probably less of a problem in that sense.

DYANI LEWIS
One final question, which is can this approach be used for other diseases like Malaria? You said that Wolbachia can effect transmission of a lot of different things, so is it a general approach?

ARY HOFFMANN
It certainly has potential against other diseases. So for instance, one of the ones we worry about is Chikungunya which is another viral disease, and that certainly seems to be blocked very effectively by Wolbachia, and of course in Australia we have Ross River Virus, which is another one of these viruses that potentially can be quite well blocked by Wolbachia. Now recently it's also been shown that Wolbachia has activity against plasmodia, probably not as much as we'd like at the moment. But of course, only one strain of Wolbachia has been tested, and it may be possible to find the Wolbachia that causes very effective plasmodium blockage. So I think yeah, Wolbachia certainly has that potential. I suspect we're probably just at the tip of the iceberg in terms of exploring these sorts of interactions, and I think it's probably one of those situations where you've just got to see what happens in the next few years in terms of the research results coming out. But of course in all those cases you still have to spread the Wolbachia.
So in all those cases, we are facing a situation where you do need to get the Wolbachia through your vector population effectively, and of course when you're talking about Malaria, there are other challenges, because it's not just one vector you're talking about. In dengue we have one main vector and we have a secondary vector as well. But it's mostly one main vector. In the case of Malaria of course, there are several vectors that you'd need to focus on. But having said that, one of the Anopheles species that's been associated with Malaria has recently been successfully trans-infected with Wolbachia and we now have a strain out there that causes at least some blockage of plasmodium and clearly that has lots of potential in terms of Malaria suppression into the future.

DYANI LEWIS

Professor Ary Hoffmann, thank you for being our guest on Up Close today and talking to us about controlling the dengue virus.

ARY HOFFMANN
Thank you Dyani.

DYANI LEWIS
Professor Ary Hoffmann is a geneticist and insect ecologist from the departments of Genetics and Zoology at the University of Melbourne. Relevant links, a full transcript, and more info on this episode can be found on our website at upclose.unimelb.edu.au. Up Close is a production of the University of Melbourne, Australia. This episode was recorded on 19 June 2013. Producers for this episode were Kelvin Param, Eric van Bemmel and myself, Dr Dyani Lewis. Audio engineering by Gavin Nebauer. Up Close is created by Eric van Bemmel and Kelvin Param. Until next time, goodbye.

VOICEOVER
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