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Alligator Serum Antibodies: New Therapeutic Avenues

Dr. Shira Johnson:
Take a test tube of HIV, add serum from crocodiles, stir well. What do you have? Well, you have far less HIV particles than the same experiment done with human serum, but what are we going to do with that? You're listening to ReachMD, the channel for medical professionals. Welcome to the Clinicians' Round Table. I'm Dr. Shira Johnson, your host, and with me today is Dr. Mark Merchant, associate professor of biochemistry at McNeese State University in Lake Charles, Louisiana.

Dr. Merchant has teaching responsibilities at the university, and he has many, many scientific publications, mostly I journals that are just a bit over my head. But his recent work with the serum of alligators come him into National Geographic, all of the science journals, and many of the news and TV stations. Today, we're discussing his recent work with alligator serum and its ability to fight infections, definitely in alligators and possibly in humans.

Thank for taking the time to be with us today, Mark. I know you've been a very busy man lately since all this news came out.

Dr. Mark Merchant:
It's my pleasure. Thank you for having me.

Dr. Shira Johnson:
First, a few questions about your work. What was your hypothesis going into this, and how did you get involved in this arena?

Dr. Mark Merchant:
I've been around alligators my entire life. I grew up...

Dr. Shira Johnson:
Personally and professionally, is that it?

Dr. Mark Merchant:
Well, yeah. I mean, you know, when I was young, I grew up fishing and hunting in the local marshes here, and of course, when you do that in this part of the world, there's lots of alligators. And of course, all kids are fascinated with alligators. But what fascinates me today as a professional is a little bit different than what fascinated me when I was a kid. We're interested in their immune systems now. Alligators are very territorial animals. They engage in territorial fighting. They bite each other's limbs off, literally, lots of very serious injuries.

But despite the fact that they live in aqueous marsh environment that harbor many potentially infectious microbes, these enormous wounds seem to heal without a lot of infection. And so, that's very interesting to us.

Dr. Shira Johnson:
So, what's the practical aspect of this? How does one get blood from an alligator?

Dr. Mark Merchant:
We go out at night, we shine a very powerful spotlight across the marsh. Like many animals, their eyes are highly reflective. We can see their eyes, drive toward the alligator, slip a noose over its neck, tighten down, wear the animal down, get into the boat as soon as possible, so as not to stress the animal, tape its mouth shut, and stick a needle in its neck, and draw blood from the spinal vein. It's in the vertebral column.

Dr. Shira Johnson:
How long does it take to do all this?

Dr. Mark Merchant:
Depends on the size of the alligator. Obviously, we want to avoid injury to ourselves and to the animals. I will let an alligator roll around as long as it takes to get it tired. Anything under four and a half feet, I'll just grab with my hands and you know, drag it in the boat, and we can tape their mouth shut immediately. And to draw a blood sample only takes a matter of a minute or two. A larger animal, obviously, with a noose, we have to let it roll around more, and it can take up to ten minutes, but not more than that.

Dr. Shira Johnson:
You have a team for this, right? Is this with graduate students that get on board for...

Dr. Mark Merchant:
Not really. I don't let students handle alligators. I don't need that liability.

Dr. Shira Johnson:
No.

Dr. Mark Merchant:
To tell you the truth, I go out with individuals in Louisiana with the Louisiana Wildlife Department here in Louisiana. I actually live in Texas, so over near my home in Texas, I have a couple friends, and sometimes my son, we'll go out and catch these alligators and bleed them.

Dr. Shira Johnson:
What was some of your initial laboratory experiments or laboratory work that sparked this, and where or when was that published?

Dr. Mark Merchant:
The very first initial experiments, I asked the very simple question, "Can alligator serum kill microbes?" First we started with bacteria, and I tried 23 different types of bacteria in my original study. And the answer was yes, it kills lots of different types, gram-negative, gram-positive. It kills them very rapidly, it kills them in a temperature-dependent manner. This was published in the Journal of Comparative Biochemistry and Physiology.

Then we moved on to look at its anti-parasitic properties. That was a pretty good study. It was published in the Journal of Parasitology. We looked at antifungal activities, and on and on. We eventually got to where we were tired of looking at activities, and we wanted to look at the mechanism. So, then we discovered, thorough the series of a couple mechanistic studies that were published in various journals, that the mechanism of antimicrobial activity of alligator serum is in fact the serum complement system.

Dr. Shira Johnson:
Not actually the antibody formation, right?

Dr. Mark Merchant:
Just to clarify, there are several different pathways for serum-complement activation. The classical pathway, actually called the classical pathway, is antibody antigen dependent. But the alternative pathway is antibody independent. And we found through some mechanistic studies that that is the pathway that is very active in alligators. That didn't preclude the fact that they may also have the classical pathway, but we know that the one we were dealing with was the alternative pathway.

Dr. Shira Johnson:
Let's break some of this down and speak in terms of future work, and where this is going. We know that this component from the alligator with the complement furiously attacks HIV, which I'll guess that alligators are not exposed to anyhow. But from a clinical aspect, what do we do with that, to have some tangible research ideas for human beings?

Dr. Mark Merchant:
For HIV, absolutely nothing. I downplay my antiviral studies because the fact that, number one, serum complement's never going to be a drug for humans. It's a series of ten rather large proteins that would elicit an immune response in humans. Even if it didn't elicit an immune response, they're very unstable. They would never have a shelf life. So, that's not in the picture.

Dr. Shira Johnson:
So, not stable, and would trigger a host reaction.

Dr. Mark Merchant:
Exactly. However, we are working, trying to isolate, feverishly trying to isolate some small cationic proteins that I've shown are produced

by their leukocytes. And we hope that these, and these do have antiviral activities, antifungal and antibacterial activities, and we're hoping that maybe those might be good candidates for something to be used in a clinical setting

Dr. Shira Johnson:
For those of you just joining us, you're listening to the Clinicians' Round Table on ReachMD, the channel for medical professionals. I am Dr. Shira Johnson, and I'm speaking with Dr. Mark Merchant, a biochemist at McNeese State University in Louisiana, who's done some very stimulating research with alligators. What about fungi? Your work showed it was reactive against fungi, and we know immunocompromised hosts succumb to fungi daily. Could you or other scientists see taking that aspect of the research a step further?

Dr. Mark Merchant:
Sure. We've shown that these extracts are very effective at killing candida yeast in vitro now. We haven't done any in vivo studies. We've shown that it's fairly effective as an anti-candida albicans agent. And we know that candida albicans is a cause of lots and lots of nosocomial infections in the US. And so, that would be exciting, if we could do something about that.

Dr. Shira Johnson:
And what about MRSA, very reactive against MRSA, which communities and hospitals are having problems with that right now in real time. Is a gator serum paving the way for other research in this area, or is it too virulent, not the serum, right.

Dr. Mark Merchant:
But the gator leukocytes, that's the one we're excited about. Just a note here, a very important note, we're not sure if, once we isolate these proteins and characterize their structure, if they will be able to be used internally in humans. We don't know if these tiny proteins are going to elicit an immune response. My inclination is to say that they probably will, but we could certainly use them externally, topically, but I'm not sure about internally. We'll just have to see.

Dr. Shira Johnson:
There was a statement in at least one article I read that said pills and creams, maybe you're referring more to the creams that contained alligator peptides could be available at local pharmacies within seven to ten years. Is that a stretch, or do you see that happening?

Dr. Mark Merchant:
No, I think that's more realistic than something that you would put in an IV drip or something like that, because if you apply them topically, there's far less chance that it will elicit an immune reaction, you know, a host immune reaction.

Dr. Shira Johnson:
What was the single most exciting discovery for you personally in this research, and why?

Dr. Mark Merchant:
There's a couple. The very first day in the lab, when we showed that alligator serum kills just all kinds of stuff, that was pretty exciting, because I didn't know what to expect. I mean, this was five or six years ago, no one had ever done anything like this. And to see that activity from day one was really exciting. The other exciting thing was when, I think I was working with a fellow scientist up in New Jersey. We were trying to isolate what was in the leukocyte extracts, and we were looking at a HPLC profile of the proteins that were in the extract, and trying to separate them.

And I was comparing an antifungal profile with the chromatogram I saw, and I saw that there were peaks of activity that matched with the protein peaks. So, I could look at this chromatogram and say, "The protein that makes this peak here has antifungal. Here's another one, here's another protein peak right here, and that protein has antifungal activity. These other ones don't." So, I could actually start to see that there was something in these leukocyte extracts that showed distinct antimicrobial activity.

Dr. Shira Johnson:
Aren't there some other animals, toads and frogs, for instance, whose blood can behave in a similar manner, at least in vitro?

Dr. Mark Merchant:
The very first antimicrobial peptide described was by Dr. Zasloff, and it was from the skin secretions of frogs. Frogs obviously have moist skin, which, you know, frogs living out in the forest and wherever, they have moist skin that's going to be a really great place for bacteria and fungi to grow. So, they actually produce and secrete these onto their skin secretions to help prevent infection. And that was the first antimicrobial peptide described, back in the late 80s, I believe.

And so, that was pretty exciting. And since then, there have been many, many antimicrobial peptides isolated from plants and insects, all the way up to humans. We produce our own. But we think there's something special about alligators and crocodiles, because they do lead a lifestyle of aggression toward members of their own species. They do put a lot of genetic pressure on each other, because of where they live, to evolve something really, really good, because if every time an alligator fights and tears a hole in another one, if they

all go belly-up and die, they wouldn't be around.

So, they've had this incredible genetic pressure to produce something really effective, and I think that they have done that.

Dr. Shira Johnson:
Did any products come on the market that were a result of the work that was done with toads or frogs?

Dr. Mark Merchant:
Not yet. There has been antimicrobial peptide on the market yet. I think we may be expecting to see our first one in the next year or two.

Dr. Shira Johnson:
And that's not from you yet?

Dr. Mark Merchant:
No, no, not from me. None from crocodile, I'm the only one working on the crocodilian thing right now.

Dr. Shira Johnson:
Where do you go to for funding? Is it going to be easier for you now to find funding? Do you think big pharma will be interested in the work that you're doing?

Dr. Mark Merchant:
Well, I have funding right now from the state of Louisiana. Once we actually isolate and start to describe the structure of these proteins, I believe then that maybe the pharmaceutical industry could be interested. I believe that maybe National Institutes of Health and maybe the National Science Foundation might be interested as well.

Dr. Shira Johnson:
What's your take-home message for our audience?

Dr. Mark Merchant:
Wow, take-home message. Well, I'm having a blast doing this stuff, and hopefully we can produce something that may help modern molecular medicine combat some really problematic things that we've seen in the last few years, namely the development of these so-called super bugs that are resistant to practically everything we have on the market today.

Dr. Shira Johnson:
Yeah, because your timing, I mean, right, when MRSA is rampant, and the drugs we have are getting resistance to everything.

Dr. Mark Merchant:
Absolutely. We've got some really nasty things that the CDC has been good enough to share with me. You know, things that are resistant to some klebsiellas that are resistant to 17 or 20 different commonly-used antibiotics. It turns out that these leukocyte extracts are actually quite effective against these.

Dr. Shira Johnson:
That's pretty exciting the CD gave these to you to work on. That's pretty exciting.

Dr. Mark Merchant:
Oh, yeah. CDC is great. They're really, really good.

Dr. Shira Johnson:
And they gave you money with it, I hope, right?

Dr. Mark Merchant:
No, no, no. They gave me the bacterial strain. I actually asked them if they wanted to collaborate, but they said that they were really busy, so I said, "Well, I can do it myself." But they gave them to me, and we ran with it. I'll be writing up that stuff for publication pretty soon. I just wanted to mention that these are in vitro tests, you know, in a petri dish. These are not by any stretch of the imagination any kind of in vivo animal or human testing at all.

Dr. Shira Johnson:
No, we can't say that too often for our listening audience, but it's still tremendously exciting that you've been able to take these steps even in vitro.

Dr. Mark Merchant:
No one goes straight to animals. Everybody, you know, starts in vitro, in a petri dish. So, that's where we are now, very early in the

game. But pretty exciting stuff.

Dr. Shira Johnson:
This came from an animal that's been around how long? How long has the alligator been around?

Dr. Mark Merchant:
Crocodilians in general have been around roughly 175 million years, 200 million years.

Dr. Shira Johnson:
Dr. Merchant, thank you for being my guest today. I thoroughly enjoyed you being on the show.

Dr. Mark Merchant:
Thank you so much.

Dr. Shira Johnson:
We've had Dr. Merchant here from Louisiana. We've been discussing potential breakthroughs in the infectious disease world through looking at the alligator serum or components from their blood. I am Dr. Shira Johnson. You've been listening to the Clinicians' Round Table on ReachMD, the channel for medical professionals. To comment or listen to our full library of podcasts, visit us at ReachMD.com. Thank you for listening.