Dr Vincent Racaniello interviewed by Robert Herriman re Influenza H7N9 gain of function experiments

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Virology Blog: http://www.virology.ws/2013/08/13/influenza-h7n9-gain-of-function-experiments-on-dispatch-radio/
YouTube: http://www.youtube.com/watch?v=cefnT2u7poc&noredirect=1#at=51

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Herriman: Well welcome back to Dispatch Radio. Earlier this week there was a letter published in the scientific journal *Nature* that has caused quite a stir amongst the scientific community, and in a nutshell, it's saying that there's a group of scientists that are interested in performing controversial experiments on the bird flu that's circulating in China right now, it's called Avian Influenza H7N9, and to date it's infected 134 and killed 43. Here to try to sort this out is Dr Vincent Racaniello, he's a Professor of Microbiology and Immunology at Columbia University. Hello Vincent, and welcome back to the show.

Racaniello: Hi Robert, thanks for having me back.

Herriman: As soon as I saw the story you came to my mind immediately. So tell me if I got this right. So we've got about 20 odd virologists and they want to do some manipulations on this virus. Is that it in a nutshell?

Racaniello: Yeah, that's basically it. The H7N9 virus which, as you know, just emerged into people this year, seems to have some potential for infecting more people, so these virologists want to do experiments on it and they wrote this letter to let everybody know exactly what they want to do.

Herriman: Sure. And these experiments are called 'gain of function' experiments. In the simplest possible terms, can you try to explain what that means?

Racaniello: So a 'gain of function' simply means that you take a virus and you change it in some way so it does something new, so it does something that it didn't do before. That's all that means. It's quite simple. So you could for example take this H7N9 virus and make it resistant to an anti-viral drug, that would be a gain of function.

Herriman: Sure. And I read your post on Virology Blog the other day, and clearly you are pro gain of function experiments. And I guess my question is, and for our listening audience, why would anybody want to do this?

Racaniello: So, to really understand how this virus works, and really any other virus, we do gain of function studies all the time. We don't make a big deal of it, we don't write letters telling the world that we're going to do them because that's not the way science works. Science works by just doing your experiments. We do this because we would like to see what kinds of changes would lead to a gain of function, and what would be the consequences. So, in the case of this virus, these investigators want to make the virus drug resistant. As you know, there are a couple of anti-virals that you can use if you get influenza – Tamiflu, Relenza - and these investigators want to make the virus resistant. And the reason they want to do that is to see if a drug resistant mutant would have any properties that would make it scarier in people. So there is really a goal to these experiments. They want to know if you change the virus what might be the consequences for people. And as I said this is done all the time but these virologists decided to tell the world about it.

Herriman: And that's probably because it's kind of déjà vu to 2011 when they, they individually did the H5N1 experiments which caused all kinds of controversy.

Racaniello: Yes, as you know as a result of that there was a moratorium on that H5N1 transmission research for a while, and part of the goal of that moratorium was to try and increase telling the public what you're doing with this virus. And I think these authors being part of that whole scenario decided it might be a good idea to tell the public ahead of time what they're going to do.

Herriman: So they're sort of playing politics with this?

Racaniello: I suppose, in a way…

Herriman: Yes…

Racaniello: …as a scientist I wouldn't do this because I think you get into trouble. As you know the press has boiled up over those letters and the headlines are incredible…

Herriman: Sure.

Racaniello: …and I think it's better to do the experiment, and if it works out publish it, and then explain why you did it afterwards.

Herriman: OK. Now there's plenty of arguments against performing such experiments. Some people are saying, and I want you to respond to each one, that these engineered strains could be accidentally or deliberately released from the lab, sparking a flu pandemic. What do you say to that?

Racaniello: I think this is very, very unlikely. The way I view it is, you have to balance what you might get from an experiment versus the potential danger. And in this case the potential benefits far outweigh the dangers. These experiments would be done under high containment, the likelihood that a virus would escape is really, really low. Plus, whenever you do a gain of function, the virus always loses something in exchange. And in the H5N1 gain of function experiments where they adapted them to ferrets, to aerosol transmission, that was a gain of function. What those viruses lost was their ability to cause disease when they spread by that route. So I don't worry about a dangerous strain getting out at all, I think that likelihood is really negligible.

Herriman: OK. And another critique is, some are saying that the animal models, such as ferrets, yeah, they can provide some information as far as risk of transmissibility and pathogenicity. However, how do you extrapolate that to humans?

Racaniello: Right. Now this is something I have always contended, you cannot make predictions about what will happen in humans based on an experiment in an animal like a ferret, or a guinea pig or whatever your chosen animal model is. But you still have to do these experiments because they provide you other kinds of information. For example, the ferret transmission experiment, with H5N1, they, the results of those were a series of genetic changes that allowed the virus to transmit in the air from one ferret to another. Those don't predict the changes that might be important in humans. However, those changes give you an idea about how it works to make a virus better to transmit in the air. In other words what is the function of these changes? And I think the function is conserved(?) between animals and humans. So they do provide a lot of information. They're not predictive, but they provide what we call mechanistic information about very specific aspects of human disease.

Herriman: Yeah. In kind of a follow-up to that, I saw in one AP report this week, one scientist, who is definitely a critic of the experiments, said, you know, we tried this with the H5N1 two years ago, you know, we got nothing out of it, you know, should we do all this work if it's not actually going to make a difference?

Racaniello: Well I would totally disagree with the conclusion that we got nothing out of it. I would send that scientist to my blog, I've got a series of posts about what we learned from those H5N1 experiments. We learned a great deal. We were shown things that we'd never understood before about what makes a virus able to transmit in the air. So I argue that we're going to learn a lot from these types of experiments.

Herriman: Yeah, and if you weren't aware Vincent, I just saw a press release from Hong Kong today, and they have a suspected H7N9 case in China right now, and so that may be number 135.

Racaniello: Yeah, I saw that on your blog this morning.

Herriman: Oh, great! Fantastic, got to love that… Anyway, Vincent Racaniello, Dr Racaniello, has a fantastic blog called Virology Blog. If you have any remote interest in the science of virology, this is the place to go. He did a fantastic article concerning these gain of function experiments, and he

makes a very strong case for performing them. And I just found it great. And also if you're interested he has a very good Facebook page too, it's called This Week in Virology, am I correct?

Racaniello: Yes, that's right facebook.com/thisweekinvirology

Herriman: Yeah, and that's a good place to go too for information and… Alright Vincent, well I appreciate you coming on and clearing the air on this and telling us what you think, I appreciate it.

Racaniello: It's always a pleasure. Could I plug my Coursera course?

Herriman: I'm sorry?

Racaniello: I teach a course on Coursera and I'd like people to know about that.

Herriman: Oh OK, go ahead, go for it.

Racaniello: I teach a virology course, it's free on the Coursera site. It's coursera.org and you can find a link to that on my blog virology.ws. It just started last week, it's free, and we take you step by step through understanding virology, so I think you'll like it.

Herriman: That's great. And I have a lot of Facebook fans that are very interested in these kind of topics, so hopefully that'll get spread around the globe, because it is a global thing. Alright, Dr Vincent Racaniello from Columbia University, thanks for joining us on the show.

Racaniello: Robert, always great to talk to you, thank you.

Herriman: Alright, same here. Bye bye.

Racaniello: Bye.

Other commentator: Alright, well, fantastic as always Bob. And it's really awesome to know that Dr Racaniello is following your work as much as you're following his.

Herriman: That's fantas…that caught me off guard a little bit. So I'm really pleased, and considering that this particular story has got a lot of, I mean a lot of the stuff we talk about here on the show doesn't get necessarily the coverage it should, this has got probably more coverage than it should have, and not being a virologist by training, it's good to read and listen to what Dr Racaniello has to say, and even reading the comments on his blogs, because not everybody agrees.

Other commentator: Yeah, it's fantastic.

Screen shot of Dr Vincent Racaniello's description of 'gain of function' virus research