This Week in Virology

with Vincent Racaniello, Ph.D., Alan Dove, Ph.D., and Angela Rasmussen

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Episode 12: Prions, lemur lentiviruses, RS virus vaccine, H5N1

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Vincent Racaniello:
I'm Vincent Racaniello and it's a Saturday in New York. It's Saturday because we had some recording problems yesterday. But I have two guests today. Alan Dove is joining us again. Welcome Alan!

Alan Dove:
Hi! Good to be back again.

Vincent:
I appreciate your taking time to record on a Saturday.

Alan:
Oh, no problem, just got done shoveling out the cars here in Western Massachusetts before we get another foot of snow dumped on us.

Vincent:
Did you get a lot of snow?

Alan:
Oh yeah. Yeah, we got about a foot last night and it's still coming down.

Vincent:
Well we didn't get much here, but as usual it paralyzes us no matter how much we get. It took me three hours to go 38 miles last night.

Alan:
Heh heh.

Vincent:
Our second guest is here with me in my office, Angela Rasmussen!

Angela Rasmussen:
Hello!

Vincent:
Welcome to TWiV!

Angela:
Thanks, it's great to be here on TWiV.

Vincent:
I know that you usually wouldn't be here on a Saturday, right? [chuckling]

Angela:
Oh never, never! Graduate students are never at work on weekends, ever.

Vincent:
Do you want to be called Angela or Angie?

Angela:
Oh, please call me Angie.

Vincent:
Ok, so Angie is actually a Ph.D. student in my laboratory. So now we have two, a former Racaniello person and a current Racaniello person. This is just coincidental, I think.

Alan:
Well, it's always encouraging to show the current graduate students that, you know, people do eventually get out of your lab.

Vincent:
[chuckling]

Angie:
Which is something that we definitely need to see. Ha ha ha.

Vincent:
Yes, of course. Well, you two have never met, you never met Alan, right?

Angie:
No.

Alan:
No.

Vincent:
Alan graduated years ago. And you will graduate in a couple of months, right?

Angie:
Exactly!

Vincent:
So I think what it means is that the people who can talk about viruses just happen to come from my laboratory!

Alan:
That must be it!

Angie:
It's true, it's the primary source for excellent people who can talk about Virology.

Vincent:
Well today we have lots of stories as usual. There's never a shortage of things to talk about in Virology, which is gratifying. The problem is deciding what to include, actually, because there are usually too many stories. Oh, Alan! How's journalism? How is science journalism? I meant to ask you.

Alan:
Oh, science journalism is busy as heck. Uh, I've been tracking down sources for three different stories, and of course you know everybody disappears next week for the holidays, so I had to get all my interviews done this week. So, it was kind of a hectic week for me.

Vincent:
So do you cover all science or just Biology-related science?

Alan:
I cover, uhm, technically I cover just about anything that comes up, but you know, in practice the big demand seems to be for Biotechnology, Molecular Biology, and so that's what I end up covering.

Vincent:
So, occasionally you do a virus story.

Alan:
Uh, oh yeah. Yeah, viruses come up a lot.

Vincent:
The last one I remember is the interview with...

Alan:
Oh, Maurice Hilleman.

Vincent:
Maurice Hilleman.

Alan:
Yes.

Vincent:
That was a fun one, right?

Alan:
Yeah, that was a blast.

Vincent:
Someday we have to talk about that.

Alan:
Yeah. Heh heh heh.

Vincent:
These giants, uh, aren't around forever, and when they're here we should talk to them and get them down digitally forever.

Alan:
Absolutely.

Angie:
Get Hilary Koprowski on here.

Vincent:
What a good idea!

Angie:
Yeah.

Vincent:
He would do it for me. Maybe I'd have to go to Philadelphia, because I don't know if he can do Skype.

Angie:
Well, probably not, but that's just a quick hour and a half away on...

Vincent:
Yeah, it's no problem. Uh, I had him here a few years ago, you may remember him...

Angie:
I do.

Vincent:
For a seminar. He was very nice.

Angie:
He gave a really interesting talk on Rabiesviruses as well.

Vincent:
Yeah, he's a very interesting... Do you know Hilary at all...?

Alan:
Yeah, yeah. I uhm, actually I've met him at a couple of events, including the one where I interviewed Maurice Hilleman. It was a star studded get-together.

Vincent:
Yeah, that's a good idea, we'll have to... let me write down. Hilary Koprowski. Actually if you go to my Columbia website we'll put a link in the notes. You can see a picture of me and Hilary...

Angie:
And Rich Kessin.

Vincent:
And Rich Kessin. I remember we went for a drink afterwards, after his seminar. And he ordered a martini.

Alan:
[chuckling]

Vincent:
With Boodles gin.

Angie:
[laughing]

Vincent:
Which I'd never heard of.

Alan:
Boodles gin!

Vincent:
Do you know Boodles gin, Alan?

Alan:
No, I don't! [chuckling]

Vincent:
Speaking of giants, though, one died not too long ago. And that's our first story. Carleton Gajdusek. He was 85 years old. I met him once, you probably never did, Angie.

Angie:
No.

Vincent:
And Alan, did you ever meet him?

Alan:
No, no I never did.

Vincent:
Carleton of course, was the scientist who found all about kuru, that interesting disease in New Guinea. The Fore people of New Guinea, they were dying from some weird neurological disease and he went there to sort it out. Apparently he was interested in these old..., and odd, or unconventional diseases. And, eventually he found that the disease which only appeared in women and children was caused by cannibalism. And what would happen would be, someone would die in the tribe, and then they would take the brain of this person and the women and children would eat it as part of the ritual. And he said this is transmitting some sort of disease and you shouldn't do it. He got them to stop and in fact, the disease went away. And now we know that this is what's called a TSE - a transmissible Spongiform Encephalopathy, which is caused by a protein. A protein gone wild.

Angie:
[chuckling]

Vincent:
Or a prion. And of course, a number of people have worked on this subsequently, but the main driver I think would be Stanley Prusiner, would you agree with that?

Alan:
Yes. Absolutely.

Vincent:
And he got the Nobel prize not too long ago for sorting this out. This is really fascinating, and in fact there are a couple of articles in the news this week about this. So basically, you get these transmissible spongiform encephalopathies - TSEs, when your prion protein, which is encoded by a gene which we all seem to have, misfolds. And the disease can be transmitted to others when they either eat the protein or somehow take it up, and there are forms where you get the infection from others like kuru, they ate the brains, they had prions in them and they got the disease. You can also have a genetic form where you have a mutated prion gene in you and at some point the protein starts to misfold and you develop the disease. And, do either of you know what is the most recent kind of TSE that there's a lot of headlines about lately?

Angie:
Would that be mad cow disease, or variant Creutzfeldt-Jakob disease?

Vincent:
What do you think?

Alan:
That would be those two things, which may be the same thing, but there's still a little bit of debate about that.

Vincent:
Ah, so right. So, there's variant CJD, which we see a lot in the UK, right?

Alan:
Right.

Vincent:
I think there were 164 cases so far, fatal cases of variant CJD in the UK. And, this is thought to be acquired by eating cows who have mad cow disease, right?

Angie:
Correct.

Vincent:
But Alan, you think it's not clear if...

Alan:
Well, I think it's fairly clear. The issue is, you know... it's the usual Koch's postulates argument. You haven't really conclusively proven this until you've isolated the pathogen and reproduced the disease, and of course, nobody is going to do that in this case, uhm, but there's ample circumstantial evidence to say that these two things are most likely connected.

Vincent:
Right. So it's called variant because this is thought to be originating from BSE - bovine spongiform encephalopathy, right?

Alan:
Right.

Vincent:
I found an article in BBC news which says "Fears raised over new variant CJD wave", and apparently there's another number of cases coming up which are thought to be maybe a new variant. So there have been so far 164 deaths and now they think that there may be 3 to 350 more cases coming up. So again, this is if you eat.., in theory if you eat meat from a cow that died of this disease or presumably has these misfolded proteins and they can transmit the disease to you..., so that would be a transmissible form as opposed to a familial or genetic form of the

disease. So again, this is all starting from the work that Gajdusek did. Of course, before Gajdusek there were also other diseases of sheep, specifically scrapie, which is also a TSE. But it was really Prusiner and others who sorted out that it would be a protein. Now, I also found a very interesting article in *PLoS Pathogens* called "Prions in milk from ewes incubating natural scrapie". Now a ewe, that would be a female sheep.

Angie:
Female sheep. [in unison]

Vincent:
Ok, gotta get that right.

Angie:
Lady sheep.

Vincent:
A lady sheep. Ewe, E-W-E. So, the prions are in the milk! This is interesting because it's the first evidence that that happens, and we thought before..., we didn't actually limit milk distribution in any way, because we didn't think prions were there.

Alan:
Right.

Vincent:
So this is a big problem, right?

Alan:
Potentially. I mean, what they found here is that the..., they can find the scrapie prions in the milk from these ewes, and, you know, granted, it's sheep rather than cattle, and cattle are the bigger source of milk that humans are drinking....

Vincent:
Right.

Alan:
...but it's certainly an unexpected result, and it's kind of a disturbing result, because you've got this food source that may have, uhm, this potentially infectious protein in it.

Angie:
Or, what I think is more disturbing about it is that it seems that normal sterilization or pasteurization techniques don't actually inactivate or kill, I guess you could say, the prion protein. So, even if you pasteurize the sheep milk or otherwise process it into cheese or some other type of dairy product, it can still contain infectious prions.

Alan:
Right.

Vincent:
Do we know how much sheep milk is consumed, globally?

Angie:
Uh, I don't.

Alan:
I don't either.

Vincent:
I would guess that it's probably limited to farm consumption. If you have a farm with sheep, you get sheep milk and you drink it, because it's good. It's like goat milk I would assume also.

Angie:
Right.

Alan:
Right.

Vincent:
It's probably not commercially a big deal. So it's the cow milk that would be the issue.

Angie:
I would say though there are a lot of sheep milk cheeses though.

Vincent:
That's right. And they might have infectious prions because you could imagine that the process wouldn't inactivate them. Yeah.

Alan:
But I think really, the, uhm, maybe the most disturbing thing is that somebody hadn't looked before now.

Vincent:
Yes. Yes.

Alan:
[laughing]

Angie:
It gives you a lot to think about in terms of food safety.

Alan:
Right, what else haven't we checked?

Vincent:
You can have a big list, sure. I assume now, this will stimulate people to check in cow milk, right?

Alan:
Right.

Angie:
I would hope so, I love cheese.

Vincent:
[laughing]
I'm not a big fan of milk, but I know a lot of people are. If your herd is free of BSE, then the milk is probably okay.

Angie:
You would hope, except for the practice of feeding cows feed that's made with other cows, which I think has largely stopped since...

Vincent:
Right.

Angie:
...mad cow disease or bovine spongiform encephalopathy was first described in the United Kingdom...

Vincent:
That's right.

Angie:
...but I think, I don't know if the practice has been completely eliminated.

Alan:
Then there's also the issue of, you know, you say if your herd is free of BSE, but remember, that for a number of years the US said "well our herds are free of BSE". And the way that the department of agriculture was able to make that claim was that essentially they weren't looking very closely.

Vincent:
Mhmmm, right.

Alan:
Uh, so again, you know, you don't find what you're not looking for.

Vincent:
Now, I may be wrong about this, but it's my impression that in the US, the department of agriculture does not examine every carcass.

Alan:
No, they don't.

Vincent:
Whereas in Japan they do, is that correct?

Alan:
I think that's correct, yeah.

Vincent:
Well, we will end it on this last sentence of the abstract, which says "it also" ("it" referring to their results) "raises some concern with regard to the risk of humans of TSE exposure associated with milk products from ovine and other TSE-susceptible dairy species." So we may hear more about this in the coming months and years. But I think that's quite interesting. Well of course, all of Virology is, isn't it? [laughing]

Angie:
Yes, of course. [laughing]

Alan:
Sure!

Vincent:
Alright, next story. "A Transitional Endogenous Lentivirus from the Genome of a Basal Primate and Implications for Lentivirus Evolution." This was a paper published recently in *The Proceedings of the National Academy of Sciences*. And, this caught my eye because they found basically... a lentivirus of course includes HIV, SIV, the simian immunodeficiency viruses, and also viruses of other animals, such as, uhm, cats and horses and a variety of others, there are lentis infecting them. And in this paper they found lentivirus sequences integrated into the chromosomal DNA of lemurs. And, again, we talked about lemurs before, Dick brought it up a couple of episodes ago, and I hadn't realized this, but these lemurs have been on this isolated island, Madagascar for 14 million years, and they haven't had contact with anyone else. So, I looked at this and it turns out this is interesting at a much higher level. So these, first of all, finding the DNA of these viruses in the genome is... the first time that this has happened. So, at least for primates, and a lemur is a primate - it's little - but, they're primates, right? And, this shows that lentiviruses can integrate into the germline. So in order to be transmitted in this way, from animal to animal it has to integrate in the germline. We know now for example, HIV only infects lymphoid cells, and we don't know that it infects the germline, but apparently at some point this retrovirus did. So that's the interesting part. And then of course, this will have people looking more and more in other genomes for these. But the other thing is, this is quite an ancient virus. When you have a viral genome integrated into the host chromosome it evolves much more slowly than viruses do, so it's a lot easier to track evolution of it. So what they could do here is

show that this is quite old. And, uh, this virus they say is basal to all known primate lentiviruses, so it predates all the ones we know, HIV and SIV for example. And the point is, that lemurs have been isolated for 14 million years, how did this get into their genome from other species, because this island is very isolated, it's hundreds of kilometers from Africa?

Angie:
I think it's about 250 miles away from mainland Africa.

Alan:
That's right.

Vincent:
And it's very deep water also, right?

Angie:
Correct.

Vincent:
And, so they have evolved alone. So this virus had probably hit them 14 million years ago, but how? Did it get them on the mainland and they made their way to Madagascar, was there a vector that could get across..., I think that's an awfully long distance for a mosquito, I think Dick said once about 25 miles is the maximum a mosquito will go, and that's only certain kinds of mosquito, so how this happened is really a mystery.

Alan:
Well unless there was a bird carrying it, uh, but that seems unlikely, that you would have something that could infect a bird and a primate at the viral level.

Angie:
I read actually an interesting book about Krakatoa, the Indonesian volcano, every time it erupts, it basically completely decimates the ecosystem on the island. But then as soon as the island..., its lava dome builds back up and it has a surface, it relatively rapidly becomes recolonized with plants, and it's because of seeds and spiders and things like that blowing...

Vincent:
That's right!

Angie:
....actually, in the wind, it's making its way there. So, again you'd have to figure out something that could conceivably infect both a spider or, you know, some kind of small insect, uh, as well as a lemur. But, that's the other possibility. In this paper, I think they talk about a bat.

Alan:
There is actually, uhm, there's some evidence now as well that you can get at least bacterial and fungal species transiting the entire Atlantic from Africa by the jet stream. So yeah, it is certainly possible that you get a high altitude transfer either through dust or through some species getting

carried across. On the other hand, it's also conceivable from the genome analysis that this is a very very ancient virus, it's perfectly believable that it's 14 million years old. And lemurs, when they got this one, they were still part of the mainland.

Vincent:
Sure. That could very well be.

Angie:
Absolutely.

Vincent:
I mean you could imagine that a... maybe an animal swam, could have gone this far, it could have been on a log and floated. I know that we have at the end of Long Island a BSL-4 laboratory called Plum Island.

Alan:
Plum Island, yes!

Vincent:
And it's a few miles from the mainland, but they told me when I visited years ago that they saw deer swimming from the mainland to the island.

Angie:
Wow!

Vincent:
And, you know, that's not good because they have foot and mouth... they used to have foot and mouth, I don't know if they still do, but animals can do odd things. So, it could have been. But this is an interesting paper... and also we should point out that it shows that these lentis are very old. We didn't appreciate that before. People tended to think they're relatively new viruses, but they're quite ancient.

Angie:
When you think about it, these endogenous lentiviruses have only been recently described as well, so....

Vincent:
Right.

Angie:
I think the more of these are discovered in various genomes.... we'll find out more about how old they really actually are.

Vincent:
Yeah, this is a really nice example of why you have to look for things. You don't always have to have a hypothesis....

Angie:
Absolutely.

Vincent:
You have to look and see what you find, and this is a nice combination of Virology and Bioinformatics and a little bit of Evolution thrown in.

Alan:
Absolutely.

Vincent:
I think this is a really interesting paper and, we'll put a link in of course, and uh, you can have a look for yourself. So that's quite cool. Now next one, Alan you picked up on this one.

Alan:
Yeah! So this is some news that just came out, uhm, from Hopkins, uh, some researchers were looking at the respiratory syncytial virus vaccine. The RSV vaccine, and this is a bit of virological history, uhm, back in 1966, the golden age of vaccine development...

Vincent:
That's right.

Alan:
So the vaccine was initially developed against RSV, and this is a virus that..., I think the estimate is that 50% of kids before age 1 end up infected with this. In most of them it ends up being a self-limiting infection, but it's you know, the usual story, you get a certain percentage of kids who get very severe respiratory disease from it and it's a significant cause of morbidity. So, I think one statistic was a couple of hundred thousand hospitalizations a year, or something like that. So it's a significant disease, it's certainly worth developing a vaccine for, uhm, and they came out with this thing in 1966, did a test group, and gave it to some kids, and this was a formalin-killed vaccine, so they took the RSV virus, killed it with the chemical formalin, very much like the inactivated polio vaccine, IPV.

Vincent:
Right.

Alan:
That was all well and good, the kids took the vaccine, but then the ones who got exposed to RSV afterwards, actually developed a worse disease, they developed an enhanced respiratory virus disease, or syndrome, compared to what they would have gotten if hadn't been vaccinated. So this very appropriately scared a lot of people off working on RSV, if the vaccine is going to make things worse than no vaccine..., and in the ensuing 40 years, no pharmaceutical company or major research program has gone after this. Uhm...

Vincent:
Can I interrupt...

Alan:
Go ahead.

Vincent:
When I was taking courses for my Ph.D. I remember this being given as an example of a vaccine that went bad and that vaccine was actually developed by Robert Chanock, who was a Virologist at NIH.

Alan:
Ahhh!

Vincent:
Do you remember Alan, what the explanation was for the vaccine failure?

Alan:
Well the original explanation..., and people have done follow-up studies on this to try to figure out what the problem was and the conventional wisdom that emerged was that the inactivation damaged the antigens in the virus to the point where they produced a sub-optimal immune response and this sub-optimal response prevented a proper immune response from developing when the real virus came along.

Vincent:
Right, in particular they thought that..., so these viruses have two glycoproteins...

Alan:
Right.

Vincent:
They have an attachment glycoprotein, and they have an F glycoprotein which is needed for fusion. And so they thought that this destroyed the F glycoprotein so they didn't make antibodies against it, and therefore these viruses could get into cells and then spread by fusion from cell to cell.

Alan:
Right.

Vincent:
And therefore cause the atypical disease. You know, it sounded good at the time.

Alan:
Right. So of course that put a damper on work on this vaccine, and uh, what these folks did, is they went back and looked at it using modern techniques, and of course we know a lot more about the immune system now, uhm, and they came to the conclusion that it wasn't that the

antigens were messed up, the problem was that the vaccine stimulated antibody production without stimulating what are called the Toll-like receptors, and Toll-like receptors in the immune system are responsible for starting the cascade of events to mature the antibody, to refine the antibody. So in fact what you're getting is an initial antibody response but you never get the antibody maturation that's supposed to occur to get neutralizing antibodies against this virus. And now, knowing this, I think the reason this is a very important bit of work, is it tells you how to fix the problem, essentially. It tells you that if you have an RSV vaccine and if you can simultaneously stimulate the Toll-like receptors, uhm, perhaps through another antibody or through adding, you know, some other agonist to the Toll-like receptors as you deliver the vaccine, you should be able to get an effective immune response against it.

Vincent:
Yeah, I think in this paper they did use a TLR agonist.

Angie:
They did, that's exactly what they used.

Alan:
Yes. So they did the experiment in mice, and found when they did this, and simultaneously stimulated the Toll-like receptors, they get what appears to be an effective vaccine.

Vincent:
So probably here, the agonist is just used to dissect the defect and prove that it's in fact this TLR deficiency....

Alan:
Right.

Vincent:
...but you probably can't use these in people.

Angie:
Right.

Vincent:
So you have to figure out how to not destroy the antigens in a way that would prevent this.

Alan:
Right.

Vincent:
At least you have an assay now, you know what to look for, right?

Alan:
Exactly, and you have a mouse system, where you can look for this and get meaningful results.

Vincent:
Yeah, this is a very nice paper. So Angie, you know a little bit about Immunology, right? [chuckling]

Angie:
I do. [chuckling]

Vincent:
So what does the TLRs and sensing of virus in the innate response have to do with the antibody affinity?

Angie:
So when you think about it, uh, your cells are exposed to all kinds of things all the time. And not all of them are going to be bad, like a virus, so the Toll-like receptors exist to recognize, first, when a virus infection is around, and to give signals that will turn on the cell basically, to both attack the virus and to recruit in the immune system. So normally the immune system is running around responding to everything all the time, but it's not necessarily dangerous, so, the response stops there. When a Toll-like receptor starts the signaling program, and says "hey, we're infected with a virus", it kicks the immune system into high gear, and then allows for isotype switching, which allows for the development of neutralizing antibodies, and recruits the T cell response, and basically brings in the power of the entire immune system. So, lacking the TLR agonist, uhm, it's not going to respond basically, so you're just going to get the most basic immune response and it's just going to stop there.

Vincent:
Hmmm.

Angie:
You're not going to take it to the next level where you're going to have lasting immunity..... and where the body is really going to recognize that, you know, it's facing an infectious threat.

Vincent:
Right.

Alan:
So the old RSV vaccine primed the body to recognize the virus as foreign, but not to recognize it as a threat.

Angie:
Exactly. And not to..., and most importantly, in terms of, you know, an effective vaccine, not to, you know have preventative immunity against it.

Alan:
Right.

Vincent:
Hmmm. Yeah this is a big deal I think, it should stimulate some real progress in an RS vaccine.

Angie:
Which is very important too because RSV is one of the viruses that's been implicated in the pathogenesis of asthma, which affects quite a lot of people and it's been shown to really start with early childhood respiratory infections, and unlike Rhinovirus, which I work on, there's only one RSV that you can develop a vaccine for, so it would be terrific if this particular virus could be controlled with vaccination, an effective vaccine.

Vincent:
Hmmm. So if you get..., the idea is if you get infected at a young age, which is the way you get infected with RS, that predisposes you to Asthma later on, correct?

Angie:
Correct. And actually it's very important that they found that the Toll-like receptors are involved in this, because one of the things that the research on Asthma and early childhood respiratory infections has shown, is that the type of response, the type of immune response the child has to the infection, actually determines whether or not that child is more likely to develop Asthma.

Vincent:
Yeah, at the moment there is very little you can do for infants, there..., you can treat them with an antiviral called Ribavirin, but that's about it, and it doesn't always work, and as you know, you can get resistance.

Alan:
Right.

Vincent:
Ok, that's a nice paper. That's a very good one Alan, but we have all nice papers on TWiV.

Alan:
Absolutely.

Angie:
Of course.

Vincent:
Now, the last story is something we haven't talked about, and we will have to talk about it more, and that is influenza, but specifically avian influenza, which seems to be coming back at the moment, it had been quiet over the summer. And now, there are a variety of outbreaks in Asia..., I saw articles on outbreaks on chicken farms in Hong Kong and in India. And this specifically is the H5N1 influenza virus strain. So we haven't talked at all about influenza, of course this is a very serious human infection, and it's also quite prevalent in birds, particularly migratory aquatic birds are infected with various influenza viruses. And they generally don't get ill. It is in them actually a gastrointestinal infection, and they shed the virus in the feces, and that's why it is very

effectively spread, and when they spread it onto chicken farms, the chickens get infected and it has a very high mortality. And the concern now of course is that in the past 30 or so years we've seen increasing evidence that the H5N1 strain in particular, which is extremely virulent in chickens and other domesticated birds, turkeys.., ah, has some ability to infect humans, there have been a few hundred cases globally in humans, and the only thing it hasn't done is to spread effectively from human to human, and that's what everyone is looking to see when that's going to happen. In this case there have been some outbreaks on chicken farms, and what you do when the farm is identified with a H5N1 outbreak, is, unfortunately you have to kill all the chickens. And the farmers don't like that, and you have to pay them of course, for each chicken. And in this outbreak in Hong Kong, the Hong Kong government after this one outbreak immediately ordered 68,000 chickens in the farm in question killed, 12,000 at a nearby farm, so you try and cull all the chickens in a geographic area to try and prevent the spread of the virus. So this is unfortunate on many levels of course because the farmers lose a lot of money and it increases the chances of spread, because the people who work on these farms of course, they're the ones who are going to get the virus and then spread it to their families, and whoever they come in contact with. So this has been in the news for many many years since I think there was a big outbreak in Hong Kong in, uhm...., I forgot the year, but I think about 16 people got infected with an H5 strain, and since then it's been in the news almost regularly. Alan, have you ever done any avian influenza stories?

Alan:
I haven't, but mainly because, you know, I'm writing for trade journals and mostly monthlies, but certainly, you know other colleagues of mine in science journalism who write for weeklies and more mainstream publications have been hitting this pretty hard. It's certainly big news and certainly worth keeping an eye on.

Vincent:
Yeah. So I do not want to minimize the importance of this whole issue, but one thing we have to remember, first of all, it has not yet changed sufficiently to be able to be transmitted among humans. And it has been circulating for many years in humans.

Angie:
Most of the people who have gotten, you know, quite ill with H5N1 influenza are people who are directly exposed to chickens...

Alan:
Right.

Vincent:
Right.

Angie:
...and literally had a chicken flapping in their face.

Vincent:
Exactly. So..., and now, that's not to say that it won't change some day to be transmitted. Everyone assumes that if it becomes transmissible, that it will maintain the same kind of virulence that it has in chickens and turkeys.

Angie:
Absolutely.

Alan:
Right.

Vincent:
And I don't know why we must make that assumption.

Alan:
Not a reasonable assumption at all, you'd actually expect the virus to become somewhat more attenuated.

Vincent:
Very prominent Virologists saying, you know, "if this virus is transmitted, it's going to be bad", I don't know why you should assume that.

Angie:
Frankly, I think it's much more likely that if there were to be a flu pandemic, which is, of course always likely, because they occur, you know, every few decades, a serious one...

Vincent:
Mhmm.

Angie:
...it would be one of the flu strains that currently infects people. H1, H2, or H3..., right?

Vincent:
Exactly. Yeah, there's good evidence that it would be..., you know the human strains are recirculated every so many years and it's good reason to believe..., and I think the number is, after about 68 years all the people who are immune to the one strain are now gone and you can now re-introduce that strain. So we're not paying much attention to those, we're paying a lot of attention to these H5s..., I'm..., I'm not sure that's such a good strategy.

Angie:
When you consider the Spanish Flu pandemic of 1918, which, according to some estimates killed 100 million people worldwide, was H1N1 subtype, uhm..., it seems that I'd be more worried about that, than this H5N1 and the possibility of what it might become.

Vincent:
I mean, I think certainly we need to keep track of this and look at the different viruses and so forth, and be ready, but I don't think everyone should assume. I found actually a very interesting blog called H5N1...

Angie:
Ha ha ha!

Vincent:
...which is done by a gentleman in Vancouver Canada.

Alan:
Heh heh!

Vincent:
...and, uh I actually put a comment there last week because he had said in one of his posts "I'm quite sure this virus is going to be the next pandemic human strain". And I wrote "with Virology you cannot be sure".

Angie:
Never!

Vincent:
[chuckling]

Alan:
No, this is absolutely worth keeping an eye one, but it's not worth keeping all eyes on. It's..., the pandemic will...

Angie:
I agree.

Alan:
...very likely come from some direction we didn't expect.

Angie:
This however, I mean of course is not only an interesting virus, it's also important for agriculture.

Alan:
It's economically....

Angie:
Certainly the economic importance is critical and I actually have to say that a couple of years ago at the pub that I watch football at every Sunday they raised the price of chicken wings by 10 cents because of bird flu.

Alan:
Oh!

Vincent:
Hmmm.

Angie:
And everybody said, well you're not going to get bird flu from a chicken wing, but it's not actually because you eat the chicken wing that you're going to get bird flu, it's because all these chickens have to be culled if avian influenza appears in the chicken farms. So if you have less chickens that can go to market the price goes up.

Vincent:
Well in Hong Kong basically they have a 21 day shutdown of live chicken trade, uhm, and they told people you have to get used to life without chicken. And, you know, they have frozen chicken, and so forth, but this could be one strategy. You know, part of the problem here is that we have huge poultry farms now in this global agri-business that we've created. And that has increased the infections with these viruses. And if we shut down that trade, which is not going to happen obviously, maybe we should stop eating chicken and turkeys and we wouldn't have to worry about it.

Angie:
[laughing]

Alan:
[laughing]

Angie:
Well then we could always eat beef except for, they have, you know transmissible spongiform encephalopathies.

Alan:
How about sheep cheese?

Angie:
Yeah, sheep cheese! [laughing] Oh wait!

Vincent:
Yeah, I heard Ian Lipkin lecture a few weeks ago. The problem is now, in the food and agricultural business now you pool thousands and thousands and thousands of animals now to make a product.

Alan:
Right.

Vincent:
And that increases the likelihood that you're going to get some kind of infection, not just viruses, but bacterial infections.

Angie:
Of course.

Vincent:
And this of course didn't happen fifty years ago!

Angie:
Right.

Vincent:
You had very limited pools of these things. So, we'll keep an eye on this, because I'm sure it will come up from time to time. Oh, one thing I noticed there was an article about the culling in India and the government wanted to kill a lot of chickens, and they had a plan to cull 20,000 fowl in a small town in India, and after 4 days they had only killed 150 because the farmers wouldn't let them, because they weren't giving them the money right on the spot. [laughing]

Angie:
[laughing]

Vincent:
So this is again an example of, it's not just the science, you know, it's a sociological issue and you have to..., if you're going to kill peoples' chickens that they use for a livelihood you have to pay them. So that was an interesting story. Ok, so that takes care of our stories for this week. We have some reader email, and our picks of the week to go through here.

Angie:
Who can't get enough Virology?

Vincent:
Exactly. It's just such a good subject. Ok, we had..., this week we just had one reader email from Everett, who got an iPod Touch as an early Christmas present, and he listens to it in the lab, apparently he does some very monotonous assays, and found our podcast. And he writes, "I was thrilled, so thrilled to find your podcasts, and I am absolutely mesmerized by them. I cannot even tell you how happy I am to listen to what I consider to be a fascinating topic, and you deliver it so well. I love the combination of science with a little bit of history, and wait patiently for your future podcasts." So that's nice. So, I thanked him, and then he answered, he thought he had a celebrity experience, or a near celebrity experience.

Angie:
[laughing]

Vincent:
Of course, I'm not a celebrity, I'm sorry. Maybe Dick is, because he was in Time magazine this week!

Angie:
He was?

Vincent:
Yeah, I had posted that on Virology blog, he had an article on vertical farming. So Dick, you're in India, you may not be hearing this, but you are a celebrity, Dick.

Alan:
Yes.

Angie:
Well so are you Vince, you do have a Wikipedia page. [laughing]

Vincent:
No no no. [laughing] And he asked if we could talk about a couple of other viruses, HTLV in Leukemia, HHV-6 and MS, EBV in Burkitt's lymphoma and NPC, SV40 and non-asbestos-related mesothelioma, because it is my understanding that the link between these viruses and their pathologies is not wholly definitive, although compelling. So sure, we will cover a lot of those in the future. Absolutely. Thanks for sending in your suggestions, that's great! This reminds me to tell you that the other day was a momentous day in history. You want to tell us about that Angie?

Angie:
Yes, it was the day that Karl Landsteiner identified that Poliovirus was the actual etiologic agent that causes poliomyelitis.

Alan:
Ah!

Vincent:
Did you know that Alan?

Alan:
I did not know that!

Vincent:
I have a blog post on this, we'll direct you to it, but December 18th is the day he announced his results at a meeting.

Angie:
Yes.

Vincent:
So of course, he probably did the experiments earlier.

Angie:
Of course, he probably discovered that in March, but...

Vincent:
But, that's a good date to have, and it's in a book called *A History of Poliomyelitis* by J.R. Paul, which is an excellent book. Although it's not our choice this week, maybe someday it will be.

Angie:
There is also another great book actually, called *Polio: An American History,* that I believe covers the topic a little bit, it's more about the social history of polio, but definitely a very interesting read.

Vincent:
Polio is a disease of which there's no shortage of books written, and we'll certainly get to those in the future. So while we're on books, why don't we do our science book of the week. And this is one I picked, it is called *Science Fictions: A Scientific Mystery, a Massive Cover-up and the Dark Legacy of Robert Gallo.*

Angie:
[chuckling]

Alan:
Dun dun dun!!!

Angie:
Yeah!

Vincent:
I have the book in my hand.

Angie:
It's very ominous, it really is.

Vincent:
It's very thick, and it's of course about Robert Gallo, who was one of the original people to identify HIV-1.

Alan:
But NOT a Nobel Laureate for it!

Vincent:
Yes.

Angie:
Probably because of what they discuss in this book, I would wager.

Vincent:
Yes. Yes, so this is written actually by John Crewdson, do you know the name Alan?

Alan:
I've heard the name, I haven't read his stuff though.

Vincent:
So John is a senior writer for the Chicago Tribune. He got a Pulitzer Prize in 1981. And this is based on a 50,000 word Tribune account of the discovery of HIV. And basically, it's why he thinks that Gallo was wrong about saying he discovered the virus, and it's beautifully written, it's incredibly well researched, it's just detailed, everything is here. I highly recommend it, it's very good. We'll put a link to that in the show notes. Uhm, speaking of books, Stephen from the UK sent us his list of science books, we had asked for people to send in suggestions, and there are a lot of books on there that I really like, so we'll be getting to them in the next weeks and months. And that brings us to our science podcast of the week. And this is a bit different one from usual, this is called Skepticality. Any of you ever listen to that one?

Angie:
I have not, but I'm curious, is that even a word?

Vincent:
Skepticality?

Angie:
Skepticality?

Alan:
Well I guess it is now, isn't it?

Angie:
I guess it is now!

Vincent:
You know, the English language is plastic.

Angie:
It's true.

Vincent:
As it should be. Uh, science and revolutionary ideas, this is a bit different from what we've chosen so far. Here's the description from the website: "Our podcast is here to bring you relevant, under-reported current events, as well as in-depth discussions from a scientific, critical,

skeptical and humorous point of view. In our travels we will tackle the beasts of pseudo science, the paranormal supernatural UFO alien encounters, misunderstood history, astronomy, space, and overwrought legends, urban or otherwise." It's well done, it's interesting, it covers a broad selection of sciences, and a bit irreverent, but that's good. So there you have it: Skepticality. Everyone, thank you so much for joining us on this Saturday today.

Angie:
Thank you for having me on the show Vince!

Vincent:
Maybe you'll come back sometime.

Angie:
I would love to!

Vincent:
Ok. Are you going to come back Alan?

Alan:
Absolutely! Yeah!

Vincent:
Very good. Ok, so Alan and I are planning to have a Top Ten Virology Story of 2008 episode. So, if you have some ideas for that, send them in. What are the top Virology stories of 2008? You know, every podcast does a Top Ten. And Virology should be no different.

Angie:
I agree.

Alan:
And please, please, please send in your ideas, because I think Vince and I have only come up with about three so far.

Vincent:
Uhm, recently...., one little technical note I made some changes to the feed of this podcast and I may have messed up your ability to retrieve it in iTunes, but it should be fixed by now, I'm sorry about that. Angie, where can people find out about you? Any website or Twitter that you'd like to give them?

Angie:
Uhm, well I have a Facebook page...., uhm, but no currently, not really. I have a blog, but it's not really about Virology, so...

Vincent:
Ok. You can find me on the Twitter, profvrr, and Alan's Twitter is on his website, which is Dovdox.org, or....?

Alan:
Dovdox.com is my website, and my Twitter if you want to go directly to it, uhm, is just alandove.

Vincent:
I'm finding that Twitter is very nice for finding out in science what's going on.

Alan:
I'm surprised at how useful it was. I was very very reluctant to start using it, because it seemed pointless until I tried it, and it's kinda handy.

Vincent:
Well you find if you follow certain people you can limit the noise extensively.

Alan:
Right.

Vincent:
So I follow people generally in science, and many people post links to stories, well guess what happened, on the 100th anniversary of the polio discovery I posted a link for example, so people tend to do that and I think that makes it interesting, and in fact some of the stories we talk about come from Twitter originally.

Angie:
I'm going to have to become part of this Twitter thing.

Vincent:
Uh, I think you need to just work in the lab, don't worry.

Alan:
[chuckling]

Angie:
Ok. Ok!

Vincent:
[laughing] But it really can be useful, and if you taylor it to your specific needs, there are already websites on how to use Twitter for your business for example.

Angie:
Well it seems like it's been incredibly helpful for you! So....

Vincent:
Yeah, exactly.

Alan:
And if you don't taylor it to your specific needs it can be an incredible waste of time, so...

Vincent:
Yes. Well the problem is you can do it from your cell phone.

Alan:
Right.

Angie:
Oh, that would be the end of me.

Vincent:
You can stand in lines and watch the Twitter stream in Twitter, you know...

Angie:
I already have a hard enough time constantly texting everybody with my teenager phone with the keyboard.

Vincent:
We are really grateful that you were listening to us, uhm, this has been "This Week in Virology", I'm Vincent Racaniello, this is the podcast where we talk about all things viruses. We hope you have a great holiday, whatever holiday you celebrate. Tune in next week again, and thanks for joining us! Bye!

Angie:
Bye!

Alan:
Bye!

Transcribed by Gertrud Rey