Transcript Details
This is a transcript of an educational program. Details about the program and additional media formats for the program are accessible by visiting: https://reachmd.com/programs/focus-on-global-medicine/synthetic-virions-to-detect-sars-origins/4081/

ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Synthetic Virions to Detect SARS Origins

Change and challenge is in the wind as 2008 comes to an end. The same is true when examining this month's ReachMD XM160, special series Focus on Global Medicine. We take a look at both the changes and the challenges impacting global medicine.

Severe acute respiratory syndrome or SARS made significant headlines in 2003 testing our global public health infrastructure. Since then, we have seen dramatic evidence to suggest that bats were the original animal host for the virus. The most recent data coming from a synthetic SARS like bat coronarvirus. How does our ability to synthesize complex viruses like this one enhance our capacity to deal with threatening passages. You are listening to ReachMD, The Channel For Medical Professionals. Welcome to the Clinicians Roundtable. I am your host, Dr. Mark Nolan Hill, professor of surgery and practicing general surgeon. Our guest is Dr. Mark Denison, Professor of Pediatrics and Associate Professor of Microbiology and Immunology at Vanderbilt University School of Medicine.

DR. MARK NOLAN HILL:

Welcome, Dr. Dennison.

DR. MARK DENISON:

Thank you, its very nice to be here.

DR. MARK NOLAN HILL:

Dr. Denison, when did your team begin its research on this project?

DR. MARK DENISON:

We have been working at coronaviruses for about 20 some years and with the SARS epidemic of course that raised the profile and importance of the viruses in the public line and so we have been working on them for a long time. We began work on SARS very soon after the epidemic.

DR. MARK NOLAN HILL:

And you originally were dealing with bat. Were other species considered?

DR. MARK DENISON:

No, well, when the SARS outbreak occurred, there was of course consideration of the animals that were being sold in the markets and strange animals to us like Civet cats and Raccoon dogs and those animals were looked for and found to carry the virus, but in the wild, they did not have the virus and so investigators in China began surveillance of other animals.

DR. MARK NOLAN HILL:

So its in a little bit, when you say sold in the market, I know you are not speaking about the United States obviously. What do you exactly mean by them?

DR. MARK DENISON:

Well, these are animals that were farmed, like chickens are farmed here to be sold for food in the markets there and they are exotic to us, but they were commonly sold in these markets and they are open markets where animals might be stacked in cages and so its thought that they probably were infected in the markets, but since they couldn't be identified in the wild, therefore they began to look in other places for how those animals could have gotten infected in the markets.

DR. MARK NOLAN HILL:

Now, one of these animals were bats?

DR. MARK DENISON:

Well, no, there were no bats, so all the bats were being considered because its like Casablanca where you round up to usual suspects and people are looking for bat because its thought that it might be involved with Ebola and several other recent outbreaks of human epidemic viruses such as Nipah and Hendra viruses and so bats were a suspect and they were looked for.

DR. MARK NOLAN HILL:

As I understand that bat coronavirus hadn't been cultured before, is that correct?

DR. MARK DENISON:

Correct, one of our main motivations was that in fact these viruses had been looked at by an unusual mechanism, which was culturing

bat secretions, particularly rectal secretions in bats and they identified sequences consistent with coronaviruses, but none of these viruses could ever be cultivated in any of our available tissue culture cell lines and so could not be studied further for their growth or replication or transmission between animals.

DR. MARK NOLAN HILL:

Now tell us about those viruses.

DR. MARK DENISON:

Well, its probably not one virus, and in fact, when they began to look in bats, they identified probably more than 20 new coronaviruses in bats, none of the bats were sick, they were just shedding them suggesting that bats may be a reservoir for all kinds of coronaviruses, particularly even they have been the source of ones that have led to colds and other things in humans and in other domestic animals, so there was no single virus and when we started to work, we began to look at actually multiple viruses to see which one's the closest to what SARS looked like.

DR. MARK NOLAN HILL:

Now when you use the word coronavirus, I have to think back on my Immunology days and medical, what exactly is that?

DR. MARK DENISON:

Well, coronaviruses are family of viruses that can contain RNA as their genetic material. They are the largest RNA viruses in terms of their genetic information. Their family, their name for the corona or crown of proteins – they look like an eclipsed sun and so thus their name for the sun and not for the bear.

DR. MARK NOLAN HILL:

Now, why common colds that are caused by certain coronaviruses, what is it about this specific coronavirus that makes it so deadly in bats, not in bats, but as bats transmit them?

DR. MARK DENISON:

It really became a deadly human virus, its not really clear that it actually causes any disease in bats, and I think what it did is the joint species and then adapted, it entered into humans and it truly was to all the data we have a new human virus, and so if you can imagine a new influenza or a new measles virus, if there is something new the humans had never seen before, they represented there for a highly pathogenic virus in humans.

DR. MARK NOLAN HILL:

Are there certain genetic components to transmission?

DR. MARK DENISON:

The main genetic component probably is the spike glycoprotein, which is on the surface of the virus, which binds to specific receptors on a host cell and allows the virus to get in and then just spread from cell to cell.

DR. MARK NOLAN HILL:

And can we predict, who among the general population might be more vulnerable to this?

DR. MARK DENISON:

It's not clear at all and our data does not yet answer the question of how the virus initially got into humans. Its likely that it was a recombination event so it may have been a bat virus co-infecting somehow a human under unusual or extraordinary conditions and that there was a recombination event between those 2 viruses that then gave the bat-type virus the ability to then spread in human cells or animal cells, one of the other or both.

DR. MARK NOLAN HILL:

How would the bat virus get to a human at all?

DR. MARK DENISON:

Well, I can imagine lots of potential strategies, bat secretions, and animals in the markets, animals getting infected with a high dose of virus sort of shutting it into a cell or into a host, which allowed it then to temporarily replicate and then a few months ingested that animal that might have allowed it then to survive. That's one potential scenario, another would be a direct contact with bat secretions, inhalation, or a bite although I don't want to begin thinking about vampires at this point.

DR. MARK NOLAN HILL:

Dr. Denison, and how specifically does this research further our capacity for identification, analysis, and even public health response to emerging viral threats?

DR. MARK DENISON:

One of the great limitations in our opinion with our ability to respond is that many viruses, that are known human viruses, for example, hepatitis C even cannot be readily cultivated in cells and so regular approaches to studying antivirals or vaccines are defective because we can grow the viruses, so in the case of an emerging virus; for example, if there was an outbreak and you could identify the source by sequencing the type of strategy we use might allow for rapid replication or reproduction of the virus to grow it in standard culture so that

it could then be studied for vaccines and therapeutics.

DR. MARK NOLAN HILL:

Why is it so difficult to grow some of these viruses?

DR. MARK DENISON:

Well, there may be several reasons, one example would be that, as I mentioned the spike protein has the binder receptor so that a virus coming out of bats just fresh out of the animal or even out of an initially infected human might not have a good ability to bind to the cell and enter the cells that are used in culture for standardly growing the virus and so that would be a real limitation to it being able to grow.

DR. MARK NOLAN HILL:

Did any animals who might have come in contact with the bat get sick?

DR. MARK DENISON:

Well, not very, there wasn't much evidence that any of the animals were that ill, we don't of course know of animals that died, they weren't tracked, but and experimentally in the laboratory many animals could be infected with SARS virus, but a few of them got ill, so there were a few models and animals where they actually sick.

DR. MARK NOLAN HILL:

Why would that be? Why would the human be so susceptible?

DR. MARK DENISON:

Its not clear that the human initially was so susceptible, but coronaviruses have perhaps an unique capacity among RNA viruses for adaptation and mutation, so rapid change, of course with any virus virulence, source of your disease may not be the goal of the virus, but that may allow it to more rapidly spread in some circumstances.

DR. MARK NOLAN HILL:

Are we learning any more about the mechanism by which SARS actually causes lung damage in humans?

DR. MARK DENISON:

We think we are. There is my collaborator basically Dr. Ralph Barrack at the University of North Carolina Chappell Hill, who was an absolute co-partner in this and this is a very joint disease, are studying how the virus adapts using a mouse model where SARS, if its passaged in mice very rapidly adapts and becomes virulent in the mouse and therefore can be studied for those mechanisms.

DR. MARK NOLAN HILL:

And just review for a second, what is the natural history of SARS when a human gets it?

DR. MARK DENISON:

Well, the natural history of SARS when humans got it was that they probably developed a disease that may have been initially actually more of a systemic disease and then it's actually 7 to 10 days had onset of severe respiratory disease looking like ARDS or acute respiratory stress syndrome that led to much of the morbidity and mortality.

DR. MARK NOLAN HILL:

How many patients would you guess that you have personally dealt with?

DR. MARK DENISON:

With SARS, none, because it was implicated mainly in China. Of course it spread to 32 countries over the period of about 4 to 6 weeks and so the real severity of this was focused in a couple of places on call in Toronto where this really had significant impact.

DR. MARK NOLAN HILL:

Did we have any in the United States at all?

DR. MARK DENISON:

There were several cases, in fact, there was one in Chappell Hill, North Carolina, but that was an imported case from someone that had traveled, so there was never endemic disease. If I could make one point about this, its not even clear to us that SARS will ever reemerge because there were a couple real limitations on the virus; for example, its ability to spread required symptomatic disease and so efforts at quarantine were very effective, so its likely that SARS may have been eradicated, but one of our goals is to try to say that there are other bat coronaviruses and we would want to be able to understand how it became a human virus, so if this happened again with the SARS-like virus, we would be prepared for it.

DR. MARK NOLAN HILL:

Are you pretty confident in terms of that statement that the SARS may not actually come back again?

DR. MARK DENISON:

Lets see. Ha, ha, ha, ha.

DR. MARK NOLAN HILL:

Ha, ha.

DR. MARK DENISON:

My wife says I am always confident, I am sometimes right.

DR. MARK NOLAN HILL:

Ha, ha, ha, smart woman.

DR. MARK DENISON:

So I think the answer is – there's no evidence that there's any naturally circulating SARS at this time. So I would say, no, I am not a 100% confident, but and thus another reason to be prepared to understand how it would spread and evolve overtime.

DR. MARK NOLAN HILL:

How did the virus get eradicated to that degree?

DR. MARK DENISON:

Well, if there were 2 Achilles heels and SARS had one as I mentioned was that it appeared to require symptomatic disease for efficient spread and so that if you isolate symptomatic individuals, you could dramatically drop its transmission as opposed to influenza, which spreads presymptomatically mostly and so its very hard to quarantine and control flu. The second one would be that the reproduction number or the number of people ultimately on average that got infected by a single SARS infected person was fairly low and so with those 2 issues, its likely that quarantine and public health measures could be very effective at controlling and ultimately getting rid of an epidemic of circulating virus in humans.

DR. MARK NOLAN HILL:

I want to thank our guest, Dr. Mark Denison. We have been discussing new research that enhances our understanding of the origins of the SARS virus. I am Dr. Mark Nolan Hill and you have been listening to the Clinicians Roundtable on ReachMD, The Channel for Medical Professionals. Be sure to visit our website at www.reachmd.com featuring on-demand podcasts of our entire library and thank you for listening.

Thank you for listening to our special series Focus on Global Medicine as we celebrate this annual holiday season. Everyone at ReachMD wishes you and your family a happy holiday and a successful New Year.

Free CME on ReachMD is now easier. Link to ReachMD's free custom application for your iPhone at www.reachmd.com.