This Week in Virology

with Vincent Racaniello, Ph.D.

Special Episode: A Paradigm for Pathogen De-Discovery

Interview with Dr. W. Ian Lipkin
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Vincent Racaniello: This Week in Virology, the podcast about viruses, the kind that make you sick.

You're listening to this week in virology. This is a special episode recorded on September 5th, 2012. I am Vincent Racaniello and with me is Professor Ian Lipkin. Thanks for joining me today, Ian.

Ian Lipkin: A pleasure.

Vincent: Today we are here talk about a paper that will be published on the 18th of September.

The title of the journal is mBio. The title is A Multicenter Blinded Analysis Indicates No Association between Chronic Fatigue Syndrome/Myalgic Encephalomyelitis and either Xenotropic Murine Leukemia Virus-Related Virus or Polytropic Murine Leukemia Virus

And let me read just the last names because I think everyone should know who's on this paper...

Alter, Mikovits, Switzer, Ruscetti, Lo, Klimas, Komaroff, Montoya, Bateman, Levine, Peterson, Levin, Hanson, Genfi, Bhat, Zheng, Wang, Li, Hung, Lee, Sameroff, Heneine, Coffin, Hornig, and Lipkin.

That's not probably the biggest author paper you've ever had right?

Ian: It's close.

Vincent: It's close. So this is the culmination of a study you have been coordinating for over a year now, is that right?

Ian: its two years.

Vincent: And it began in 2009 with the report that XMRV, a new retrovirus might be involved with chronic fatigue syndrome and it's been quite a ride since then. There have been a few positive studies but mostly negative ones.

So can you tell us what why was this study undertaken that you have coordinated?

Ian: There are two issues in pathogen de-discovery.

One of course is to persuade the scientific community that you've done everything necessary to address the question whether or not you've made a substantive link or not.

The other is to do everything you can for the community that you're trying to serve which are uh... the patients the families of those who are afflicted with the disease.

And although many in the community have felt for a long time that this issue was settled. There are many members of the community have not felt that to be the case.

And the people who participated in this study who were critical in generating the data that led to the whole XMRV polytropic murine leukemia virus link to the chronic fatigue syndrome myalgic encephalomyelitis were Harvey Alter, Judy A. Mikovits Frank Ruscetti, Shyh-Ching Lo and, of course, the people who work with them.

Now although some would say that these individuals retracted their papers. When you talk to them, they did not in fact retract those papers. They will tell you that they were pressured by journals to retract, to participate in retraction. So while the journals may have retracted the papers, the authors did not.

And until the authors have a chance to go over the original information, the original assays, to try to test these with well characterized samples and then find those, find the hypothesis wanting, they are not going to be willing to come out in public and say you know we have made an error. It was an honest mistake, but we find no evidence for this link between these viruses and this disease. And this is why in fact the study was undertaken.

It was undertaken with very strong support even after some of the negative papers began to appear from both from Tony Fauci, Francis Collins, Tom Friedman, and Harold Varmas because they realized it was critical that we address this in a forthright coherent comprehensive indisputable fashion.

So what we set out to do was to identify cases using criteria that were established by the laboratory people as well as the best clinicians in the field. They were collected over wide geographic area so that if there were differences in the causes of chronic fatigue syndrome in one part of the United States or another we would not be confounded by just looking at one area. This is very important.

We made certain that the controls we selected were matched well and we collected the samples that the investigators responsible for regional work wanted us to collect. We coded them, we sent those samples to them, we allowed them to use whatever assays they wanted to use.

The only thing we insisted upon was that the criteria for calling a sample positive or negative had to be set up in advance and that once they were established they could not change.

We then allowed them to proceed and they found what they found. Once we collected all those data, if there was any discrepancy from one sample to another, because they received more than one sample, we tried to reconcile them.

And at the end of the day what we found, in fact, was that although the laboratories were able to recognize the positive controls, those were provided to us by John Coffin, there was no association between chronic fatigue syndrome or myalgic encephalomyelitis, if you prefer, and or either of these two viruses.

No one found any sequences by PCR. Serology was a little more tricky because we don't really have positive controls for it and the results were somewhat discordant. But again there was no association between the presence of antibodies as described by Frank Ruscetti and status of the case.

When all these data were assembled we met in teleconference and everyone agreed that the hypothesis had been tested and found not to hold up.

I will say that in deep appreciation of the sincerity of all the investigators, everyone held to their word. They are speaking out and saying we feel that this study was fairly done. We feel that the hypothesis has been tested and we find no association between the viruses that we previously reported and this disease.

Now I've been involved with other sorts of studies where we've tried to look at the role of infections and chronic diseases -- ALS and adenoviruses, borna disease and chronic fatigue syndrome, in measles virus and MMR and autism. I've never had an opportunity before to get as many people involved so that when we're finished there's absolutely no question but that we've tested it and found that there's no link. I'm hopeful that this is going to settle the issue once and for all.

There's been a side benefit to this whole process, and that is we've established a working group of people who were capable of collecting materials. We've been able to store sera and PBMC so that other investigators who want to do either microbiology or genetics or proteomics will be able to access those samples through the NIH.

There will be calls for proposals and there will actually be funding associated with that during the interim. We offered the laboratories and the investigators in the clinical sites who were engaged with this work to put forward proposals to do something with these materials in advance of that RFA though without any funding.

Several groups applied, two of them were selected by the entire team and they will be receiving plasma samples that they can then study. The primary focus has been on microbiology and genetics but I'm sure there will be other applications as well. So we've been able to hold back as much of the sample as possible.

I know some in the community, the scientific community, feel that this was not money well spent, but the fact is I think that we've obviated a lot of missteps that might have followed with clinical trials and such for antiretrovirals.

In addition we've been able to establish a sample bank that will be helpful for years to come and we've been able hold, I think, the attention of the community.

Vincent: So the samples that are going to be available are the samples collected as part of this study?

Ian: That's correct.

Vincent: There are 147 case patients, 146 matched controls.

Ian: That's correct.

Vincent: And you have enough material for many years of investigation.

Ian: Well it depends on how greedy people are, as usual, but there are there at least 15 PBMC samples. Now those are difficult to aliquot, each with a million cells. Those will go to individual projects.

The plasma, however, we can aliquot and for people who want to do proteomics, who do microbiology using these plasma samples, we have enough for probably 50 laboratories.

Vincent: So tell me how these samples were selected. You mention that all the investigators were given the opportunity to participate in that. So did each group have x number of patients for this study, how did that work?

Ian: Yes, so our initial, so we initially did a power calculation trying to figure out how many samples we needed based on the worst- and best-case scenario from the Mikovits paper in the and the Lo paper, so we could determine the minimum set. Based on those calculations we sought 150 subjects with disease and 150 who were matched controls.

We brought in more than that obviously because as we began to examine these people and they met clinical criteria we collected their blood. We also sent those bloods off, before deciding to include them, to a clinical laboratory here at Columbia and we used other laboratories as well, commercial laboratories to make sure that they didn't have hypothyroidism or some sort of cryptic hepatitis or anything that might confound the diagnosis of chronic fatigue syndrome.

And so we initially, given we had six sites across the United States; the notion was that each one was going to get 20 to 25. At the end of the day, some were more successful in recruiting than others were. But on average we had somewhere between 20 and 30 patients selected per site and with matched controls.

Now the laboratories, the clinicians met and the laboratorians met, everyone decided, and again we agreed on what the criteria that would be used should be. We used the most stringent criteria possible. So we selected people who met the Canadian criteria and they also had to meet the Fukuda criteria.

We also decided that we wanted to select people who had a prodrome that was consistent with an infectious disease—fever, night sweats, lymphadenopathy, swollen lymph nodes anything suggestive of an infection—so that we would give the hypothesis the best possible chance of success, which has not been done in the past. So that there would be no way to go back a priori and criticize the study design and say if you'd looked at this population you would have found XMRV or P-MLV.

It is critical that you do that. If you just go into a freezer and try to pull out cases that have been previously called positive, you can always say, well maybe there was a thaw, maybe a titer dropped, who knows what could have gone wrong.

In this instance everything was pristine from the selection of the cases, the criteria that were used, the processing of the materials.

So the samples were sent to us overnight, we purified PBMC using standard classical methods. Everything was stored in freezers here so there was no possibility for contamination, and we have had no P-MLV or XMRV in our laboratories.

All the assembly we do is done in positive pressure conditions so we don't have to worry about contamination of materials. In fact we didn't have any evidence of contamination so we set it up again so that people could do what they wanted to do. So that this means some labs did things that other people didn't do.

The FDA analyzed PBMC as well as plasma, as did Mikovits, Ruscetti, Hanson laboratories. The plasmas was really only analyzed alone, it was analyzed at the CDC.

Now during the course of this study lots of things happened that made it very difficult to continue. I think that was Harold Varmas who said this is worth a paper itself or maybe a movie.

Vincent: Didn't you do that already?
Ian: As you may recall Judy Mikovits had difficulties in the WPI. The WPI, which stands for the Whittemore Peterson Institute. The 'P' in WPI stands for Peterson who doesn't talk to the Whittemores anymore. So that's another story in itself.

Vincent: He is on this paper right?

Ian: Yes, he's on this paper as well, he was one of the original people who, with Paul Chaney, described this group at Incline Village where this syndrome was early to be reported.

Then Judy Mikovits wound up afoul of the WPI and she wound up in jail which was quite remarkable because I wound up involved with the negotiations trying to broker an agreement between her lawyers, and Judy Mikovits, and the Whittemores to get her out of jail.

Essentially what happened was when it began to look as though the hypothesis was unraveling, the people began to push the onus of responsibility onto to Mikovits for that work, and, of course, she wanted to have access to her lab notebook so that she could at least describe what she'd done and relate it to the individuals there.

She took those lab notebooks and I had conversations with Harvey Whittemore about whether or not she should have access to her notebooks.

I would say I understand that you want to keep the original lab notebooks, but every scientist is entitled to have copies of his or her records. How else can they talk about what they've done, replicate their work, provided detailed protocols and so forth? Well, that didn't rest very well. She was accused of stealing intellectual property. Well, if the hypothesis doesn't hold up, where's the intellectual property?

So there were all these things that were circling and then we had to find a way for her to be engaged in the study.

Maureen Hanson at Cornell agreed to receive samples processed by Frank Ruscetti. Harold Varmus agreed to allow Frank Ruscetti to continue to participate in the study and receive samples and characterize them.

At one point the CDC said you know we don't really have the time and energy to invest in this and I appealed to Tom Frieden.

I said, look we really need to close this loop once and for all so that we don't have another situation with MMR and autism which lingered, as you know, for more than a decade and we still have people who are reluctant to vaccinate their children with MMR despite the fact that you know that's been clearly laid to rest. So everybody got onboard, pushed this very strongly and well this was the result.

Vincent: So Judy was.... How did Judy participate in this, in all of this?

Ian: While Judy was in jail, and after Judy got out of jail, she was in contact regularly with Frank Ruscetti and with Maureen Hansen and was responsible for the study design, and for making decisions about how you call a sample positive or negative, and review the data, and participated in writing the paper.

There was a lot of negotiation in the drafting of this paper, as you might imagine, because it's very sensitive, but everybody signed off on this.

We went through literally 50 different iterations of the paper, and after it was signed-off on by all the authors, then it first had to go up the chain at the NIH and the CDC so that they could approve it as well.

Vincent: Do you have the original Word document with all the changes embedded in it? That might be an historical document.

Ian: Yeah, the problem is it crashes.

Vincent: It's too big.

Ian: It's too big for mac.

Vincent: So none of the samples used were samples from any other previous study. Is that correct?

Ian: That's true. These are all..., well I can't say any previous study, but any previous study in which these people had been engaged.

Vincent: Right, okay. And the positive cases, the individuals diagnosed with CFS, were these individuals who had the disease for varying lengths of time -- short, medium, long?

Ian: Yeah, so you know in the paper we spent a fair amount of time talking about of the nature of the disease. One of the challenges of course with a disease like this one is that because it's called chronic fatigue syndrome you can't get there during the acute period, during the acute ictus. The mean age at illness onset was 35, plus or minus 10 years. The mean duration was about 16 years, plus or minus 8.5.

There isn't anybody here… it is not like we were able to get people six months after the onset of the illness which would be the closest you could be and still have a diagnosis of chronic fatigue syndrome. I don't really see any way in which such cases are going to be found.

Vincent: You received blood samples in your lab. Is that correct?

Ian: That's correct. So the patients would be seen, bloods would be drawn, they would be sent to us.

Vincent: Because they were drawn somewhere else, right?

Ian: Yes, the bloods were all drawn in commercial phlebotomy suite, then they were shipped to us overnight, they were received which means receiving five days a week because they also have clinic on Fridays.

We would then process them and we would aliquot them and we would code them with barcodes and then we would send off a sample of plasma to clinical laboratories to test for things that we wanted to know about. And this hasn't been done before in the past either.

We looked at a wide range of parameters that we thought might be important as exclusionary diagnosis. Now I mentioned some of these already, like evidence of liver disease and so forth. Table one has a whole series of different things that we examined and you can look at all the various exclusionary criteria.

Once those laboratory values came back, we then decided which of the samples would be taken and would be submitted to the individual labs for testing.

Vincent: So what was that, what was the cut down from the original samples to what was actually tested for viral sequences, the 147, 146?

Ian: I don't remember the total but that is how we got down to 147, 146. It wasn't as though we drew 200, for example. A lot of these cases were excluded at an earlier time point because they simply didn't meet various criteria.

Vincent: So one of the tests that were..., so then you sent these coded samples out to the various labs and then you said they could do what they wanted with them, assay them in the ways that they wanted and one of the ways that CDC and FDA did was to do PCR on plasma or PBMC, right?

Ian: Correct.

Vincent: So, in some cases, this was RT-PCR that they would use.

Ian: That is correct.

Vincent: They would produce RNA from the samples, reverse transcribe it. What kinds of primers were used for the PCR? Was this agreed upon by everyone?

Ian: No, no, that's a critical point and I appreciate your bringing that up. For the purposes of this study design I really don't care what primers people use because if I ask you and you've previously reported something as being positive, to use my primers, and you don't get a finding that correlates with what you previously reported, you'll simply tell me that this is because I forced you to use my primers.

So we wanted to circumvent that criticism. So the one thing we did do is we said to people whatever primers you want to use, whatever reagents you want to use—after, obviously the point of collection, we can't vary that—that is entirely up to you.

You tell us where you want to purchase these primers and we will pay for them. So what we then did is we actually arranged for various commercial suppliers to provide reagents to people who needed them but they were the reagents that they designated, and they list them, and you can obviously look up what they've used and these differ from laboratory to laboratory.

Now we did ask that people go back and sequence their products and see what they found. But that's not terribly informative.

What's really critical, obviously, is the end result and that is to say, can you confirm or refute the finding of the relationship between the viruses and disease. And that's where, of course, nothing was found, right.

Vincent: So the CDC and FDA both did RT-PCR of plasma, so that's looking for virus, correct?

Ian: That's correct. Or looking, well I don't know that....

Vincent: RNA sequences.

Ian: Nobody was doing the viral purification protocol so it's not like they did a nuclease treatment and then extracted. They were just taking plasma and doing traditional extraction.

The FDA wanted to access PBMC. Now, as you may recollect from the early days, of the response of the criticism of the Mikovits paper... what Mikovits Roscetti said was that the key was the growth of these cells which then allowed expression of virus. So, we provided the reagents that were required to culture the PBMC so that they could test that hypothesis.

That didn't make any difference, that didn't but it could conceivably have done so. But it didn't, right.

Vincent: Right.

Ian: So those were also negative.

Vincent: So those were, that was PCR of cultured PBMC.

Ian: That is correct.
Vincent: This is not RT-PCR, this is extracting DNA.

Ian: Yes, correct. But again the key issue here is the culture. The FDA did not culture themselves, and this is one of the reasons why it took so long to get through this study.

Because you have to be able to culture these cells and sometimes, you know, uh... Frankly Ruscetti found that he wasn't able to propagate the cells. So we had to send them another aliquot, and he had to try again so that then takes several weeks.

Then after that was done, the PCR was done, whether it was plasma or PBMC, all the PCR was done for that group at Maureen Hansen's laboratory up at Cornell.

Vincent: So we looked for viral RNA or DNA which would be integrated DNA presumably, right?

Ian: Correct.

Vincent: All negative on the case, the positive cases, the CFS/ME cases which are a 147. None were positive in any case for PCR or RT-PCR.

Ian: Correct.

Vincent: The same for the controls which is a 146. Zero for all of the RT-PCRs and PCRs, including the cultured PBMCs, right? So that CDC, FDA, and Mikovits, Roscetti and Hansen. So that's resoundingly negative.

Ian: So the only issue is the plasma, serology.

Vincent: Right. And what was done there? Tell us how that's done.

Ian: Well he, Roscetti, has a proprietary assay that he uses to test for antibodies reacted with... react with cells. As you see there was no difference between cases and controls. Controls 6.2%, cases 6.1 %, and because we don't have a positive control, I really don't know what that means.

Now, many, many years ago, I was asked by CDC to look into the potential role of borna virus and chronic fatigue syndrome. You see this was back in the mid-1990s to late 1990s, there was a report that came out of Japan suggesting that borna virus was implicated and 50% of cases were reported to have nucleic acids There was a family found where 3/4 of people in the family had borna virus nucleic acids and were also antibody positive.

So Brian Mahy was then Director of DVRD, who ran afoul, as you may remember, of this whole issue of whether not enough money was being invested in this research, asked me to look into this. I looked at the gulf war syndrome, which was also very topical at the time, and I looked at these chronic fatigue syndrome patients, many of them coming out of a clinic that was run in the Karolinska, which at that point was one of the best clinics for CFS in the world.

We found no evidence of borna-virus nucleic acids and our lysates were positive but our western blots were negative. When I tried to report this finding, I wound up going to progressively less impressive journals until I finally wound up at the one in which it was published.

There was a great deal of reluctance to publish the paper because the saying at that point was, you're just not good enough at doing this and this was why it's all negative.

It took almost two years to publish that particular paper, which is how I learned the lesson of making certain that the people who originally do the report are the ones who are engaged in proving or disproving the concept.

At that point the one thing that struck me was that many of these individuals, I think it was close to two-thirds, something like 67%, were reactive with borna-virus proteins and lysates but negative in western blot. They were also reactive with flag and beta-galactosidase and I was left to conclude that they had polyclonal B cell activation.

At the very end of this paper, which appears in the Journal of Neurovirology, I said, you know, these patients are clearly sick in some way, they have some immunological activation, I don't know why, but it's not borna virus.

In this instance, when you compare the serology between the case and controls you don't find that discordance, you don't find more activity in the CFS patients then you do in the controls. But I am convinced, after working in this field for a very long time that this is a bona fide syndrome.

I don't believe that it necessarily has a single cause. I don't pretend to have insights into the pathogenesis of CFS.

One of the things that we want the community to take away, very clearly, is that the people who have been engaged in this study, and many others around the world, are committed to trying to understand why they're ill.

We have reagents; we have resources now they can be applied to this task. Just because this particular hypothesis hasn't borne fruit does not mean that there won't be an answer downstream and we're trying to do that work as rapidly and efficiently and rigorously as we can.

Now one of the other things that I think is important for your listeners to take away from this particular investigation is that we need to have rules for interpreting data. We need algorithms by which when people have a tantalizing finding it can be tested.

We've got Koch's postulates and people use Koch's postulates to this day, but they don't serve us very well in this era when we don't have an animal model for a disease and we don't have the ability to grow the organism necessarily.

I have another paper that is under review right now. It's not on chronic fatigue syndrome but it’s specifically about the issues of how you talk about levels of certainty, levels of confidence in the association between a finding and a consequence. I hope to be able to talk with you about that at a later time.

Vincent: What kind of rules are you thinking about?

Ian: Well I have three levels. The lowest level is the phenomenon. You know you find something but it doesn't tell you necessarily that there is any linkage.

The next level talks about finding something in association with an organ that's affected, it looks at clusters of disease where you find something, it examines burden, it talks about biological plausibility based upon analogies to other systems. So for example, you know this virus causes cancers in cows, it could equally well cause cancers in humans, a papillomavirus sort of an example.

And the last level, the most compelling level of course, which I call level three is where you either complete Koch's postulates or you demonstrate that a very specific drug can eliminate disease or you demonstrate that by vaccination the incidence of disease drops dramatically. Of course Koch's postulate is the gold standard, but I don't think it's essential.

Vincent: In this case, the XMRV CFS story, how did we not follow those rules?

Ian: Well, I think with the initial publication we had an association, we had some epidemiological data that suggested that there were differences between cases and controls, but that you can be confounded there. Let me give you a couple of examples.

There was one particularly poignant one a few years ago where someone thought they'd found the cause of the disease. I don't want to go into more details because I don't want to embarrass these people.

In essence, it was a respiratory disease, it was a disease of children and unfortunately these samples were collected during an outbreak of respiratory disease in a given geographic location and the controls came from a different, during a different time of the year. As a result, there was this respiratory pathogen that was passing through the population that had nothing to do with the disease in question.

So you probably know what I'm talking about. That's why we decided to select all of the cases within a certain timeframe so that we could be certain that we weren't just simply looking at an outbreak that was passing through a community. In addition, this is the reason why we decided to go for geographic diversity as well.

Vincent: So the virus XMRV was originally identified in a screen of prostate tumors. Although your paper has nothing to do with prostate cancer, there are still some individuals who believe that there may be an etiological role for this or a related virus in that disease, any thoughts on that?

Ian: Well, I agree and you know the strategy that I would pursue in this sort of work. I suggest if you really wanted to address that rigorously, though I'm not, I am not eager to jump back into

the world of XMRV and I don't intend to. As I explained, I've done my bit for NIAD for the year in this respect.

I think what would be required would be the people who originally publish that work should be sent blighted samples collected from individuals with disease and they should be asked to test them and report their findings.

Until the original group that makes the report withdraws the finding based, either because they say we made an error that we're admitting to or they retest new samples and say we've done the best we can do, approach this problem rigorously. That question is going to be open.

I think that's unfortunate and it's a disservice to patients who are continuing to pursue this hypothesis. It is imperative that we find ways to rapidly address and reconcile these kinds of findings with other data so that we can move on.

Vincent: Well it seems that that requires people to work together and you were sort of a third party in this case so you were able to get this to work and it's probably why NIAD came to you in the first place but when you have people having different findings it is hard to get them to talk to each other. So what do you do? You call them up and say, hey?

Ian: How do you get to yes is very difficult. I find that breaking bread with a little bit of alcohol is quite helpful.

Vincent: Yes, but what if you don't drink? Break the bread?

Ian: It's even better.

Vincent: So you mentioned just a few minutes ago, you hope this is your last association with XMRV. Yet it sounds like you're interested in CFS/ME. So what's the future with that?

Ian: I am indeed. What we are doing is… we have two efforts underway. First, with the Hutchins Family Foundation we've received some support to pursue pathogen discovery and biomarker discovery in people with CFS/ME.

What we've done is to go to all of these clinicians and others who have previously found agents using commercial laboratories and have constructed a massive PCR system that allows us to rapidly look at their leading candidates. In addition, we're going to be pursuing high-throughput sequencing on the Illumina platform.

We're also doing RNA seek, we're looking for RNA markers, we're looking for linked RNAs, any other sorts of insights we might have that will enable us to understand the pathogenesis of the disease or develop markers that could be used for diagnosing people or making predictions about who's likely to respond.

We also have a large proteomics project associated with this.

I am completely unbiased with respect to what we find. We are using unbiased high-throughput sequencing, proteomics, same sort of thing; it really is a discovery platform.

Vincent: What about the microbiome. Could this have some role in the disease and it should be looked at?

Ian: The microbiome… Unfortunately in this project we were not allowed resources to do those kinds of collections which I think is something that needs to be done. On the auspices of the Hutchins Family Foundation, we are indeed collecting rectal swabs. So we will be able to look at those types of materials.

Vincent: The other issue is that there are a lot of individuals who have followed this story, many with the disease, many of them accept or will accept the conclusion and hope to move on; but there will be a vocal cadre of them who don't buy it, and some of them will say, well you haven't looked in the right place. Why PBMCs, how do you know that is where the action is?

Ian: Well that's a good point, and that's another reason for doing this study as we did. We gave these investigators an opportunity to specify what samples they wanted and they wanted PBMC, and they wanted plasma, and they wanted an opportunity to culture the PBMC.

So when you start a study like this you have to have ground rules. The ground rules that I insisted on are the criteria for K selection, for sample collection, for sample processing, for analysis, for reporting have to be established in advance and that's the only control that I'm applying from the outside.

So you can never exclude the possibility that had we looked someplace else we would have found something different; but given that the original reports were based upon similar types of samples, similar types of analyses, these individuals felt comfortable with saying we believe that this study was fair.

We have a press conference on the 18th where Harvey Alter, Judy Mikovits, and Frank Ruscetti will be present and they will have an opportunity answer questions from the press.

Based on my understanding of what we've talked about, there won't be any surprises. They're going to say, you know, we put our full weight, enthusiasm, belief, confidence in what was done here and we feel that we were given a fair shake and that I think it's time to move on.

Vincent: In fact, this podcast will be released on the 18th and I have a part of the press release which shows that what you're saying is correct. Everyone seems to be agreeing here and I should read the last….

Ian: The last quote from Mikovits.

Vincent: Yes. Would you mind if I read that sentence, “It will have been spoken?”

Ian: Not at all, not at all.

Vincent: “Although the once promising XMRV and MLV hypothesis have....”

Ian: No, no, start higher than that.

Vincent: You want me to go higher than that.

Ian: “I greatly appreciated the opportunity....”

Vincent: Okay. “I greatly appreciated the opportunity to fully participate in this unprecedented study, unprecedented because of the level of collaboration, the integrity of the investigators, and the commitment of the NIH to provide its considerable resources to the CFS community for this important study.

“Although I am disappointed that we found no association of XMRV/ P-MLV to CFS, the silver lining is that our 2009 science report resulted in global awareness of this crippling disease and has sparked new interest in CFS research.

“I am dedicated to continuing to work with leaders in the field of pathogen discovery in the effort to determine the etiologic agent for CFS.”

I ask.... Well the next quote is yours… so that we know what you think.

Ian: Well that's okay, the important quote is hers and I think this takes an enormous amount of courage and class.

Vincent: It always does to admit you're wrong, but that's the key, right. That's the key to moving forward, right? And that's good to hear.

Of course in your paper the discussion begins, "Our results definitively indicate that there is no relationship between CFS/ME and infection with either XMRV or P-MLV."

And everyone signed off on that you say?

Ian: They've all signed off on it. Everyone has read the press release.

Vincent: I would agree with XMRV for sure and P-MLV as far as you've shown here, but maybe somewhere else in the body there's another virus that is causing this or some pathogen. You are not ruling that out? And I don't think you said that.

Ian: Oh, I am heavily invested personally and professionally in that search. Not personally but professionally.

Vincent: Professionally. And when you find it we will have you here to talk about it

Anything else you'd like to say before we wrap up?

Ian: Thank you.

Vincent: Thank you for coming by, I appreciate it. So the press conference is going to be live streamed I understand?

Ian: Indeed.

Vincent: And we will put a link at Virology.ws and TWiV.tv so that everyone can find it and listen to it as well on the day of the 18th.

Ian Lipkin is a professor in the Center for Infection and Immunity at the Mailman School of Public Health at Columbia University. Did I get everything right there?

Ian: Perfect.

Vincent: Thanks for joining me today.

Ian: A pleasure.

Vincent: I am Vincent Racaniello and you can find me at virology.ws.

You've been listening to a special episode of This Week in Virology. Thanks for joining us. We'll be back next week.

Another TWiV is viral.
