Excellent exposition on community concerns about the Lipkin study (by asleep on the People with ME Forum)

http://peoplewithme.com/thread-1271-post-7589.html#pid7589

28 June 2012

From asleep:

My view on the Lipkin "XMRV" study is one of strong suspicion and skepticism. I will preface this by saying that I am hopeful that he will produce a quality study that provides scientific answers and isn't swept into town in a tsunami of self-righteous political triumph. But I would be shocked if he actually does.

The main problem is that everything Lipkin has said and done to date with regard to this study is indistinguishable from astute politicking aimed at ensuring that this study seals off this line of research once and for all. I'm not saying that this is definitely the case, merely that Lipkin has yet to do anything to logically preclude this motivational possibility. Through a lens of such politics, all of his "maverick" actions are perfectly coherent:

** Carrying on with the study in defiance of criticism: The negative faux "replications" and the BWG didn't successfully put out the political fire, so another study is necessary. However, it must be carefully framed as the final word (an absolute nonsense concept in science) and conducted by someone who has delicately jockeyed themselves into a superficial position of agnosticism. Despite patients being admonished endlessly about "following scientists instead of the science," it is hoped that they will in fact follow someone down a path of corrupted science based solely on his appearance as caring and even handed.

** Getting Mikovits and Ruscetti involved: This is necessary to give the appearance of actually trying. Someone who accepts the carefully cultivated image of Lipkin's agnosticism would likely to a double-take at any attempt that entirely excludes the primary proponents. The narrative key is to have them "involved," even using their own tools and methods, but to remove crucial elements of the process from their control (in this case cohort selection; sample collection, processing, coding; overarching study design and analysis).

** Saying a number of "open minded" things about ME: Words are free and never warrant suspension of skepticism prior to actions (in this case the actual scientific quality Lipkin produces with his study). In fact, the use of hopeful words to prime the populace for destructive action is a timeless political tool, a "fig leaf."

Again, I must stress that I'm not accusing Lipkin of being motivated in this way, nor am I attacking him. I am simply pointing out a possible motivation that is entirely consistent with what has been said and done thus far. It won't be until his study is published that we will be able to evaluate the

integrity of his actions and words. It is entirely in his hands to produce research that is rigorous, logical, and measured in its conclusions.

There are, however, a number of aspects to this study that would suggest this political motivation is more than a mere possibility:

** Requiring participants to pre-accept results in order to participate (i.e. gagging them): It's hard to imagine any legitimate reason why an honest study would require this. It reeks of a totalitarian attempt to control the message after publication and marks an effective continuation of gags on Mikovits.

** The very nature of the study: Why yet another "do-or-die" test under novel conditions? This is akin to demanding that because someone claims evidence of a novel phenomenon, they must immediately know enough about it to always reproduce it under any conditions presented to them. Yes, blinded and controlled reproducibility is crucial, but not at square one of understanding (unless, perhaps, your goal is to exclude additional understanding...). I think that the only honest approach to get to the bottom of things at this point is for Lipkin to sit down with Mikovits and Ruscetti and see what they are finding and then work closely with them to flesh out the many unknowns surrounding these possible viruses (e.g. better contamination controls, better understanding of viral life cycle and tropism and reservoirs, better understanding of the role of collection and processing, better understanding of methodological nuances and sequence variations). If they cannot find some agreed upon explanation such as contamination, they can at least acquire enough understanding to devise a blinded test that will reasonably control for these current unknowns, which necessarily plague this Lipkin study. Interestingly, this is the precise approach that DeFreitas recommended to the CDC, which they declined due to the cost of a plane ticket. Yet surprisingly the CDC found the funds to force upon her a series of eerily similar, premature, CDC-controlled "do-or-die" tests that "disproved" her finding.

** The secrecy of the design: Obviously the details will be known upon publication, and any criticisms levied thereafter. Obviously the study cannot begin until the design has been worked out, so why not release the details ahead of time, especially if (with a straight face) you intend it to be "definitive"? Wouldn't you want to tidy up any overlooked loose ends before starting, as it would be laughable to genuine scientists to hear of a fatally flawed study being sold as the last word? The reason for the secrecy cannot be that Lipkin is ensured of producing a flawless study and therefore it would be pointless to air the details publicly, as that would imply that the whole peer review process is unnecessary. Is the canard about "that's not the way it's done" so deeply entrenched that it cannot be put aside to make sure this all-important study is robust? Or is it just easier for criticisms to be conveniently lost in the media frenzy that will accompany a negative study?

** The possibility of this study being used to discount all retroviral involvement: In Lipkin's letter from last December, he says the study will "address the question of whether a retrovirus is associated with disease." There are already serious questions about whether this study will even adequately look for relevant MRV sequences (see below), which is a small subset of all retroviruses. The question of whether a retrovirus is involved is far far beyond the scope of this study, esp if they don't do extensive testing for reverse transcriptase, extensive searching in non-blood tissues, and extensive, unbiased deep sequencing. If the study is negative, I fully expect many "lazy" media articles to "accidentally" state that the involvement of a retrovirus has been definitively ruled out in ME.

From the perspective of patients, there is only one outcome of this study that could be devastating. That is if MRVs are involved in ME and this study renders research into this area politically infeasible and scientifically suicidal, as it would mean there will never be full understanding of or a reliable treatment for the root cause. It's far worse to seal the only path to freedom than it is to wander a bit further down a dead-end. Unfortunately, the Lipkin study seems poised to deliver this nightmare.

I think it's also worth considering some of the extraordinary implications if this study is actually positive. It would mean that Fauci (who has presided over decades of government negligence in this disease), following years of successful legal, political, media, and pseudo-scientific attacks on this finding, has inexplicably allowed his star pupil to reveal the truth just before the political finish line. It would mean unavoidable realization by the public (in an election year no less!) that not only is there a new retrovirus loose in the population, but that it has been negligently allowed to spread and destroy lives for decades by the government health agencies. It would mean catastrophic cost escalation for health insurers. It would mean that the BWG and many of the negative studies would almost have to be investigated for fraud. It would mean a fall from respectability for many of the "top" retrovirologists. It would expose the psychobabblers for what they truly are. It would mean very uncomfortable questions about viral origin and government knowledge. It would force a re-evaluation of all of the previous "rumor viruses," thus exacerbating all of these other issues. Simply put, it cannot be allowed to happen.

Lastly, I want to enumerate just some of the open questions that would have to be left on the table if this study is negative and successfully sold as "definitive":

** What about issues of cohort selection, sample collection and processing, viral life cycle and tropism adversely affecting the study? After all, the BWG failed in its duty to better elucidate these issues, so they now represent unknown variables in Lipkin's study. When you don't even know what variables you should be controlling and accounting for, your conclusions are wholly unreliable.

** What about novel sequences found by Hanson, O'Keefe, the Lithuanians, and Grossberg? None of these are close enough to VP62 to be simply written off as contamination, so leaving them unexplained (and likely un-searched-for in Lipkin's study) shows an extreme lack of scientific ingenuity.

** What about Mikovits's unsequenced isolates? It seems laughably disingenuous to claim that something is not there when you haven't even bothered to take a small step (sequence the isolates) to identify precisely what you're even searching for (the ME virus sequences). Not even Judy knows at this point exactly what sequences she found originally.

** What about Dr. Snyderman's results? If Lipkin is the maverick some claim, and the deep sequencing expert some claim, and he's serious about getting to the bottom of this disease, how could he possibly not take on such a straightforward case that others have turned down out of fear?

** What about an ARV clinical trial? Putting aside all the disingenuous "concern" from non-patient onlookers, it would be completely trivial to find very willing volunteers. Dr. Snyderman's data

alone is more than was necessary to launch trials of Rituximab, a far more dangerous drug.

** What about the PC and BPH results? If the ordained ministers of Science have proclaimed that MRVs don't exist in ME, it would be rather incongruous for these studies to persist.

** What about searching for reverse transcriptase? Seems odd to say you found no sign of RVs when your search was limited to specific--but unknown--sequences and never extended to more generic markers of RV infection.

** Why has no attempt been made to test tissues? Evidence from the macaque study as well as behavior of MRV-like viruses in other animals would strongly suggest that blood is not the ideal place to look, esp until more is understood about the virus.

** What about all of the still-unexplained non-PCR results (serology, IHC, FISH)? These cannot be simply written off as contamination, and the explanations to date (cross-reactivity, etc) have not be supported by anything other than desperation and guesswork.

** Philosophically and practically, could the axioms of modern retrovirology ever permit the discovery of a slowly replicating exogenous retrovirus with some vague semblance to human or animal ERVs? I believe this is essentially the question that anciendaze has been positing for some time. In essence, the axioms and assumptions that rule the field exclude any MRV-like virus from ever being "found" in humans as any MRV-like virus would have enough similarity to endogenous sequences and be close enough to limits of detection to always be reflexively dismissed as contamination.