Kevin Sullivan's Rebuttal to the Perth Group

Below is my reply to the Perth Group. I have e mailed a PDF to include pictures and other information that may not appear on facebook, I encourage facebook users to read it in its PDF format. I have asked them to put my reply on their web site. In the PDF format I have colored the points from the PG's reply to Kevin Sullivan in blue and italicized them for ease of reading.

I will first start with a brief apology. I want to acknowledge I was wrong for calling Dr. Turner "Mr. Turner". I will use your earned title from here on out.

I know I have been asked to discuss a lot about the initial isolation of the virus. I am not avoiding the subject. I am not accepting defeat on the issue, nor am I conceding you the point. I am trying to focus on the comments in the PG's reply to me first. Regardless, there is not much more that can be said about it. All that both sides have to go by are the published papers. No new insights that have not been discussed before are going to pop up. I do not have access to lab notebooks or any unpublished figures. I think the isolation is sufficient while you see it as fundamentally flawed. I do not currently have the resources or time to isolate the virus by your standards (I lack access to patient blood), although I am confident in my ability to do so. I realize and accept that this is the foundation of your argument and in your opinion (or at least the impression I am given) all the HIV work after that is invalid. Hopefully we can move beyond the first papers and consider the body of work that has been amassed since 1983. Since we are striving for a scientific discussion I would ask you to consider the other facts that are present.

In this forum and others many have claimed that using examples from other biological systems does not suddenly prove HIV exists. This is true. However I would like to point out that technology has advanced since the early 1980s and techniques common1984 are no longer commonplace. Since the Perth Group has been active in arguing their point of view in court you may understand this legal example. I am no lawyer, nor claim a full understanding of the way the legal system works. However, many interpretations of the law are based on precedent. Over time some older precedents are replaced with newer interpretations of the law or they are forced to change when new or unforeseen circumstances are presented. I merely provide examples from other systems to acknowledge a new technology or concept that is accepted by the scientific community.

*"Re the RAK papers you wrote: "I reviewed some of the information that you provided. One of the key points to your argument that HIV testing is flawed comes from the papers on the RAK antigen". You did not say where you obtained "the information we provided" but in regard to "HIV" testing, we have never argued our case using "the RAK antigen" or RAK antigens or any other data in*

*Rakowicz-Szulczynska's papers. Indeed, our principal paper on "HIV" antibody testing was published several years before Rakowicz-Szulczynska's published her findings. What we argued then and subsequently is the absence of proof the "HIV" antibody tests are specific for "HIV" infection. Hence, in framing our arguments it was not only impossible to use Eva Rakowicz-Szulczynska's data, there was no need to. The only way to prove the specificity of the antibody tests is to compare the presence or absence of a positive test with the presence of absence of "HIV" – as determined by isolation/purification. That is, to use "HIV" itself as the gold standard. This has never been reported, making it impossible to know how many, if any, seropositive individuals are infected with a retrovirus "HIV". Biotechnology companies are well aware of this deficit and it is regularly asserted as a disclaimer in their antibody test kit packet inserts."*

I got the reference from some of your material I read ("The Perth Group Revisits the Existence of HIV"). I am not sure if you have insinuated that HIV testing was flawed or not because of these papers. The initial observations were based on reactivity to one anti-HIV antibody. Any conclusion saying that antibody testing is flawed because there was cross reactivity of one anti Env antibody with cancerous cells is not a sound argument. There are many types of antibody with different levels of specificity. All antibodies, even if they recognize the same protein are not created equal. Many antibodies used in lab say on the packaging that they are for research purposes only not diagnostic usage. This is because they work good enough for the lab but have not been stringently tested for diagnostic purposes. Does your group have any evidence that the specific ant-env antibody MAb 5023 (DuPont Co.) (From EM. Rakowicz-Szulczynska 1994, Novel family of gynecologic cancer antigens detected by anti-HIV antibody) was used for HIV-1 testing? Is there any western blot using serum from patients that are positive for the RAK antigen to show that they have antibodies that specifically react with the antigen? In the case of HIV it has been demonstrated that these patients have antibodies reactive for the proteins many accept to by HIV proteins.

In addition you use the detection of small HIV-like sequences to plant the seed of doubt that HIV sequences are viral in origin in "The HIV Genome Paper". In this document you point out that "You wrote: "Why is it only found in patients who according to the establishment has HIV?" First, this is not true as evidenced by Rakowicz-Szulczynska's's findings.' In the Parenzee case your group made the argument (I found this quotation from "The Perth Group Revisits the Existance of HIV"

"The prosecution witnesses claimed that the "HIV" nucleic acids are unique to this "virus" and cannot be found anywhere else. In our cross-examination we submitted evidence that this is not the case. This evidence included a paper published by Dr. Eva Rakowicz-Szulczynska *et al*, researchers from the USA, who showed that nucleic acid sequences similar to the "HIV" env and gag genes were found in 95% of breast and gynaecological cancer in women and prostate

cancer in men.12-15 "The DNA fragments amplified in seven blindly selected breast cancer samples were sequenced. The breast cancer DNA sequences showed at least 90% homology to the HIV-1 gene for p41".

In their summary, which the Judge himself read to the court, the authors of the above studies concluded: "The results obtained strongly suggest that the long-postulated breast cancer virus may in fact be related to HIV-1".12" (From the Perth Group Revisits the Existence of HIV)

It is for these reasons that I bring the papers up.

*"You wrote: "The HIV envelope protein gp160 is a polyprotein that is cleaved into gp120 and gp41". Not true. To the contrary, gp160 and gp120 are polymers of gp41 which, according to Montagnier, is actin."*

Apologies, but can you provide my the reference for this quote, or possibly a link to the full quotation if it is not readily accessible?

*"You wrote: "As a friendly suggestion I would not use this series of papers as a cornerstones to your argument in the future". We appreciate friendly suggestions but this suggestion is arcane. If these DNA sequences are, as Dr. Foley says, "clearly [HIV] subtype B, which is typical for North America", but are not caused by infection with "HIV", then what are they? How did they arise? If they are "clearly [HIV] subtype B, which is typical for North America", but not of viral origin, then we repeat, the notion that "HIV" DNA is unique cannot be substantiated. There must be ways of acquiring "HIV" DNA which are not a retroviral infection. This is a significant problem for the HIV theory of AIDS. Is this why you are recommending we do not use it? Do you intend to simply ignore these data?"*

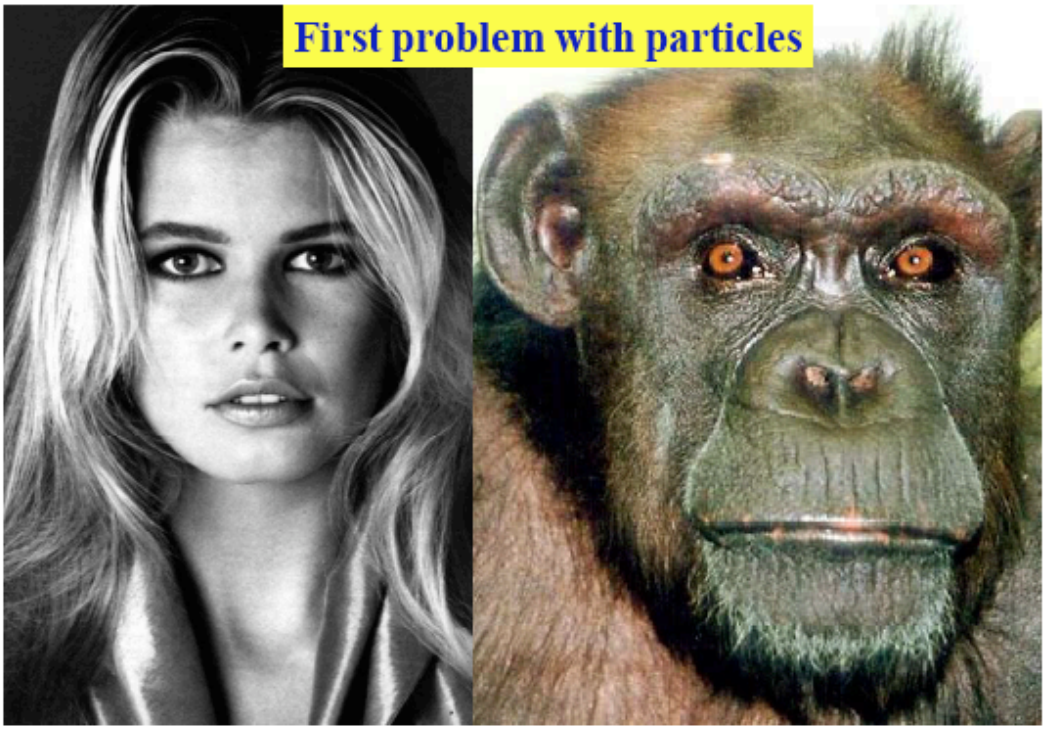
I do not want to really dwell on the RAK antigen story for too long. I think you were missing the point I was making though. I do not doubt that the reported sequences are a close match to those reported for gp41. However, the scientific work done in those papers is quite sloppy. Sloppy work always causes doubts to the validity of results. If you do not believe me, I am sure if you gave the papers I referenced to a group of critical reviewers they would find many flaws. If you like I can go point by point over them. The initial papers on HIV isolation are more technically sound and you see the disagreement we have. So yes, the sequences she presents are exactly what Dr. Foley says they are, however I do question their origin. It is a little suspicious. Oncogenisis and tumor proliferation are complex processes and occur for different reasons. I find it hard to believe that in many different types of cancer all of the cells magically have similar sequences spontaneously appear. Since she is pushing forward the possibility of a new tropism for HIV or a new virus she must prove it. For me 100bp of sequence does not establish the presence of any new agent, or a virus we know with a different tropism (non-immune cells would represent a different tropism for HIV). We know that 10kb of sequence has been recovered numerous times over

from HIV patients. Today's PCR tests have more specific primers, and sequencing is likely rely on fragments much more meaningful than 140bp. Am I wrong in that statement?

*"You wrote: "In your literature you equate this difference to mistaking an attractive model for a chimpanzee"."*

*"Incorrect. We used a taxonomical analogy to illustrate the difference between type C and type D particles. To say that at one and the same time "HIV" is a type C and a type D particle is no different from saying an object is simultaneously an attractive model and a chimpanzee. And given that "HIV" is also classified as a lentivirus it must now rate as a "Holy Trinity"."*

I am sorry, you are right, I missed one of the finer parts of your argument. I accept it as an illustration and not an insinuation. The image and caption are below.




To say that "HIV" is a type-C particle and a lentivirus is no different from saying that an animal is both a human and a gorilla.

For those on facebook the caption states "To say that "HIV" is a type-C particle and a lentivirus is no different from saying that an animal is both a human and a gorilla" However, after looking at the picture I am inclined to say that is a chimpanzee rather than a gorilla. Mind you I am no primatologist but based on the location and size of the ears, and the flat top to the skull (lacking a prominent sagittal crest), nasal structure and general overall appearance it does appear that this is a chimpanzee.  Was that the point of the picture, a subtle joke?

Yes, some of the PRIMARY literature on HIV did classify it incorrectly. This has been rectified and it has been classified properly. The first EM from 1983 is unclear, I cannot tell what particles those are because I cannot see a good picture of the core structure. The electron dense ring in the budding/just budded virions is reminiscent of a type C virus. It is important to state many of the viruses look the same while budding or just after budding since the electron dense core has not finished condensation. They next classify it as type D because of images in “Selective Tropism of Lymphadenopathy Associated Virus (LAV) for Helper-Inducer T Lymphocytes “ Type D particles have cylindrical shaped cores. Lentiviruses have cone shaped cores. It is possible to mistake the two, especially considering lentiviruses were thought to be weird animal viruses, they were not commonly worked on so scientists were not familiar with them.

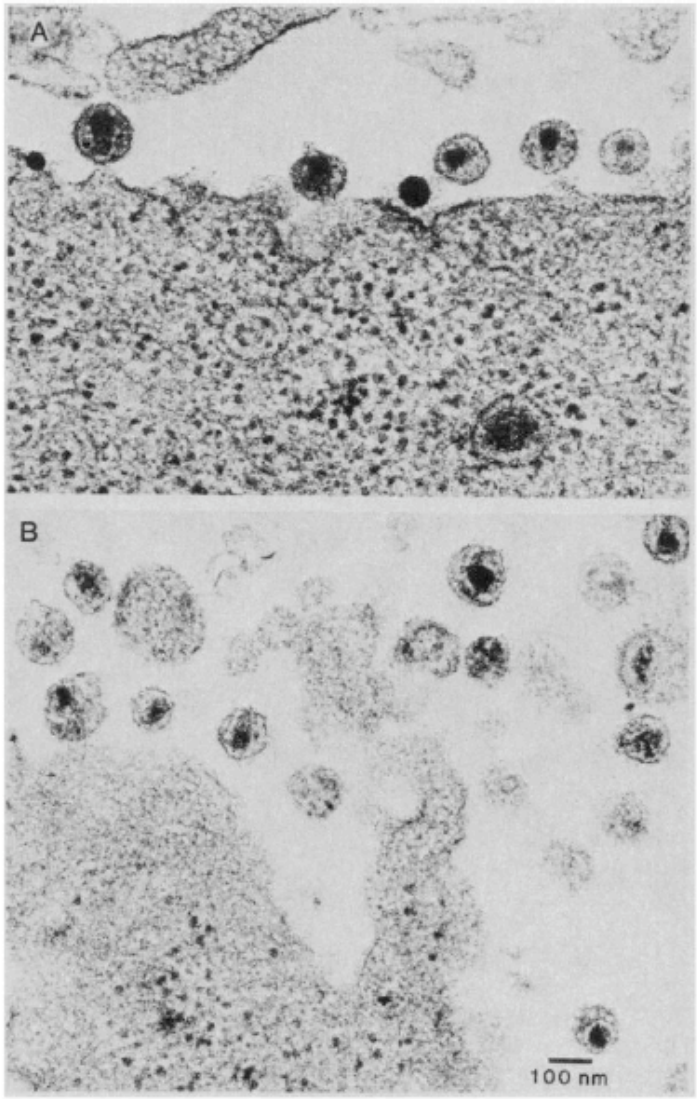



Fig. 2. Electron microscopy of viral particles in ultrathin section. (A) Portion of a T4 lymphocyte from a healthy donor, which had been infected by the virus isolated from patient E.L. Note the numerous mature particles with eccentric dense core in the external space. These particles are morphologically similar to D particles such as those found in Mason-Pfizer virus or the virus recently isolated from simian AIDS (*27*, *28*). However, no antigenic relatedness was found between the p25 of the human virus and the p27 of Mason-Pfizer virus (*29*). (B) Portion of a T4 lymphocyte from patient E.L. at the time of virus production. Note the abundant mature virions around a piece of altered cytoplasm.

(Selective Tropism of Lymphadenopathy Associated Virus (LAV) for Helper-Inducer T Lymphocytes Author(s): David Klatzmann, Francoise Barré-Sinoussi, Marie Thèrése Nugeyre, Charles Dauguet, Etienne Vilmer, Claude Griscelli, Francoise Brun-Vezinet, Christine Rouzioux, Jean Claude Gluckman, Jean-Claude Chermann, Luc Montagnier Source: Science, New Series,

Vol. 225, No. 4657 (Jul. 6, 1984), pp. 59-63)

This is some of the morphology information from the Fields Virology Retrovirus Chapter. As you can see budding and mature viruses can look different. It also takes careful work to properly classify a virus based on morphology. I still contend, as would many others in the field contend that sequence is better than morphology.

**TABLE 55.1**
**RETROVIRUS GENERA**

| New Name | Examples | Morphology |
|---|---|---|
| Alpharetrovirus | Avian leukosis virus (ALV)<br>Rous sarcoma virus | C-type |
| Betaretrovirus | Mouse mammary tumor virus (MMTV)<br>Mason-Pfizer monkey virus (M-PMV)<br>Jaagsiekte sheep retrovirus | B, D-type |
| Gammaretrovirus | Murine leukemia viruses (MuLV)<br>Feline leukemia virus (FeLV)<br>Gibbon ape leukemia virus (GALV)<br>Reticuloendotheliosis virus (RevT) | C-type |
| Deltaretrovirus | HTLV-1, -2<br>Bovine leukemia virus (BLV)<br>STLV-1, -2, -3 | – |
| Epsilonretrovirus | Walleye dermal sarcoma virus<br>Walleye epidermal hyperplasia virus 1 | – |
| Lentivirus | Human immunodeficiency virus (HIV) type 1<br>Human immunodeficiency virus type 2 (HIV-2)<br>Simian immunodeficiency virus (SIV)<br>Equine infectious anemia virus (EIAV)<br>Feline immunodeficiency virus (FIV)<br>Caprine arthritis encephalitis virus (CAEV)<br>Visna maedi virus | Rod/cone core |
| Spumavirus | Human foamy virus | Immature |

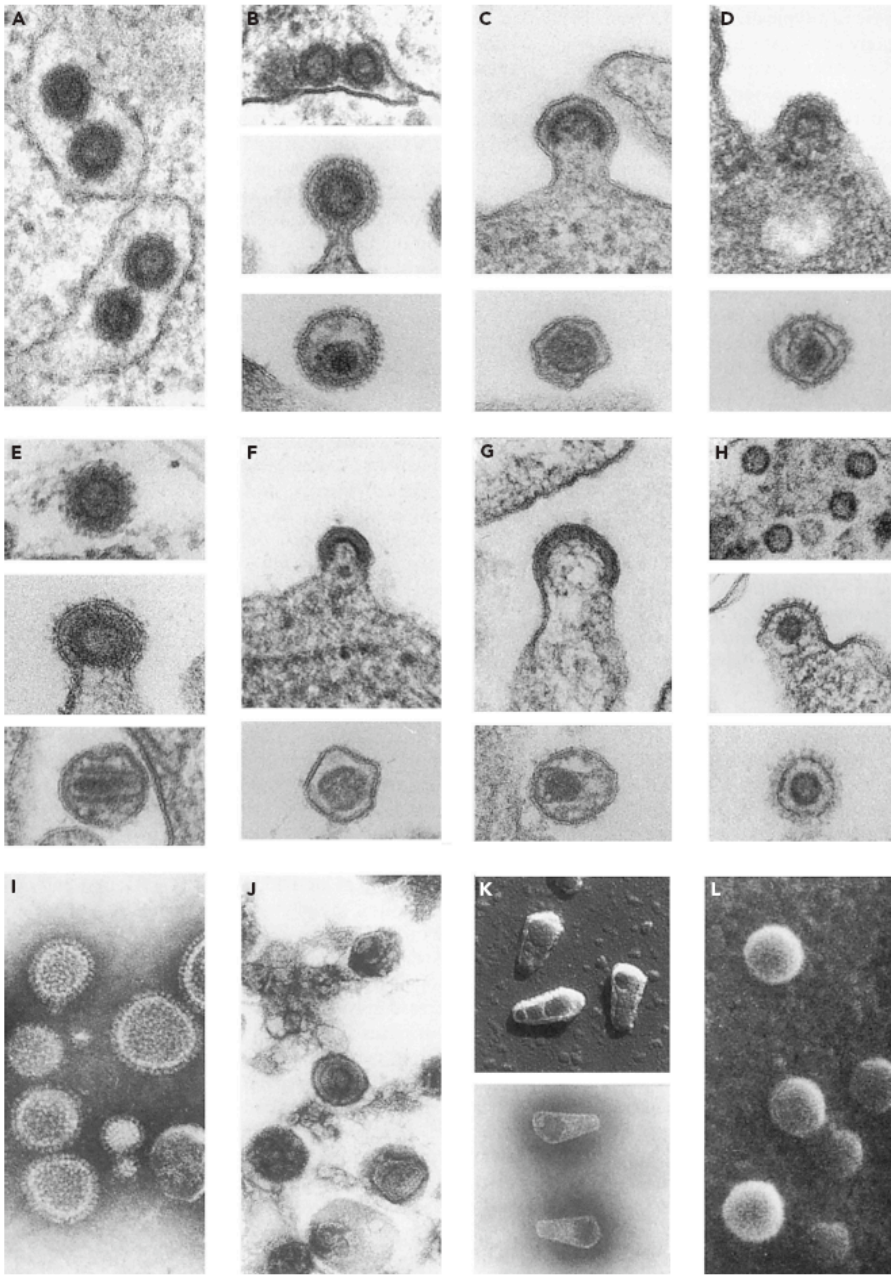



**Figure 55.1** Electron micrographs of representative virion particles. The diameters of all the particles are approximately 100 nm. **A:** Type A particles. Intracisternal A particles in the endoplasmic reticulum. **B:** Betaretrovirus. Mouse mammary tumor virus, MMTV; type B morphology (*top*, intracytoplasmic particles; *middle*, budding particles; *bottom* mature extracellular particles. **C:** Gammaretrovirus. Murine leukemia virus, MuLV; type C morphology (*top*, budding, *bottom*, mature extracellular particles). **D:** Alpharetrovirus. Avian leukosis virus; type C morphology (*top*, budding; *bottom*, mature extracellular particles). **E:** Betaretrovirus. Mason-Pfizer monkey virus; M-PMV; type D morphology (*top*, intracytoplasmic A-type particles; *middle*, budding; *bottom*, mature extracellular particles. **F:** Deltaretrovirus. Bovine leukemia virus, BLV (*top*, budding; *bottom*, mature extracellular particles. **G:** Lentivirus. Bovine immunodeficiency virus (*top*, budding; *bottom*, mature extracellular particles). **H:** Spumavirus. Bovine syncytial virus (*top*, intracytoplasmic particles; *middle*, budding; *bottom*, mature extracellular particles. **I:** Betaretrovirus. Mouse mammary tumor virus, MMTV; type B morphology, visualized by negative staining with phosphotungstic acid. **J:** Gammaretrovirus, visualized as pseudoreplica stained with uranyl acetate. **K:** Lentivirus. Purified cone-shaped cores of equine infectious anemia virus (*top*, cores visualized by shadow casting technique; *bottom*, cores visualized by negative staining with phosphotungstic acid. **L:** Budding retroviral particles visualized by scanning electron microscopy. (Micrographs are courtesy of Dr. Matthew Gonda; reproduced from Coffin JM, Hughes SH, Varmus HE, eds. *Retroviruses*. Cold Spring Harbor, NY: Cold Spring Harbor Press; 1997, with permission.)

I will address your section with the title “You wrote: ‘Lack of a spike protein’”.

The quote you used was from a heading to one of my sections to address some references. Specifically in your reply document “’You wrote: “The HIV envelope protein gp160 is a polyprotein that is cleaved into gp120 and gp41”. Not true. To the contrary, gp160 and gp120 are polymers of gp41 which, according to Montagnier, is actin’”. Many HIV researchers believe that gp160 encoded by the Env gene is the precursor to the spike in question. My paragraph under that heading is as follows. “Many criticisms are focused on the fact that the glycoprotein that mediates entry is not easily visualized using standard EM techniques. I would guess that antibody binding to this protein would not be sufficient to prove its existence on the outside of the viral particle. The reason why it cannot be easily resolved by EM is probably due to insufficient electron density and size (although admittedly I am not an EM expert). If you look at electron micrographs of *Vesicular stomatitis virus* (VSV) you will not observe any spikes or knob proteins. VSV is a virus that is known for its prolific ability to infect a diverse array of cell types and species using its glycoprotein VSV-G. A related virus, rabies is indistinguishable in shape (see above why shape is a poor indicator of virus) also lacks pronounced spikes or knobs. I doubt that your group would fail to acknowledge the existence of both rabies and VSV. “

I never say there is a lack of the spike protein in the above quote. My reply was in response to how clearly defined spikes may not be easily resolved using some EM techniques.

To your insinuation your group claims that it does not exist.

*“In 2003 Kuznetsov and his colleagues reported a study utilising atomic force microscopy that contradicted what all “HIV” experts claim. They reported*

*“We suggest that spikes, knobs, observed by negative-staining electron microscopy may be an artifact of the penetration of heavy metal stain between envelope proteins. Indeed, the term “spike” appears to have assumed a rather imprecise, possibly misleading definition, and might best be used with caution”. In other words, this posits zero knobs on the so-called “HIV” particle. “*

In response taken from Kuznetsov et al., 2003. I feel that the quote you pulled from the text of the document is a little misleading. Your “In other words, this posits zero knobs on the so-called “HIV” particle” is the wrong conclusion taken from the work. The full quotation from the discussion section is as follows. The link to the full paper (free full text) which I encourage all to read is (http://jvi.asm.org/cgi/content/full/77/22/11896?view=long&pmid=14581526)

“We suggest that the spikes observed by negative-staining electron microscopy may be an artifact of the penetration of heavy metal stain between envelope proteins. Indeed, the term “spike” appears to have assumed a rather imprecise, possibly misleading definition, and might best be used with caution. In the work of Briggs et al. (6), the spikes on the surfaces of HIV

virions protruded about 7.5 nm, which is not inconsistent with the height above the virion surface that we observe by AFM for the tufts of protein. On the other hand, spikes of envelope protein are described on the surfaces of HFV that extend 13.8 nm above the surface (69), nearly twice the length of those on HIV. The gp41-gp 120 combination is probably better described as mushroom shaped, with large, exposed exterior surfaces. The number of these gp120 clusters on individual virions, taken as the average from many particle images and assuming that one-third to one-half of the virus was visible, is close to 100 _ 20. This number is similar to that obtained by TEM (20) and the 70 to 140 trimers per virion estimated for simian immunodeficiency virus (9), but it is significantly greater than the 7 to 14 trimers per virion estimated for HIV by Chertova et al. (9). There is one complication, however, that could make our estimate somewhat problematic, and that is the quantity of host cell membrane proteins that may be incorporated into viral envelopes upon budding. If the amount is comparable to that of gp120, then substantially less of the gp120 could be present. That is, some of the protein tufts we observed might represent cellular proteins. It is not known whether virus envelope protein promotes exclusion of cellular proteins from the viral membrane, nor are there reliable estimates of the amount of cellular proteins generally incorporated. Examination of cell membranes from uninfected host cells by AFM, however, reveals a distribution of protein shapes and sizes that are far more diverse than we see on the more or less uniform surfaces of viruses. In particular, there is a much higher proportion of small proteins of _10 nm on normal cell surfaces. The appearance of the virus surfaces is not, in most respects, similar to host cell surfaces, and in particular, the many small proteins are lacking. Thus, we believe that the envelopes of the virions visualized by AFM are composed predominantly of gp120."

From this full discussion of their result they explain how their result is different from others. Nowhere in the entire document do they ever claim that there is no gp120 or gp41 on the cell surface. What they are arguing is that the model of a trimer on the cell surface may not be correct. Their results show that there may be multimers of gp120-gp41 on the cell surface. They propose their mushroom model to describe this. This is significantly different from your conclusion that "In other words, this posits zero knobs on the so-called "HIV" particle." Your statement is misleading. They are arguing that the idea of a punctuate spike structure (trimer) on the surface may not be entirely correct. To that end they are saying that the idea of a spike may be misleading to some, for example it appears to have misled you. However, they did observe the envelope protein on the cell surface. Therefore the virus would still be able to mediate fusion. This envelope was not shed super rapidly.

To encompass many of your points above about the Env protein and its detection.

We can agree that any virus is too small to see with the naked eye. Therefore we have to use special techniques to view them, all of which have pros and cons. For example, EM techniques, both scanning and transmission, rely on fixation and stains. Cryo-EM reconstruction relies on averaging. All EM techniques use ionizing radiation that does damage cellular structures. AFM can only see topological differences. Crystallography, is a snapshot in non-physiological conditions often with changes to the parent molecule. I am not saying that any of these approaches are fundamentally flawed and/or unusable; however, it is important to understand that how you test something determines your result. It

takes a number of independent approaches to truly understand something and make sure any observation is not an artifact of the test.

Would you like to have a separate discussion on GP120 shedding?

*"It appears you are stuck on the notion that, because some particular DNA sequence is not found in normal healthy humans this proves the sequence must be exogenously acquired. You, like the "HIV" experts, seem to believe in an invincible, unalterable DNA hiding behind a force-field the envy of Darth Vader. You do not seem to appreciate that a new DNA sequence could arise in situ, in vivo, de novo. Your view is not shared by eminent biologists."*

As a scientist, biochemist and a retrovirologist who applies evolutionary principals to my work, I feel that I appreciate genomic plasticity more than most. Although some refer to DNA as the "immortal coils" most scientists in fact appreciate they are subject to many changes and rearrangements. In fact this is one of the reasons why there are ongoing projects to sequence the genomes of tumor tissue and common cell lines. Restriction fragment length polymorphism analysis (DNA fingerprinting) relies on the fact that DNA polymerase sometimes has trouble copying repetitive sequences giving rises to the loss or gain of repetitive sequence. Immunology accepts that single cells can acquire new functional sequence in their genes that make antibodies or T cell receptors. Gallo appreciated that DNA can change when he was selecting cells that could support HIV replication (H9 cells ) in his paper "Detection, Isolation, and Continuous Production of Cytopathic Retroviruses (HTLV-III) from Patients with AIDS and Pre-AIDS Author(s): Mikulas Popovic, M. G. Sarngadharan, Elizabeth Read, Robert C. Gallo Source: Science, New Series, Vol. 224, No. 4648 (May 4, 1984), pp. 497-500" Different cells supported differential replication; this could either be from differences in gene expression or the loss/gain of other genes. One theory of protein evolution is domain shuffling, in which random events cause new domains to be associated to give rise to new functionalities. Mobile elements in DNA can move, take out or insert new sequence. Some key principles are that all of these events are random processes and many rely on bulk movements of genetic units. Genomic sequencing has not found an endogenous lentivirus in humans or any relative closer than a lemur. Since humans or our close relatives do not have endogenous sequences resembling HIV than these would have to "arise *in situ, in vivo, de novo*." Full length sequences of what we call HIV can be amplified from patients we claim to be infected with the virus. Importantly, these sequences are coming from one mRNA transcript. If we say HIV is 10,000 base pairs the chances of randomly acquiring 10,000 bases in a row to match an HIV sequence is 1 in 4^10,000. Provided that there can be as a rough number 20% sequence diversity that is still 1 in 4^8,000. It is impossible that a full length sequence could be made by random chance by a single cell in its lifetime. If you want to invoke the fact that it is possible that some endogenous retrovirus could be mutated by random chance to look like HIV or if mobile elements move some domains near each other, I cannot

calculate those odds. However, it would still take numerous insertions/deletions and mutations. HIV has accessory genes that are not present in the endogenous viruses. To make HIV in a cell from scratch, you have to provide that cell with a selective advantage as many many things would have to occur for an HIV-like genome to appear. This cannot happen all at once. Many acknowledge that HIV is cytotoxic (kills cells), a cell that is making HIV from scratch would need to get around this. Scientists argue this virus kills people, a person would have to be ok as this sequence is forming. It is doubtful there is any benefit to making a single virus "arise *in situ, in vivo, de novo"*. Furthermore, we do not see HIV in one cell, or even in one cell of the same lineage. Therefore according to your argument many cells all over the body all at the same time are randomly arriving at the same sequence (given some error), the same way, at the same time while cranking out a ton of this RNA into the blood. That goes against all probability. We then have to consider that this happens in many people al over the world. The odds of that happening are astronomical.

*"Although more than half a century has passed since the Nobel laureate Barbara McClintock discovered the phenomenon of transposition, which can lead to the appearance of new genotypes and phenotypes, at present it is still generally accepted that any time one finds a particular stretch of RNA in a cell, for example, in a T-lymphocyte, unless RNA or DNA has been introduced from outside, all T-cells, regardless of their physiological state or stresses to which they are subject, will contain a corresponding stretch of DNA. In other words, the DNA (genes) in a cell are invariant and all RNA molecules in the cell are subservient to a matching length of DNA. However, according to McClintock, the genome can be restructured and not only by transposition. In her Nobel lecture of 8th December 1983, she said, "rapid reorganisation of genomes may underline some species formation. Our present knowledge would suggest that these reorganizations originate from some "shock" that forced the genome to restructure itself in order to overcome a threat to its survival...Major genomic restructuring most certainly accompanied formation of new species". The "genomic shock" which leads to the origin of new species may be "either produced by accidents occurring within the cell itself, or imposed from without such as virus infections, species crosses, poisons of various sorts, or even altered surroundings such as those imposed by tissue culture. We are aware of some of the mishaps affecting DNA and also of their repair mechanisms, but many others could be difficult to recognize. Homeostatic adjustments to various accidents would be required if these accidents occur frequently. Many such mishaps and their adjustments would not be detected unless some event or observation directed attention to them...Unquestionably, we will emerge from this revolutionary period with modified views of components of cells and how they operate, but only however, to await the emergence of the next revolutionary phase that again will bring startling changes in concepts"."*

I am not sure what you are trying to prove with this passage. Your quote "at present it is still generally accepted that any time one finds a particular stretch of

RNA in a cell, for example, in a T-lymphocyte, unless RNA or DNA has been introduced from outside, all T-cells, regardless of their physiological state or stresses to which they are subject, will contain a corresponding stretch of DNA. In other words, the DNA (genes) in a cell are invariant and all RNA molecules in the cell are subservient to a matching length of DNA." Are you arguing that RNA can appear in a cell without a DNA template? A 10kb RNA fragment will not appear from nowhere in a cell. There may be some fundamental principles of biology that you are missing. The class of polymerase that makes the mRNAs to make proteins in the cell (and HIV genomes) requires a DNA template to make long RNAs. Nearly all polymerases require a template. Now not all RNA sequences match DNA sequences. This is accepted. First introns are removed from mature mRNAs, this means that two regions that are adjacent on the mRNA may not be on the DNA. However, the sequence of each unit is found in fairly close proximity (on a genomic scale) on the DNA. mRNAs get a poly A tail, this is not encoded in the DNA. Some RNAs can be edited by enzymes so their sequence will not match that of the template. These are all accepted facts. However no spontaneous mRNA will appear without a corresponding DNA element, especially at a length of 10kb.

Second, your quote from Barbra McClintock does not reflect the true intention of her statements. Once again you may be ignoring some underlying principles of biology. As a background for others, she studied corn as a model system for genetics. Specifically she looked at corn kernels, which are one half of the reproductive bodies on the plant. This is ½ of the genetic contribution to a new plant. Because of their haploid nature single mutations or changes to the genomes of these kernels will be inherited and present in nearly every cell of the new plant. She studied corn kernels because for genetics you need large numbers of plants to observe rare changes. When you try to grow corn from a plant that has been mutated or has a genetic flaw you only see the "winners" as progeny, i.e. the plants that had compensatory changes required to grow. Her points of view should not be considered on the individual level, but rather on the species level, she even comes out and talks about speciation. Taking the example of viral stress in a plant. It does the plant no good if only one somatic cell makes a change that prevents infection. However if this mutation occurred in a kernel it can be passed on long after the parental plant died from the infection. There is a fundamental difference between the cell, the multicellular organism and the species as a whole. The organism is not about the individual cell, the cell cannot survive without the whole. Even a subset of cells cannot survive without the organism. The changes to drive survival from stress must be in every cell or nearly every cell. The same is true in a human. If you want to talk about the separate changes to immune cells as they mature we can do that. In that case "mutations" in single cells can be beneficial. However, this mechanism is isolated to specific loci of the genome and should not be used as a pretext to argue how HIV pops out of cells.

*"As far as the PCR is concerned, researchers from several institutions from the*

*USA pointed out in 1996: "To evaluate the sensitivity and specificity of PCR, investigators must ascertain whether study participants are infected with HIV. Typically, a new test is compared with a superior reference (or gold standard) test…The lack of an appropriate reference test (for HIV PCR) substantially complicates evaluation". Even if a gold standard did exist, the specificity of the PCR still could not be determined for the simple reason, that this test, as the same researchers point out, is not standardised". "The criteria for determining when PCR gave positive results varied among the studies". Even when the lack of standardisation is ignored and totally unsuitable gold standards are used, such as the antibody test, the specificity of PCR varies from 40% to 100% leading researchers from different institutes in the USA to conclude "Our investigation produced two main findings. First, the false-positive and false-negative rates of PCR that we determined are too high to warrant a broader role for PCR in either routine screening or in the confirmation of diagnosis of HIV infection. This conclusion is true even for the results reported from more recent, high-quality studies that used commercially available, standardised PCR assays…We did not find evidence that the performance of PCR improved over time"."*

Can you please provide a reference(s)?

*"How do you know the similar DNA shared by two people is that of a retrovirus?"*

If you take RNA or Proviral DNA, clone it, express it in cells, harvest the supernatant and put that on target cells they will become infected. You could do this from any patient with sufficient viral load. If you sequence that plasmid or directly sequence viral RNA from a patient the sequence obtained is most closely related to other retroviruses.

*"In 2007 Laura Geretti from the Department of Virology, Royal Free Hospital, London UK, wrote an article entitled "The use of phylogenetic analysis as evidence in criminal investigation of HIV transmission". This paper made it quite clear it is impossible to use DNA sequences data, including phylogenetic analysis, to prove two individuals harbour an identical "HIV" genetic sequence. Geretti and her colleagues concluded "Consequently, even with the appropriate controls, phylogenetic analysis cannot 'prove' transmission".*

This is the conclusion section from the paper which can be found in its full text from http://www.ncbi.nlm.nih.gov/pubmed/17661846

"Conclusion
It is important that everyone involved in the criminal justice system is made fully aware of the limitations of phylogenetic analysis before using its findings as conclusive evidence of HIV transmission between two individuals. Phylogenetic evidence, in the context of other clinical and epidemiological evidence, can provide support for linkage between cases, but cannot, in itself, be proof of

transmission. Expert witnesses should acknowledge the limitations of the inferences that might be made and choose the correct language in both written and verbal testimony. Over-interpreting the results of phylogenetic analyses is unacceptable, regardless of how convinced an expert may be of the guilt or innocence of the accused. “

The major points of the article state that this analysis cannot provide 100% proof that the transmission occurred as the accuser may state, however it can be used as part of the evidence to make a case provided the technique is applied properly. It also clearly states that this technique can be used to clear someone of charges. The technique can establish if a person is in a chain of transmission. It is more difficult to tell who gave the virus to whom or in what order, however, it is able to show that people are part of a linked chain, showing transmission of the virus.

*“You wrote: “Looking for this enzymatic activity (which is rare in human cells and only occurs under a defined set of conditions) is much easier than looking for something unknown by PCR”. Two problems here: 1. RT activity is not rare in human cells. 2. You cannot look for something new by PCR before you have the primers and probes you need to look for it. These can only be obtained by first purifying the viral particles. Please give us the proof that anyone has purified the “HIV” particles.”*

I still contend that RT activity at the levels reported for HIV isolation, and subsequent HIV study is rare if not absent in human cells. Can you provide me references that clearly state that it is somewhat common for many different types of cells harbor high levels of RT activity.

“You wrote: “Your group is 100% right, poly T is not specific in any way for viral RNA, it will pick up any cellular mRNA in addition to vRNA”. Is poly T a typing error? Do you mean poly A or RT? If so, you cannot claim RT activity or poly(A) RNA are retroviral and not cellular. And without such proof there can be no proof for the existence of “HIV”.”

I was talking about using a primer for the RT reaction that was poly T (thymine) that would bind to the poly A tail on mRNA and viral RNA (vRNA). I talk more about RT later in this document.

“(i) RT activity, and not the enzyme reverse transcriptase as you claim. (The cellular DNA polymerases γ and β can also reverse transcribe RNA into DNA)”

I am not up on all of my polymerase biochemistry, can you provide me with the references for the DNA polymerases efficiently transcribing RNA into DNA. It is not that I don’t trust you, but without a bit of research I cannot comment. I don’t really know where to start.

*"(ii) three proteins, p80; p45 (p41); p25 (p24) which reacted with antibodies in BRU's serum."*

*"Then, for no reason whatsoever, they ignored the p80 protein and the antibody which reacted with it. In the case of p45 (and presumably the antibodies which reacted with it) they claimed it was cellular actin (the molecular weight of actin is 41,000). The p24 protein was said to be "HIV" and the antibodies which reacted with it, "HIV" antibodies. Because none of the proteins which sedimented "exactly where one would predict viral particles to settle" (the 1.16 g/ml band), did not react with an antibody to HTLV-I p24, they claimed to have discovered a new retrovirus, consisting of only one protein, p24. Fourteen years later, in July 1997, during a videotaped interview conducted by the French journalist Djamel Tahi, Montagnier stated: "analysis of the proteins of the virus demands mass production and purification. It is necessary to do that". Then, astonishingly, he said that in 1983 he did not purify the virus: "I repeat we did not purify". And, unbelievably, in what they called "purified, labeled virus" they were unable to find any particles with "the morphology typical of retroviruses". In a similar interview conducted in December 2005, Charles Dauget, the Pasteur Institute electron microscopist, confirmed that in the "purified" virus, they found only cellular debris. In other words, Montagnier accepted that his 1983 evidence did not satisfy his own criteria necessary to prove the existence of a new retrovirus, or even a retrovirus. Obviously, since Montagnier found RT activity in a "finite band" which had cellular debris but no retrovirus particles, the enzyme can only be cellular. And it can have nothing to do with a retrovirus and much less with transmission of a retrovirus, even if detected in an infinite number of consecutive cultures. Similarly, any protein present in the "finite band", irrespective of its reaction with antibodies present in BRU's serum, including p24, must be cellular. Ditto for any RNA including poly(A) RNA and primers and probes based on this particular RNA. In conclusion, in 1997 Montagnier admitted that his 1983 evidence did not satisfy even his own criteria necessary to prove the existence of a new retrovirus, "HIV".*

*Our questions to you are: "*

Before I answer this I realize what I say may be taken out of context or misused beyond my intent. In reference to the "Isolation of a T-Lymphotropic Retrovirus from a Patient at Risk for AIDS" I stated before, this paper is an initial report. It is not the most stellar display of research science in history. Yes, you do point out some weak points in the data. I will give you credit when I reply to your question 1. I will offer a counter of positive points to your argument in response to your question 2.

*"1. Do you agree with our analysis of Montagnier's data – yes or no?"*

Yes, I agree for the most part with some points from your critical analysis.

Yes, RT activity may not be exogenous retrovirus specific. However, spreading transmissible activity in conjunction with particles does favor a viral agent. The RT activity appears to be specific for a reverse transcriptase instead of a standard DNA or RNA polymerase. Sedimentation indicates that this RT is associated with something of uniform density that appears to be distinct from other labeled RNAs. RT activity alone is insufficient to 100% prove a viral agent is there, but it is one piece of evidence.

Yes it is odd they ignored the 80kd band; if I were reviewing the paper I would have asked about it. Based on what was presented I cannot say if that was actin or not. I would have asked them to use a monoclonal antibody to prove that it was actin. It is worth noting that actin is incorporated into HIV virions and HIV proteins do interact with it so it is likely to be present in an IP. Since it is an internal cellular protein there would be less reason for antibodies avoid auto reactivity. You are right that the evidence aside from weight and presence in multiple samples does not unambiguously show it is actin. In their defense they do say that it *may* be actin they do not say it *is*.

I would like to see the interviews you cite and if any EMs of the debris that may be around before I comment on that.

Yes, I agree that the EM of the virus in this paper is not that good. Looking at the virus it would be very difficult to determine what family of retrovirus it is. It only shows budding virus and the level of detail in the cores of released virus is insufficient to 100% tell what type of particle it is. This could be why it was misclassified.

No, I do not agree with the general conclusion that all HIV work is invalid because of these shortcomings.

*"2. If no, could you please explain where and why we are wrong?"*

Aside from the points that we can agree are not very strong. This paper does offer many positive points.

1. The sample was taken from someone in a specific risk group. That person was displaying the symptoms of the ARC as it was referred to around this time. It was recognized that a deficiency in T cells, specifically CD4 was found in patients with advanced disease, AIDS. It was hypothesized that this virus was killing CD4 T cells, which could make it difficult to grow the virus in someone lacking the target cells. Their attempt to trying to grow the virus from someone prior to the onset of AIDS appears to have been a good starting source of infected cells.
2. They attempt to culture the virus. They use the patients own cells first and detect RT activity (more on that later). If they had stopped here I would agree with you, something weird could be going on. More tests would

need to be done. Also, I know there are criticisms that the cells were stimulated, they stopped PHA treatment after 3 days but virus was detected at day 15. They take blood from another individual, isolate the T cells, and split the culture in two. They coculture those cells with the ones from the at risk patient. Donor cells were RT- to start. RT in the coculture was not detected until day 15, while the non-cocultured cells remained RT- for 6 weeks even though those cells were treated similarly. No natural infectious human endogenous retrovirus has been isolated. This clearly shows spreading RT activity. Two explanations are possible 1. A retrovirus is replicating. 2. The cells from the patient are somehow harboring RT activity while growing in the culture. They do the same assay with umbilical cord T cells. Again, only the cultures that had products from BRU (patient 1?) had RT activity. I would be convinced at this point that they have something interesting going on that would either be one of the two possibilities I listed.

3. There is so much talk related to the RT. I am not a polymerase/RT expert so my conclusions may be wrong. The RT activity "likes" conditions similar to an established retrovirus. You are right cellular activities could mimic apparent RT activity. They control for this in 3 ways. 1. They use radioactive uridine (U). DNA polymerases do not readily polymerize using U. 2. They use actinomycin D which inhibits RNA polymerases (I think it lowers the activity of DNA polymerases as well) so incorporation of U would come from RNA polymerases. 3. They use a poly T primer which would bind to the poly A tail of mRNA or vRNA (yes poly A stretches are in the genome as well, but actinomycin D treatment and use of uridine lower the chances a common DNA or RNA polymerase is acting on DNA. The polymerase "prefers" an RNA template. Only some DNA polymerases can use an RNA primer, and the use of U makes this unlikely. Efficient RNA dependent RNA polymerase activity is not robust in cells. Do you object to this analysis?
4. The sedimentation indicates that whatever they are purifying with RT activity is uniform in density. This supports the viral hypothesis.
5. Reactivity of infected cells to antibodies from patient 1 (especially the use of patient 2) lend credence to the idea that something viral is going on. The fact that the controls were not stained lower the possibility of the disorder being caused by autoimmunity. Autoimmunity, to the best of my knowledge, would not be consistent with RT activity or virus production.
6. The EM of viral particles supports the viral hypothesis.

*"3. If yes, don't you think that like us, you, as a scientist, must question the generally accepted view that in 1983 Montagnier discovered a new retrovirus, "HIV"? And thus, like us, become a dissident? "*

Honestly, my reaction to this single paper would be as follows. My first reaction would be that this is interesting. My second reaction would be to reread it and critically analyze it. I would have come up with many questions and looked at all

of its deficiencies. I would imagine this is the same reaction the members of the PG would have had and we would have come up with many of the same things. I then would have found the idea of a viral agent intriguing. I would say the evidence suggests that a retrovirus may have been present in patient 1 (BRU), its link to AIDS would be unclear at best. Scientists never like a sample size of one. The serum of patient 2 helps but still does not fully eliminate any alternative really strange possibilities. I would have then done what many others in the scientific community did in 1983, I would have eagerly awaited follow up publications from this group, but specifically from independent groups. These came in from1984-present. Gallo's lab isolated many viruses from patients. Due to the controversies associated with Gallo I will not talk about his data. Jay Levy et al., "Isolation of lymphocytopathic Retroviruses from San Francisco Patients With Aids" Science, Aug 24, 1984, pp.840-842. would constitute an independent isolation. Others continue to do so to this date.

In summation, I agree with you that the initial paper does have some details lacking. I feel, especially given the technology at the time, that it is a sufficient support of an interesting finding. The goal was to get the idea out there. As an initial paper it is o.k.: no initial paper is complete or covers as much as an eager reader wants. Initial papers put ideas out there for others to validate and expand upon. I feel that for HIV this has been done.

*"You wrote: "I truly believe that people are entitled to believe and practice whatever they want provided it does not cause others harm. I truly believe your group preaches views that do harm others and society as a whole".*
*We do not "preach". We write scientific papers based on our research and interpretation of the HIV/AIDS literature. If you find errors, or do not agree, do what true scientists do, write the editors of the journals where we have published and defend your thesis. The fact that you accuse us of harming "others and society as a whole", means you have either not read or understood our papers. There is no scientific basis to your claim. Public health policy based on our views is more stringent than that recommended by the HIV experts. People who do not understand this fact reveal their ignorance of our views."*

I will say I let my emotions get the best of me. I am fine carrying out a rational scientific conversation about this topic. I will debate you as long as your group will debate me. Naturally, I do believe that I am right, but will critically review all sources, just as if it was a scientific paper undergoing peer editing. If your arguments are convincing or you present me with data that 100% refutes my position I will concede the point.

What does get me worked up is when our little scientific discussion has implications that go beyond the scope of science. I don't think the Perth Group would deny the fact that most of the medical and scientific communities believe that HIV is a virus and it does cause AIDS. This does not automatically make you wrong, but obviously to overturn convention you need convincing data. I do not

agree with supporting, giving credence to, or not correcting people who make statements to change medical and safety practices – i.e. specifically stopping or not starting medication or forgoing safe sex practices -- in the absence of sufficient data to support their opinions. Those actions are tenets of what is considered to be good medical practice; it would be irresponsible for us to advise them otherwise without convincing scientific data. Less data is required to debate, there is much less on the line, however it does take a more stringent level of proof to change medical practices. I encourage you to work at systematically and scientifically proving your point. It should also be noted, that it is not sufficient to provide counterarguments (without much hard data) to research conducted and published in the early 1980s. It is now 2010, and if you wish to overturn a hypothesis as well supported as that of HIV causing AIDS you must counter all research that supports that hypothesis to date.

This message is only a response to your reply to me. I tried to keep it shorter by not including new topics. I know that although I was careful and tried to reply to as many things as possible there will likely be the need to clarify and discuss some points, or move onto new topics. In order to keep our audience captive and speed up our rate of communication can we talk about specific topics or shorter aspects of debate section by section?