Reconciliation between Pure Scientists and AIDS-Dissidents:

Could an ancient retrovirus, RNA-interference and stress be the answer to the divergent opinions ?

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Summary:

In this article, based on scientific publications, I present a new theory on the cause of AIDS. The latest scientific research is combined with well known facts and put into a new context. The outcome is that there is no infectious HI-Virus.
The provirus, described in scientific publications, seems to be an ancient retrovirus, established during evolution in our genome, normally acting as a nearly suppressed part of the genome that can be partly activated under certain circumstances like oxidative stress and malnutrition leading to T-cell decline and disease.
Aids diagnosis is a vague statement and testing for HIV is not evidence based and thus disapproved.
But if we all work together we can improve the situation for the people who are suffering from health problems.

Overview:

I. Introduction: Testing for HIV

Since the claim that HIV is the cause of AIDS in the 1980th there is a never stopping discussion between "AIDS dissidents" and scientists. Why?
The answer is that there are many facts that make it difficult to believe, that there is a virus that causes the multiple various symptoms of AIDS. I will only try to give an answer to scientific reasonable doubts:

1. The ELISA test for HIV antibodies has a high sensitivity and a low specificity as claimed by the company , Abbott, themselves. **[1]** Thus they recommend a second test in case of positive testing.
2. The test serum of patients tested for HIV has to be highly diluted which differs from other laboratory tests for infective diseases like Measles, Varicella, Mumps, Cytomegalovirus and Epstein-Barr Virus.

If the test serum of patients tested for HIV is not highly diluted than everybody tests positive! **[2]** Due to Giraldo this outcome could mean:

- Everybody has a HIV infection?
- Everybody has antibodies to HIV?
- The test is not specific for HIV?

Indeed the test kit reacts at least with 50 more "substances". **[3]**

3. The second test – done in some countries after a positive result in the ELISA test for HIV is the "Western Blotting " test. The interpretation of the test results varies in different regions of the world. That means, having a positive result in one part of the world and travelling with the blotting test result to another part of the world would declare you healthy in that other country. [**4,5,6]**
4. Concerning to L. Montagnier, one of the 2 scientists that are named the discoverers of HIV, he himself does not claim to have ever purified the virus **[7]** which is in fact the "gold standard" in virus proof in scientific work. **[8]**

As a result of the afore mentioned we have no test standards, no virus proof and no evidence.

THAT´S WHY WE SHOULD STOP TESTING FOR AIDS !
IN ADDITION: A POSITIVE TEST RESULT COULD FRIGHTEN PEOPLE TO DEATH!
The Nocebo-effect is due to involvement of the cholecystokinin-system. **[8a]**

5. Concerning the high number of people said to suffer from AIDS all over the world, but specifically in Africa and the fast developing countries, most people are not tested at all.
The WHO "Bangui definition" is sufficient to be diagnosed for AIDS due to criteria of having symptoms like itching, coughing and diarrhea for more than 1 month.
6. In Africa most tested persons are pregnant women, because they are the ones that visit hospitals during pregnancy and those institutions are capable of testing says Christian Fiala, physician in Vienna, Austria. Pregnant women express more antibodies as other humans due to the changed situation in the body, fighting against foreign antigens of the fetus. **[9]**
For more explanations concerning positive HIV tests in pregnant women, newborn babies and multiple mothers see the chapter V of this article on pregnancy .

<u>The conclusion is that we have no standards for diagnosing AIDS.</u>

II. What evolution teaches us

The new scientific results in research concerning the human genome have changed our mind tremendously. Humans and chimpanzees, which diverged from a common ancestor some 5 million years ago, differ in their genome sequences only about 1 – 2 %. We are aware that only about 3% of our genome is coding. The other 97% were long named "junk " DNA. As to Jamil Baccha they are "spam from the dark age". **[10]** All living creatures from plants to humans comprise a big quantity of proviruses fixed in our germ lines and providing us with a fossil record of viruses long extinct in the population. **[11, 39]**
In humans, there are about 80.000 proviruses and their remnants many of them ancient retroviruses, comprising about 6-8% of the genome, or about twice as many as genes.
John M. Coffin, Professor of Molecular Biology and Microbiology, Tufts University: " There is more provirus in us than there is us in us." [12]
The former "junk" DNA is now investigated for these sequences, which are dedicated to gene regulation processes, promoter sequences, transposons, jumping genes (Barbara Mc Clintock won the Nobel Price in 1983 for her discoveries in maize), micro RNAs and RNA interference and may be more research in the future will lead to new discoveries we are still not aware.
The "Central Dogma of Biology", which states that DNA is transcribed to RNA and then translated to proteins can now be extended because of the various amounts of RNA that are translated from the DNA of our genome regulating cell processes without being translated into proteins. In addition we are aware of a process which transcribes RNA into DNA which is used by Retroviruses.

III. The regulation of the genome of the provirus

The scientific literature – concerning HIV – is nearly exclusive based on the **provirus, which is about the integrated DNA into the human genome.** "The provirus might have been a former virus, derived from a chimpanzee virus progeny, that gave rise to a virus, that could infect humans. It might have lost downregulation of the NEF-gene, which made it more infectious". **[13]**
The 3 main genes of the provirus are gag, pol, env and some more genes that are due to recombination of parts of the integrated DNA thus comprising more possibilities for coding. TAT for instance is a provirus transcription activator and the LTR (long terminal repeat) is a binding site in provirus activation for RNA synthesis.
Some of the molecules that are working together in the regulation of gene expression in the T-cells are **host factors:** Nuclear factor Kappa Beta (NFκB) and his inhibitory unit p50, Histone deacetylase1 (HDAC1 also known as sirtuin 1), RNA polymerase II, small hairpin RNAs. The Nobel Price for Medicine of 2006 was awarded to C. Mello and A. Fire for their breakthrough in research concerning RNA interference in *Caenorhabditis elegans*. **[14]**
The publication from S. A. Williams et. al.claims that activation by NFκB p50 promotes HIV latency through histone deacetylase recruitment and repression of transcriptional initiation. Knockdown of p50 expression with specific small hairpin RNAs reduces HDCA1 binding to the latent HIV LTR and induces RNA polymerase II recruitment, but only short virus transcripts are generated. **[15]** Synthesis of full-length viral transcripts can be rescued by additional expression of TAT.

Having a closer look to NFκB shows that this molecule is very well known for being activated in inflammatory processes of the cell and transported into the nucleus for binding. **[16]** The histone deacetylases, like Sirtuin, lead to repressive changes in heterochromatin. **[15, 17]** RNA interference and micro RNAs can trigger gene expression or inhibition.**[18,19]** As to Alexander Spirin, Moscow, RNA molecules, embedded in protein particles called "informosomes" are found in many cells of the body, including germ-cells. **[20]** They might imitate particles similar to viruses. The RISC - **R**NA- **I**nduced **S**ilencing **C**omplex - might also elucidate more details **[21,22]** concerning m-RNA which is attached to proteins. It is a ribonuclein paricle composed of a single-stranded short interfering RNA (si-RNA) and an endonucleolytically active Argonaute protein, capable of cleaving m-RNAs complementary to siRNA. RNA interference can be a hereditary molecule, that means it might be transported via germ cells and involved in regulating processes in the next generation.**[23,24]** Thus small RNA molecules and attached proteins might explain the false pretences for HIV. But even the latest scientific research from Nolwenn Jouvenet, Paul D. Bieniasz & Sanford M. Simon in "*Nature* advance online publication 25 May 2008 **[24a]**, gives new suspicion for particles produced inside the cell and transported to the surface : "…Here we describe quantitatively the genesis of individual virions in real time, from initiation of assembly to budding and release. We studied fluorescently tagged derivatives of Gag, the major structural component of HIV-1—which is sufficient to drive the assembly of virus-like particles[6]—with the use of fluorescence resonance energy transfer, fluorescence recovery after photobleaching and total-internal-reflection fluorescent microscopy in living cells…."

IV. About molecular response to oxidative stress

Oxidative stress is caused by Reactive Oxygen Species (ROS). They are generated mainly by two processes: 1. The oxygen dependent pathway of microbial killing by myeloperoxidase, an enzyme which produces free radicals for the destruction of bacteria. 2. The mitochondria produce ROS during electron transport for the generation of energy as ATP. ROS can cause damage to mitochondria and other components of the cell like the nucleus thus leading to energy deprivation and chromosomal damage resulting in mutations.**[25]** The balance of the cell is depending on a balanced oxidation/reduction status which includes a normal pH of 7.4. For promoting the stability there are molecular redoxsystems in the cell like katalase superoxiddismutase, and the Thioredoxin system. This system is provided by another system called Glutathione. Both systems comprise a pair of oxidized and reduced molecules called Thiredoxin Tr (the oxidized form) and TRX (the reduced state) and in addition we have Glutathione which forms a dimer GSSH if oxidized and occurs as GSH if reduced. These redoxmolecules are selenoproteins and therefore Selen is an indispensable component of the cell. **[26]** The dismutases are dependent on Cu/Zn in the cytosol and Mn in mitochondria. The glutathione system is involved in the promotion of telomerase activity, an enzyme which contains a reverse transcriptase that is responsible for cell division in fast dividing cells like germ cells, white blood cell progenitors, some stem cells and cancer cells. For a healthy organism there has to be a balance in this system. If the GSH concentration is too high this could lead through activation of telomerase to cancer. If the GSSH concentration is too high this will result in damaging cell components due to destruction by free radicals. **[27,28,29]**

V. Combining stress response with provirus activation or Don`t mix up the cause and the outcome

In response to T-cell activation by stimuli like ROS **[30]** NFκB is transported into the nucleus. This process is promoted by several other factors like TRX1 **[31]**, the Mitogen activated kinase (MAPK, JNK) **[32]** , Tumour Necrosis Factor (TNF) **[33]** , and other molecules that are involved in the process. NFκBp50 binds to the LTR of the provirus thus regulating gene expression via HDCA and small RNAs. **[15]**
Small RNAs coded by the provirus might inhibit HDCA binding and induce transcription of m-RNA resulting in translation of proteins. **[34]** HIV-TAT down regulates telomerase activity in the nucleus of human CD4+ T-cells. TAT is released by actually infected T-cells either in vitro or in vivo. **Picomolecular concentrations, promote the growth of activated endothelial or CD4+ T cells. Micromolecular concentrations of extracellular Tat are instead capable of inhibiting antigen-driven T-cell proliferation. [35]** The results show that expression of the provirus genes is sensitive to activation of TAT and the concentration of the TAT protein. In contrast anti provirus medications would be molecules targeted against Pol II and TAT. **[36] HDCA inhibitors are developed as antineoplastic drugs** in cancer thus promoting apoptosis. **[37,38]** To summarize the afore mentioned: We should expect that everybody expresses to some extent the integrated silenced proviral genes.

VI. Pregnancy

Pregnant women have to fight against the foreign antigens of the embryo / fetus in their body as 50% of the genes come from the paternal site. It is estimated that for avoidance of these problems, the immune status of the women shifts from cell-mediated immunity toward humoral immunity. **[39]** This would explain the diminished amount of T-cells and the high concentration of antibodies in the ELISA-Test. They are normally produced from the B-cells during pregnancy. There is evidence that females might fight male transposons through RNA interference in studies concerning Drosophila. **[40]**
Cracken et al. **[41]** state a downregulation of NFκB in T-cells of pregnant women, which is essential for the maintenance of the cytokine profile required for pregnancy success. Thus pregnant women and their fetus or women who have delivered and their newborn babies who test HIV positive might follow the normal biological requirements of an evolutionary process. **[42]** This means being tested HIV positive is a sign for applying a biologically successful tool in the interaction of mother and child survival in the uterus.

VII. How to avoid getting ill

Referring to the afore mentioned the cause of activation of the endogenous retroviral genes that now contribute to our entire genome is oxidative stress. **[43]** Oxidative stress is often caused by infections and an impaired metabolism, because of malnutrition, missing vitamins and micronutritional elements . They are needed for the normal biochemical reactions in the cell which is well documented in textbooks used for teaching in Medical Universities. Selen is part of the selenoenzymes of the glutathione and thioredoxin complex. Thus nutrition and good sanitary conditions as well as pure drinking water and improved living conditions are on the top of the list for preventing diseases specifically in poor regions of the world. Much too high concentrations of vitamins could counteract health because the natural induction of expression of the thioredoxin system depends on a low dosis of ROS **[44]**.

Concerning AIDS diagnosis we have to be aware that most "AIDS patients" might just suffer from glucose deprivation which means hunger **[45,46],** malnutrition, diarrhoea, tuberculosis, malaria and sexually transmitted diseases like chancre and infections by clamydia. Stressful conditions must also be avoided by birth control and use of condoms. Legal and illegal drug abuse as well as some chemical substances like specific pesticides, that are not used in the "Western World" any longer but are exported to "3rd World Countries" are also counteracting to a good health status. As to the WHO- report "What are the key health dangers for children?" Nearly 10 million children under the age of five die each year – more than 1000 every hour – but most could survive threats and thrive with access to simple, affordable interventions. …Malnutrition contributes to more than half of the deaths. … Over 90% of children with HIV are infected through mother- to child transmission, which can be prevented with antiretrovirals as well as safer delivery and feeding practises. … About 20 million children under five worldwide are severely malnourished, which leaves them more vulnerable to illness and early death. About two-thirds of child deaths are preventable through practical, low-cost interventions. WHO is improving child health…". **[47]**
So think about what might promote the life of mother and child and what might do harm!

VIII. If we all work together

Scientists are eagerly discovering the main tools for gene regulation specifically the biology of small RNAs is on the top of concern and might give better insights to gene and cell functions and metabolism. This might help fighting diseases, specifically chronic diseases. The Nobel Prices in Medicine of 2006 and 2007 are due to these outstanding scientific research results. But we are aware, that science can also be prone to error. Thus the freedom of discussing new insights in science and medicine has to be promoted by government, scientists and also the industry for more acceptance.
The P*harmaceutical Industry* is more challenged because of the big variety of diseases that are a threat to human beings.
AIDS committees could teach people in practising a healthy lifestyle and birth control and make the use of condoms more accepted.
People who are diagnosed with AIDS should not trust any test result and not believe in a fate. They should try to improve their health by avoiding "stress factors" and claim for medical care for any disease, which should be provided to everyone. Abuse of legal and illegal drugs are counteracting to health.
Organizations and governments should help to improve the life of poor and under- or malnourished people by enforcing their power. They should also spread the truth.
We are no longer living in the mediocre and the earth is no disc. No reactions like those Galileo Galilei or Giordano Bruno had to suffer from should be possible after the century of enlightenment. We should expect, that the truth is disseminated with joy. And we are obliged to use freedom and responsibility for generating more satisfactory conditions for the life of all people. Scientific knowledge - specifically of medicine - has to be more openly discussed for everybody.
We are responsible for what we do and what we neglect. Spreading anxiety and fear is beneath a democratic and humane society and the main difference between animals and humans is responsibility. We should be proud of the evolution of our character. To combine knowledge with love is the most noble-minded trait we can show.
People should begin to trust more in their own power to improve a healthy life style – also in the "Modern World" and they should start being more interested in creating their own thoughts and decisions for an informed but autonomous way of health and life.
So: Who won the fight? The answer is: All mankind!

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