

GENE OR VIRUS IN HEALTH AND DISEASE: IT`S ALL ABOUT SELF AND NON-SELF

Abstract

In this paper a new paradigm is proposed concerning the gene / virus hypothesis. Ever since the publication of the Human Genome Project (HGP), non protein coding genes have been in focus as regulatory elements in cellular interactions. The “HIV” data are shown to be statistically and not specific for a defined virus. As “HIV sequences” have been demonstrated to be universal in gene bank probes of many species, and can even be found in human chromosome 8, testing for “HIV” has no scientific basis. Stress and nutrition regulate health and disease as well as epigenetic interactions. Evolution is a never-ending process and our ancestors, Neanderthals and Denisovans contributed to human diversity, specifically to the HLA complex. Microorganisms and horizontal gene transfer also made us human by expressing their genes in symbiotic adaption. But they also might be recognized by the immune system as non-self, resulting in attacks. The concept of a virus is discussed as a term, which cannot be defined universally, as it depends on interactive situations. Health is a complex process depending on many environmental factors, even social ones contributing to gene expression and balance of the living system.

- I. The So-Called “HIV-Genome”
- II. “HIV-Sequences“ Are Everywhere
- III. Stress and Evolution
- IV. What HLA Diversity Tells Us
- V. Evolution: Horizontal Gene Transfer and Endogenization
- VI. Gene Expression, Self and Non Self
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I. The So Called “HIV-Genome”

The “HIV sequence database” of the Los Alamos National Laboratories does not indicate a specific sequence of the “virus genome”, but a statistical average value of the so-called genes of HIV from numerous data from the so-called “provirus” [1],[2],[3],[4],[5],[6]:

[1] <http://www.hiv.lanl.gov/content/sequence/HIV/REVIEWS/HXB2.html>

Numbering Positions in HIV Relative to HXB2CG

[2] <http://www.hiv.lanl.gov/content/sequence/HIV/COMPENDIUM/2012/hiv1dna.pdf>

HIV/SIV complete genome

[3] <http://www.hiv.lanl.gov/content/sequence/HIV/COMPENDIUM/2012compendium.html>

HIV sequence compendium 2012

[4] <http://www.hiv.lanl.gov/components/sequence/HIV/sra/sra.comp>

HIV sequence components

[5] <http://www.hiv.lanl.gov/content/sequence/NEWALIGN/align.html>

HIV sequence alignments

[6] <http://www.hiv.lanl.gov/content/sequence/HIV/mainpage.html>

HIV sequence data base

[39] Graphic 1, [40]

Conclusion: “HIV” is not a real existing virus but a statistical construct!

II. “HIV-Sequences“ Are Everywhere

Using a statistical database (BLAST) from Miguel Romero Fernandez-Bravo of March 17th, 2014 he recognized that “HIV-sequences” are found in genome databank probes of many organisms including microorganisms, plants like Zea mays, rice, sesame, in mice and human chromosome 8 as well as in the genome of ancient Homo sapiens neanderthalensis [7]. Humans who tested positive for HIV and were infected by leishmaniasis could be reacting because of “HIV sequences” in Leishmania major. Sequences were also found in malignant tissues of persons not “infected with HIV” whose non tumorous cells were not “HIV contaminated”. Even if the sequences were not of endogenous origin, they would contaminate tests, which make them of no scientific value for finding a virus. There are other studies that found sequences of “HIV” in Human chromosome 8 and plants. [8] / [Graphic 2]

Conclusion: “HIV” sequences are everywhere (at least endogenous in “homo sapiens neanderthalensis”, in human chromosome 8 and tumor tissue), consequently the existence of “HIV” being an infectious exogenous virus has not been proven!

III. Stress And Evolution

As already mentioned in my paper “Reconciliation between Pure Scientists and AIDS-Dissidents: “Could an ancient retrovirus, RNA-interference and stress be the answer to the divergent opinions?” [9] Stress plays an important role for disease and “HIV positive testing”. In addition it has been known for quite some time (Gosh D.) that there is a glucocorticoid receptor binding site in the “HIV” Long Terminal Repeat, which means, that stress hormones are of concern. [10]

Oxidative stress might be the major affecting “HIV” dementia. The authors provide a rationale for antioxidant and neuroprotective therapy. [11]

As Steve W. Cole et al. point out in *Genome Biology* **2007** - “*Social regulation of gene expression in human leukocytes*” influences human health due to the fact that human genome-wide transcriptional activity is altered in association with a social epidemiological risk factor. [12] Impaired transcription of glucocorticoid response genes and increased activity of pro-inflammatory transcription control pathways provide a functional genomic explanation for elevated risk of inflammatory disease in individuals who experience chronically high levels of subjective social isolation.

Stress is a major driving force of evolution, which can lead to changes in adaption or extinction of species (Parson 1991 and 2005) Eviatar Nevo 2011 [13]. As stated in *Conclusions and Prospects at all organized levels of genes, genomes, phenomes, and biomes*, abiotic (thermal, chemical, climatic) and biotic (parasites and pathogens) environmental stressors usually increase genetic and genomic diversity. A high degree of genomic diversity in nature is adaptive as structural, expressional, or regulatory polymorphisms all coping with diverse stresses.

Conclusion: Stress drives disease and fast evolution by inflammation and change of genetic and genomic diversity.

IV. What HLA Diversity Tells Us

The genes, which have a major impact on immunity, are located in the Major Histocompatibility Complex (MHC) also called Human Leukocyte Antigens (HLA) on chromosome 6. For blood transfusion, the blood groups and proteins of the transfused cells in the donation are of concern in respect to rejection reactions, which can induce allergic or even life-threatening conditions, because of incompatibility of proteins from donor to receptor. Thus blood has to be tested for lack of allergic antigens concerning different blood groups. The HLA region is the most polymorphic in the human genome, as it has to adapt evolutionarily to the ever-changing environment (i.e. microbes, nutrition). It is known to harbor most genes that have a relation to gene expression in certain known diseases. Over 70 conditions are listed in the “*Genetics Home Reference*” of the *U.S. National Library of Medicine*, some of which are involved in immune dys-regulation such as Graves disease.

Anti HLA-DR monoclonal antibody results in inhibition of hematopoiesis in canine and human models. Inhibition of hematopoiesis is associated with apoptosis (cell death) in a proportion of marrow cells (cells for renewal of blood cells) as stated by Lee [14]. Thus, antibodies to unmatched HLA proteins can lead to decline of blood cells. Reduced T cell count is diagnosed as a major impact in “HIV infection” and “AIDS”.

Maternal HLA Homozygosity and Mother-Child HLA Concordance Increase the Risk of Vertical Transmission of HIV. [15] JID 2008: 197 (15 April) Mackelprang et al. pp. 1156-1161

As previously reported in my former papers, pregnancy and progesterone have an impact on driving the pregnant women's immune system from cellular immunity to antibody production (T1 to T2 switch). Thus, "infection" might induce increased diversity to the child, which promotes immune fitness by rendering the immune system of the offspring to stimulate more diversity by creating new HLA genes, which is of advantage in response to environmental stimuli from microbes. In this case, nature is protective by stimulating evolution of new genes in the child from a mother, whose HLA diversity is limited by HLA homozygosity.

There is a significant component of heredity in the susceptibility to HIV-1 in identical twins infected with the same viral strain, which progressed at a similar pace, whereas their fraternal twin had a different clinical course (Draenert et al. 2006). [16]

"The infection of the germ line can lead to viral genes becoming inherited in host alleles. A broad range of retroviral and non retroviral virus groups are now recognized as part of modern genomes". [17]. Katzourakis et al. 2010. Endogenous viral elements in animal genomes. [18]

Conclusion: There is a strong impact on the genetic components known as "HIV" which are influenced by the diversity from the genes of the HLA system. The variety of the HLA genes has an impact on health and disease. "HIV" transmission from mother to child might become life promoting for the offspring, leading to new genes for the HLA system. In some constellations allergies might result.

V. Evolution: Horizontal Gene Transfer and Endogenization

The ENCODE Project Consortium. An integrated encyclopedia of DNA elements in the human genome [19] states that at least 80 % of the human genome is involved in significant biological activity, even though most of it is not made up of genes that code for proteins. Important interactions across the entire genome regulate millions of "switches" that affect various ways that different cells interpret the same genetic information.

Horizontal transfer of viral genes to eukaryotic genomes are conserved and expressed in eukaryotic organisms, suggesting that these viral genes are also functional in the recipient genomes. RNA viruses may play significant roles in the evolution of eukaryotes. [20]

It is known that bacteria can transform the mammalian genome in vitro. Riley et al. (2013) propose that this occurs through bacterial genes acquired by somatic cell lateral gene transfer in cancer samples. [21]

New information concerning "HIV" came from Prof: Didier Raoult /Marseille, [22] who proposes, that an HIV cure may occur through HIV endogenization in humans, as observed for many other retroviruses in mammals, rather than clearance of all traces of HIV from human cells which defines viral eradication. Many species including humans, exhibit remnants of other retroviruses in their genomes that question such possible endogenization of HIV. As reported by research from two persons not infected by routine RNA and DNA testing with no signs of disease were found to have integrated inactive "HIV DNA" in their genomes.

The p24 family proteins are regulators of vesicular trafficking as Kaminska et al. from the Institute of Biochemistry and Biophysics in Warsaw, Poland stated in 2010. [23]

Evidence for functional transfer of micro RNA by exosomes comes from the research of Montecalvo et al, who detected it between mouse dendritic cells via exosomes [24]. In a paper by Zhang et al. cloning and sequencing of small RNAs in human serum revealed that plant miRNAs represent about 5% of mammalian miRNAs. [25]. The “HIV” genome is known to encode lncRNAs, miRNAs and vsRNAs [37], [38]. Host and “HIV” RNA regulate each other vice versa. Global Co-evolution of Human Micro RNAs and their Target Genes contributed to higher brain functions, and skills underlying human evolution. The recently evolved human miRNA-941 and its acquired targets showed relatively low conservation, which is consistent with the predicted theories of co-evolution of these elements and mi-RNA in recent human evolution. [26]

Conclusion: Horizontal gene transfer and endogenization of microbial genes, as well as transport of micro RNAs and proteins for different processes between cells and in cellular functions provide a more complex view of gene expression in the evolutionary context. Mammals even harbor plant mi-RNA, which indicates a normal environmental genetic interaction in the evolution of species.

VI. Gene Expression, Self And Non Self

Nutrition has a huge impact on health and disease. As already mentioned in my paper “Reconciliation between Pure Scientists and AIDS-Dissidents: Could an ancient retrovirus, RNA-interference and stress be the answer to the divergent opinions?” Hunger, malnutrition, vitamin deficiencies, and contaminated water attack health, whereas healthy food, pure drinking water, glutathione, vitamins and minerals (i.e. selenium, zinc) promote health. A publication from the Pakistan Journal of Nutrition by Hamid and Masood from the Department of Biochemistry, University of Kashmir, states that food allergies caused by lectins from a variety of different plants like seeds, cereals, potatoes, soya and beans could initiate diseases like celiac disease, autoimmune diseases, rheumatoid arthritis, obesity, cardiovascular disease and insulin dependent diabetes mellitus. [27] They function as both allergens and hem agglutinins and are able to provoke IgM and IgG antibody production. They are blood type specific, highly allergic and alter host resistance to infections. They interact with lymphocytes from the gastrointestinal mucosa and might induce failure to thrive. In addition they might reduce natural killer cell activity directly and through disruption of the intestinal flora, by weakening the body’s most important defenses against invaders. Ingestion of lectins also has major cholecystokinin-mediated effects on gastrointestinal function and growth. Many lectins are powerful allergens and *prohevein*, the principal allergen of rubber latex has been engineered into transgenic tomatoes for its fungi static properties. [28]

It is known that regulatory T-cells (Tregs) control the balance of the immune system through switches between the T1 and T2 reactions. A Treg cell-specific ablation of the E3 ubiquitin ligase *Itch* in mice caused massive multiorgan lymphocyte infiltration and chronic T-cell activation, and the development of severe antigen-induced airway inflammation. [29]

Most of the human genome is transcribed into protein- noncoding RNAs (ncRNAs) including small and long ncRNAs (lncRNAs). “HIV-1” replication relies on various cell functions. More than 200 human genes are necessary for this process. [30]

The lnc RNA *Neat* is essential for the integrity of the nuclear paraspeckle substructure, which is important for “HIV-1” replication. There are many questions that have to be answered including the role of the cellular nucleolus, paraspeckles, lncRNAs (*Neat*) and the replication

of “HIV.” [31] In addition the role of Piwi-interacting RNAs, (piRNAs) which exist in abundance, as recognizing any ever turned on gene as “self” and allows it to be expressed, will be of further interest for future studies. Findings indicate that competing epigenetic pathways generate trans-acting signals that can silence or activate homologous genes. An organism seems to have a memory of all the previous gene sequences it has ever expressed before: piRNAs initiate an epigenetic memory of non-self RNA in the *C.elegans* germline. [32]

Many natural products from plants have long been recognized as excellent sources of new anti-“HIV” drugs, like limonoid and nomilin from Citrus bergamia and betulinic acid from the leaves of *Syzygium claviflorum*. The reverse transcription activity of “HIV-1” can be partly inhibited by aqueous dandelion extract of *Taraxacum officinale*, which augments the potential therapeutic efficacy and has no negative side-effects like many pharmaceutical products [33]

Conclusion: Activation of gene expression, (food) allergy, self and non-self differentiation and application of treatments which do not exhibit side effects in therapeutic treatment might be a more effective way of treating “HIV” named diseases, which might lead to the multiple diseases called “AIDS”. The aforementioned findings provide a new perspective on health and disease.

VII. New Prospects In Science And Epigenetic

If a body produces its own gene packages into protein envelopes and another organism receives them, the particles might be neutral, positive or harmful for the subject. They might be attacked, which identifies the particle as a harmful virus.

If somebody is allergic to pollen or other material (i.e. fish proteins) and another person is not, the first reacts with its immune system maybe through inflammation and the other does not.

The term “virus” is not a clearly defined entity; it is defined by the interaction of a body’s reaction to a non-self particle as described above. If the particle is produced in the body’s own cells, it is not a virus but may be an endosome or exosome in cell communication.

It can be attacked by the body’s own immune system, which defines the reaction as autoimmunity. Health depends on the balance of the interacting partners in self and non-self and thus is very individual as it depends on gene expression, epigenetic, living conditions and mental and spiritual activity. But it is very strongly influenced by social conditions, which promote health if they are recognized as positive. Thus the vaccination concept cannot be universal as individuals are unique in their cellular “equipment” and thus reactions like uncontrolled inflammation or autoimmunity might follow or the procedure might not even be protective for a defined “germ”, which could be identified as unnecessary to be attacked.

To summarize the aforementioned: What is of concern is the reaction between self and non-self. As much as 98% of the human genome that was once named “junk” are now being studied for their contribution to our metabolome specifically in health and disease. Long non coding RNAs and micro RNAs as well as piwi RNAs are of interest. **And we have to take into account, that there is a cytoplasmatic inheritance which comprises a vast number of molecules, natural ingredients in germ cells like free DNA, many RNAs and proteins, interacting in processes of gene regulation and gene expression.** They do not work as sole entities but in harmony. Thus, a gene or molecule cannot be described as a single entity but as a part in a certain context that changes over its lifetime and under evolutionary aspects. You cannot adequately describe the impression of a picture by counting the pixels that comprise it. The music from an orchestra results from multiple interactions and might be played differently at other times by the same persons. This is why we are at the edge of a total new scientific paradigm regarding what creates life, health and disease. It is the **fluent** interaction of millions of components that interact symbiotically when we feel well. The microbial world is the

material we are made of, and so are our brothers and sisters from the human world and the creatures living with us. **Bacteria and other microbes as well as “viruses” (transport particles of genetic material enveloped for protection in a protein core) may exist externally (in the environment), internally (gut and everywhere in the body) and integrated into the genome of the individual, acting as genes.** There they might regulate gene expression and receptor presentation as well as modulation of antibody synthesis in cooperation with other entities. Our microbial world depends on our food, living conditions and social contacts. Without these interactions, natural evolution will be disturbed in a way that counteracts health. If the pace of evolution is too fast (stressful conditions) disease may occur. But after recovery, the immune system and the nervous system, which interact, will show some change by having participated in adaptive learning processes. Findings of Peter Parham indicate that HLA genes have a different origin in populations worldwide. Originally, researchers were investigating HLA genes to determine the role they play in whether or not the body rejects tissue transplants. The final variant of HLA that they sequenced, called HLA-B*73, "surprised us by having an exceptionally unusual sequence, suggesting it might have an archaic origin," according to Peter Parham, an immunogeneticist at Stanford University, as reported to Live Science. The investigators suggest that modern humans, on their exodus from Africa, acquired this odd variant from the Denisovans in west Asia, which may have provided protection and immunity to whoever had it against the local germs in the area at the time. Another HLA gene variant, called HLA-A*11, is absent from African populations, but represents up to 64 percent of versions of the gene in East Asia and Oceania, with the greatest frequency in people from Papua New Guinea. A similar situation is seen in some HLA gene types found in the Neanderthal genome. These variants are common in European and Asian populations, but rare in African populations. "We are finding frequencies in Asia and Europe that are far greater than whole genome estimates of archaic DNA in modern human genomes, which is 1 to 6 percent," said Parham. [36] Within one class of the HLA genes, the researchers estimate that Europeans owe half of their variants to interbreeding with Neanderthals and Denisovans, Asians owe up to 80 percent and Papua New Guineans up to 95 percent. "The likely interpretation was that these HLA class variants provided an advantage to modern humans and so rose to high frequencies", Parham said Aug. 25 2014 /Science). In addition the new scientific research projects, concerning **epigenetic** interactions with the genome, by regulating methylation, acetylation, chromatin remodeling and other processes that might become heritable give new insights to the actions that influence the fate of an organism. [34],[35]. Without the so-called “HIV”-sequences (regulation of gene expression) we would not expand HLA, which is necessary for diversity and adaption to the ever-changing environment.

Conclusion: A virus (translation is “poison”) cannot be defined as a particle. The term depends on an interaction between a non-self particle of a nucleic acid with a core protein, which is transmitted in an exogenous manner that leads to an immune attack response by the receptor organism. It has to be recognized as non-self. As humans (and other living creatures) differ in their genes and specifically in the HLA system of immune recognition, the HLA system is of concern in the so called “fight against invaders”. We need to carefully monitor its place in the process of evolution; for example horizontal gene transfer is a natural process that has acted on evolution for millions of years. The “fight against HIV” and “HIV eradication” might do much harm, as these genes serve to regulate our immune system and its evolutionary development. Cytoplasmatic inheritance is a normal biological concept and has nothing to do with the transmission of a virus. Epigenetic processes should be more in the focus of research. The different RNA molecules and their actions are tremendous. We can fight the so-called “AIDS” diseases, which do not have a common scientific definition, by improving living conditions as explained in my papers and my web-book.

<http://www.christl-meyer-science.net/en/>

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Numbering Positions in HIV Relative to HXB2CG

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HIV/SIV complete genome

[3] <http://www.hiv.lanl.gov/content/sequence/HIV/COMPENDIUM/2012compendium.html>

HIV sequence compendium 2012

[4] <http://www.hiv.lanl.gov/components/sequence/HIV/sra/sra.comp>

HIV sequence components

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HIV sequence alignments

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HIV sequence data base

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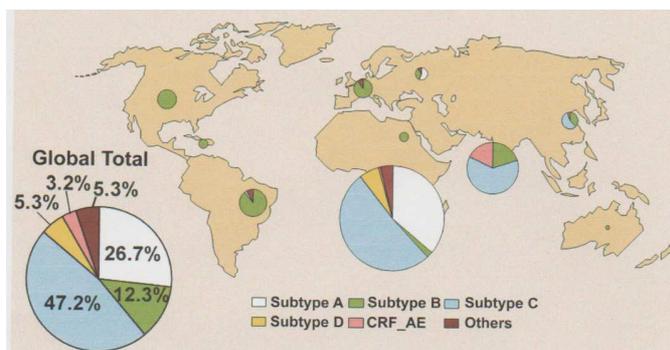
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Graphic 2:

BLAST sequences

Human chromosome 8 / Human Immunodeficiency Virus type 1

NCBI Blast:dbj|D38677.1| (125 letters) 06/02/14 22:52

BLAST®

Basic Local Alignment Search Tool

[NCBI/ BLAST/ blastn suite-2sequences/ Formatting Results - F810M939114](#)
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Blast 2 sequences

dbj|D38677.1| (125 letters)

RID [F810M939114](#) (Expires on 02-08 04:52 am)

Query ID [gi|807799|dbj|D38677.1|](#)
Description HUMCIET171 Human chromosome 8
 Homo sapiens cDNA 5'.

Molecule type rna
Query Length 125

Subject ID [gi|1906382|gb|K03455.1|HIVHXB2CG](#)
Description Human immunodeficiency virus type 1 (HXB2), complete genome; HIV1/HTLV-III/LAV reference genome
[See details](#)

Molecule type nucleic acid
Subject Length 9719
Program BLASTN 2.2.29+

Graphic Summary

Distribution of 1 Blast Hits on the Query Sequence

Description	Max score	Total score	Query cover	E value	Ident	Accession
Human immunodeficiency virus type 1 (HXB2), complete genome; HIV1/HTLV-III/LAV reference genome	119	119	53%	1e-30	99%	K03455.1

Alignments

Human immunodeficiency virus type 1 (HXB2), complete genome; HIV1/HTLV-III/LAV reference genome
 Sequence ID: [gb|K03455.1|HIVHXB2CG](#) Length: 9719 Number of Matches: 1
 Range 1: 6348 to 6414

Score	Expect	Identities	Gaps	Strand	Frame
119 bits(64)	1e-30()	66/67(99%)	0/67(0%)	Plus/Plus	

Features:

```

Query 59  GTACCTGTGTAGAAGGAAGCAACCACCACTCTATTTTGTGCATCAGATGCTAAAGCATAT 118
Sbjct 6348 GTACCTGTGTGGAAGGAAGCAACCACCACTCTATTTTGTGCATCAGATGCTAAAGCATAT 6407

Query 119  GATACAG 125
Sbjct 6408  GATACAG 6414
  
```