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Origin and evolution of viruses: Escaped DNA/RNA sequences as evolutionary accelerators and natural biological weapons

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Summary Knowledge of the origin and evolution of viruses could provide a better understanding of a number of phenomena in the field of evolution such as the origin and development of multi-cellular organisms, the rapid diversification of species over the last 600–700 million years and the lack of transitional forms in the evolution of species (''missing links'') etc. One of the possible effects of escaped DNA/RNA sequences or viruses on the evolution of multi-cellular organisms, especially vertebrates, could be the phenomenon of horizontal transmission and dissemination of genes. Interestingly, if so, this effect could be considered as a model of primeval and natural genetic engineering. Other possible links between the evolution of multi-cellular organisms and viruses are connected with the fact that viruses represent the source of different forms of selective pressure such as epidemics of infectious diseases, autoimmunity, malignant alteration, reproductive efficiency, etc. At the same time, these two models of ''long-term evolutionary relations'' could represent ''key factors'' in the evolution between viruses and multi-cellular organisms. The capability of a genome to produce and emit DNA/RNA sequences or de novo created viruses which can be a vector of genes horizontal transmission and/or cause selective pressure on concurrent or predator species gives a new characteristic to viruses – the possibility of their acting as natural biological weapons. Finally, possibly evolutionary advantages of this genome capability could be one of explanations for the phenomena such as genome instability and its ability to emit DNA/RNA sequences and/or de novo created viruses, as well as evolutionary conservation of this unique phenomena.

The origin and evolution of viruses

In contrast to other microbes and multi-cellular organisms, the origin and evolution of viruses is mostly unknown. Our knowledge concerning their origin is lost in a sea of conjecture and speculations, hardly supported at all with precise scientific evidences. For example, viruses have never been detected as fossil particles, probably because they are too small and too fragile to succumb to fossilization processes. Even in fossilized biological

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materials such as plant leaves or insects in amber, preserved nucleic acid sequences of viruses have never been detected. Hence, evolutionists are limited in their ability to precisely reconstruct an evolutional history of viruses. However, in spite of all the difficulties in understanding their origin and evolution, several theories more or less successfully explain the basic observed facts [1–3].

Due to the fact that the genome of viruses underlies mutation and genetic recombination, viruses probably evolve according to a form of natural selection, very similar to that governing other living things. It seems that this simple fact may well provide enough support for scientific acceptability of several commonly discussed hypotheses on virus origin and evolution. Currently, there are three such hypotheses. The first hypothesis is the so-called theory of ''regressive evolution'', which proposes that viruses descend from free-living and more complex parasites. According to this theory, ancestral viruses developed a growing dependence on host-cell intracellular ''machinery'' through evolutionary time, while retaining the ability to auto-replicate, like mitochondria that have their own genetic information and replicate on their own [2–4]. The second hypothesis is the so-called theory of ''cell origin'', which assumes that viruses reflect their origin from cell DNA and/or messenger RNA, which acquired the ability to auto-replicate, create extracellular virions, exist and function independently. Finally, there is the theory of ''independent'' or ''parallel'' evolution of viruses and other organisms, which assumes that viruses appeared at the same time as the most primitive organisms [1,3,4].

Whatever the advantages and disadvantages of each theory are, the ability of every cell (excluding cells without a nucleus, e.g., the erythrocytes of mammals) to release DNA/RNA sequences or de novo created viruses is unique and amazing. At the same time, the cell's ability to release DNA/RNA sequences shows a high level of evolutionary conservation. These facts might be well enough motifs for identification of positive selective pressure that could be linked with this genome ability, as well as a highly important thesis for better understanding of origin and evolution of viruses, and even life as we know it [3–5]. Several factors of positive selective pressure could play important role in development and evolutionary ''symbiotic'' linking (conservation) of genome and its ''instability'', which is probably responsible for cell ability to emit de novo created viruses: (i) the possibility of horizontal and vertical dissemination of gene blocks, and their incorporation into the cell genome of new hosts; (ii) the possibility of acceleration of evolutionary processes, which could result in rapid diversification of species and sometimes quicker and better adapting to environmental conditions; (iii) the possibility that de novo created viruses can act as natural biological weapons against predator and/or concurrent species.

There are a number of complex molecular life forms that blur the boundaries between cells and viruses. Also, there are pieces of self-replicating genetic material found in bacteria, e.g., episomes, which evolve independently of their hosts, and can even move from one host to another – but carry genetic information that may be toxic or beneficial, even essential, to their host. In the case of the beneficial role of episomes, many bacteria would be unable to reproduce at all without them. Episomes are, in many ways, quite similar to viruses – except that they only reproduce themselves when their hosts do, whereas viruses reproduce themselves hundreds of times, causing disease. According to this way of thinking, viruses probably co-evolve with their hosts, like any ''good parasite''. There appears to be quite a lot of justification for this idea, especially from studies of viruses such as *papilloma* viruses, endogenous retrovirus-like sequences in animal genomes, and *herpes* viruses. For example, the divergences of primates and of birds related to chickens have been traced by comparing the types and sequences of retroviral-derived sequences in their genomes. It has also been repeatedly shown that the closest relatives of human *papillomavirus* types infecting particular tissue types (e.g., cutaneous wart types, genital mucosal types) are those viruses infecting similar tissue types in other primates, indicating that these tissue preferences were well established before the divergence of humanoid apes from the primate line [1,3,4].

Viruses as evolutionary accelerators

The model of living beings evolving based on genome changes and the ability to adapt to positive and/or negative selection pressures is widely accepted among evolutionists. However, it is hard to imagine that the evolution of life is based on accidental and isolated gene mutations and that this model of evolution finally brought about the form of life we know today. One of key arguments against a model of evolution based on the accidental changes of isolated genes is the simple fact that gene mutation is a relatively rare event and hence, according to this model, evolution would be very slow. Many evolutionists argue that life on the Earth would still be at the bacteria and seaweed

stage, if genetic changes were based only on accidental changes of isolated genes. Considering the fact that most mutations are sources of negative selective pressure, the minor percentage of accidental mutations of genes that might cause positive selective pressure, theoretically, could not result in the evolution of living beings and the diversity of species that we know today. Certainly, this opinion does not completely exclude participation of accidental isolated gene changes in the evolutionary processes, but the influence of these events on the evolution of life probably is minimal and marginal [3,4,6].

With the exception of the mutations of isolated genes, several different mechanisms can lead to genome changes. These mechanisms are recombination, transposition, translocations, inversions, deletions, duplications, transduction and other unpredictable, chaotic and yet unremarkable genetic events which, in contrast to mutations, lead to great changes of genome. Significant genetic changes can probably result in ''great evolutionary displacement'' and acceleration of evolutionary processes. Incidentally, this hypothesis might represent an acceptable explanation for the many ''missing links'' in palaeontology and the state of our knowledge regarding the origin of life and species. Put quite simply, what we call the ''missing links'' probably never existed, due to ''rapid'' and large-scale changes which, for as yet unknown reasons, have implicated, from time to time, every living creature in the last billion years. Consequently, we can conclude that the evolution of living beings probably has not been based on gradual and ''fine'' passing forms. In this story, viruses could be an important factor in the theory of ''rapid and big evolutionary steps'' based on great changes of genome. Several mechanisms might be included in this evolutionary scheme: (i) horizontal transmission of genes between individuals of identical or even different species; (ii) vertical transmission of genes and bi-directional vertical transmission between mother and offspring in viviparous species; (iii) genome destabilization and induction of new changes of genome; (iv) increasing genome instability. Finally, the advantages of the rapid evolution of living beings and a possible link of this phenomenon with viruses could be an acceptable explanation for the ''symbiotic'' connection of the genomic ability to emit DNA/RNA sequences and/or de novo created viruses. This phenomenon could lead to evolutionary conservation of genome instability as a universal genome characteristic [6,7].

Recombination is a far more powerful way for DNA to change. This model of genome remodelling takes whole blocks of genes and moves them to different locations. These new locations could be elsewhere in the same genome or in the genome of a different host. One of recombination mechanisms is transduction by viruses that works in both prokaryotic and eukaryotic organisms. The discovery that large blocks of genetic instructions can be swapped and transferred among living beings is a clue that the insertion of new genes could be the mechanism that assists evolution. If viruses can transfer eukaryotic genes across species boundaries, and can install their own genes into their hosts, the case for the new mechanism is even stronger. Viruses do just that [1,3,4,6,7].

Viruses as natural biological weapon

From the standpoint of medical science, instability is a highly undesirable feature of a genome as it is very often a source of malignant alteration of cells, spontaneous abortion, autoimmunity, genetic diseases, emerging and even the re-emerging of new viruses. In contrast to this, speaking in a Darwinian sense, the evolutionary advantages of genome instability are probably more important than potential and real negative consequences of this phenomenon. In addition, emitted DNA/RNA sequences and/or de novo created viruses can operate as natural biological weapons against predator and/or concurrent species. This possibility could also be the source of positive selective pressure supporting evolutionary conservation of features such as genome instability and its ability to emit its own sequences [8–11].

Viruses apparently can, and obviously do, make big jumps in hosts every now and then. It seems almost certain, for example, that *arthropods* are the original source for a number of virus families infecting insects and mammals — such as the *Flaviviridae* — and probably also of viruses infecting insects and other animals and plants — such as the *Rhabdoviridae* and *Reoviridae*. For example, *picornaviruses* of mammals are very similar structurally and genetically to a large number of small RNA viruses of insects and to at least two plant viruses, and — as the insect viruses are more diverse than the mammalian viruses — probably had their origin in some insect that adapted to feed on mammals (or plants) at some distant point in evolutionary time. The majority of existing viruses relevant to humankind are zoonozis. In spite of the fact that animals are the source of many viruses pathogenic to humans, the most important factor in the

dissemination of viruses is the fact that humans live in a manner which increases the possibility of transmission of new viruses from their endogen hosts (animals) to humans. *Rodents* and *arthropods* are also included in transmission of viruses from one species to another, especially in an urban milieu where their vector role is multi-amplified. Other animals, especially primates, represent important sources of viruses potentially pathogenic for humans. In this context, we can mention a few emerging or even re-emerging, new extremely virulent and dangerous viruses which cause diseases such as Ebola, Marburg and Congo-Crimean haemorrhagic fever, Hantavirus lung syndrome, Korean haemorrhagic disease, SARS-Co virus, and of course, HIV1 and HIV2 [1,3,4,7].

HIV is important problem for humankind and also a good example that can support our hypothesis on viruses as natural biological weapons. It is now generally accepted that HIV is a descendant of simian immunodeficiency virus (SIV). Certain simian immunodeficiency viruses bear a very close resemblance to HIV-1 and HIV-2. For example, HIV-2 corresponds to a simian immunodeficiency virus found in the *sooty mangabey* monkey (SIVsm), widely known as the *green monkey*, which is indigenous to western Africa. The more virulent strain of HIV, namely HIV-1, was, until very recently, more difficult to place. The closest counterpart that had been identified was the simian immunodeficiency virus that was known to infect chimpanzees (SIVcpz), but there were significant differences between it and HIV. In addition, it was reported that frozen tissue taken from a chimpanzee carried a simian virus (SIVcpz) which was almost identical to HIV-1. The chimpanzee came from a sub-group of chimpanzees known as *Pan troglodytes troglodytes*, which were once common in west-central Africa. It is claimed by some researchers that this shows that these chimpanzees were the source of HIV-1, and that the virus at some point crossed species from chimpanzees to humans. However, it was not necessarily clear that chimpanzees were the original reservoir for HIV-1 because chimpanzees are only rarely infected with SIVcpz. Also, there is opinion that wild chimps became infected simultaneously with two simian immunodeficiency viruses (SIVs) that had ''viral sex'' to form a third virus capable of infecting humans and causing AIDS [12—15]. Sharp et al. [16] discovered that the chimp virus was an amalgam of the SIV infecting *red-capped mangabeys* and the virus found in greater spot-nosed monkeys. The authors believe that the hybridisation took place inside chimps that had become infected with both strains of SIV after hunting and killing the two smaller species of monkey [16].

The hypothesis that HIV evolved from SIV is based on the many similarities between these two viruses, especially at the genetic level. The two viruses are genetically very similar and are transmitted in the same way. However, HIV only causes AIDS in humans and SIV only causes AIDS in monkeys. The SIV virus, like HIV, is found in blood. This can provide support for the belief that HIV entered man via monkey's blood. For this, possible routes include drinking the blood of monkeys, eating raw monkeys or perhaps direct exposure of humans to monkey blood [13,14,16]. Finally, the possibility of interspecies sexual transmission cannot yet be excluded.

Conclusion

The opinion that viruses simply cause infectious diseases is over-simplified and archaic. Their role in nature and their influence on the evolution of other living things is probably of greater and, even, crucial importance. The ability of a genome to emit de novo created viruses and the evident evolutionary conservation of this property strongly suggests that emitted DNA/RNA sequences could be important in the evolution of life. Practically, this means that viruses could be important sources of positive selection pressure on certain species, thus opening up the possibilities of: (i) horizontal dissemination of genes; (ii) rapid and large-scale evolutionary changes by way of unstable genomes; (iii) a role as biological weapons directed against concurrent and/or predator species.

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