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MOLECULAR STRATEGIES OF VIRAL REPLICATION AND THEIR IMPACT ON THE EVOLUTION OF GENOMES OF CELLULAR ORGANISMS

Abstract

The article explores the fundamental role of viruses as generators of genetic variability and driving force of macroevolutionary processes in the biosphere. Molecular biological strategies of virus replication are analyzed within the paradigm of the Baltimore classification, which considers the genome type as a determinant of transcriptional logic and adaptive potential of viral lineages. Attention is focused on enzymatic replication systems – RNA-dependent RNA polymerase (RdRp) and reverse transcriptase (RT), devoid of an error correction mechanism. It is proven that the high frequency of incorporation of non-complementary nucleotides and structural variability due to template changes lead to the formation of quasispecies – highly dynamic populations of genetically related subvariants, which ensure evolutionary plasticity and survival of the virus under selective pressure.

The molecular mechanisms of viral genome integration into host cell chromosomes as a basic pathway of horizontal gene transfer are outlined. Obligate integration of retroviruses mediated by viral integrases with co-optation of cellular proteins for chromatin navigation are considered, as well as the mechanisms of lysogeny of temperate bacteriophages, which determine the genetic plasticity of prokaryotes and their acquisition of new phenotypic traits (in particular, pathogenicity and stress resistance). The phenomenon of the formation of endogenous viral elements (EVE) because of ancient integrations into eukaryotic germline cells, which became a substrate for the emergence of new regulatory sequences, is described.

Hypotheses of the origin of viruses are synthesized. The concept of polyphyletic origin is asserted, according to which different viral classes evolved independently from distinct predecessors (plasmids, retrotransposons) through horizontal gene transfer, gene loss, and recombination, which makes it impossible to identify a single common ancestor.

The central aspect of the work is the analysis of the consequences of viral-cellular coevolution through the mechanism of molecular exaptation – co-optation of viral genes by host organisms to perform new biological functions. The molecular basis of the formation of morphophysiological structures and immune mechanisms based on integrated viral sequences is presented. Examples are detailed: fusogenic activity of retroviral syncytin proteins during placentation; the origin of the neuronal gene Arc, which provides intercellular communication and synaptic plasticity, from a retrotransposon; the transposon origin of RAG-recombinase enzymes responsible for somatic recombination of gene segments in the vertebrate adaptive immune system; the evolution of the CRISPR-Cas adaptive immune system of bacteria from casposons; the role of endogenous retroviruses in maintaining the pluripotency of embryonic stem cells (HERV-H) and the functioning of their LTR regions as transcriptional enhancers (MER41). It is argued that viruses are a critical architectural element in the formation of genomes and the evolutionary complexity of cellular biological systems.

Keywords: Baltimore classification, virus replication, quasispecies, horizontal gene transfer, endogenous retroviruses, coevolution, molecular exaptation, origin of viruses, endogenous viral elements, gene co-optation.

Introduction

Despite the debatable status of viruses as living organisms in classical biology, in the context of evolutionary studies they are considered full participants in the global exchange of genetic material [1]. Morphological, ecological or pathogenetic criteria have traditionally been used to systematize this diversity. However, in the context of studying replicative strategies and origin, the classification proposed by D. Baltimore is of key importance. The Baltimore classification structures viruses by the type of nucleic acid of the genome and the mechanism of synthesis of template RNA. Each group uses a different molecular strategy for transferring information from the viral genome to the cellular translation apparatus. Class I – double-stranded DNA viruses. The genome is represented by a double-stranded DNA molecule. mRNA synthesis occurs on the viral DNA matrix using cellular or viral DNA-dependent RNA polymerase. Class II – single-stranded DNA viruses. The genome contains a single-stranded DNA molecule. Before transcription begins, cellular DNA polymerases synthesize a complementary strand. The formed double-stranded DNA serves as a template for mRNA synthesis. Class III – double-stranded RNA viruses. The genome consists of double-stranded RNA. mRNA synthesis is conducted exclusively by the viral RNA-dependent RNA polymerase. This enzyme is structurally part of the virion and is transported into the cell during infection. Class IV – positive-sense single-stranded RNA viruses (hereinafter +ssRNA). The genome is represented by the +ssRNA strand. Viral RNA has the polarity of cellular mRNA and is directly translated by the host ribosomes. The primary translation product is the viral RNA-dependent RNA polymerase, which is necessary for further genome replication. Class V – negative-sense single-stranded RNA viruses (hereinafter -ssRNA). The genome contains the -ssRNA chain. This molecule is not capable of direct translation. Synthesis of complementary mRNA catalyzed by viral RNA-dependent RNA polymerase, which is delivered to the cell in a complex with the viral genome. Class VI – single-stranded RNA viruses with reverse transcription. The genome consists of +ssRNA. Viral reverse transcriptase synthesizes double-stranded DNA on the viral RNA template. The synthesized DNA is integrated into the host cell chromosome in the form of a provirus. Transcription of mRNA from the provirus is conducted by cellular RNA polymerases. Class VII – double-stranded DNA viruses with reverse transcription. The genome is formed partially by double-stranded DNA. After penetration into the cell, the genome is repaired by cellular enzymes to a full-fledged double-stranded episomes. Cellular RNA polymerase synthesizes pregenomic RNA. It simultaneously functions as mRNA and a template for the synthesis of new viral DNA genomes by viral reverse transcriptase [2,3].

Each class is an isolated evolutionary strategy for overcoming cellular barriers. Genome type rigidly determines the molecular logic of transcription and replication, which determines the adaptive potential of a particular viral lineage.

1. Molecular mechanisms of generating genetic variability

The high rates of evolution and adaptation of viruses to new environmental conditions or host immune responses are due to the unique structural organization of their genomes and the specificity of their enzymatic replication systems. RNA-dependent RNA polymerase (RdRp) and reverse transcriptase (RT) play a significant role in the generation of genetic diversity of RNA-containing viruses and retroviruses.

In +ssRNA and -ssRNA viruses, replication is mediated by a virus-specific enzyme, RNA-dependent RNA polymerase (RdRp). A fundamental evolutionary feature of RdRp is the lack (with rare exceptions, such as coronaviruses) of 3'-5' exonuclease activity, i.e., an error correction mechanism [4,5]. This leads to a high frequency of incorporation of non-complementary nucleotides during the synthesis of new RNA strands. To compensate for the low fidelity of copying and to optimize the overall replication cycle, +ssRNA viruses have evolved the ability to compartmentalize replication in virus-induced organelles (ROs). The formation of membrane structures such as spherules (*Flaviviridae*), double-membrane vesicles (*Coronaviridae*) or tubules (*Bunyamwera*) serves a dual evolutionary function: local concentration of viral polymerases, helicases and template RNA and spatial isolation of double-stranded replication intermediates. Since the emergence of double-stranded RNA in the cytoplasm is identified by cellular sensors of innate immunity (e.g., RIG-I) as a foreign molecule, and its membrane isolation is necessary to prevent premature triggering of the immune response. a similar strategy of hiding genetic material is also inherent in large DNA viruses that form cytoplasmic virus factories [6].

In turn, in non-segmented -ssRNA viruses, the genome of which is represented by a single continuous RNA molecule instead of separate fragments, adaptation to rapid evolution is realized through the mechanism of competitive

encapsidation. The synthesized antigen (+ chain) is instantly covered with the nucleocapsid protein N directly during synthesis. During normal transcription, the polymerase stops at specific regions of the genome to form individual mRNAs. The binding of the N protein to the newly synthesized RNA physically hides these termination signals from the enzyme. Blocking the signals forces the polymerase to work in a high-processivity mode – the enzyme does not detach from the template and continuously synthesizes a single full-length genome, maintaining the basic level of mutation generation [7]. Retroviruses of the *Retroviridae* family use a different strategy for generating genetic diversity, based on RT activity. In addition to the fact that RT also lacks a repair mechanism and generates point mutations, the algorithm for converting ssRNA to dsDNA itself provirus is a source of structural variability. The process of reverse transcription requires a complex mechanism of template changes, the so-called "jumping". RT initiates synthesis from a tRNA primer at the primer binding site (PBS), reaches the 5'-end, after which the viral RNA region is degraded RNase H. RT then "jumps" to the 3'-end of the template to continue elongation and form long terminal repeats (LTRs). When a cell is co-infected with two different strains of retrovirus, RT can jump between two different genomic RNA molecules. This is the primary molecular mechanism of homologous recombination in retroviruses, leading to the instantaneous emergence of new genetic variants [8,9].

The consequence of the error-prone enzymes (RdRp and RT) combined with rapid replication cycles is the impossibility of fixing a single wild-type genome. Instead, quasispecies are formed – populations of genetically related mutant variants of the virus within a single host [10]. The evolutionary advantage of quasispecies lies in the transition from individual to collective fitness. Mutant variants in a population are capable of complementation. Even lethal or defective genotypes can be maintained in the pool by proteins synthesized by other full-fledged virions in the same cell. The presence of a wide range of subvariants of the viral genome in the composition of a quasispecies provides evolutionary plasticity, allowing the population to instantly adapt to changes in tropism, the action of antiviral drugs, or pressure from the host immune system [11].

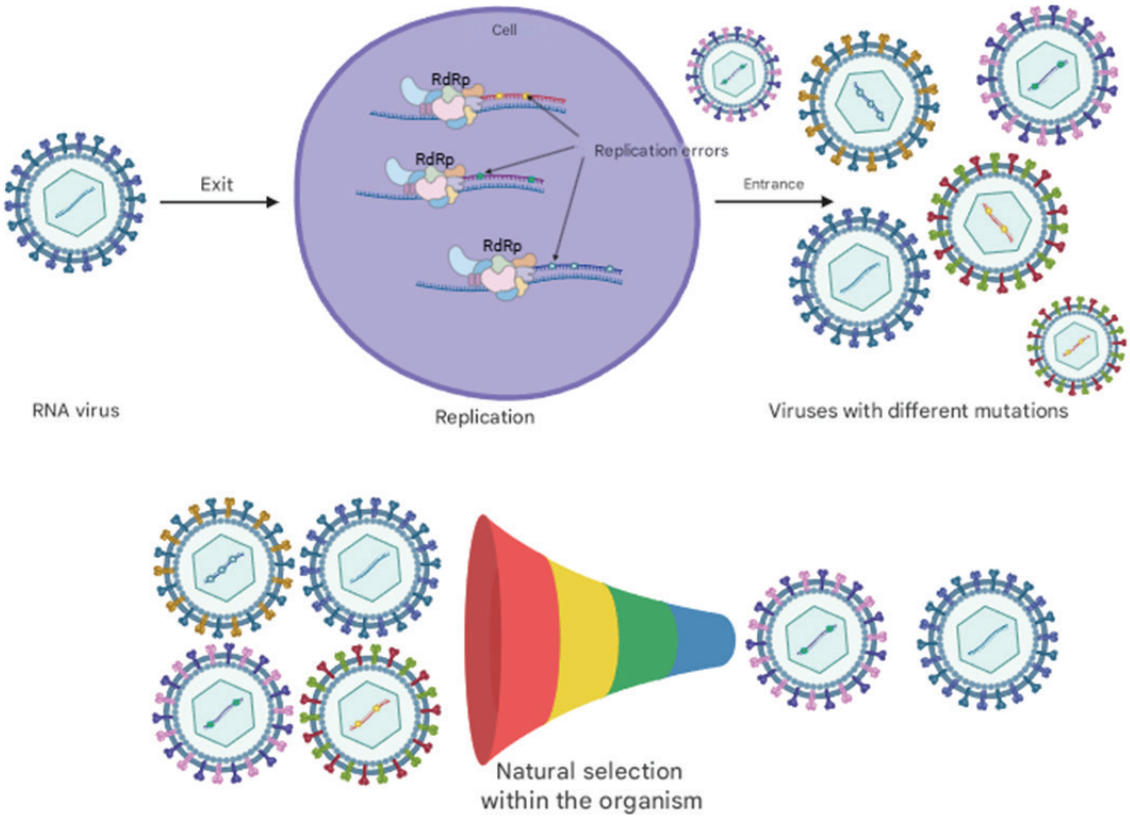

Fig. 1. Scheme of the formation of quasispecies

2. Integration mechanisms and horizontal gene transfer

The ability of viruses to integrate their genetic material into the chromosomes of host cells is one of the main mechanisms of horizontal gene transfer in the biosphere. Depending on the class of viruses, this process may be an obligate step.

For retroviruses, integration of proviral DNA into the host genome is a prerequisite for productive infection. After reverse transcription is completed, a preintegration complex is formed, the key enzyme of which is viral integrase. It conducts 3'-processing of the terminal regions of viral DNA, cleaving two nucleotides from the 3'-ends of both strands to create reactive sticky ends [12,13].

An important evolutionary feature of retroviral integration is its non-randomness: viruses co-opt cellular proteins to navigate chromatin. The integrase of human immunodeficiency virus uses the host factor LEDGF/p75 to direct the provirus to active transcriptional domains, while the murine leukemia virus interacts with BET proteins. Integrase catalyzes a strand transfer reaction, joining the 3'-ends of viral DNA to the 5'-ends of host DNA, after which cellular repair systems fill in single-stranded gaps [12,14].

In prokaryotes, the key agents of horizontal gene transfer are temperate bacteriophages, capable of switching between lytic and lysogenic pathways. The choice of strategy is tightly regulated: the high stability of the viral protein CII activates the synthesis of the repressor CI, which blocks lytic genes and converts the phage into a prophage state. Physical integration of the phage genome into the bacterial chromosome is provided by the viral integrase with the obligatory participation of the bacterial factors IHF and Fis. In the prophage state, the viral DNA replicates passively together with the host genome. Integrated prophages contain genes that change the phenotype of the bacteria [15–18]. Direct evidence is the acquisition of pathogenicity by *Corynebacterium diphtheriae* and *Vibrio cholerae,* which produce diphtheria and cholera toxins exclusively through the expression of genes within integrated prophages. The balance between integration and excision provides the bacteria with dynamic genetic plasticity [19–22].

Unlike retroviruses and temperate phages, eukaryotic ssDNA viruses (*Parvoviridae*) usually do not encode their own integrases and replicate episomally. However, molecular genetic studies have recorded numerous traces of their ancient integration in eukaryotic genomes – endogenous viral elements (EVEs). These sequences were formed as a result of the integration of viral genomes into germline cells with subsequent vertical inheritance. Their presence became the evolutionary material for the emergence of new regulatory sequences and changes in the chromatin architecture in the host genome [23,24].

Endogenous parvovirus elements have been identified in vertebrate genomes – integrated sequences of the *rep* and *cap* genes of ancient parvoviruses, the integration of which occurred approximately more than 30 million years ago [25].

A modern example of the ability of ssDNA viruses to integrate into the genome is adeno-associated virus (AAV), which demonstrates a unique mechanism of site-specific integration into the *AAVS1* locus on human chromosome 19 [26]. The process is initiated by the viral Rep protein, which recognizes the RBS (Rep binding site) and makes a single-strand break, forming a covalent bond with the host DNA and releasing the 3'-OH group. This free end serves as a primer for cellular polymerases, which copy the viral genome by template switching [27].

Integration of viral genes into host genomes provides evolutionary innovations. Sequences that originally served the infectious cycle of the virus acquire new functions in eukaryotic organisms. They become the basis for the formation of new tissues, transcriptional networks, and immune systems. a list of key features of multicellular organisms that arose as a result of horizontal transfer of viral genes is given in Table 1.

3. Evolution of viruses and theories of their origin

The origin of viruses is still a matter of debate. The three main theories of viral origin – the virus world theory, the gene escape theory, and the cellular regression theory – cannot fully explain the origin of the virosphere, as viruses exhibit a huge diversity of both replicative and morphological, infectious, and adaptive strategies.

Therefore, it is impossible to trace their single common ancestor. Accordingly, the theory of the polyphyletic origin of viruses arises, that is, the absence of a single common ancestor, analogous to LUCELLA, the last universal common ancestor, in cellular organisms [43,44]. The diverse groups of viruses most likely arose from different ancestors. ssDNA viruses probably arose several times independently as chimeras: the replication proteins were obtained from plasmids, the capsid proteins from RNA viruses. RNA viruses, Baltimore classes 3–5, are descended from a common ancestor that had an RdRp, but horizontal gene transfer, frequent gene loss or recombination events have divided them into distinct groups. Reverse transcription

Table 1

Key features of multicellular organisms that arose as a result of horizontal transfer of viral genes

Feature (property)	Biological function of the trait	Gene or regulatory element that provides a trait	Virus – gene donor	Source
Placentation in mammals	Fusion of trophoblast cells to form immune tolerance to the embryo	*syncytin-1, syncytin-2*	Endogenous retroviruses *HERV-W, HERV-FRD (env)*	[28]
Placentation in skink-like lizards (*Mabuya*)	Fusogenic activity in the placenta of viviparous lizards	*syncytin-Mab1 (Mab-Env1)*	Endogenous retrovirus *(env)*	[29]
Formation of the myelin sheath in vertebrates	Activation of myelin basic protein (MBP) gene transcription through binding to SOX10 factor	*RNLTR12-int* (non-coding RNA)	Endogenized gammaretrovirus	[30]
Synaptic plasticity and memory in tetrapods	Transport of mRNA between neurons in extracellular vesicles (capsid-like structures)	*Arc*	*Ty3/ gypsy (gag)* family retrotransposon	[31]
Adaptive immunity of jawed vertebrates	Catalysis of V(D)J recombination to generate antibody and T-cell receptor variability	*RAG1, RAG2*	DNA transposon superfamilies *Transib* (transposase)	[32,33]
Pluripotency of primate embryonic stem cells	Recruitment of coactivator complexes, prevention of premature cell differentiation	LTR sequences and long non-coding RNAs	Endogenous retrovirus *HERV-H*	[34]
Adaptation to a starchy diet in hominids	Providing novel tissue-specific promoter for enzyme overexpression in salivary glands	*AMY1* (regulatory region)	Retroviral element *HERV-E*	[35]
Immune regulation in humans	Regulation of immune response genes through STAT1/IRF1-dependent pathways (enhancer activity)	Regulatory area near *AIM2*	Endogenized gammaretrovirus *MER41*	[36]
Antiviral protection of human cells	Physical blocking of the cellular receptor ASCT2 to prevent infection by exogenous retroviruses	*Suppressyn (SUPYN)*	Endogenous retrovirus *HERVH48*	[37]
Development of the feto-placental complex	Trophoblast cell proliferation and differentiation, vascular development, transplantation tolerance	*PEG10, PEG11/RTL1*	Endogenized gammaretroviruses	[38]
Regulation of development and fertility in insects (*Nilaparvata lugens*)	Ensuring normal morphogenesis and reproductive function of grasshoppers	*NlToEVE14*	Endogenized toti-like virus (ToEVE)	[39]
Genomic stability in humans	Involvement in cell cycle regulation and microtubule formation	*EBLN-1, EBLN-2*	Endogenized bornavirus	[40]
Resistance to retroviral infections in mice	Blocking the infectious cycle of murine leukemia virus (MLV) at the post-cell entry stage	*Fv1*	Endogenous retrovirus of *the ERV-L* family *(gag)*	[41]
Immunosuppression by parasitic braconid wasps (*Braconidae*)	Delivery of immunosuppressive genes into the caterpillar body to protect the laid parasitoid eggs	Genes of structural proteins of virus-like particles	Polydnaviruses (derived from nudiviruses)	[42]

viruses, Baltimore classes 6–7, have a common origin from retrotransposons [45]. All three mechanisms have likely occurred in the evolution of diverse groups of viruses.

4. Coevolution of viruses and their hosts

Since viruses are obligatory intracellular parasites and require a cell to carry out their genome, their rate and direction of evolution are directly dependent on the evolution of the host. The evolution of other organisms under the influence of positive selection for resistance to viruses forces them to adapt to infections. As a result, there is a so-called "arms race" between the virus and the host.

Although it is generally accepted that 8% of the human genome is exclusively composed of classical endogenous retroviruses, the total proportion of mobile genetic elements of viral origin is as high as 45% [46]. Ancient integration of retroviruses has provided the molecular basis for the formation of key morphological structures in vertebrates. For example, in placental mammals, syncytin proteins are encoded by the *env* genes of endogenous retroviruses. *HERV-W* and *HERV-FRD.* These viral proteins provide fusogenic activity – the fusion of trophoblast cells with the formation of syncytiotrophoblast and also form the immune tolerance of the mother's body to the embryo. The formation of the myelin sheath of nerve fibers in vertebrates depends on the endogenous retroviral element *RNLTR12-int.* This sequence is transcribed into a non-coding RNA, which binds to the transcription factor *SOX10* and specifically triggers the expression of myelin basic protein (MBP) in oligodendrocytes [30,47].

Viral and subviral elements determine the functioning of higher nervous activity through mechanisms of intercellular communication. The *Arc* gene, important for synaptic plasticity, long-term memory formation and neurocognitive processes in tetrapods, evolved from a retrotransposon of the *Ty3/gypsy* family. The Arc protein has retained the ability to oligomerize, inherent in viral Gag proteins, and forms structures homologous to viral capsids. These capsid-like complexes capture their own mRNA Arc, transported to synaptic terminals and are released into the extracellular space as part of extracellular vesicles. Uptake of these vesicles by neighboring neurons provides horizontal transfer of genetic information, which locally modifies synaptic plasticity without involving the nuclear apparatus of the recipient cell [31].

The adaptive immunity system of jawed vertebrates is based on molecular mechanisms borrowed from mobile genetic elements. The process of V(D)J recombination, which generates antibody and T-cell receptor variability, is catalyzed by the proteins RAG1 and RAG2. These enzymes are derived from the DNA transposase transposon superfamilies *Transib*. Evolutionary transformation has transformed the "cut and paste" mechanism characteristic of autonomous transposons into a regulated process of somatic recombination of gene segments. Instead of mobilizing its own genome, the co-opted RAG transposase specifically recognizes recombination signal sequences (Recombination Signal Sequences – RSS) on host chromosomes, creating double-stranded DNA breaks required for the assembly of unique antigen-recognition receptors [33].

In primates, transcripts of the endogenous retrovirus *HERV-H* constitute a significant fraction of the total RNA pool in embryonic stem cells and are obligatory for the maintenance of a pluripotency state. *HERV-H* long terminal repeats contain binding sites for key pluripotency factors (*OCT4, SOX2, NANOG*) and act as enhancers. Long noncoding RNAs transcribed from *HERV-H* loci serve as molecular scaffolds that recruit coactivator complexes to specific regions of the genome, preventing premature cell differentiation [34].

In the hominid lineage, adaptation to a high-starch diet was accompanied by amplification of the salivary amylase (*AMY1*) gene. Integration of the *HERV-E* retroviral element near the ancestral *AMY1* gene provided a novel tissue – specific promoter that initiated overexpression of the enzyme directly in the salivary glands, whereas the original gene was expressed predominantly in the pancreas. The presence of multiple homologous retroviral sequences at this locus triggered unequal crossing over during meiosis, which ensured an increase in the number of copies of the *AMY1* gene in the human genome [35].

In bacteria, particularly *Escherichia coli,* the presence of integrated prophages critically affects viability and stress resistance. For example, the deletion of nine cryptic prophages from the genome *E. coli* K-12 leads to increased sensitivity of the bacterium to oxidative stress and the action of quinolone antibiotics. At the molecular level, this protection is provided by specific phage genes: Kil protein*,* encoded by prophage *Rac*, during cellular stress, binds to the bacterial protein FtsZ and inhibits its polymerization, thereby blocking cell division and giving the bacteria time to repair damaged DNA. In the process of coevolution, a number of protective mechanisms of viral origin have been formed. The phenomenon of superinfection exclusion is

that the already integrated virus expresses surface or cytoplasmic proteins that physically block host cell receptors or prevent translocation genome of secondary viruses [48,49].

CRISPR-Cas system, which provides adaptive immunity of bacteria against phages, arose through the co-optation of casposons – self-synthesizing DNA transposons. The main adaptation enzyme Cas1, which cuts and integrates new viral spacers into the *CRISPR* locus*,* is an evolutionary descendant of the casposon transposase, which has lost the ability to move autonomously, but has retained endonuclease activity for the directed incorporation of foreign DNA fragments [50].

Conclusions

Viral replication generates fundamental genetic variability in the biosphere. The constant accumulation of viral mutations leads to the formation of quasispecies. Quasispecies ensure continuous adaptation of the virus to the host's selective pressure. The mechanisms of integration of viral genomes into the genomes of other organisms provide global horizontal gene transfer. The coevolution of viruses and hosts is realized through molecular exaptation. Viral elements are the structural basis for the emergence of complex aromorphoses. The molecular logic of viral replication directly determines the macroevolutionary complexity of cellular organisms.

References

1. Stefano GB, Kream RM. Viruses Broaden the Definition of Life by Genomics Incorporation of Artificial Intelligence and Machine Learning Processes. Curr Neuropharmacol. 2022 Oct;20(10):1888-93. doi: 10.2174/1570159X20666220420121746
2. Baltimore D. Expression of animal virus genomes. Bacteriol Rev. 1971 Sept;35(3):235-41. doi: 10.1128/br.35.3.235-241.1971
3. Koonin EV, Krupovic M, Agol VI. The Baltimore Classification of Viruses 50 Years Later: How Does It Stand in the Light of Virus Evolution? Microbiol Mol Biol Rev. 2021 Aug 18;85(3): e00053-21. doi: 10.1128/MMBR.00053-21
4. Jia H, Liu S, Rao G, Liu Q, Wu J, Cao S, et al. An evolutionarily unique viral RdRP suggests a common dual function feature of the priming element. Sci Adv. 2025. Apr 18;11(16):eadv9640. doi: 10.1126/sciadv.adv9640
5. Ghosh S, Biswas S, Mohanty R, Misra N, Suar M, Kushwaha GS. Structural and Phylogenetic Analysis on the Proofreading Activity of SARS-CoV-2. Curr Microbiol. 2025 Apr;82(4):149. doi: 10.1007/s00284-025-04130-3
6. Deng H, Cao H, Wang Y, Li J, Dai J, Li LF, et al. Viral replication organelles: the highly complex and programmed replication machinery. Front Microbiol. 2024 Jul 31;15:1450060. doi: 10.3389/fmicb.2024.1450060
7. Ortín J, Martín-Benito J. The RNA synthesis machinery of negative-stranded RNA viruses. Virology. 2015 May;479-480: 532-44. doi: 10.1016/j.virol.2015.03.018
8. Pedersen FS, Mikkelsen JG. Retroviral Replication. In: Encyclopedia of Life Sciences [Internet]. 1st ed. Wiley; 2021 [cited 2026 Apr 08]. p. 1-12. Available at: https://onlinelibrary.wiley.com/doi/10.1002/9780470015902.a0029306 doi: 10.1002/9780470015902.a0029306
9. Heng X, Herrera AP, Song Z, Boris-Lawrie K. Retroviral PBS segment sequence and structure: Orchestrating early and late replication events. Retrovirology. 2024 Jun 17;21(1):12. doi: 10.1186/s12977-024-00646-x
10. Domingo E. QUASISPECIES. In: Encyclopedia of Virology [Internet]. Elsevier; 1999 [cited 2026 Apr 08]. p. 1431-6. Available at: https://linkinghub.elsevier.com/retrieve/pii/B0122270304002405 doi: 10.1006/rwvi.1999.0240
11. Sardanyés J, Perales C, Domingo E, Elena SF. Quasispecies theory and emerging viruses: challenges and applications. Npj Viruses. 2024 Nov 14;2(1):54. doi: 10.1038/s44298-024-00066-w
12. Lesbats P, Engelman AN, Cherepanov P. Retroviral DNA Integration. Chem Rev. 2016 Oct 26;116(20):12730-57. doi: 10.1021/acs.chemrev.6b00125
13. Suzuki Y, Craigie R. The road to chromatin – nuclear entry of retroviruses. Nat Rev. Microbiol. 2007 Mar;5(3):187-96. doi: 10.1038/nrmicro1579
14. Desfarges S, Ciuffi A. Retroviral Integration Site Selection. Viruses. 2010 Jan 12;2(1):111-30. doi: 10.3390/v2010111
15. Feiss M. Cohesive Ends. In: Reference Module in Life Sciences [Internet]. Elsevier; 2022 [cited 2026 Apr 08]. p. B9780128225639000536. Available at: https://linkinghub.elsevier.com/retrieve/pii/B9780128225639000536 doi: 10.1016/B978-0-12-822563-9.00053-6
16. Casjens SR, Hendrix RW. Bacteriophage lambda: Early pioneer and still relevant. Virology. 2015 May;479-480:310-30. doi: 10.1016/j.virol.2015.02.010
17. Gabig M, Obuchowski M, Srutkowska S, Wegrzyn G. Regulation of replication of λ phage and λ plasmid DNAs at low temperature. Mol Gen Genet. 1998;258(5):494-502. doi: 10.1007/s004380050760
18. Fokine A, Rossmann MG. Molecular architecture of tailed double-stranded DNA phages. Bacteriophage. 2014 Apr;4(2): e28281. doi: 10.4161/bact.28281
19. Kimsey HH, Waldor MK. CTXφ immunity: Application in the development of cholera vaccines. Proc. Natl Acad Sci. 1998 Jun 09;95(12):7035-9. doi: 10.1073/pnas.95.12.7035
20. Safa A, Sultana Jime J, Shahel F. Cholera toxin phage: structural and functional diversity between *Vibrio cholera* biotypes. AIMS Microbiol. 2020;6(2):144-51. doi: 10.3934/microbiol.2020009
21. Buck G, Groman N, Falkow S. Relationship between β converting and γ non-converting corynebacteriophage DNA. Nature. 1978 Feb;271(5646):683-5. doi: 10.1038/271683a0
22. Parveen S, Bishai WR, Murphy JR. *Corynebacterium diphtheriae*: Diphtheria Toxin, the *tox* Operon, and Its Regulation by $Fe2^{+}$ Activation of apo-DtxR. Fischetti VA, Novick RP, Ferretti JJ, Portnoy DA, Braunstein M, Rood JI, editors. Microbiol Spectr. 2019 July 19;7(4):7.4.4. doi: 10.1128/microbiolspec.GPP3-0063-2019
23. Feschotte C, Gilbert C. Endogenous viruses: insights into viral evolution and impact on host biology. Nat Rev. Genet. 2012 Apr;13(4):283-96. doi: 10.1038/nrg3199
24. Rybicki EP. Virus genomes and their replication. In: Cann's Principles of Molecular Virology [Internet]. Elsevier; 2023 [cited 2026 Apr 08]. p. 125-66. Available at: https://linkinghub.elsevier.com/retrieve/pii/B9780128227848000040 doi: 10.1016/B978-0-12-822784-8.00004-0
25. Belyi VA, Levine AJ, Skalka AM. Sequences from Ancestral Single-Stranded DNA Viruses in Vertebrate Genomes: the *Parvoviridae* and *Circoviridae* Are More from 40 to 50 Million Years Old. J Virol. 2010 Dec;84(23):12458-62. doi: 10.1128/JVI.01789-10
26. Maurer AC, Weitzman MD. Adeno-Associated Virus Genome Interactions Important for Vector Production and Transduction. Hum Gene Ther. 2020 May;31(9-10):499-511. doi: 10.1089/hum.2020.069

27. Krupovic M, Forterre P. Single-stranded DNA viruses employ a variety of mechanisms for integration into host genomes. Ann NY Acad. Sci. 2015 Apr;1341(1):41-53. doi: 10.1111/nyas.12675
28. Mi S, Lee X, Li X ping, Veldman GM, Finnerty H, Racie L, et al. Syncytin is a captive retroviral envelope protein involved in human placenta morphogenesis. Nature. 2000 Feb;403(6771): 785-9. doi: 10.1038/35001608
29. Cornelis G, Funk M, Vernochet C, Leal F, Tarazona OA, Meurice G, et al. An endogenous retroviral envelope syncytin and its cognate receptor identified in the viviparous placenta *Mabuya* lizard. Proc Natl Acad Sci. 2017 Dec 19;114(51). doi: 10.1073/pnas.1714590114
30. Ghosh T, Almeida RG, Zhao C, Mannioui A, Martin E, Fleet A, et al. A retroviral link this vertebrate myelination through retrotransposon-RNA-mediated control of myelin gene expression. Cell. 2024 Feb;187(4):814-30.e23. doi: 10.1016/j.cell.2024.01.011
31. Pastuzyn ED, Day CE, Kearns RB, Kyrke-Smith M, Taibi AV, McCormick J, et al. The Neuronal Gene Arc Encodes a Repurposed Retrotransposon Gag Protein that Mediates Intercellular RNA Transfer. Cell. 2018 Jan;172(1-2):275-288.e18. doi: 10.1016/j.cell.2017.12.024
32. Roth DB, Craig NL. VDJ Recombination. Cell. 1998 Aug;94(4):411-4. doi: 10.1016/S0092-8674(00)81580-9
33. Kapitonov VV, Jurka J. RAG1 Core and V(D)J Recombination Signal Sequences Were Derived from *Transib* Transposons. Nemazee D, editor. PLoS Biol. 2005 May 24;3(6):e181. doi: 10.1371/journal.pbio.0030181
34. Lu X, Sachs F, Ramsay L, Jacques PÉ, Göke J, Bourque G, et al. The retrovirus HERVH is a long noncoding RNA required for human embryonic stem cell identity. Nat Structure Mol Biol. 2014 Apr;21(4):423-5. doi: 10.1038/nsmb.2799
35. Ting CN, Rosenberg MP, Snow CM, Samuelson LC, Meisler MH. Endogenous retroviral sequences are required for tissue-specific expression of a human salivary amylase gene. Genes Dev. 1992 Aug;6(8):1457-65. doi: 10.1101/gad.6.8.1457
36. Chuong EB, Elde NC, Feschotte C. Regulatory evolution of innate immunity through co-option of endogenous retroviruses. Science. 2016 Mar 04;351(6277):1083-7. doi: 10.1126/science.aad5497
37. Frank JA, Singh M, Cullen HB, Kirou RA, Benkaddour-Boumzaouad M, Cortes JL, et al. Evolution and antiviral activity of a human protein of retroviral origin. Science. 2022 Oct 28;378(6618):422-8. doi: 10.1126/science.abq7871
38. Ono R, Nakamura K, Inoue K, Naruse M, Usami T, Wakisaka-Saito N, et al. Deletion of *Peg10*, an imprinted gene acquired from a retrotransposon, causes early embryonic lethality. Nat Genet. 2006 Jan;38(1):101-6. doi: 10.1038/ng1699
39. Huang HJ, Li YY, Ye ZX, Li LL, Hu QL, He YJ, et al. Co-option of a non-retroviral endogenous viral element in planthoppers. Nat Commun. 2023 Nov 09;14(1):7264. doi: 10.1038/s41467-023-43186-2
40. Horie M, Honda T, Suzuki Y, Kobayashi Y, Daito T, Oshida T, et al. Endogenous non-retroviral RNA virus elements in mammal genomes. Nature. 2010 Jan;463(7277):84-7. doi: 10.1038/nature08695
41. Best S, Tissier PL, Towers G, Stoye JP. Positional cloning of the mouse retrovirus restriction gene *Fvl*. Nature. 1996. Aug; 382(6594):826-9. doi:10.1038/382826a0
42. Bézier A, Annaheim M, Herbinière J, Wetterwald C, Gyapay G, Bernard-Samain S, et al. Polydnaviruses of Braconid Wasps Derive from an Ancestral Nudivirus. Science. 2009 Feb 13; 323(5916):926-30. doi: 10.1126/science.1166788
43. Villarreal LP. Evolution of Viruses. In: Encyclopedia of Virology [Internet]. Elsevier; 2008 [cited 2026 Apr 08]. p. 174-84. Available at: https://linkinghub.elsevier.com/retrieve/pii/B9780123744104007068 doi: 10.1016/B978-012374410-4.00706-8
44. Krupovic M, Dolja VV, Koonin EV. Origin of viruses: primordial replicators recruiting capsid from hosts. Nat Rev. Microbiol. 2019 Jul;17(7):449-58. doi: 10.1038/s41579-019-0205-6
45. Koonin EV, Dolja VV, Krupovic M, Varsani A, Wolf YI, Yutin N, et al. Global Organization and Proposed Megataxonomy of the Virus World. Microbiol. Mol Biol Rev. 2020 May 20;84(2): e00061-19. doi: 10.1128/MMBR.00061-19
46. International Human Genome Sequencing Consortium, Whitehead Institute for Biomedical Research, Center for Genome Research; Lander ES, Linton LM, Birren B, Nusbaum C, et al. Initial sequencing and analysis of the human genome. Nature. 2001 Feb 15;409(6822):860-921. doi: 10.1038/35057062
47. Kaján GL, Doszpoly A, Tarján ZL, Vidovszky MZ, Papp T. Virus-Host Coevolution with a Focus on Animal and Human DNA Viruses. J Mol. Evol. 2020 Jan;88(1):41-56. doi: 10.1007/s00239-019-09913-4
48. Wang X, Kim Y, Ma Q, Hong SH, Pokusaeva K, Sturino JM, et al. Cryptic prophages help bacteria cope with adverse environments. Nat Commun. 2010 Dec 21;1(1):147. doi: 10.1038/ncomms1146
49. Haeusser DP, Hoashi M, Weaver A, Brown N, Pan J, Sawitzke JA, et al. The Kil Peptide of Bacteriophage λ Blocks *Escherichia coli* Cytokinesis via ZipA-Dependent Inhibition of FtsZ Assembly. Kearns DB, editor. PLoS Genet. 2014 Mar 20;10(3):e1004217. doi: 10.1371/journal.pgen.1004217
50. Krupovic M, Makarova KS, Forterre P, Prangishvili D, Koonin EV. Casposons: a new superfamily of self-synthesizing DNA transposons at the origin of prokaryotic CRISPR-Cas immunity. BMC Biol. 2014 Dec;12(1):36. doi: 10.1186/1741-7007-12-36

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МОЛЕКУЛЯРНІ СТРАТЕГІЇ ВІРУСНОЇ РЕПЛІКАЦІЇ ТА ЇХНІЙ ВПЛИВ НА ЕВОЛЮЦІЮ ГЕНОМІВ КЛІТИННИХ ОРГАНІЗМІВ

У статті досліджено фундаментальну роль вірусів як генераторів генетичної мінливості та рушійної сили макроеволюційних процесів у біосфері. Проаналізовано молекулярно-біологічні стратегії реплікації вірусів у межах парадигми Балтиморської класифікації, яка розглядає тип геному як детермінанту транскрипційної логіки та адаптаційного потенціалу вірусних ліній. Увагу сфокусовано на ферментативних системах реплікації – РНК-залежній РНК-полімеразі (RdRp) та зворотній транскриптазі (RT), позбавлених механізму корекції помилок. Доведено, що висока частота інкорпорації некомплементарних нуклеотидів та структурна мінливість унаслідок зміни матриць призводять до формування квазівидів – високодинамічних популяцій генетично споріднених субваріантів, які забезпечують еволюційну пластичність та виживання вірусу в умовах селективного тиску.

Окреслено молекулярні механізми інтеграції вірусного геному в хромосоми клітин-хазяїв як базовий шлях горизонтального перенесення генів. Розглянуто облігатну інтеграцію ретровірусів, опосередковану вірусними інтеразами з кооптацією клітинних білків для навігації по хроматину, а також механізми лізогенії помірних бактеріофагів, які зумовлюють генетичну пластичність прокаріотів і набуття ними нових фенотипових ознак (зокрема патогенності та стійкості до стресів). Описано феномен утворення ендогенних вірусних елементів (EVE) унаслідок стародавніх інтеграцій у клітини зародкової лінії еукаріотів, що стали субстратом для виникнення нових регуляторних послідовностей.

Узагальнено гіпотези походження вірусів. Стверджується концепція поліфілетичного походження, згідно з якою різні вірусні класи еволюціонували незалежно від відмінних попередників (плазмід, ретротранспозонів) унаслідок горизонтального перенесення генів, втрати генів та рекомбінацій, що унеможливлює ідентифікацію єдиного спільного предка.

Центральним аспектом роботи є аналіз наслідків вірусно-клітинної коеволюції через механізм молекулярної екзаптації – кооптації вірусних генів організмами-хазяями для виконання нових біологічних функцій. Наведено молекулярну базу формування морфофізіологічних структур та імунних механізмів на основі інтегрованих вірусних послідовностей. Деталізовано приклади: фузогенна активність ретровірусних білків синцитинів у процесі плацентації; походження нейронального гена *Arc*, що забезпечує міжклітинну комунікацію та синаптичну пластичність, від ретротранспозона; транспозонне походження ферментів RAG-рекомбінази, відповідальних за соматичну рекомбінацію генних сегментів у системі адаптивного імунітету хребетних; еволюція адаптивної імунної системи бактерій CRISPR-Cas від каспозонів; роль ендогенних ретровірусів у підтриманні плюрипотентності ембріональних стовбурових клітин (*HERV-H*) та функціонування їхніх LTR-ділянок як транскрипційних енхансерів (*MER41*). Обґрунтовано, що віруси є критичним архітектурним елементом у формуванні геномів та еволюційному ускладненні клітинних біологічних систем.

Ключові слова: Балтиморська класифікація, реплікація вірусів, квазівиди, горизонтальне перенесення генів, ендогенні ретровіруси, коеволюція, молекулярна екзаптація, походження вірусів, ендогенні вірусні елементи, кооптація генів.

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