Mini-Review Article

Introduction of RNA virus evolution

Hoorieh Soleimanjahi[1*], Taravat Bamdad[1], Elham Ahmadi[1]

[1] Department of Virology, Faculty of Medical Sciences, Tarbiat Modares University, Tehran, Iran

Received: March 6, 2015; Accepted: April 20, 2015

Abstract

Several viruses, in particular RNA viruses, have high mutation rates and relatively short generation times. Particle stability during infection in nature or in laboratory triggers the evolutionary event toward different mechanisms such as genome segmentation, point mutation and recombination. The frequency of mutant genomes increase and modify the previous distribution, which, consequently, lead to emergence of a new infectious particle. Mutation and selection are the most fundamental processes in evolution. High mutation rate of RNA viruses has an important role in viral fitness. Therefore, it increase our understanding about molecular biology of viral infections and their evolution by selection, mutation could reliably determine our ability to challenge destructive viruses. This review focuses on existing impressions of genetic organization and mechanisms of RNA viruses evolution.

Keywords: Evolution, Molecular biology, RNAvirus

***Corresponding Author:** Hoorieh Soleimanjahi. Tel: (+98) 21-82883561; Email: soleim_h@modares.ac.ir

Please cite this article as: Soleimanjahi H, Bamdad T, Ahmadi E. Introduction of RNA virus evolution. Arch Med Lab Sci. 2015;1(1):37-41.

Introduction

The rise of emerging viruses is rooted in their evolutionary power , so they evolve much faster than antiviruses. The most emergent diseases are recently described or raised in their predominance. The RNA viruses are able to generate mutations for adaptation in new environments (e.g, new host), therefore the reason why most RNA viruses are most comparable to new diseases, originates from their basic evolutionary power. Viruses can jump from species to species which is a way to make them more virulent and in some cases in a new host, a new disease may occur. Some of the viruses have been around for a long time with continual threat to human health such as rotaviruses, and some viruses such as HIV and SARS are somewhat new recognized viruses. Although HIV has been recognized in a monkey infected with virus and the SARS relatives could infect various animals, these viruses were completely new when encountered human. So they are completely novel and it is difficult to predict what those are going to be [1]. Understanding the origin and evolution of viruses is important issue because evolution gives us some rules and helps to predict the potential risk for various diseases. If we know how viruses and other pathogens evolve, we are better able to treat them and this helps to protect us from new emerging diseases. Another important reason to study evolution is development of vaccines that prevents transmission and studying drug resistance strains, which may emerge during therapy [1-4].

In recent years, the interest of evolutionary biologists in the mechanisms, consequences and evolution of genetic robustness has been revived by new and powerful techniques that allow the tracking and manipulation of viruses. RNA viruses have elevated mutation rates to increase their adaptability. RNA viruses provide unique insights into the patterns and processes of evolutionary change in real time [1, 2].

Mechanisms of virus evolution

In 19th century, viruses have been extensively recognized as disease-causing agents. Virus-mediated diseases have motivated molecular biologists to intensively study these pathogenic agents in order to find ways to eradicate them. As a result, many of the important findings of modern molecular biology have been derived from extensive work on the interaction between viruses and their host cells. As a known fact, understanding the evolution remains one of the most challenging problems in biology and need to prompt understanding of the origin of viruses [3]. Although the significant advances in metagenomic surveys of viral biodiversity and what the results might mean for viral origins, a more detailed exploration of the virosphere should certainly be a main research concern. It has become increasingly clear that many RNA viruses have the capacity to exchange genetic material with one another, and to acquire genes from their hosts [4]. In addition to production of mutations (raw material of evolution), these viruses also possess mechanisms in order to eliminate parts of their genomes with accumulative venomous changes and to create beneficial combinations of mutations in an efficient manner. The phenotypic similarities and homologies among diverse types of viruses are a common subject in viral origins. Fundamental mechanisms of viral evolution such as the error-prone nature of RNA-based replication and what this means for the evolution of genome size and complexity, can shed light on the ancestry of viruses [4]. Two distinct but not mutually exclusive types of genetic exchange take place in RNA viruses. Firstly, genetic reassortment which occurs between multipartite viruses involves transaction one or more of the discrete RNA molecules of the segmented viral genome. The second main process, recombination, can occur in either segmented or unsegmented viruses when `donor' nucleotide sequence is introduced into a single, flanking acceptor' RNA molecule to produce a new RNA containing genetic information from more than one source. Both recombination and reassortment occur at highly variable frequencies in RNA viruses [4,5]. In the present study, we review some present opinions on the evolutionary aspects of RNA viruses, and focus on the different mechanisms and factors that might explain the evolutionary forces in RNA viruses. Viruses usually have been marginalized from evolutionary biology and despite advances of various aspects of virus evolution, tracing the origin of viruses is difficult. Also study of RNA viruses has direct useful implications in virus researches. Therefore, the evolution and emergence of RNA viruses might be as a good starting point for people with background in evolutionary biology [4, 6].

Mechanisms of RNA viruses recombination

Rates of recombination vary dramatically among RNA viruses. Recombination has been associated with the expansion of viral host range, increase or decreases in virulence, the evasion of host immunity and the evolution of resistance to antivirals. However, the evolutionary reasons for its occurrence remain uncertain. Recombination is favored by natural selection to eliminate deleterious mutations or create well adapted genotypes. Recombination can take place either within a single genomic segment as RNA recombination or exchange of entire genomic segments between segmented viruses as reassortment. ‘Copy choice’ recombination is the most widely accepted model of RNA recombination. In this process, RNA-dependent RNA polymerase (RdRP) in most RNA viruses, and reverse transcriptase (RT) in retroviruses switched from one RNA molecule (donor) to another (acceptor), by this means generating an RNA molecule with mixed ancestry. Various factors influence template switching (i.e secondary structure) [5, 7, 8]. RNA recombination is ‘homologous’ when occurs between sequences with high similarity, and ‘non-homologous’ when two non-related RNA molecules are involved, that often produce deleterious genotypes. It should be noted that defective interfering particles (DIP), observed in most viruses, contain shortened viral genomes, and are probably produced through a copy choice mechanism, depending on low processivity of RNA polymerases [7].

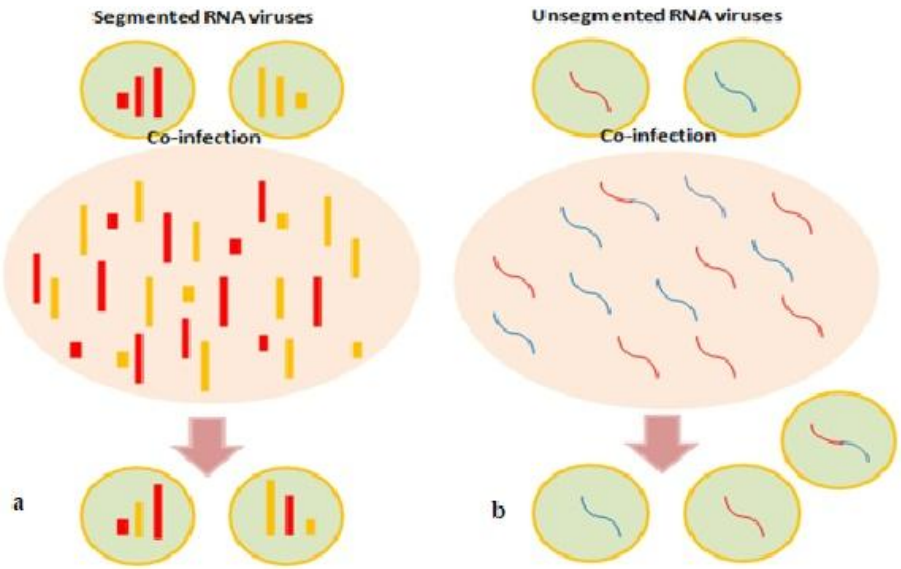

Figure 1. Co-infection of a cell by genetically distinct viral strains can lead to the generation of recombinant viruses. This process can occur in both non-segmented and segmented viruses. a. reassortment, b. recombination.

Mutation

RNA viruses have a high mutation rate between living species due to distinctive style of replication, especially mediating their RNA polymerase and reverse transcriptase which do not have a proofreading function. This disability considerably increases the number of random genetic changes introduced into viral genomes [3].The mutation rate is a feature that can be developed by natural selection, and explained by diverse aspects of viral biology, such as genomic architecture and replication speed. Viruses have very small and compact genomes, short generation times and extremely large populations and hypersensitivity to deleterious mutations which make them to be more potential for mutation [7, 9, 10]. Most mutations have harmful fitness effects, however, as a fact, by increasing the size of genome, the rate of mutation and production of beneficial mutations increase. There is a strongly inverse association between mutation rate in the time of genome replication and genome size, although there is evidence of abnormally low or high mutation rate for a specific genome size, which suggests that mutation rate is a optimized features by opposing selection pressures. High rate of mutation usually results in fitness loss while, low rate mutation is more probable to increase the fitness in nature [4, 7].Therefore, it is expected that any increase in genome size and complexity result in reduction of error rate or a buffering state against the effect of deleterious mutations (i.e., mutational robustness). Significantly, RNA viruses are still undergoing mutation and despite the application of chemical mutagens inducing fitness losses, error rates have been progressively reduced over evolutionary time. On the other hand, faster replication of RNA viruses along with rather short genomes size migh is favored by natural selection. The balance among the generation of mutants and the action of selection leads to a dynamic population structure, known as 'quasi-species' [4, 11].

Mechanisms of genetic robustness in RNA viruses

If RNA viruses show high mutation rate, how do they face deleterious mutations? Although at the first glance, it might sound paradoxical, high rate of mutation results in robustness at the population level. The efficacy of deleterious allele elimination or contribution of more suitable mutations by natural selection depends on population size. It was shown that more crowded lineages might become more robust at the population level, while individual sensitivity to

mutation is usually increased. This strategy relies on the efficient elimination of mutated genotypes in population and the preservation of the non-mutated genotypes. The evidence suggests that during RNA virus evolution, the fitness of RNA viruses increases. Robustness is defined as a reduced sensitivity to perturbations (inheritable) affecting phenotypic expression [8, 12]. Because a strong effect can be produce by mutations, in the presence of redundancy and buffering mechanisms as a consequence of adaptation, the fitness of genomes is only mildly affected. Robustness may occur when several copies of a single gene are existing such as what seen in retroviruses, when several genes contribute to the same function or through biochemical mechanisms. Gene duplication, rearrangement, polyploidy, use of alternative pathways or involvement different chaperone proteins may compensate the lost function. In principle, genetic robustness may differ from individual to individual and has a heritable basis which affects the probability of survival. In general, the selection pressure for increasing robustness depends on the rate of mutations [8, 12] .

Beside these mechanisms, host variation and environmental conditions often have a strong effect on fitness. Differences in cell types and tissues within a given host, differences in host species, or the presence/absence of antiviral responses, seasonal cycles of infectious diseases all represent instances of host and environmental heterogeneity [8, 13].

Reassortment

Reassortment is the second form of genetic exchange that has been described in RNA viruses. It is restricted to segmented viruses, as it involves packaging of segments with different ancestry into a single virion. In RNA recombination, reassortment requires a cell to be infected with more than one virus, although reassortment does not require the physical proximity of parental genomes during replication. It is hypothesized that segmented viruses have been arosen following co-infection of a single cell by two or more viruses, which through complementation they evolved to be functional together [7]. The genome packaging of different segmented viruses is not entirely a random process. Many positive-sense single-stranded RNA ((+)ssRNA) plant viruses contained segmented genomes which are encapsidated into separate particles. To produce new progeny of viruses a common host must inoculated with a high multiplicity of infection (MOI) which leads to mixed infections. There is extensive variation in the rate of reassortment among animal segmented viruses such as influenza A, rotaviruses and with low frequently in Hanta and Lassa viruses. Reassortment between different subtypes of influenza viruses play a key role in the genetic variation and reassortant viruses ultimately emerged pandemic. It was supposed that a defined packaging signal in the different segments of genome results in serial packaging of genomes. Furthermore, a random packaging mechanism in particle size dependent manner is suggested. In both modeles of packaging, the exchange of individual segments and emergence of a new reassortant virus may occur [7, 9, 14] (Figure 1).

Conclusion

In this review, we have outlined what we considered to be the main important features regarding the genetic composition and organization of the RNA viruses. The study of viral evolution has developed quickly in the last 30 years. Therefore must be tried deals with the “cause and consequence of evolutionary change in viruses” and links the mechanisms of viral evolution within their hosts to the epidemiological outcomes that helps to better understand evolutionary biology, epidemiology, ecology and population genetic and treatment. Viruses are a serious problem; however, they constitute very powerful tools for experimental evolution and antiviral treatments. Increasing our understanding of the roles of selection, mutation could determine our ability to contest harmful viruses. We need to determine the rate of adaptation and kind of molecular changes that are associated with fitness.

Conflicts of Interest

The authors declare that there are no conflicts of interest.

References

1. Condayan C. Adaptation and Evolution: The Life of an RNA Virus Microbe world. 2010;1-2.
2. Elena SF, Sanjuan R. Adaptive value of high mutation rates of RNA viruses: separating causes from consequences. J Virol. 2005;79: 11555-8.
3. Kim M. Biological view of viruses: creation vs evolution. Journal of Creation. 2006;20:1-2.
4. Holmes EC (2011) What Does Virus Evolution Tell Us about Virus Origins? J Virol 85: 5247-9655.
5. Worobey M, Holmes EC. Evolutionary aspects of recombination in RNA viruses. J Gen Virol. 1999;80:2535-43.
6. Holmes EC. The Evolution and Emergence of RNA Viruses. Syst Biol. 2010;59:610-2.
7. Simon-Loriere E, Holmes EC. Why do RNA viruses recombine? Nat Rev Microbiol. 2011;9:617-26.
8. Santiago F. Elena, Sanju´an R. Virus Evolution: Insights from an Experimental Approach. Annu Rev Ecol Evol. 2007;38:27–52.
9. Flint SJ. Genome Replication and mRNA Production by RNA Viruses. In: Flint SJ, editor. Principles of virology: molecular biology, pathogenesis, and control. Washington: ASM Press. 2000;190-525.
10. Duffy S, Shackelton LA, Holmes EC. Rates of evolutionary change in viruses: patterns and determinants. Nat Rev Genet. 2008;9:267-76.
11. Lauring AS, Andino R. Quasispecies theory and the behavior of RNA viruses. PLoS Pathog. 2010.
12. Elena SF, Carrasco P, Daros JA, Sanjuan R. Mechanisms of genetic robustness in RNA viruses. EMBO Rep. 2006;7:168-73.
13. Dowell SF. Seasonal variation in host susceptibility and cycles of certain infectious diseases. Emerg Infect Dis. 2001;7:369-74.
14. Cline TD, Karlsson EA, Freiden P, Seufzer BJ, Rehg JE, et al. Increased pathogenicity of a reassortant 2009 pandemic H1N1 influenza virus containing an H5N1 hemagglutinin. J Virol 85. 2011.