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Theoretical Analysis of the Evolution of Viral Epidemic Strains Based on Molecular Epidemiology: Implications for Public Hygiene Prevention and Control

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Abstract: Throughout history, epidemic viruses have posed significant challenges to human progress, threatening lives and imposing substantial socioeconomic burdens. Even when certain strains evolve to become less fatal, their long-term health impacts persist. Understanding viral evolution mechanisms is thus crucial, as it enables dynamic monitoring of viral indicators and the implementation of targeted preventive measures based on virulence and infectivity. This paper reviews recent literature from the past five years, synthesizes widely accepted theories on epidemic virus evolutionand discusses their implications for public health strategies. Noteworthy theories include coevolution, host jump, and immune escape, with the first two being particularly instructive for public hygiene. Professional staff should apply cutting-edge methodology to the optimization of the viral datasets. Furthermore, the relevant department should adopt appropriate theories in monitoring the trends in viral evolution, maintaining vigilance regarding emerging strains that infect humans.

Keywords: molecular epidemiology, public hygiene, virus, viral evolution

1. Introduction

The evolution of epidemic viral strains refers to virus undergoing changes in genetic structures over time, eventually leading to the emergence of new viral strains with novel biological traits. Getting knowledge of viral evolution is essencial to progresses in the field of public health. Though much concerning work has been done, a current summary of related hypotheses or theories and its implication on public hygiene are little proposed.

This paper initially reviews the prevailing hypotheses regarding the viral origin, subsequently addressing the targeted perspectives of the academic community. It then succinctly outlines the established knowledge on viral evolution, encompassing mutation and horizontal gene transfer, both of which are pivotal in the evolutionary process of viruses. Additionally, hypotheses that remain in need of further verification—such as immune escape, virus-host coevolution, and host jumps—are discussed in detail. Each hypothesis is examined based on its definition, underlying mechanisms, and practical cases, presented in chronological order for clarity. This paper eventually highlights contemporary public health strategies and offers insights into how theoretical advancements can inform and enhance public health systems. It is anticipated that these insights will contribute to more effective control and mitigation of the spread of viral epidemic strains.

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Through synthesizing these diverse aspects, this article aims to provide a holistic framework for understanding the complex evolutionary history and the ongoing dynamics of epidemic viral strains. Additionally, it encourages relevant departments to integrate concerning theories to optimize disease prediction models and safeguard the universe health, thus boosting the development of public hygiene.

2. Viral evolution and corresponding public hygiene strategies

2.1. The emergence and development of virus

2.1.1. The origin of virus

The origin of viruses remains a contentious topic in academia, with five primary hypotheses proposed to date: the regressive hypothesis, escape hypothesis, virus-first hypothesis, RNA world hypothesis, and lab leak hypothesis, listed chronologically.

The escape hypothesis, initially supported by the discovery of transposons, posits that viruses originated from genetic material that 'escaped' from host cells. This theory is supported by observed gene homology between viruses and their hosts. However, the discovery of Mimivirus, Mamavirus, and Megavirus, each containing numerous genes absent in other viruses, challenged it and revived interest in the regressive hypothesis. The latter suggests viruses evolved from complex ancient organisms through progressive gene loss, though structural disparities, such as the lack of ribosomes, cast doubt on its validity.

The 1970s saw the emergence of the virus-first hypothesis, aligning with Walter Gilbert's RNA world hypothesis, which holds that viruses or virus-like entities predated cellular life. This gained traction with the discovery of viroids and virusoids in the 1990s and was further supported by viral protein folding family analyses post-2010, highlighting the conservation of ancient structures. Concurrently, the RNA world hypothesis in viral evolution linked the simplicity of RNA viruses to remnants of an RNA-based primordial world, though the relationship between DNA and RNA virus complexity remains unclear.

Amid the COVID-19 pandemic, the lab leak hypothesis surfaced, but lacks substantial evidence and is more related to biosafety ethics than the fundamental mechanisms of viral origins, thus receiving limited academic attention.

2.1.2. Established knowledge on viral evolution

Viral evolution is fundamentally driven by mechanisms such as mutation, genetic recombination, horizontal gene transfer and selective pressure. These processes encompass both spontaneous changes in the viral genome and the acquisition of genetic material from external sources, including other viruses and host organisms. As these mechanisms are well-established and extensively documented in the scientific literature, this paper will not delve into a detailed discussion of them.

2.1.3. Theories and hypotheses to be tested

Based on established theoretical frameworks, several novel hypotheses and models have been proposed to explain viral evolution in greater detail.

One of the most widely recognized evolutionary strategies is immune escape, which allows viruses to evade host immune responses and ensure their survival. This mechanism includes strategies such as antigenic modification, suppression of host immune responses, and establishment of intracellular latency, all of which enable viruses to evade detection and elimination by the host immune system. Immune escape is primarily driven by genetic mutations, including but not limited to antigenic drift,

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antigenic shift, immune checkpoint mimicry, and interference with antigen presentation. A notable example is the study on circulating SARS-CoV-2 spike N439K variants, which demonstrated that a receptor-binding motif (RBM) mutation, N439K, confers the ability to evade antibody-mediated immunity while maintaining viral fitness comparable to the wild-type strain. This conclusion was supported by experimental evidence showing that the N439K variant retained high-affinity binding to the human ACE2 receptor and exhibited efficient replication in cultured cells [1]. Despite these advances, the mechanisms underlying immune escape remain incompletely understood at present. Unresolved questions include the genetic and molecular basis of the observed inter-individual variability in immune responses towards the same virus. Therefore, further research is essential to elucidate the precise mechanisms of immune escape and to inform the development of targeted therapeutic interventions.

Another significant area of research interest is virus-host coevolution', a concept closely related to immune escape. Coevolution describes the evolutionary arms race between viruses and their hosts, a phenomenon particularly evident in long-term infections. This process can be categorized into two distinct modes: antagonistic coevolution and adaptive coevolution. To date, several studies have identified general outcomes and traits of coevolution [2]. Moreover, researchers have revealed a correlation between the frequencies of G-quadruplex-forming sequences (PQS) in double-stranded DNA (dsDNA) viruses and their hosts, suggesting a close coevolutionary relationship and reciprocal mimicry in genome organization [3]. Additionally, studies have demonstrated that viruses can drive coevolution through epigenomic modulation, influencing host gene expression and immune responses. Concurrently, host defense mechanisms have evolved and become more sophisticated over time [4]. However, several questions remain, including the maintenance of long-term evolutionary equilibrium, the generalizability of cross-species coevolution patterns, and the precise molecular mechanisms driving these interactions. The last phenomenon to be discussed in this paper is the host jump, which denotes the process by which a virus transitions from its original host species to infect a new host species, typically facilitated by genetic mutations or ecological interactions. This mechanism is pivotal in driving zoonotic disease outbreaks and the emergence of infectious diseases. Research suggests a pattern in host jumps, suggesting that cross-species transmission frequently occurs on an evolutionary "backbone" of long-term virus-host co-divergence [5]. Over a decade ago, studies on the precise mechanisms of host jumps revealed that viruses can adapt to new hosts through mutations, enabling them to bind to specific receptors of the new host. However, uncertainties remain, such as whether specific types of mutations consistently lead to host jumps.

Several determinants influence host jumps. Environmental factors, including the frequency of interactions between different host species, play a significant role. Host characteristics are also critical, as evidenced by a study on the rapid adaptive radiation of cichlid fishes in Africa's Lake Tanganyika and their associated viruses. This study found that cross-species transmission events were only observed within members of the same fish family, underscoring the importance of close genetic relatedness as a key determinant of rapid host jumps in viruses [6]. Additionally, the evolutionary potential of the virus itself is a determinant. Viruses with high mutation rates can enhance their binding affinity to host receptors, while those with low mutation rates may expand their host range through mechanisms such as pan-host adaptation.

Host jump is typically characterized by accelerated adaptive evolution via horizontal gene transfer. While this phenomenon may exhibit some correlation with coevolution, it's distinct in its emphasis on rapid adaptive changes that occur when a virus transitions to a new host, as opposed to coevolution. Understanding the interconnections between these phenomena is critical for advancing viral evolutionary research and public health strategies.

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2.2. Enlightenment on public health system

Understanding the comprehensive landscape of viral evolution has enabled society to develop numerous strategies to curb the spread of viral infections. Traditional measures include controlling infection sources, interrupting transmission routes, and protecting vulnerable populations through practices such as mask-wearing, avoiding crowded spaces, and vaccination. In recent years, advancements in virus surveillance and genomic sequencing have emerged as critical tools in epidemic prevention. The World Health Organization (WHO) and national Centers for Disease Control and Prevention (CDC) actively monitor viral mutations in real time via systems like the Global Influenza Surveillance Network (GISN). Beyond GISN, other global real-time surveillance networks have been established, leveraging international collaboration and data sharing to track and analyze viral genomic variations. These efforts provide a scientific foundation for informed public health decision-making.

A key priority in improving viral surveillance is ensuring the acquisition of comprehensive and high-quality data. However, significant gaps remain, particularly in data from developing countries and remote regions. For instance, genomic data across diverse viral strains and long-term surveillance data are often insufficient. Notably, a recent study on farmed fur animals identified high-resolution genome sequences of 125 vertebrate-related viruses using advanced methodologies. This research significantly expanded the known diversity of viruses and their host ranges. By employing a single-sample library construction strategy, the study analyzed mixed viral infections at the host individual level and identified potential "high-risk" viruses with frequent host-jumping behaviors, such as norovirus and Getah virus. Integrating interdisciplinary approaches—including ecological and geographical distribution, evolutionary dynamics, and public big data—the study revealed the ecological and epidemiological characteristics of these viruses across spatial, population, and organizational dimensions. These findings offer valuable insights for public health systems [7]. Building on this study, relevant organizations and research groups can adopt similar methodologies to further enrich viral databases. Integrating cross-disciplinary data into a centralized data hub will enhance our understanding of viral evolution and expansion. Given the critical role of host-jumping events in emerging infectious diseases, surveillance efforts must extend beyond human infections to include a broader range of animal hosts, which remain largely underrepresented in current studies. In the realm of antiviral drugs and therapies, multi-targeted therapies show significant promise. Inspired by mechanisms of immune evasion, scientists have developed strategies to enhance host immune responses. However, clinical data on these therapies remain incomplete. To address this, relevant organizations should recruit more volunteers by educating the public on the principles of these therapies and providing financial incentives. Expanding data resources in this area will be crucial for the refinement and efficacy assessment of these therapeutic approaches.

Furthermore, research on virus-host coevolution underscores the need to transition public health strategies from static to dynamic approaches. Given the continuous evolution of viruses, a forward-looking perspective is essential. Artificial intelligence (AI), already a ubiquitous tool in daily life, holds immense potential for academic applications. By training AI models with enriched, multidisciplinary datasets, as is mentioned above, researchers can develop predictive models to forecast viral evolutionary trajectories and potential outcomes. This would enable the proactive deployment of targeted health prevention and control measures.

While many enigmata in viral evolution remain unresolved, ongoing advancements are expected to further optimize public health systems. By embracing interdisciplinary collaboration, innovative technologies, and dynamic surveillance, we can better anticipate and mitigate the impacts of viral threats.

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3. Conclusion

After a thorough examination of the current evolutionary theories of epidemic strains, we may be able to more effectively integrate them with AI technology and apply this integration to the statistical prediction of epidemic trends, thereby revealing the transmission dynamics of epidemic strains across different times, spaces, and hosts. Furthermore, these theories will also contribute to the development of new vaccines, such as drugs designed to target the immune escape capabilities of viruses, making a significant contribution to global health. In the near future, employing novel cross-research methods and more advanced strategies to enhance the data hub, while also emphasizing the inclusion of multidisciplinary data and surveillance of animal hosts, holds great scientific significance for strengthening the public health system. However, the current research on viral evolution presents notable limitations: a significant proportion of studies predominantly focused purely on non-human viruses or common human-infecting viruses, lacking forecasts on what their next host would be or whether they would transfer to mankind, under a long period of evolution. Given the established phenomenon of host jumping, it is imperative to maintain vigilance and investigate emerging viruses that originate from other animal species. Future research should focus on encompassing a broader spectrum of epidemiological viruses to enhance our understanding of viral evolution and its implications for public health.

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