

Pathogenesis Studies of HIV/AIDS, A General Viral Topic

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Abstract

HIV/AIDS treatment is still incurable. To resolve this challenge, HIV-induced pathogenesis processes—including viral infection, HIV reservoirs, HIV latency, invading to human cell/genome, human immunity dysfunction, AIDS symptoms/episodes and finally human mortalities must be understood. By HIV pathological studies, we can improve HIV therapeutics a great deal. In this editorial, we give these sides of topics in every possible pathways and details (both diagnostics and therapeutics). The relationship between HIV-induced pathogenesis and target therapies is emphasized.

Keywords: HIV; AIDS; Human Genome; HIV Infection; Viral Pathology; Virus Therapy; Animal Model; Human Immunity; Clinical Therapeutics; Human Immune Dysfunction

Backgrounds

Human biological characters of easy HIV accessibility mechanisms (entering, lurk and a cascade of pathogeneses) in infected patients is a critical issue in the different fields of HIV/AIDS studies [1-7]. Still a hot topic, HIV-induced pathogenesis study is a gateway between disease progress diagnostics and curable therapeutics. It is a sort of sequencing cellular pathogeneses, accumulating molecular abnormal events and human physiological dysfunction in human bodies. Unfortunately, we have known little about these patterns of molecular linkages and pathologically sequential processes now. Lacking valuable information about pathological relationships between early stages of molecular abnormality and final irreversible mortality steps is the drawbacks in the field of HIV/AIDS studies. Thus, any creative subjects aiming at revealing overall HIV-induced pathogenesis in infected patients and AIDS episode- including virus survival, duplications, parasite at different types of human cells and organs, dysfunctional activity against normal human immunity and human mortalities are all welcome and have greatest medical significances/potentiality [1-7].

The details of these patterns of HIV-induced pathological molecular/routes are depicted in Figure 1. Feasibility and mortalities of different routes of HIV infection and inhibitions is available. These types of HIV pathogeneses are likely to general routes of other viral infection [8-10].

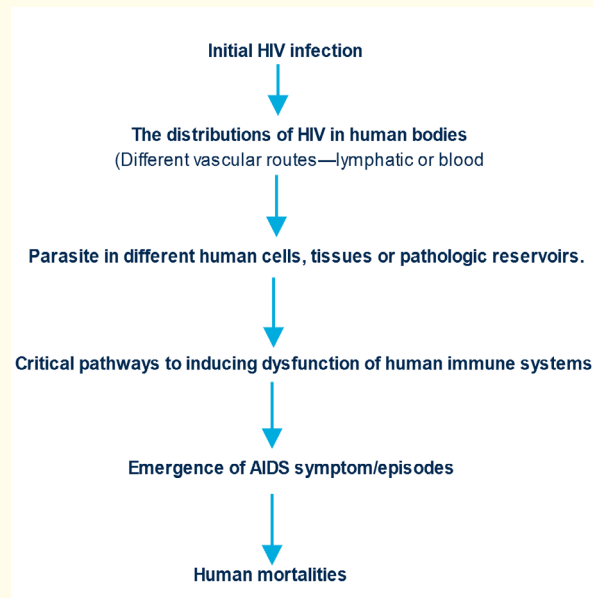


Figure 1: General pathways of HIV-induced pathologic cascade and human mortalities.

The distributions of HIV in human bodies via vascular routes

The distribution of HIV in human bodies via different vascular routes (lymphatic or blood) is initial process for disease progresses after HIV infection. A great number of human cells or tissues can parasite HIV viruses, such as brain, neural, intestinal tissues and so on. Neutralizing HIV by chemotherapeutic agents, animal/human antibody or other types of bio-therapeutic options is generally applied but insufficient for complete HIV managements. Many HIV containing reservoirs can protect usual medical interventions and therapeutics, such as chemotherapeutic agents. More systemic or symptom scientific studies are urgently needed to solve this issue.

HIV-induced molecules or pathogenesis courses in infected human cells that can trigger various host defensive mechanisms:

- Viral attachments on host cell membranes (cell membrane signal ligands etc)
- Viral entry (cellular co-receptors or extra-cellular molecules etc)
- Transcription/replications of virus and HIV copies in cells and viral load in plasma (cell plasma components and enzymes—retro-RNA polymerases etc)
- Human HIV reservoir established
- HIV latency
- Viral envelop
- Human genomic penetrations (integrases or recombinases etc)
- Viral egress by human cell viral copying (diseased cell lyses or decompositions by host/cell defensive mechanisms such as interferon, cytokines, interleukin and so on)
- Human physiological abnormalities (high fever, wasting, metabolic symptoms and so on)
- Host immune system impairments and dysfunction (activated lymphocytes, especially T-helper lymphocytes etc)
- Emergence of disease complications and causations of AIDS symptoms and episodes (co-infected with other microbial or viruses or HIV-induced cancer etc)
- Human mortalities (co-diseases)

Key Factors and Pathways Linking with Disease Progresses or Host Defensive Mechanisms Participations

Human mortalities

Deepest virus infections such as avian flu, plagues, Ebola and so on can cause quick widespread human deaths and dreadful catastrophe immediately [8-10]. HIV-induced human mortality is, however, long and no definite time scale [1-7]. Until now, people are still unknown about these differences. Accordingly, finding the exact biological molecules, pathways, mechanisms and mortalities that these differences of deepest viruses kill human beings is beneficial for anti-infective agent developments, clinical therapeutics and epidemic managements.

Human vaccine developments and challenge schedules

Viral vaccines especially many raw inactivated viruses or chicken egg modified viruses are widely accepted to treat the healthy and sick humans. They are often the first option of many doctors and virologists. However, HIV vaccine therapeutic paradigms have yet been found. From our perspectives, important factors causing slow progresses of HIV vaccine perfections might come from lacking deep understanding into virus-induced pathogenesis and immunological impairment mechanisms by HIV and shortage of funds to implement phase II and phase III clinical trials for so varieties of potential vaccines ready for experimental evaluations and clinical verifications [11].

Most virologists believe that a vaccine is the easiest and one of the most effective therapeutic options we can rely upon because of a number of excellent examples across the history have been previously found for many deadly viruses, including small-pox and so on. Yet previous work failed to copy these vaccination paradigms in new emerging deadly virus infections, such as HIV and so on, especially to those who have been infecting with viruses for a certain amount of times in human bodies [1-7]. To these patients, therapeutic efficacies of vaccines are greatly compromised. Possible reasons behind scene can be speculated from different pathogenesis phases and therapeutic innovations;

Genome wide study of HIV-penetration into human genomes

One of the most harmful HIV-induced pathogenesis steps might come from virus-penetration into human genomes of infected cells or tissues [12]. Despite our proposed roadmap [13], this challenge remains to be experimentally verified. If this hypothesis has been finally proved, a great difference in clinical trials can be made [12-14]. Unfortunately, no marked breakthrough in this respect has been available. This study is still not overwhelmed, yet hopes still remain [14] (Table 1).

Methods	Possible evaluation	Ref
Biophysically monitor the interactions and binding between pure DNA and HIV segments	Integrase inhibitors	15
<i>In vitro</i> pathogenesis study of HIV in infected animal and human cells	Biotherapy and other therapy	13, 15
<i>In vivo</i> genomic or bioinformatics study of HIV and its therapeutic relationships	Different forms of vaccines and antiviral drugs	13
Establishing relationship between HIV and human genome changes for susceptible loci in infected patients	Pathogenesis and therapeutic studies	12

Table 1: Different levels of genomic study for HIV infection, pathogenesis and therapy.

In future, the heavyweight of genomic sequencing forces might be transformed from biomedical major students into mathematics or physics major students or scholars because the laboratory protocols for computation or alignments of different DNA pieces into a whole genome will take longer times and efforts than handling genetic sequencing devices and machines by biomedical major students [16-18]. For computational work, the mathematics or physics major students must be smarter and advantageous over biomedical major students [16-18]. So, it is foreseeable that mathematics or physics major students might be at least parts of working force suitable for genomic

sequencing and data analysis. The contributions by mathematics or physics scientists can be no less than that by biomedical scientists for genomic sequencing alignments and data analysis from larger-sized genomic pool for different backgrounds of human genomic information, such as diversity of human genomes in different gender, age, ethnic groups and races and so on.

Pathologic Patterns

Clinical immune-dysfunctional characters of HIV in human bodies

Many different patterns of human immunity components or lymphocytes might be major forces for HIV neutralizing, disease control, viral-copy inhibitions and even viremia clearances. From present knowledge, these different patterns of human immunity components and lymphocytes act differently among various progressive stages of HIV infections within human bodies [5-7] (Table 2).

Major disease phases	Symptomatic characters	Time after HIV infections	Possible immune-activities
HIV transmissions	Detectable HIV viremia in human blood	4 - 11 days	Cellular membrane molecule and receptors
Infected symptoms	Fever, rash, fatigues, diarrhea and elevated liver enzyme level etc	2 - 6 weeks	Cytokine or inflammatory mechanisms
Peak of HIV viremia	Highest viral copies and load in human blood	3 - 8 months	Cytotoxic T lymphocytes; CTL
Establish of chronic infections	Stable RNA copies in patient's blood	1 years	Neutralizing antibodies or balance of human defensive
AIDS occurrence	Co-infection and cancer	No definite time-scale	Dramatic immune-decline
Mortality	Unknown mechanisms	Two years after AIDS	If no treatment

Table 2: Clinical aspects of HIV progression and active immunity counteractions.

Heterogeneity of wild-type HIV virus genome

HIV viruses are not uniform in genome. Heterogeneity of wild-type HIV virus genome makes it difficult for uniform vaccine manufacture. It is so big an obstacle that makes HIV vaccine development slowing down and less fruitful.

Latency status of HIV in infected patients

Latency status of HIV in infected patients is the main causalities for therapeutic resistance and failures. Long-lasting HIV latency can survive for several week antiretroviral therapy (ART) or even longer. This is one of the most important pathogenesis characters of HIV and therapeutic pitfalls. Further investigations are underway [20-21].

Different sites of HIV viremia reservoirs

Different organs or sites of HIV viremia reservoirs in human bodies are obscure topics up-to-date. The history of HIV reservoirs knowledge is quite long, but remains to be an unresolved issue from therapeutic consideration. As the human tissues of HIV reservoirs can contribute as barriers for HIV from the attacks of most types of therapeutic agents. Owing to these protective activity of HIV reservoir bodies, HIV infection is difficult to be cut off from HIV infected patients. Thus, this topic is important and meaningful in the field of HIV/AIDS therapeutic studies.

Host Defensive Mechanisms and Immune Dysfunctions

Host defensive mechanisms are key elements for preventing and inhibiting HIV-induced pathogenesis and mortalities. Currently, host defensive mechanisms are widely studied as human immune systems-best represented as immune-related molecules such as cytokine,

interleukins, interferon, antibodies as well as different types of immune activated cells, such as macrophage, cytotoxic T-lymphocyte, antibody-secreting B-lymphocytes [22-23]. These types of researches are very suitable for HIV/AIDS diagnostics and therapeutics-common goals of understanding human immune systems and dysfunctions. In our perspectives, expanding funds or moneys should be allocated for this kinds of scientific investigations because these items of money payments are somewhat like one stone kills two birds.

Currently, we only understand the superficial relationships between pathogenesis progresses and human immune dysfunctions. Genetic-, molecular-, animal cell-, human cellular- or body relationship between them are especially obscured, or at least incomplete. As a result, most human immune system functionalities are still mysteries to us, which leads to poorly manipulate capability of human immune system from our reaches. Apart from genetic/genomic understand of HIV in human cells or bodies, HIV-induced human immune dysfunction is a golden-mine for further scientific therapeutic discoveries. Yet, these pieces of golden ores cannot be alchemized unto golden harvests at this stage. Next generations of HIV-pathogenic researches must stride longer paces than ever before. Human immune functionalities are multi-layers that encompass genetic-, molecular-, cellular and whole-body organizations. Today, we can't focus our attentions only on a specific HIV-induced components or pathways due to insufficiency of HIV knowledge education and propaganda. Deeper understanding into HIV-pathogenic processes must be constantly renewed and theoretically highlighted [24].

Detrimental Processes Relating to Human Mortalities

Pinpointing key components or pathways regarding HIV-induced mortalities is not an old fashion for therapeutic interventions. Many co-infections or HIV-induced tumors are attributed to human mortalities is still a forward discipline. Promotions of HIV-induced pathogenesis or mortalities are unavoidable avenues of HIV studies. Generally speaking, most of these pathways are parallel with pathways of HIV-induced immune dysfunction mechanisms in this stage of HIV study. Even this type of HIV pathogenic study has been progressed slowly over the past decade comparing with HIV pathogenesis/therapeutic study relating into human mortalities.

Conclusion

A great number of HIV-induced pathogenesis molecules and pathways have been discovered. But it needs to transform from bench to the bedside. New translational studies from experimental investigations into clinical paradigms are quite necessary and have great medical/biological significance. These new trends will lead us into higher horizons of HIV-infection treatments and eradications.

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