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HIV Vaccination, Current Drawbacks and Future Perspectives

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Abstract: *Creating high effective and safe vaccines are always the first intuition and study of priority interests among majority virologists because many successful paradigms can be traced back for more than two hundred years. One possibility of curing HIV/AIDS is by employing effective HIV vaccines. A lot of factors can affect the identifications, assessments, verifications and smooth developments of HIV vaccines worldwide. In order to promote HIV vaccine developments and clinical HIV therapeutic achievements, this mini-review gives in depth information of this field in new era (present drawbacks and perspectives).*

Keywords: *HIV, AIDS, drug toxicity, HIV vaccination, viral pathology, virus therapy, animal model, human immunity, therapeutic vaccines*

1. BACKGROUNDS

Creating high effective and safe vaccines are always the first intuition and study of priority interests from majority virologists because many successful paradigms can be traced back for more than two hundred years. One possible final solution of curing HIV/AIDS is by employing effective HIV vaccines.[1-8] A lot of factors can affect the identifications, assessments, verifications and smooth developments of HIV vaccines worldwide. Despite being fulfilled by animal models first, some clinical studies have been proved to be peril. For example, some chilly evidences have been reported that tested normal human by HIV vaccine challenges can acquire HIV after long-term silence and only very limited HIV-infected patients or normal persons have been proved useful in late-staged infected patients by conventional HIV vaccinations [4-8].

Most virologists believe that vaccine is the easiest and one of the most effective therapeutic options we can rely upon because of many excellent examples across the history. Yet previous work fails to obtain effective therapeutic vaccines for many deadly viruses, including HIV/AIDS, especially to those who have been infecting with viruses for certain amount of times in human bodies [9]. To these patients, therapeutic efficacies of vaccines are greatly compromised. Possible reasons behind scene can be given from pathogenesis phases and different angels;

Pathogenesis of viral infectious consequences and phases;

- Viral attachments on host cells
- Viral entry
- Transcription/replications of virus and increasing copies and viral load
- Human genomic penetrations

- Egress of viral by human cell viral copying
- Human physiological abnormalities (high fever or hemorrhages and so on)
- Host immune system impairments and dysfunction
- Occurrences of disease complications

Deadest virus infections such as avian flu, plagues, Ebola etc can cause quick widespread human death and dreadful catastrophe worldwide [9-11]. Until now, people are still unknown about the exact pathways and mechanisms these deadest viruses kill the human beings. Thus, 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. From our understandings and retrospectives, important factors causing slow progressions of vaccine manufacture might come from lacking deep understanding into virus-induced pathogenesis and immunological impairments by HIV virus in humans and shortage of funds to implement phase II and phase III clinical trials for so many types of potential vaccines ready for experimental or clinical evaluations.

2. Genomic Study of HIV-Penetration into Human Genomes

The most harmful HIV pathogenesis might be virus-penetration into human genomes of infected cells or tissues [12-17]. Despite possible roadmap of these genomic study has been proposed [13], this hypothesis has been finally proved and make great difference in clinical trials [15-16]. No marked breakthrough in this respect has been reported. If it is true, almost all chemical drugs will be useless when human genome in infected cells are integrated with HIV. Studying the HIV-integrating to the genomes of different animal or human cells/tissues in HIV-infected patients might be a paramount task in current HIV-treatment study. This study is still not overwhelmed in this era yet hopes remain [17].

Systemic genome-wide study for understanding the relationship between human genomic makeup and virus-penetration is unavoidable avenue to in-depth study of HIV/AIDS. These researches are not only on biology or pathology, but also on technical improvements and innovations. Drafting human genomes is much easier now owing to the advent of next generation sequencing (NGS) [18-21]. This dramatic technical improvement might finally assist to solve this mystery of HIV integration into human genomes by unprecedented speed of genome sequencing and least amount of money (15,000-50,000 times faster and low budget 7,500 USD per genome).

3. Cost-Effective Concerned

A great amount of different vaccines can be designed and produced. Yet single vaccine clinical investigations will cost a fortune. We know that more than one hundred different types of HIV vaccines have been proposed, each type of vaccines of phase II or phase III clinical trial needs at least one hundred thousand USD. Present tight budget of biomedical researches cannot support all these studies for sufficient funds [1]. Similarly, many clinical evaluation or verification studies are sometimes risky and ethically problematic owing to incomplete understanding of pathogenesis and progresses of HIV in human bodies. Moreover, it seems unlikely to clear up HIV by vaccine alone [2-3, 15-16]. Since many new hypotheses relating to HIV vaccine developments and clinical applications are difficult to be systematic investigations for lacking funds and scientific knowledge of HIV pathogenesis in patients, some revolutionary preclinical evaluating systems in animals might be useful. It is nonetheless, the first step depending on the excellent productions of effective vaccines and antiviral drugs.

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. We here hypothesize that patients with different HIV genome mutations or translocations may be inhibited by different vaccine formulation. It is discovered that the most effective vaccines can only produce antibodies neutralizing at largest 30% of HIV in infected patients [15].

Sites, Routes and Pharmaceutical Forms of HIV Vaccinations

Sites, routes and pharmaceutical forms of vaccines might affect therapeutic efficacies of HIV vaccinations. We welcome systematic evaluations and verifications of these technical improvements (such as nano-particle) and therapeutic innovations. Since HIV viruses can parasite different types of human tissues, vaccine injection location may affect the therapeutic outcomes in infected patients. These medical and pharmaceutical studies may reach unexpected information and impacts in HIV/AIDS therapies.

Is therapeutic combination key solution?

A lot of clinical evidence shows that vaccine alone may not be a final solution for HIV infected patients. Given as lessons from invention of HAART therapies [22], combinations HIV vaccines with other therapeutics (such as antiviral chemicals or biotherapies) might be new possibilities of improving therapeutic outcomes. Lack clinical investigation, even animal studies of this kind may be mayor drawbacks in present studies.

4. FUTURE DIRECTIONS

In future, several avenues may be gone through via following solutions
Emphasizing the developments of therapeutic HIV vaccines by studying both pathologic-related pathways & therapeutic-related functionalities/activities
Building excellent comparative systems that evaluate therapeutic efficacies and outcomes among different types of HIV vaccines
Find out and reevaluate if it is useful by combinative therapeutics
Study the cost-effective of each biological step and technical details by vaccine challenging and disease inhibitions
Perfect the vaccine evaluating systems by rodent models (genetic engineering mice, GEM etc) that can replace and reduce the burdens by using high intelligent animals like apes for ethical concerns [23]
Explore new types and generations of HIV vaccines, especially therapeutic ones (more versatile and less side-effects)
Evaluations of challenging sites, longitudes, schedules and pharmaceutical forms of HIV vaccinations
Excellent meta-analysis work about HIV vaccinations and therapeutic outcomes

Since future directions about HIV vaccinations and developments could be multi-routes and need hard work, cooperation between academia, pharmaceutical companies and governmental funding bodies may facilitate these movements and receive unexpected feedbacks. Similarly, global communications and cooperation may be also fruitful.

5. CONCLUSION

The developments of effective therapeutic vaccines for deadly viruses (such as HIV) are modern medical challenges that need the efforts of ideas, human resources and a great amount of moneys. We

sincerely wish that new generations of therapeutic vaccines for deadly virus infections can be developed and effectively treat the viruses along with other types of therapeutic means. We look forward the fulfillments of our dreams—eradicating HIV from infective patient's bodies.

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Competing interesting

Authors have declared that no competing interests exist

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