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Opinion

Three Immunity Statuses against Viral Infections in Human

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Abstract

In this century, viral infections are still a serious threat to the safety of human life and health. Millions of people were infected by viruses every year worldwide, and many of them died from the infections. In recent decades, outbreak pandemics of SARS, influenza, and especially SARS-Cov-2 (nCov-2019) have been witnessed. To protect people from viral infections, vaccine is one of the most important approaches. But to develop a vaccine against a viral infection, the status and its regulation of the human immunity against a viral infection must be explored and known well. As a reference for the protection approach or strategy to control viral infections, based on the reports or publications in recent years, we present our new perspectives about human immunity statuses against viral infection, and conclude the statuses as three basic types: efficient immunity status, non-efficient immunity status and separated immunity status.

Viral infection is a serious threat to the safety of human life and society, and the interaction between viral violence and human immunity is never stopped

From the beginning of 2020, everybody in the world has been facing or suffering from the threat of SARS-CoV-2 induced disease (COVID-19). In recent decades, as a serious threat to the safety of human life and society, outbreak pandemics caused by viral infections have been witnessed,[1–4] especially coronaviruses (CoV),[2,4] influenza viruses (Flu-V),[1] human immuno-deficient virus (HIV), hepatitis B virus (HBV), hepatitis C virus (HCV)[3] and Ebola virus (EBOV).[5]

As the host, the target identification, interaction of viral particles and cells, cell infection, and viral replication in a cell are mediated by the viral surface receptors and antigens (Fig. 1a), and the antigens generated during their life cycle (Fig. 1b). The interaction between human immunity and viral violence is never stopped, and the balance between them is frequently broken and a new one is continually formed.

The interaction between a virus and its host forms a relatively stable balance which is antiviral immunity status. The antiviral immunity status is important for people to understand and choose how to control the viral pandemic and develop new vaccines.[6,7]

Human immunity against viral infection can be concluded as three statuses

The interaction between a virus and its host is very different depending on the viral strain and host individual, which yields a variety of antiviral immunity statuses. We conclude all antiviral immunity statuses of human as the three basic types as follows (Fig. 2):

Efficient immunity status

Human immunity presents an efficient immunity status to inhibit viral replication even to protect the human body from viral infection again. The efficient immunity status can be re-sorted as two subtypes.

Complete efficient immunity status

Human immunity provides an efficient immunity status to protect the human body from a recurrent viral infection for a long time even whole lifetime, such as the immunity against smallpox vi-

Keywords: Viral infection; Immunity against viral infection; Immunity status; Vaccine.
Abbreviations: ACE2, angiotensin-converting enzyme 2; CoV, coronavirus; EBOV, Ebola virus; Flu-V, influenza Virus; HBsAb, hepatitis B surface antibody; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immuno-deficient virus; HSV, herpes simplex virus; HTV, hantan virus; HMV, human measles virus; HPV, human poliovirus/human papilloma virus; IAV, influenza A virus; IBV, influenza B virus; nCov-2019, new coronavirus 2019; RT-PCR, real-time-polymerase chain reaction; SARS-Cov-2, severe acute respiratory syndrome coronavirus 2.
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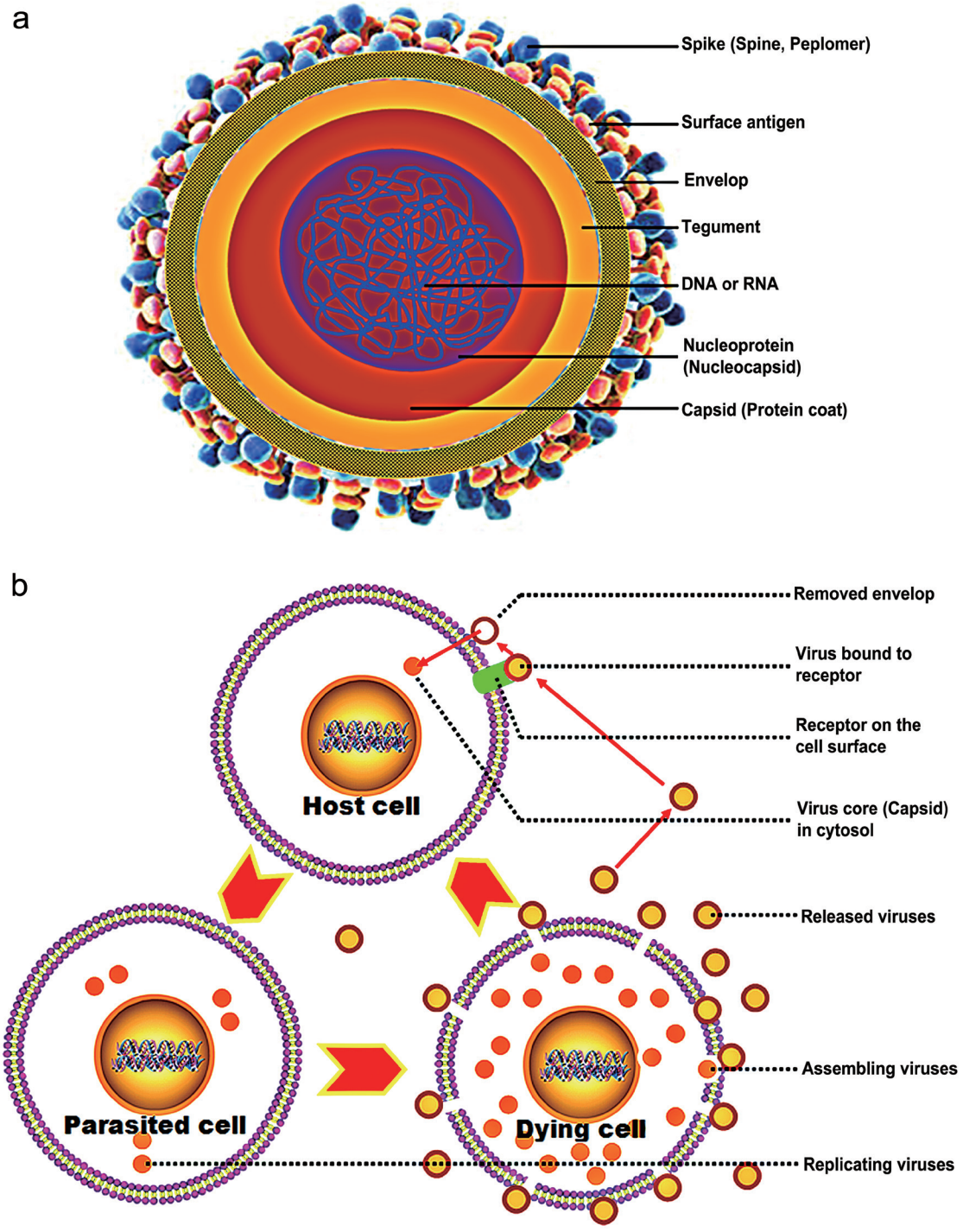

Fig. 1. Virus structure and life cycle. (a) Model of virus structure; (b) Illustration of virus life cycle.

rus (variola virus), HTV (hantan virus), HPV (human poliovirus), HMV (human measles virus), *etc*.

Incomplete efficient immunity status

The typical instances are the immunities against Flu-V (influenza viruses), CoV (coronaviruses), HPV (human papilloma virus) and HSV (herpes simplex virus). Incomplete efficient immunity status presents a protective immunity for a year or longer than a year protection usually and the viral particles will not be cleaned thoroughly, so the virus exists in the infected body for a long time and forms a new balance between viral violence and immunity, then the viral pandemic will be temporarily inhibited.

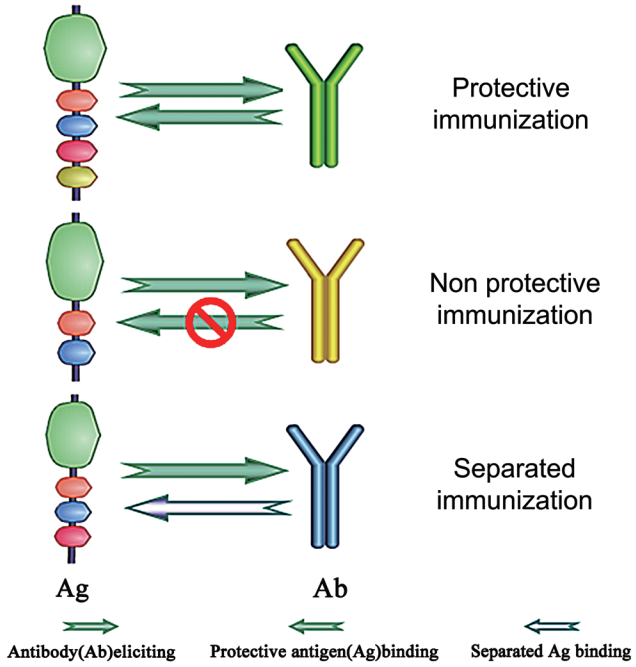

Fig. 2. Three types of immunization status against virus infections.

Non-efficient immunity status

The human body doesn't show any protective immunity to inhibit or clean the viral replication or spread in the body, such as HIV (human immunodeficiency virus), and HCV (hepatitis C virus).

Separated immunity status

The human body does not show any protective immunity to inhibit or stop the viral replication or spread in the body when the hosted body contains a virus. More importantly, the protective antibody elicited by the protective antigen will never appear in the hosted body, and the antibodies elicited by other antigens appear but without any function to inhibit viral replication or spread in the body. The antibody, HBsAb induced by HBsAg of HBV (hepatitis B virus) appears only in the body that contains no viral particle but was immunized by vaccine or subclinical infection. Positive HBsAb means there is no HBV in the body that was immunized by HBV vaccine or subclinical infection. The positive HBsAg detection means that the infected bodies will keep HBV with their whole life, and it is impossible that the HBsAb appears in the body with HBsAg positive.

Human immunity against SARS-CoV-2 infection is incomplete

So far, 30 more strains of coronavirus have been identified and named,[8] and 7 of them were confirmed to be able to infect humans (Table 1).

The coronavirus caused diseases, especially COVID-19 are threatening global public health, social safety, and economic development. The advances on the neutralizing antibodies (nAbs) against SARS-CoV-2 were reported.[2] The S antigen (Spike glycoprotein) of coronavirus is the main target of antibodies, and it is the ligand of the ACE2 (angiotensin-converting enzyme 2) that is the receptor

Table 1. Coronaviruses

Groups	Hosts	Coronaviruses
α	Humans and others	HCoV-NL63
		HCoV-229E
β	Humans and others	HCoV-OC43
		HCoV-HKU1
		SARS-CoV
		MERS-CoV
		SARS-CoV-2
γ/δ	Avian (bird) and others	.....

SARS-CoV-2 S bind to, and the S epitopes can elicit neutralizing antibodies upon SARS-CoV-2 vaccination.[2,9,10] But to date, there is no evidence from clinical data to confirm that SARS-CoV-2 induced antibody presents the protective immunity to the human body persistently because some recovered COVID-19 patients and SARS-CoV-2 infected people discharged after continued negative results of RT-PCR tests were re-infected with positive detection for SARS-CoV-2.[11,12] Therefore the pandemic of COVID-19 was projected to continue to resurge in contagion as late as 2024 or likely longer.[13] SARS-CoV-2 presents high homology to SARS-CoV virus,[14,15] but the information known about SARS-CoV immunity is insufficient because its pandemic lasted for a limited period and did not resurge.

To date, the topics about how SARS-CoV-2 interacts with the human immune system and causes "incomplete efficient immunity status" presented some hosts' responses of cytokines from basophils,[16] mast cells,[17] dendritic cells.[18] The detailed mechanism for this topic is complicated and still not known well, and the discussion about the mechanisms of the three human immunity statuses against viral infections is not a major topic of our perspective. But anyhow, the incomplete efficient immunity status of the human body caused by SARS-CoV-2 has been well proved as the brutal truth.[19]

Influenza viruses, especially influenza A and B viruses (IAV, IBV) cause outbreak pandemics frequently worldwide, the high mutation rates allow their evasion of host immunity,[20,21] and therefore induce an incomplete efficient immunity status in humans. SARS-CoV-2 was also reported as a virus with a high mutation rate,[8,9,14,15] and based on the current clinical data, like human immunity against influenza virus infection, it is well validated that human immunity against SARS-CoV-2 infection is incomplete efficient immunity status. As such, annual booster shots against COVID-19 will benefit people's protection in the future.

In any case, viruses, including SARS-CoV-2 virus, always try to form their symbiosis with human beings. From 1918, IBV has been interacting with human beings for longer than a hundred years, and finally IBV succeeded.

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Conflict of interest

The authors have no conflict of interest related to this publication.

Author contributions

Study concept and design (HYC, HY), acquisition of data, analysis and interpretation of data (XL, CSN), drafting of the manuscript (HYC, HY), critical revision of the manuscript for important intellectual content (HYC, HY), administrative and material support (HYC), and study supervision (HYC). All authors have made a significant contribution to this study and have approved the final manuscript.

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