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Coronavirus Pandemic

Can the novel coronavirus be transmitted via RNAs without protein capsids?

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Abstract

The existing knowledge is insufficient to explain some infection events of SARS-CoV-2, and new ideas about the transmission modes may be needed. The present study proposes that the RNAs of this virus might be infectious and that the transmission of these RNAs might be one route of transmission of SARS-CoV-2. I speculate that SARS-CoV-2 RNAs are infectious based on the following rationale and offer a putative mechanism: RNA is the most important biomolecule of the novel coronavirus for expression and replication, free RNA strands of SARS-CoV-2 have the potential to remain suspended in the air and retain their biological activity, and some exogenous RNAs can enter the host cell after contact. Further studies are needed in order to verify this hypothesis. It is worthwhile to compare the effects of SARS-CoV-2 components (e.g., virus particles, positive RNA strands, negative RNA strands, and virus proteins) with symptoms to study the mechanism of asymptomatic infection. If additional detection results show that the proportion of RNA in the environment is higher than the proportion of RNA in the novel coronavirus particles, this would suggest the potential presence of free RNA genomes of SARS-CoV-2 in the environment. Research on the temporal and spatial distribution of infectious SARS-CoV-2 RNA strands is necessary. The nucleic acid test of SARS-CoV-2 should target not only positive RNA strands but also negative RNA strands. For medical purposes, studying environmental RNAs (eRNAs) is important. I believe that further investigation of the infection capabilities of viral RNAs will yield useful information.

Key words: SARS-CoV-2; transmission; RNA.

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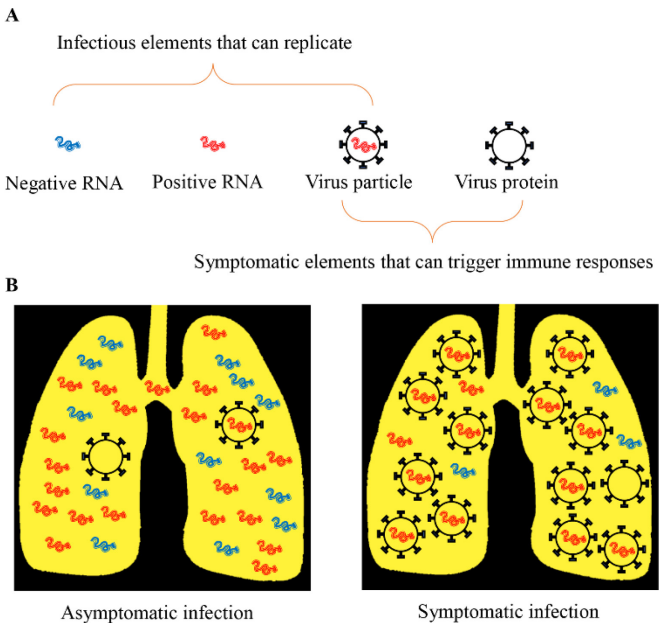
The transmission of the deadly novel coronavirus SARS-CoV-2 occurs rapidly [1-5], and asymptomatic infection with this virus has been reported [6-8]. Existing knowledge is insufficient to explain some infection events, and new ideas related to the transmission modes are needed. Herein, I propose that the RNAs of this virus might be infectious and that the transmission of these infectious RNAs might be one route of transmission of SARS-CoV-2.

I speculate that SARS-CoV-2 RNAs are infectious based on the following rationale and offer a putative mechanism. First, RNA is the most important biomolecule of the novel coronavirus and can be released by virus particles and infectious cells. During SARS-CoV-2 attack on host cells, positive RNA strands enter the cells and eventually destroy the cells through their expression and replication, virus assembly, and so on [9]. Capsid particles can protect RNA strands and bind to host cell membrane receptors to enter cells, but they have no replication capacity. If free RNA strands without protein shells can enter host cells, they can complete the biological process as SARS-CoV-2 particles do. Second, free RNA strands of SARS-CoV-2 have the potential to remain suspended in the air. Compared to virus particles, RNAs can remain airborne more easily. The molecular weight of the novel coronavirus RNA genome is 1×10^4 kDa, approximately one-five hundredth the molecular weight of the coronavirus particle. In the air, the RNA can be stable for more than a few minutes; for example, during RNA extraction, dry RNAs can be stable at room temperature for 10 minutes. Moreover, studies of synthetic genomes have confirmed that naked nucleic acid molecules *in vitro* can retain their biological activity [10]. Although it is not known how long coronavirus RNA strands can survive in the air, in some cases, a few seconds may be enough time for them to encounter a new host. Third, it remains unclear whether SARS-CoV-2 RNAs enter the host cell after contact through other ways besides binding channels formed by viral proteins and host cell membrane receptors. It has been reported that cells can engulf some tiny particles, such as small viruses and nanoparticles, through endocytosis [11,12]. Thus, the epidermal cells of the respiratory tract and digestive tract of a new host may engulf coronavirus RNAs. In addition, novel coronavirus RNAs may enter cells

through wounds or use the components of damaged cells to synthesize virus particles. The transmission of some infectious pathogens via free RNAs has been reported. Viroids, which cause diseases in higher plants, can infect host cells as RNAs [13]. Viroids comprise RNAs without a protein coat and can enter plant cells through tiny holes [14].

Evaluating the possibility of RNA transmission requires a suitable method for determining the presence of free coronavirus RNAs in the environment. A positive result of a nucleic acid test of novel coronavirus in the environment does not prove that there are novel coronavirus particles in the environment but merely indicates the presence of coronavirus RNAs. If additional detection results show that the proportion of RNA in the environment is higher than the proportion of RNA in the novel coronavirus particles, it suggests the potential presence of free RNA genomes of SARS-CoV-2 in the environment. A related issue regards the role of external RNA-degrading enzymes, e.g., RNases. Why do humans and many organisms release stable RNA-degrading enzymes on their skin and into the environment? One reason is that exogenous RNA is dangerous; thus, many organisms secrete RNA-degrading enzymes outside the body as an immune mechanism. The relationships between the survival rates of free SARS-CoV-2 RNAs and activities of RNA-degrading enzymes should be investigated.

Figure 1. The relationship between symptomatic infection and RNA infectiousness.



A, Infectious and symptomatic elements of SARS-CoV-2; B, Lungs with SARS-CoV-2 infection.

Research on the temporal and spatial distributions of infectious SARS-CoV-2 RNA strands is necessary. One aspect relevant to the temporal distribution issue is the lifespan of RNA strands. It seems that there are large differences in the fate of novel coronavirus RNA strands between host cells and the air, although the fate of these strands in the air is poorly understood. Another aspect relevant to the temporal distribution issue is the infectious activity of RNA strands. The relationship between the infectious activity and age of the RNA might be complex [15]. If the spatial distribution of RNA strands and virus particles is known, the safety distance from a SARS-CoV-2 carrier can be estimated. Methods for detecting the spatial distribution of novel coronavirus RNAs should be developed. I suggest that spatial array methods be explored. To detect the spatial distribution of novel coronavirus RNAs within a certain area (e.g., a crowded place) via a spatial array method, I suggest the following series of steps: establish sampling sites in the area → place sampling media in each site → after a certain period, collect samples for RNA level detection → analyze the distribution of RNAs and the direction of RNA transmission.

It is worthwhile to compare the effects of SARS-CoV-2 components on symptoms to study the mechanism of asymptomatic infection. The components of novel coronavirus that are related to infection and the development of symptoms mainly include virus particles, positive RNA strands, negative RNA strands, and virus proteins. Suppose that RNA-containing elements (virus particles, positive RNA strands, and negative RNA strands) are infectious factors and protein-containing elements (virus particles and virus proteins) are factors causing symptoms (Figure 1A). The patterns of combination of these factors will decide whether an infectious person has symptoms (Figure 1B); for example, if the pattern mainly entails the replication of RNA strands in host cells, then the carriers are asymptomatic but can transmit the novel coronavirus RNA strands. In the pattern of symptoms, the viral proteins and virus particles are produced in large numbers, resulting in symptomatic and infectious patients. The variable latency period of the novel coronavirus in hosts, ranging from a few hours to a few weeks, might also be explained by the above speculated patterns of combination of infectious and symptomatic factors. Moreover, the proportions of virus particles, positive RNA strands, and negative RNA strands exposed to new hosts might affect the latency period.

The nucleic acid test of SARS-CoV-2 should target not only positive RNA strands but also negative RNA

strands. Negative RNA strands are not present in the particles of the novel coronavirus, but the detection of negative strands would confirm that the tested person is infected, and such individuals might be contagious, as described above. The detection of nucleic acid fingerprints and full sequences of negative RNA strands can help evaluate the risk of infection in the environment and significantly reduce the frequency of false negative results in the nucleic acid test.

In summary, the concept of SARA-CoV-2 RNA infectiousness can aid the study of the infectious mechanisms of viral diseases, and experimental and clinical validation of this concept is urgently needed. In light of the possibility of SARA-CoV-2 RNA infectiousness, more stringent protective measures need to be developed to protect healthy people. For medical purposes, studying environmental RNAs (eRNAs) is important. I believe that further investigation of the infection capabilities of viral RNAs will yield useful information.

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