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Short Commentary

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Proposal Methodology to Prevent SARS Cov2 Infection by Deactivating RNA Polymerase

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Abstract

SASR COV2 is infecting over the world. That is the biggest corona-virus pandemic from the last flu pandemic in 1918 until now. Too many efforts are done to prevent the pandemic, but effective success is still expecting. In which, looking for a vaccine is a long time to hope. In this paper, the deactivation of the RNA polymerase enzyme is proposed. The radioactive isotope of Mg is used to replace the stable Mg in an active site of the enzyme. The method is simple to understand and easy to be done. Hoping that this method will be discussed and accepted and it needs the collaboration of the interdisciplinary scientists.

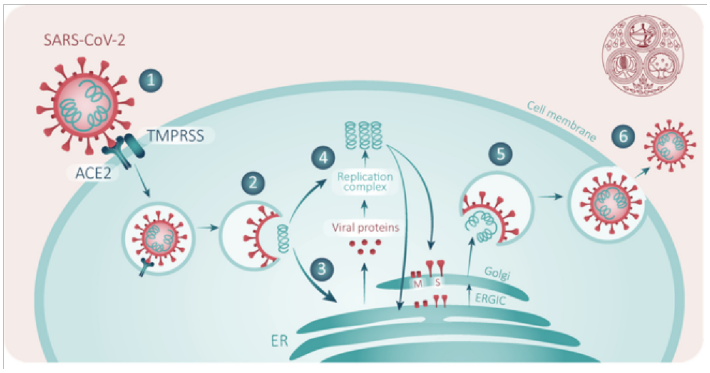
Keywords: Cloning RNA;RNA replication; Radioactive isotope; SARS-CoV2 infection

Introduction

SARS-CoV2 itself cannot reproduce because it does not replicate itself see the **Figure 1** [1,2]. So it has to ask the host cell to clone RNA for help. When SARS-CoV2 enters the human cell, they continue to delve into the cell nucleus and use the host's RNA polymerase (*RNAp*) to clone its RNA. It is conceivable that the human patient's *RNAp* is an RNA replication machinery of SARS CoV2. The multiplier depends on many factors and elaborate studies are required to determine it. The viral RNA after cloning combines with its specific proteins in the human patient cell's cytoplasm that it creates to new SARS-CoV2s then emerges from the host cell and continues to infect other cells with the same replication process as above. There are several ways to limit SARS-CoV2 infection.

- Prevent SARS-CoV2 at entering cells.
- Prevent SARS-CoV2 from cloning RNA.
- Destroy SARS-CoV2 with medication or immunotherapy (vaccine).

Our proposed option is to prevent SARS-CoV2 from replicating RNA by deactivating the host cell's *RNAp* with the use of Magnesium radioisotope.



(1) Spike protein on the virion binds to ACE2, a cell-surface protein. TMPRSS2, an enzyme, helps the virion enter. (2) The virion releases its RNA (3) Some RNA is translated into proteins by the cell's machinery (4) Some of these proteins form a replication complex to make more RNA (5) Proteins and RNA are assembled into a new virion in the Golgi and (6) released.

Figure 1: SARS-CoV-2 Replication Cycle. [1,2].

RNAp is a cofactor enzyme composed of a specific protein in green color, see the **Figure 2** [3-6] combined with metal Mg ions located in the active site. The function of the enzyme is to clone RNA molecules, was taken from the DNA molecule in the cell

nucleus. The role of Mg ions is very important and indispensable. In the absence of Mg ions, the enzyme is inactivated and the replication of the *RNAs* is stopped. After mRNA, tRNA, and RNA were cloned, they help to synthesize specific cellular proteins.

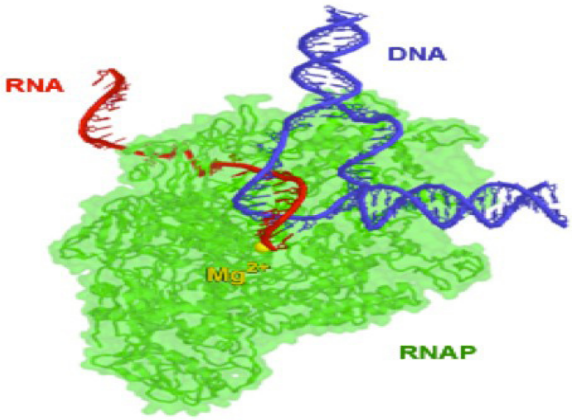


Figure 2: The *RNAp* structure in 2D [3].

The radioactive nucleus when the beta decaying will transform into the nucleus immediately behind it due to an increase in a positive charge. In the case of Mg, decay beta will transform into Al, and if Al continues beta decay it will turn into stable Si.

A proposal methodology

Assume that a stable Mg ion in RNA polymerase can be replaced with beta decay isotope, Mg^{28}. Mg^{28} has a half-life of 21 hours, emitting 3 beta particles with different energies, accompanied by gamma rays, X-rays, and bremsstrahlung radiation. When Mg^{28} decays, it converts to radioisotope Al^{28}, this isotope continues to decay beta then converts to stable Si^{28}. Both of the following isotopes are within the *RNAp* activity site but they are not the same as a cofactor of the enzyme. As a result, *RNAp* is inactivated. RNA replication of the SARS COV2 virus was stopped.

Possible consequences and side effects: When the SARS CoV2 RNA is not cloned, the infection process is stopped. We can look at how superior is this radioisotope therapy and what side effects it might have. That is:

- Removal of SARS CoV2 has entered the host cell because it has lost its only RNA when trying to replicate.
- Block the RNA replication process of SARS CoV2 leads to the spread of infection to new cells will be stopped.
- When introducing the radioactive substance into the cell, not only *RNAp* but also Hexokinase and DNA polymerase also compete to use Mg^{28}. The metabolic processes that these enzymes catalyze may be disrupted. The radiation can be bombarded within the cell, free radicals formed in the radioactive trajectory will disturb the metabolism of the cell. So not only will the infected cells have a metabolic disruption, but the healthy ones will be affected. These are important side effects and need to be taken into account in *invitro* and pre-clinical studies before conducting clinical trials.
- Physically, the active needs of the Mg-containing enzymes will produce Mg^{28} uptake. Therefore, any enzyme that works at a high frequency will be a place of high absorption for Mg^{28}. When a cell is infected with SARS CoV2, the need for viral RNA replication is many times greater than the need for regeneration of healthy cells through the phases G0, G1, S, G2, and M so that the flow of Mg^{28} in the blood will provide cells with SARS CoV that are cloning more RNA than healthy cells. And when *RNAp* is inactivated, the virus needs to replicate so new *RNAp* will continue to form, and thus the demand for Mg^{28} will increase until the amount of Mg^{28} in an intracellular fluid due to decay is balanced or less than the amount of stable Mg, the process stops. Therefore, to *RNAp* inactivation to be prioritized, we need to provide Mg^{28} so that its concentration in the cell is greater than the constant of stable Mg concentration.
- When a cell is infected with SARS CoV2, because the virus hijacks the RNA replication function, the specific proteins that the cell's RNA produces will not be synthesized. Regardless of how these cells will be damaged and will die. But when this infected cell copies the viral RNA at high frequency, the amount of Mg^{28}, Al^{28} in the cell will emit radiation. Owing to this feature, a radiation scan can be done on infected cells. Radiography may show that infected tissues other than the lungs instead of having x-rays or CTs.
- The effected dose given by radioactive isotopes for infected tissues can be calculated so low as to the least damaging. It is possible to use calculated and experimental simulation programs on *invitro*experiments.

The *invitro*experiment tests the proposed methodology:Experimental lots: lung cell is cultivated in Petri disk with and without Mg^{28} traces, and not infected and infected with SARS CoV2.

- Lung cells are not infected with the virus, do not mark Mg^{28}. Lot 1.
- Uninfected virus-infected lung cells marked with Mg^{28}.Lot 2.
- The infected lung cells do not mark Mg^{28}. Lot 3.
- Pulmonary infected cells marked with Mg^{28}. Lot 4.
- Marking dose of 1000Bq, 2000Bq, 3000Bg..Mg^{28}/1M cell to find the optimal dose.

Test criteria:

- The survival rate of Lot 2 cells compared to Lot 1.
- The most important characteristic proteins between lots 1, 2, 3, and 4.
- Number of cells infected with the virus over time between lots 3 and 4.
- Number of cells recovered between lots 3 and 4.
- Density of viruses in lots 3 and 4.
- Number of cells killed by the virus in lot 3.
- Number of dead cells from Mg^{28} lot 2, Lot 4.
- Number of cells killed by virus + Mg^{28}. Lot 4.

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Discussion

This is the idea for the method of inactivating RNA polymerase by radioactive isotope Mg^{28} without any experimental evidence to verify it. Logically, SARS COV2 has only one way of replicating its RNA through the host cell's *RNAp*, so stopping this unique clone can stop the spread of SARS COV2. There have been many studies on inactivation of *RNAp* with natural and artificial chemical compounds [4,5] but it seems that the success of these trials is still a dream. The method of using radioactive isotope Mg^{28} to inactivate *RNAp* is a completely new method, which is very simple in theory and easy to experimentally verify. Compound $(Mg^{28})Cl$ is commercially tested [6].

Recommendation

After the methodological testing, methodology can be applied in animals, preclinical experiments and clinical trials. It is thought that if this less expensive method is successful, the effect will be tremendous. It is recommended that epidemiological, biological and medical scientists work together to test this method. The author will be pleased to participate with scientific advisory function in the field of nuclear physics and methodology.

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