

Coronavirus Outbreaks: Nanomedicine and Future Perspectives

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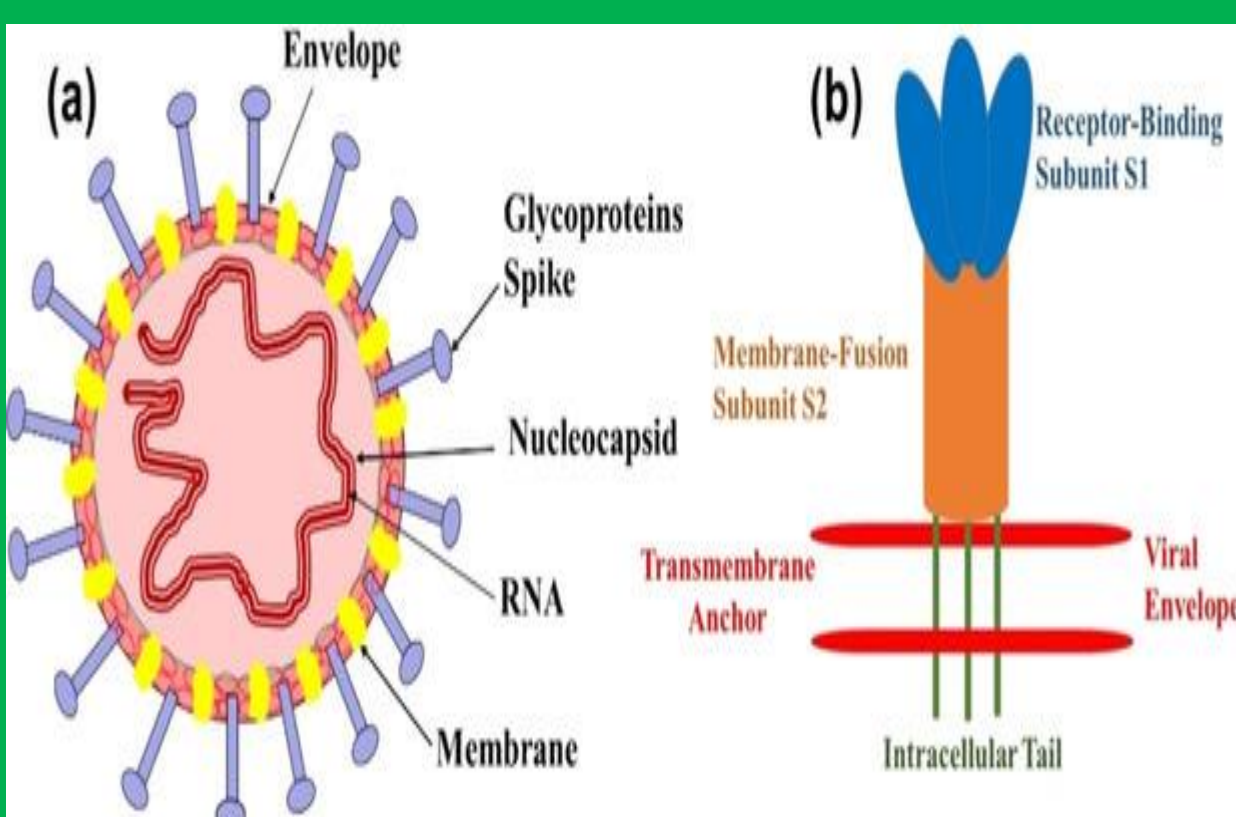
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INTRODUCTION

- In last two decades, entire world faced three outbreaks of coronaviruses like SARS, MERS and Now, COVID19.
- The first case of recent outbreak of COVID19 was recognized at Wuhan, Hubei, China five months ago.
- Later, it spread in the whole world and affects global health as well as global economy in very short duration.
- From the early 1900s to date, around 250 viruses species have been evolved, and these keep up increases in the coming years
- Here, describe the role of nanotechnology and herbals to combat COVID19.

(a) GENERAL STRUCTURE OF COVS (b) PREFUSION COVS SPIKES



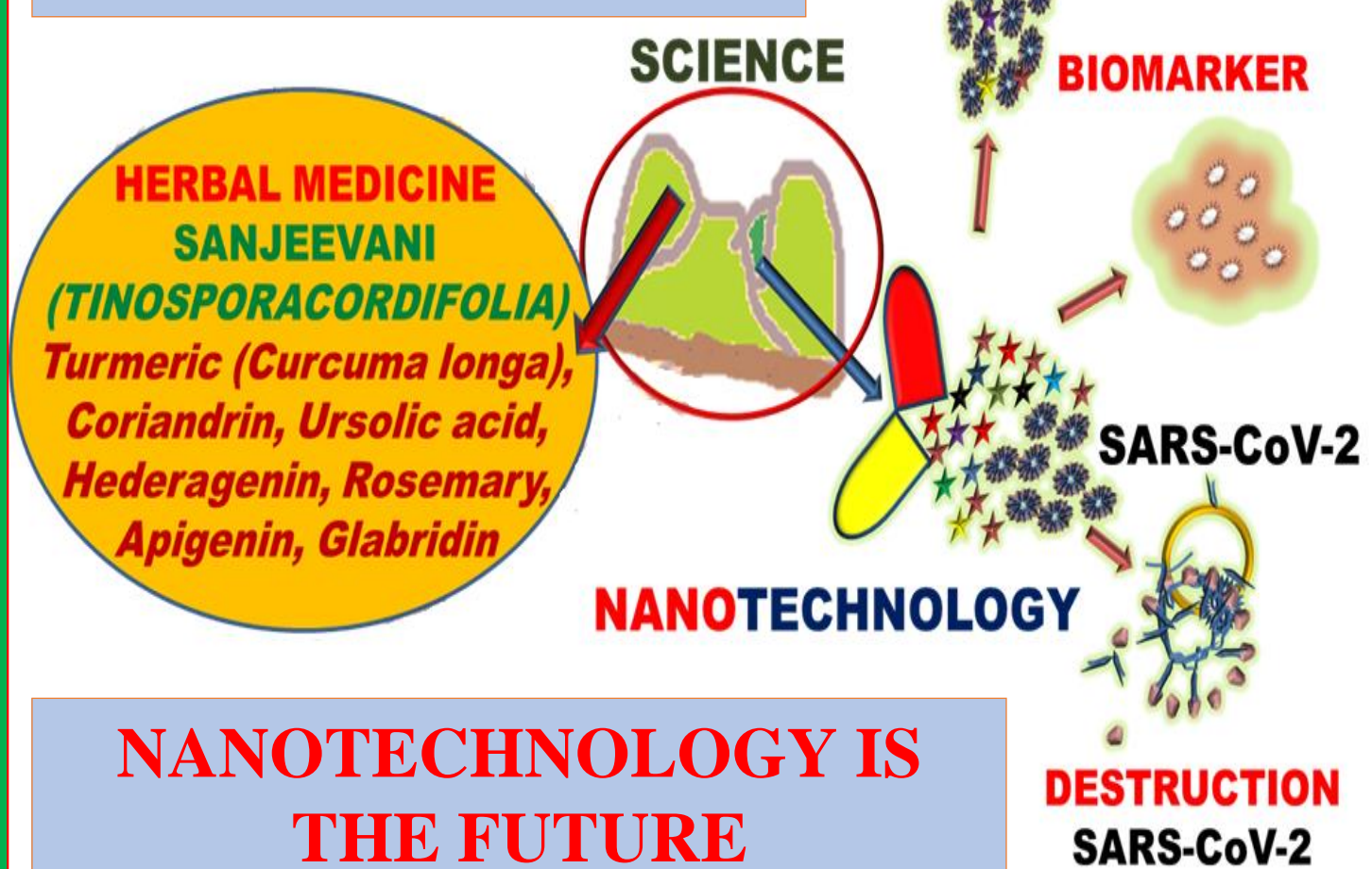
HCOVS AND THEIR CLINICAL SYMPTOMS

HCoV s	Clinical Symptoms	Incubation Period
HKU1	Fever, Cough, Respiratory Tract Illness (RTI), Sneezing, Dyspnea, Pneumonia	2-4 days
229E	Fever, Chills, Cough, Acute Rhinorrhea, Malaise, Nasal Congestion and Discharge, Headache, Throat Sore	2-5 days
OC43	Fever, Cold, Cough, Sputum, Dyspnea, Headache, Nasal Congestion and Discharge, Sneezing, Throat Sore	2-5 days
NL63	Fever, Cold, Cough, Respiratory Distress, Wheeze, Rales, Rhinorrhea, Tachypnea, Hypoxia	2-4 days
MERS-CoV	Fever, Cough, Cold, Shortness of Breath, Gastrointestinal Symptoms, Sore Throat, Arthralgia, Diarrhea and Vomiting, Pneumonia, Acute Renal Impairment, Multiple Organ Failures, Rapid Kidney Failure	2-13 days
SARS-CoV	Fever, Cough, Cold, Rigor, Shortness Of Breath, Gastrointestinal Symptoms, Myalgias, Headache, Malaise, Dyspnea, Respiratory Distress, Diarrhea, Pneumonia	2-11 days
SARS-CoV-2 (COVI D-19)	Fever, Coughing, Cold, Sore Throat, Nasal Congestion and Rhinorrhea, Diarrhea, Asymptomatic, Organ Function Damage, Acute Kidney And Cardiac Infection, Liver Dysfunction, Pneumothorax	2-14 days but in some cases extended to 24 days

HISTORICAL BACKGROUND

1962, Chicago USA	● HCoV 229E; Respiratory infections among medical students at University of Chicago
2002-2003, Netherlands	● HCoV-NL63; Replicated faster in monkey kidney cells as compared to HCoV 229E
2003, Hongkong	● SARS-CoV; Outbreak of severe respiratory infection in China
2003, Frankfurt, Germany	● SARS-CoV; patient traveled Singapore, Hong Kong, New York and During a stopover in Frankfurt, Germany on day 7
2003-2004, Shenzhen, China	● SARS-CoV; isolated from civet cats, the study revealed that it might be originated from animals
2009-2012, Kenya	● HCoV 229E, NL63, OC43, HKU1; Out of 417 samples, 2.4% HCoV-NL63, ~3% OC43, ~2% HKU1, 1% 29E.
2012, Jordan, Saudi Arabia	● MERS-CoV; Relatives are bat coronaviruses HKU4 and HKU5, 60 years old man died due to renal failure and respiratory infection.
2012, UK	● CoV of unknown origin; severe respiratory infection, the patient traveled from Qatar and Saudi Arabia.
2001-2013, France	● HCoV-OC43; genomic studies helped to understand the dynamics of evolution of CoVs
2014-2017, USA	● HCOVs OC43, NL63, 229E, HKU1; Out of 854575 cases; 2.2% OC43, 1.0% NL63, 0.8% 229E, 0.6% HKU1.
2019, China	● SARS-CoV-2; Responsible for COVID-19, severe respiratory infection which turned into global pandemic.

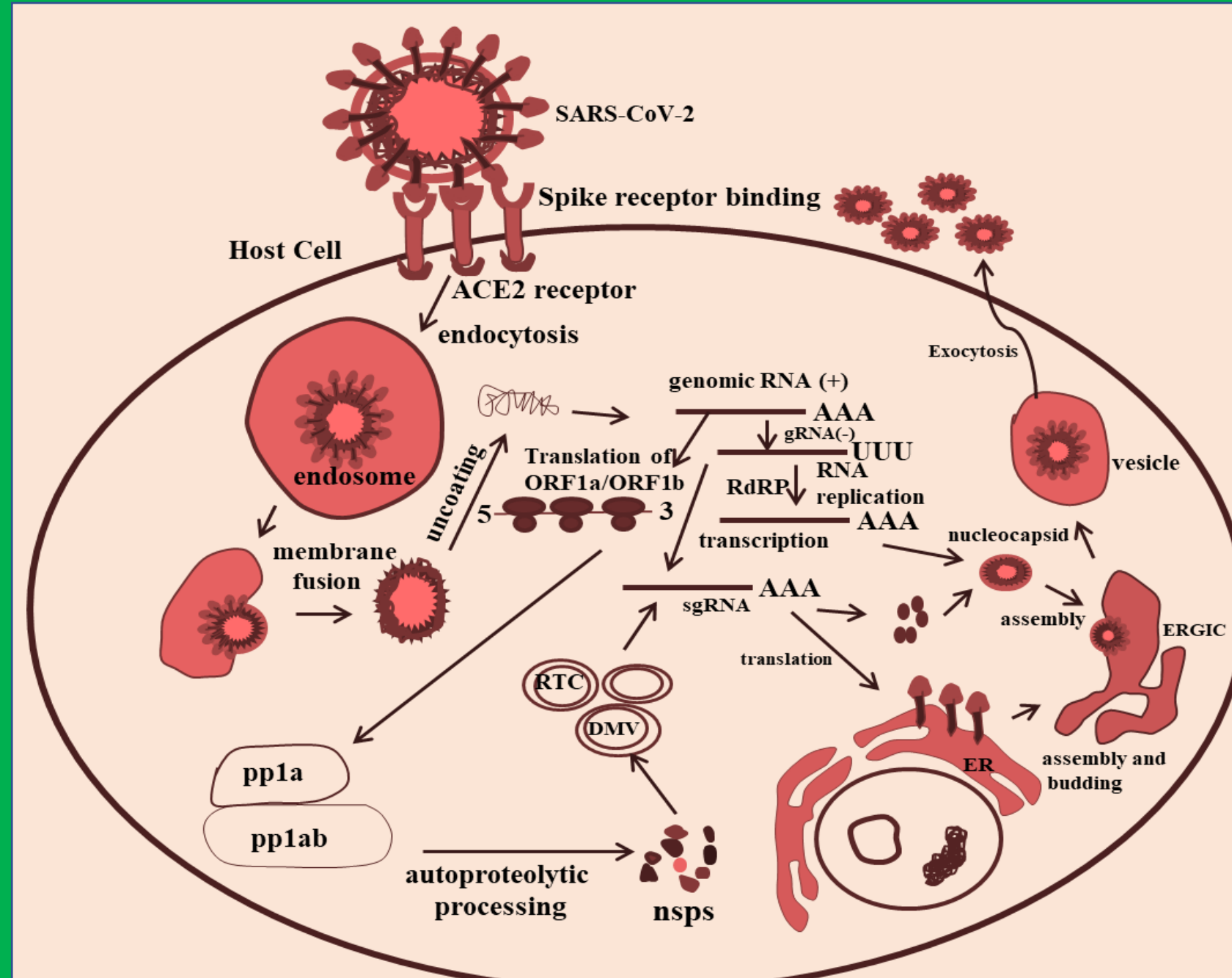
GRAPHICAL REPRESENTATION



FUTURE CHALLENGES AND PERSPECTIVES

- Controlling and development of vaccines for the outbreak of infectious diseases such as COVID19 need fast action.
- Scientists could be encouraged toward the use of nanomaterials for targeting viral structures and depriving the impact of such novel viral infections.
- The application of nanosensors, new tools offers massive advantages in the diagnosis of viral diseases.
- The development of nanosensors will be beneficial due to low cost, rapid - detection tool and can help in the epidemics
- The herbal drugs designed using specific parts of increase the resistance against the emerging and re-emerging viruses and bacteria.

SCHEMATIC OVERVIEW OF SARS-COV-2 LIFE CYCLE IN HOST

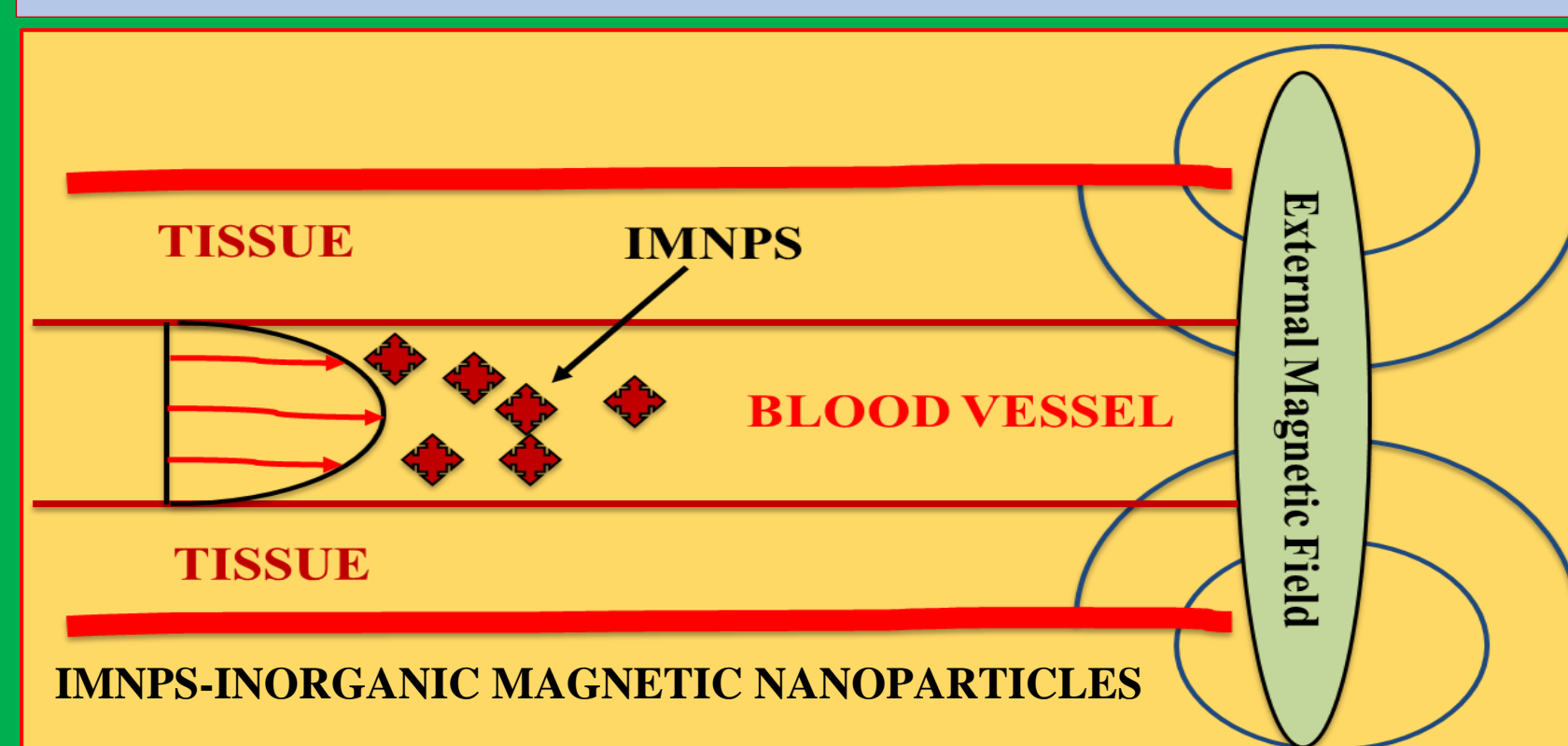


Modified schematic overview of SARS-CoV-2 life cycle in host cells, gRNA-genomic RNA; ERGIC-ER-Golgi intermediate complex; sgRNA- subgenomic RNA; RTC-replication transcription complexes; DMV- double-membrane vesicles; RdRP- RNA-dependent RNA polymerase.

FUNCTIONS OF NON-STRUCTURAL PROTEINS (NSPS)

nsp1	Promotes degradation of cellular mRNA as well as blocks translation of host cell, obstructive distinctive immunity reaction, inhibit interferon (IFN) signals
nsp2	Some functions are not known, holds to prohibitin proteins
nsp3	Multi-domain large transmembrane protein • N protein interact with Ac and Ub11 domains • Cytokine expression promote due to ADRP activity
nsp4	Potential transmembrane scaffold protein, Role in DMVs formation
nsp5	chymotrypsin-like protease (3CLpro), main protease (Mpro), cleaves viral polypeptides, inhibit interferon (IFN) signals
nsp6	Restrict expansion of autophagosome, Potential transmembrane scaffold protein, DMV formation
nsp7	Formation of hexadecameric complex with nsp8 and nsp12, role as a processivity clamp and primase for RNA polymerase
nsp8	Forms hexadecameric complex with nsp7 and 12, may act as primase as well as processivity clamp for RNA polymerase
nsp9	RNA binding protein, Dimerization
nsp10	Stimulates 2'-O-MT and ExoN activities, Scaffold protein for nsp14 and nsp16
nsp12	Primer and RNA-dependent, RNA polymerase
nsp13	RNA helicase, 5' triphosphatase
nsp14	Exoribonuclease activity for viral genome proofreading, N7-Mtase activity adds 5' cap to viral RNAs, 3'-5' exoribonuclease,
nsp15	nsp15 endoribonuclease, evasion of dsRNA sensors
nsp16	2'-O-Methyltransferase (2'-O-Mtase); avoiding MDA5 recognition, negative regulation of innate immunity

ILLUSTRATION OF IMNPS BASED DRUG DELIVERY SYSTEM



A. Gupta, S. Kumar, R. Kumar, A. K. Choudhary, K. Kumari, P. Singh, V. Kumar (2020), COVID-19: Emergence of Infectious Diseases, Nanotechnology Aspects, Challenges, and Future Perspectives ChemistrySelect, 5, 7521-7533.

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