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Research Article

# Nanoparticle Conjugated Antibody and Crispr-Cas 9 DNA Editing Enumeration Reveals the Possible Vaccination Against Spontaneous “IS::Tn::IS” Based Corona Mutants

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## Abstract

Global corona pandemic forced scientists worldwide, to search the reason for its spontaneous changes of infective mode, (i.e. the changing sequence of m-RNA (Messenger Ribonucleic acid), that mainly being transmitted by the corona virus membrane coat fusion to lung alveolus cell and cause infection.). In this paper the author attempts to describe, the cause of rapid mutation of m-RNA, that has changed the viral spike protein structures, adhering and fusing nature of corona, to infect host spontaneously and caused global pandemic. To elaborate the camouflaging of corona pandemics, the author has considered the function of transposable element, the jumping gene, illegitimate, spontaneous, recombination mutational problem. The said gene was discovered by Nobel Laureates madam Prof. Barbara Mc Clintock, 1940 in USA on Maize. Later this was studied in microbes by Prof. H. Saedler and Prof. P Starlinger in Germany. “IS::Tn:: IS”DNA (Insertion Sequence Flanked Transposable elements.IS::Tn::IS supports the spontaneous illegitimate recombination of surface spike proteins of corona. Tn in presence of IS (insertion sequence), was studied in DNA and RNA mutations, rearrangements and antibiotic resistance in Escherichia coli K-12 experiments. In addition, the author emphasized the possible development of AAIR (Antiadherent Immune response)in Balb/C mice, imagining the author’s concept of nano-coating, and Crispr/Cas-9 transposons of Nobel laureates madam(s) Prof. Duodna and Charpentier, 2020, as used in DNA repairing, and is inspired to be used for Corona RNA and to combat corona pandemics. Due to spontaneous DNA mutations, and the morphological change of corona spike proteins disturb the development of stable vaccinations. Corona treatments by nanoparticle, conjugated antibodies (plasma), AAIR and CRISPR-cas-9, DNA editing, perhaps, to be the ultimate solution to prevent corona like respiratory pandemics in future world.

***Keywords:*** *Microbes; Corona; Vaccine; Transposons; and Spike (S) Protein*

## Introduction

It is emphasized that spontaneous mutations of DNA/RNA is the basic cause of global pandemic of corona. The reason has been speculated that jumping gene type transposons are present in corona and are involved to rearrange m- RNA corona infections. The philosophy of transposons (Tn) was first discovered and observed by Prof. Barbara McClintock in USA on maize by observing segregating colour changes on maize seeds and proposed that the change of color of maize seeds are caused by (Tn) Transposons jumping gene [1]. In 1940 she discovered that and obtained Nobel Prize in 1983. Later Prof. P. Starlinger and Prof. H. Saedler studied the presence of IS::Tn::IS in bacteria *Escherichia coli*. The integration and multiplications/jumping gene from one place to other, from one gene/plasmid to other have

been studied in various manner by different scientists [2,3]. IS::Tn::IS was also found in Mu bacteriophages and many other bacterial and animal viruses [4-7]. Researchers, all over the world studied transposons among bacteriophages to study bacterial evolution, to differentiate bacterial pathogens, transforming non-pathogenic *Escherichia coli* to pathogenic *Escherichia coli*. The presence of IS was also studied by the author on fimbrial (pili) expression, Lac-and Gal-OP (Operons), regulating surface antigens and sugar fermentation in Escherichia coli. However in present context of corona infections, no such IS::Tn::IS transposon, responsible for corona spike (s) proteins mutations, have been reported. So the author was curious enough to search information regarding the presence of IS in Corona [8-10]. Some possible figures are reproduced to justify the power of IS::Tn::IS, involved in genetic illegitimate recombination, mutations and evolution (Figure 1a-1f).

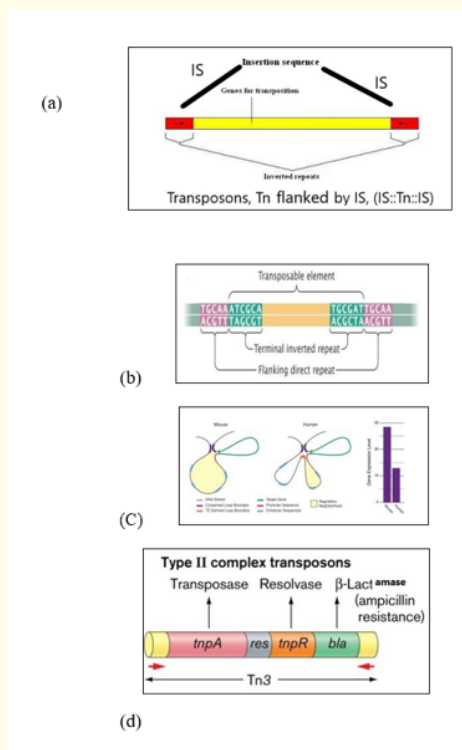

***Figure 1:*** *Figure 1a shows one transposons, flanked by IS elements (IS::Tn::IS), Figure 1b shows the repeats and inverted repeats DNA sequences involved of IS elements. Figure 1C shows the mechanism of Tn enzymes involved in illegitimate recombination and rearrangements. Cut and Paste and Copy and Paste are responsible in palindromic mutation. The foreign DNA have been identified in such illegitimate recombination where IS elements support to insert foreign DNA into host recipients [1]. Involved histograms in figure 1C, signifies the comparative nature, the frequencies of chromatin folding, among mouse and human. It shows that transposons based chromatin folding in mouse is higher compared to human. IR (Immune Response) in mouse is therefore found stable, compared to human. MHC-HLA gene, responsible for IR in human chromosome 17 is more susceptible compared to chromosome 6 in mouse [2-9]. Chromatin loops are important for gene regulation because they define a gene's regulatory neighbor- hood, which contains the promoter and enhancer sequences responsible for determining its expression. Remarkably, transposable elements (TEs) are responsible for creating around 1/3 of all loop boundaries in the human and mouse genomes and contribute up to 75% of loops unique to either species. When a TE creates a human-specific or mouse-specific loop it can change a gene's rearrangements and illegitimate recombination but also the reason for increasing antibiotic resistance in bacteria and evolution living world. Figure 1d represents the ampicillin resistant Tn. Figure 1e shows the maize seeds color segregation, as caused by transposons. Figure 1f is reproduced with the legendary personality of Barbara Mc Clintock, who identified and discovered this Tn, causing colour change of maize seeds in 1931, and received Nobel Prize in 1983 [1]. IS based Tn (Transposons) are involved in higher and lower groups of plant and animal kingdom, including the evolution of viruses and bacteria.*

Tn3 ampicillin resistant with inverted regulatory neighborhood, leading to altered gene expression. The illustration shows a hypothetical region of the human and mouse genomes in which four enhancer sequences for the same target gene fall within a conserved loop. In this example, a TE-derived loop boundary in the human genome (orange bar) shrinks the regulatory neighborhood, preventing two of four enhancers from interacting with their target gene's promoter sequence. The net result is reduced gene expression in human relative to mouse. Looping variations such as these appear to be an important underlying cause of differential gene regulation across species and between different human cell types, suggesting that TE activity may play significant roles in evolution and disease.

The method was studied by radio isotopic IS DNA labelling and southern hybridization. The method proves also how one IS elements jumps from plasmid to chromosome and back to plasmid. The study inspired not only to study genetic repeats of IS3.

The camouflaging infective nature of SARS COV- 2 corona virus, covid-19, associated with Tn, as proposed by the author [10-14]. Jumping-genes as retro transposons [9] hijacks special cells called nurse cells, the invasive nature of DNA driving evolution, and causing diseases. Almost half of our DNA sequences are made up of jumping genes, known as transposons. They jump around the genome in developing sperm and egg cells and are important in cellular evolution [15] and cause new mutations that lead to diseases. Remarkably little is known about when and where these movements started in development of reproductive cells. The key process that ensures their propagation for future generations with possible genetic disorders. Animals have developed a powerful DNA rearrangement, using suppressing activities of jumping gene. Non-coding pi RNAs [15-17], that recognize jumping genes and suppress their activity.

Some information has been recorded that virus, Covid-19, originated from Wuhan, China, and was spread all over the world, represent no RNA variations. Measurement of antibodies to SARS-CoV-2 will improve disease management, if used correctly. In late 2019, China reported a cluster of atypical pneumonia causative agent, responsible for severe acute respiratory syndrome (SARS), rapidly spreading across the globe through human interactions and respiratory transmissions and pandemic.

Sequencing and searching the presence of IS elements in Covid-19 ss RNA are seems to be essential to understand pandemic and the delayed process of vaccination. 8 copies of IS1 and other number of copies of IS2, IS3 were identified in chromosomes and plasmid of *Escherichia coli* and other enteric infectious of water, soil and environment born. IS was also observed in plasmids of hybrid *E. coli*-K-12. It is obvious for the author that by observing the changing copies of IS significantly influenced the infective modes of bacteria, viruses and their evolution [10,14]. Compared to wild types that could have been widely used for the diagnosis of acute (current) SARS-CoV-2 infections [16,17].

To study and to compare the infective mode of corona and other SARS and MERS, H1N1, viruses, it is essential that parallel to their phonotypical SEM (Scanning Electron Microscopy) views, molecular biology of those viruses are need to be studied. By searching IS1 insertion sequence among all possible corona mutants, their wild types, it is essential also to search IS among pneumococcus and other related microbes, that predominate infections and increasing fatality. After an incubation period of 3 days, corona virus can cause the symptoms of a common cold, including nasal obstruction, sneezing, runny nose, secretions and coughing [16-18].

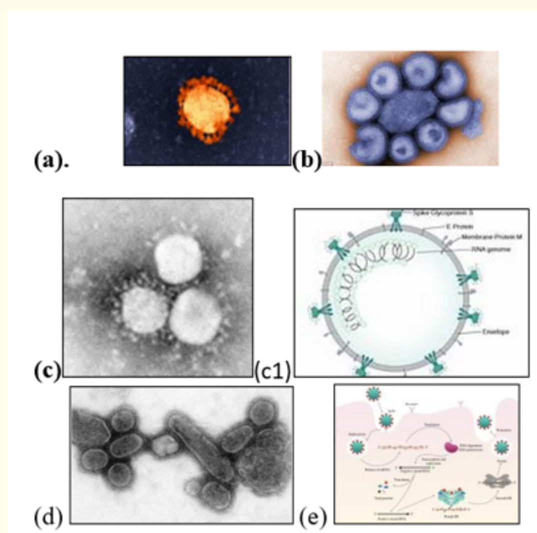


***Figure 2:*** *(a) show the SEM (Scanning Electron Microscope) views of H1N1, (b) Influenza virus colony, (c) SERS-COV-2 virus aggregating by their spike proteins in colony formation. The molecular structure of -COV-2 RNA-virus, ss RNA (Figure 2c1) transcribe coat- spike (S) glycoprotein, enzymatically initiating ACE-I, II (angiotensin converting enzyme, I and II) surface activities of host cell [19,20]. ACE-I and II help corona to adhere membrane of lung cells. OC43 haemagglutinin type virions are released from host cells after rupturing respiratory cell membrane. New virions transmit the infection via airborne droplets to the healthy recipients. Virus replicates/multiply spontaneously in support of ss m-RNA and r-RNA of respiratory lung cells. (d) shows the structure of virus caused outbreak of Spanish flu in 1918 pandemic. Viral clusters, and molecular biology significantly represent the similarities of their spike proteins, and colony formations of virus. The envelope glycoprotein is the characteristic feature, the chemistry of adherence of virus, the replication and synthesis of spike protein. Figure 2e shows the proposed cycle of m-RNA ss RNA, Covid-19, that directly involved for rapid growths of spike (S) proteins, the capsid formation and multiplying virus particles in lung cells. 3' ss m-RNA of Covid-19, recognizes 5'r- RNA of infected cells, translate glycoprotein, envelope membrane matrix protein and new corona virus particles, to spread infections.*

Coronaviruses as reported found in avian and mammalian species, resemble morphologically and phenotypically similar, but differ by their antigenic structures. Even coronaviruses of human and cattle are found antigenically similar, varied by their pathogenic expression. As common colds symptom, respiratory infections, corona viruses, invade many different tissues for initiating MOF (multiorgan failure) and fatal deaths of corona patients.

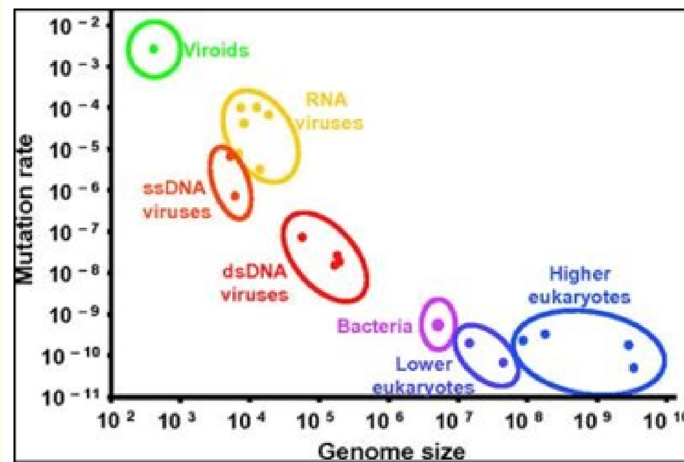


***Figure 3a:*** *At the frequencies of 10^-2, represent it spreading and infective potentialities. The new strain has changed its spike proteins, the regions of its outer protein coat/shell that infect alveoli cells. The change makes it a much more efficient predator. It passes quickly from cell to cell in our bodies, copying itself at a furious pace. Baric's experiments help to explain why the 614G strain, which first emerged in Europe in February, has quickly dominated worldwide spread [19]. He says that the virus likely jumped out of bats and discovered a brand new population of human hosts, with more than 7 billion of us on the planet to infect. None of us has any immune defenses against it, so we are prime targets. Viruses with genetic advantages that help them copy themselves faster and jump more quickly between hosts to survive and to cause pandemic", says Baric, who is one of the world's foremost experts on coronaviruses. His new study is published in the journal Science.*

As reported most human coronaviruses fall under two serotypes, OC43-and 229E- surface antigen protein expressions [1]. Figure 3 shows as per genomic length and the frequency of mutation. Viruses remain at the top.

The new study backs up earlier research by a team of scientists led by Bette Korber, PhD, at Los Alamos National Laboratory in New Mexico. The team first noticed the rapid spread of the new strain and questioned whether the virus wasn't evolving to become more easily passed between people. Nov. 13, 2020 -- The virus that causes COVID-19 is not the same strain as what first emerged from China. A new study shows it has changed slightly in a way that makes it more contagious to humans. Compared to the original strain, people infected with the new strain -- called 614G -- have higher viral loads in their nose and throat, though they don't seem to get any sicker. But they are much more contagious to others.

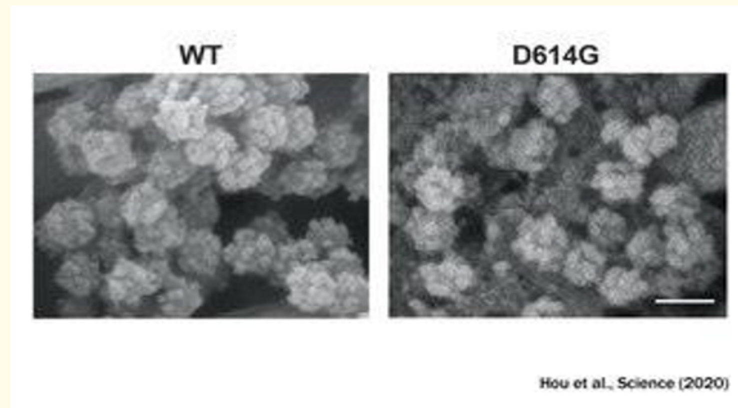


***Figure 3b:*** *Shows the fine surface antigenic variations among old (WT) virus strain compared to the new one. It shows that except fine surface antigen change, no any vigorous morphological change is identified, says Ralph Baric, PhD, a professor of epidemiology, microbiology, and immunology at the University of North Carolina at Chapel Hill. In new experiments, it was observed, that the animals who were infected with the new 614G strain., infect the animal much more quickly to the new heathy animal compared to the animals, who were already infected and were recovered.*

After establishing the experimental procedures, (Materials and Methods), it was easy to correlate the concept of AAIR (Antiadherent Immune response), if IS1 similar sequence is found among variable mutants and if antibody against IS1 is being developed in Balb/c mice similar to 026: EPEC (Enteropathogenic Escherichia coli), surface antigenic fatal diarrea, similarly with corona mutants and wild type, then it is also possible to develop IS1 based antibody AAIR again corona.IS based antibody will recognize the mutants, changing rapidly spike (S) proteins, responsible to adhere lung alveoli cells. It is therefore essential to search the presence of IS elements among corona and other respiratory viruses, SARS, MERS and other respiratory viruses.

Cloning of said IS element DNA sequence into pBR322 and recently developed vectors, cloned hybrid plasmid was transformed into *Escherichia coli* K-12 C600, Yale strain [11-14]. An AAIR in Balb/C albino mice could have been possible to develop. Isolation of pure hybrid fimbriae (pili) surface antigen of *E. coli* K-12 was used sterile peritoneally into mice to observe AAIR among mice similarly 026: EPEC fatal diarrhea also with all respiratory viruses. In experiment the author observed that the potential AAIR against 026: EPEC diarrhea in mice. Immunized mice were found all healthy, even at higher dose of infections. The said AAIR could be applicable to protect all variants of corona, if IS1 similar common gene is identified among all isolated SERS, MERS, corona, and respiratory viral mutants [3].

The coronaviruses were originally grouped into family "Corona", the "Crown" constituted by glycoprotein, (Figure 2c). Most human corona viruses fall into 229E and OC43 antigenic variants, as already reported. These differ in both antigenic determinants and culturing requirements. 229E-like antigenic variants can usually be isolated in human embryonic fibroblast cultures. OC43-antigenic variants was isolated from suckling mouse brain. There is little antigenic cross-reactions were observed, caused independent epidemics. Further to that, it is reported that human coronaviruses are, predominantly containing amino peptidase-N and sialic acid-containing (APNSA) receptors [19,20] (Figure 3).

There are 7 mRNAs are involved in such envelop proteins. For assembling virus particles to form matured corona viruses, and their release in the from membrane bound buds formations, resembled their growths similar to vegetative growths of yeast cells. Studies in both

organ cultures and human volunteers, enumerate that corona viruses are extremely fastidious and grow only in differentiated respiratory epithelial cells to make infected cells vacuolated and damage. The cell damage triggers the inflammatory nasal secretion, and swelling to stimulate sneezing in respiratory airways, increasing body temperature rise. The growth of opportunistic bacterial species, *Bacillaceae, Coccaceae, Chlamydomonas*, influence the increasing inflammation, pathogenically support corona to damage mucocilliary activity of the respiratory, urinary tract and lung, and to bring the patients to death [21]. Interferon (IF) can protect against infective stage of corona, but it's functionality against corona in human immune response is not understood.

Because coronavirus infections are not common and are IF(Interferon) based. Many individuals have specific antibodies in their nasal secretions that can protect against infection. Most of these antibodies are directed against the surface projections and neutralize the infectivity of the virus. Cell-mediated immunity and allergy have not been studied properly and intensively to confirm the mode of corona inflammations. Even the epidemiology of inflammatory coronavirus colds is not well defined and studied. Herd Immunity concept is also an alternative approach to observe infection movement, pass through communities, during winter in families, schools, and locality to mitigate corona infections [11-15].

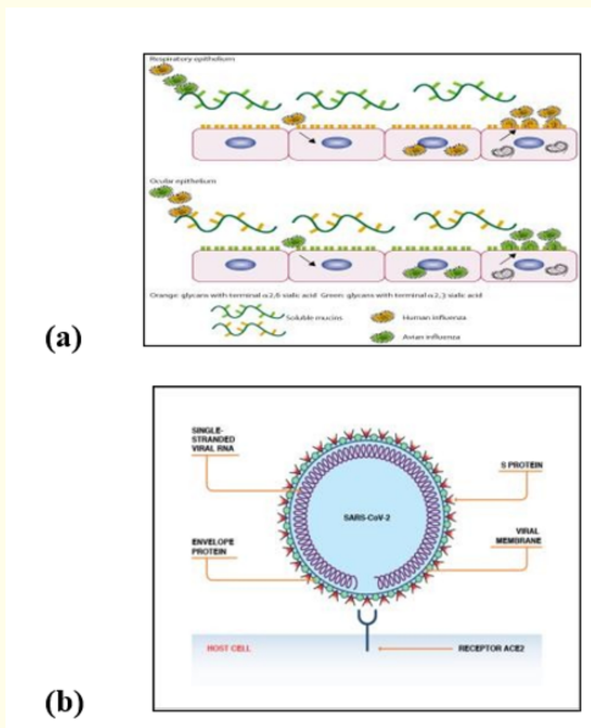


***Figure 4:*** *Figure 4a and 4b describe the presence of two enzymes and chemical components (APNSA, ACE), involved in attachment of influenza viruses (a) and corona (b) on the surface of human respiratory systems [19,20].*

## Materials

(a) IS-DNA probe, (b) Hybridization buffer solution, Instruments to work with bacteria and viruses. LH (Laminar Hood), Autoclave, UV-Lamp, sterilizing alcohol, (c) Respiratory viruses lytic buffer, (d) Nitrocellulose filter, (e) Micropipettes (f) Temperature controlled water bath with shaker, (g) Polymerase Chain Reaction instrument, manual and real time, (h) Serotyping arrangements.

## Methods

IS probe-DNA was prepared by Prof. Heinz Saedler, Institute of Genetic Engineering, Biology-III, Albert Luedwig University (ALU), Freiburg, Germany during 1980. Dr. John Cullum, FRS, a visiting faculty, my colleague, guided to study transposable element in microbes, Brahma., *et al*. [10]. Later the author took the said probe to Max-Planck institute of Immubiology, ALU, Freiburg, Germany to study the infective natures of different *Escherichia coli*, EPEC (*Enteropathogenic Escherichia coli*), ETEC (*Enterotoxigenic Escherichia coli*) and UTIEC (Urinary tract Infecting *Escherichia coli*) in presence and absence of IS.

IS probes were used to study and to differentiate the genetic expression of fimbriae (pili) as the mains cause of bacterial adherence, and the expression of colonization factor antigen (CFA). P32 alpha d ATP radio isotope was used to label IS DNA Probe and to hybridize the donor and hybrid recipients of plasmid and chromosomal DNA, to observe the presence of IS in hybrid plasmids. DNA and chromosomes were chopped by restriction enzymes (REs). EcoR, Pst1, Sal, Hind II, BamH1, Hapa, RE(s) were used to separate small fragments of plasmids and to clone foreign DNA of MRHU(+) positive isolated plasmid DNA [11-14].

IS cloned hybrid plasmid expressed hybrid fimbriae (pili) could be used to search the presence of IS homology DNA/RNA in different mutants of corona, MARS, SERS, and respiratory viruses. Considering the proposed IS::Tn::IS viral spike gene cloning (ssRNA) the hybrid plasmid could be used similar manner to search the presence of IS homology DNA/RNA sequences among all mutant variants. AAIR development is responsible to protect viral adherence.

IS probe could be isolated and purified from the known source of *E. coli* k-12 hybrid strains, containing plasmid. The presence of IS could easily be searched by southern and western blot. IS1, IS2, IS3...IS10, different DNA-probes can also be used to search the presence of IS among corona respiratory viruses [10]. DNA probes were labelled against radio-isotope p32 alpha (α) d ATP, and in addition of buffers dGTP, dCTP, dTTP combined nucleotides. (ss) DNA IS element in presence DNA polymerase. Radio isotope labelled IS probes could identify the presence of IS in corona viruses. ss RNA of viruses could easily be hybridized as per Southern [21]. At a time many virus es could be tested in the form of western Blot. Tagging single drop of virus lysates, on NC (Nitrocellulose) filter membranes and were denatured by NaOH buffers. NC-membrane filters were then dried in temperature controlled vacuumed dryer and were then put into hybridized solution containing radioisotope ss IS DNA probe, immerged with PEG (Polyethyl Glycol). Hybridization solution was gently shake overnight at 65$^{o}$ C closed temperature controlled water bath. Southern, Western and Northern blots are all made similar fashion, varying slight the buffers. To confirm the presence IS DNA in viral DNA/RNA, Southern blot was sufficient (Figure 5a) [21].

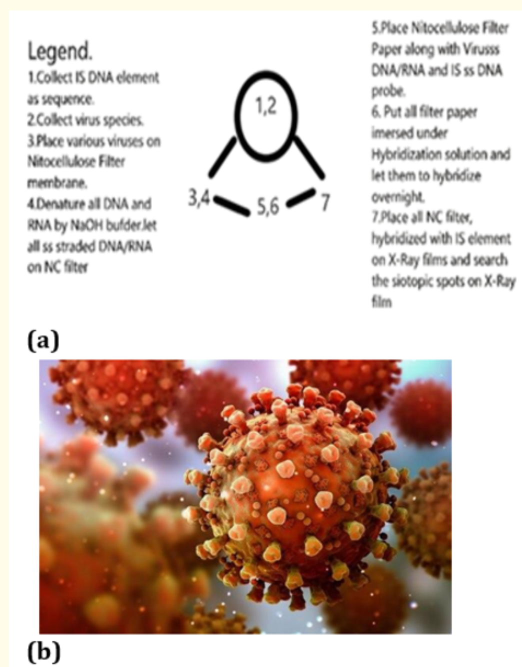


***Figure 5:*** *(a), Legend: 1 Collect IS DNA Element from DNA bank→2.Collect Viral Species carefully with proper protections and mask →3. Place the various species on NC-Filter at vacuum on, 4 number in one round filter membrane 2-4 inch in NC filter diameter →4. Denatured all tagged viral solution by NaOH buffer for releasing their ss RNA→ Place NC filter in Vacuum dryer at 35-37oC for 2 hours→5. Put all dried NC filter with ss RNA into ss IS- p32 alfa d ATP labelled probe for hybridization solution, overnight at 65oC in a closed water bath in gentle shaking. →6. Take the filter carefully from hybridization and place them on clean Watman blotting paper to dry them open. →7. Put all IS labelled hybridized virus RNA/DNA on Kodak X-Ray filter in Dark at least for a week, in a series of routine work. → 8. Take out in dark the film and put them in film exposer solution of Kodak and for visualization. → Chopped RNA/DNA by Restriction Enzyme (RE) of Pst1 and EcoR1 could be effective to search IS localization in copies in ssRNA, ds RNA of viruses as reproduced by RE in AGE (Agarose gel Electrophoresis) similar to any DNA molecular studies, involved for screening Corona ss RNA and hybridisation. 5b shows the figure of one active corona virus. The dangerous living particle has taken out 10 millions lives in USA. The spike proteins can be attacked by nanoparticle baes IS antibodies, if found that majority of these viruses significantly hybridized with IS based DNA/RNA sequence. A vast study is required to establish the community of virus group, through radioisotope hybridization.*

### Vaccine model interpretation and experimental proposals

As reported in Nature, more than 90 vaccine companies are being involved to develop against SARS-CoV-2 vaccine. The research teams in companies and universities globally are using experiments and begun injecting the formulations into volunteers under safety trials. Others have started testing in animals. Mutational effects of transposons might be different among corona MERS, HIV viruses. Although the mode of infection and transmission of these viruses are different, air, dust, water, human and animal born. The "host-vs.-graft" IR and will remain mostly same in T-cell based humoral immunity. Rate of mutations have accomplished viruses, the search of host and vectors. The insect (arthropods), water, air and dust, higher and lower groups of animal, are all involved as carrier of corona. Origin of corona, from different animal sources Bat, Camel and Pangolin, compared to HIV, of blue monkey in Africa, create confusion to design vaccine.

The most important part of these viruses are the surface lipid conjugated spike glycol-protein and epigenetics of ss, RNA replication, transcription and translations. The mode of rapid infectivity of corona viruses are basically depend on such coats, the adaptive nature of mutations "host-vs.-graft", long and short distance, transmitting and propagating power. Viruses are clever, compared to bacteria. For designing vaccine against such infective agents, IS mediated hybridization perhaps would be a breakthrough. To classify infective and non-infective corona, IS based hybridization study is important [7,9,15,16].

## Conclusion

Virus Bacteria, Fungi, Mould and Algae are belonging to organised (Fungi, Mould and Algae (eukaryons) and unorganized bacteria and Virus (prokaryons) nucleic acid cells. Our body cell system belongs to eukaryotic cells and tissues. Viral cells as prokaryon carry ss, (single stranded), or ds (double stranded) RNA or DNA and transposons. Compared to bacteria, viruses can only survive, if host for such viruses are found [14]. For survivals, viruses adapt environment spontaneously by mutations and participate evolution. Bacteria and viruses follow their metabolic activities, either in the form of symbiosis, partial full parasitic nature, "host–vs -graft" immune responses (IR).

Bacteria at the size, of 1 micron (μ) to 10 micron (μ) irrespective to host, have their own metabolic system. On the other, viruses are fully host specific, change from non-pathogenic to pathogenic, lytic to lysogenic phases. Based on signal received from hosts, bacteriophages in case of bacteria and retro and adeno viruses in case of animal and human propagate by means of infections. As per host and environment they colonize and grow in normal and extreme, acidophilic (pH1-2), mesospheric and thermophile environments. Lambda, Psi-ex, T4 viruses share their existence by transforming DNA to RNA among adeno-, retro- and rhino, animal viruses (human, animal, bird and insect) to sustain host specific activities [14,15].

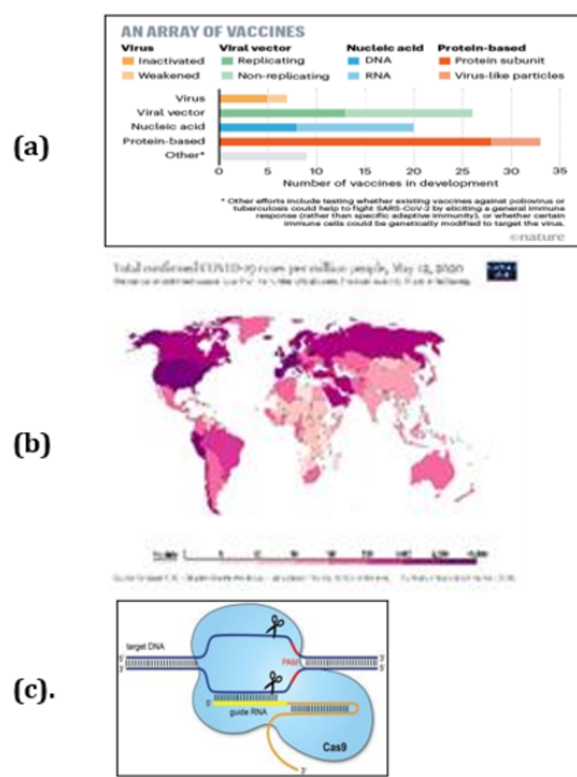


***Figure 6:*** *(a) Shows vaccine designs in support of isolated surface protein virus, m-, r- RNA, and or by attenuated virus, RNA/DNA. (b) Represents the Covid-19 pandemic, spreading globally and are being indicated by pink (less effected countries) → Violet (countries with increasing trends) and →Dark (potentially effected countries). However these colors are changing rapidly (i.e. the changing corona of India from 17th to 1st. Recently scientific news say that in Jan-Feb of 2021, the rate of corona infection could perhaps be 2 lacs/day among 1.3 billion Indian population, USA, and Brazil remain in 1st and 2nd position. The viral strains are changing. (c) Represents the repairing mechanism of Crispr/Cas-9 transposons, protein. Crispr/Cas-9 mechanism is used to repair pathogenic corona to nonpathogenic corona sequence, if Crispr/Cas-9 transposons is modified by nonpathogenic influenza virus coat spike proteins.*

Computation simulation could be used to search the sequence homology and to use them in Crispr/cas-9 repair mechanism [23]. The hybrid plasmid has been designed by the author [10], was associated with HA-(Haemagglutinin) gene, indirectly represent the adherence and colonization. Hybrid strains *GE-Eoli-K-12* surface fimbriae expressed AAIR, (Antiadherent immune response) in Balb/C mice to combat 026: EPEC fatal infection [12], CRISPR (Clustered Regularly Interspaced Short Palindromic Repeat/Cas9 protein as transposon, recently discovered could also be involved to repair Corona [11-13]. Cas-9 protein transposons will search RNA homology in pathogenic corona, precisely cut and repair corona [14-20]. The prophylaxis of “Plasma Therapy” [22-28] against corona could be useful as non-specific IR in trial and error experimentation. To increase immunity against particular serotype of corona. PCR, RTPCR (Polymerase Chain Reaction) could be efficient in routine checking, diagnosis, monitoring corona.

A mammoth approach is essential to manage the prophylaxis of corona infection, comprising drug design, CRISPR/Cas-9 and IR base small molecule as transposons based DNA vaccine, that will target (Major histocompatibility Complex based Human link Antigen) MHC/HLA, gene expression and to secret interleukin, interferon (IL, IF) protein, activating CD8, CD4, T-B-and Macrophages (Granulocytes and Basophiles) to kill mischievous/unknown infective elements like SARS COV-2 virus, n-COVID-19 infections. AAIR (Antiadherent Immune response) concept is primarily used to block adherence of corona like viruses, predominating the spread infections. Corona spike proteins as main machineries to adhere lung cell, camouflage the body immune response (IR) by humoral immune response, activated by vaccination.

The proposed corona AAIR could be disturbed by mutation of “IS::Tn::IS” transposons, spontaneously changing spike protein characters. T-lymphocyte, B- lymphocyte, Macrophage based IR prophylaxis, allow corona virus not to adhere on lung cell and to proliferate. In support of ACE-I and II, corona infect the body. If the said RNA/DNA get mutated, then the structure of spike protein will change. The T-cell will not recognize the said virus and will fail to inform b-cell to develop antibodies to develop AAIR, so it is essential that IS based IR to combat all mutants of corona. The corona viral prophylaxis in this search will be large.

Viruses in this series can be varied from mild cold: → Influenza→ Flu→ MERS→ SARS and Corona-Covid-19.

To combat corona, the author proposes two viable concepts; one is nanoengineering (nano-coating), nanoparticle conjugated antibody to protect trachea and, lung alveoli and the other is the application of CRISPR/Cas 9, DHA editing/repairing pathogenic corona tonon-pathogenic flue viral RNA [29,30]. Over time, new variants of viruses are expected to occur. All viruses constantly mutate their genetic code. These variants can emerge and disappear spontaneously. Though sometimes selective pressure allows the variant to persist through adaptive evolution, multiple variants of the SARS-CoV-2, COVID-19 has been documented globally persist. The emerging concern of corona variant has been first identified in the United Kingdom with an unusually large number of mutations and indicates the first variant of concern (in December 2020) carries 23 mutations compared to the wild-type SARS-CoV-2, with 14 non-synonymous (amino acid altering) mutations. Six synonymous (non-amino acid altering) mutations. These mutations lead to changes in protein structures, eight of which occur in the spike protein (Figure 3b and 5b). This is highly unprecedented as most SARS-CoV-2 variants have only a few mutations that accumulate at a relatively consistent rate over the time [29].

## Acknowledgement

This paper has been dedicated to late Prof. S. Basu, my “Guru” who left us on 25th December 2020.

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