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SARS-CoV-2 Infection Inhibition by Gene Manipulation

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Abstract

Owed to unique coronavirus (Covid-19) outbursts, the year 2020 perceived an unforeseen contagion condition. If the patient has concomitant diseases at once, the situation can become unfluctuating shoddier. The privation of identification for a viral related contagion due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is considered liable for the fiasco of practicable handling. Clustered regularly interspaced short palindromic repeats (CRISPR)/Cas system has made it possible the use of sophisticated technologies in order to modify target genes. Furthermore, it is presently being employed to prevent viral reproduction. As a result, it's possible that SARS-CoV-2 communal could be destructed by CRISPR/Cas system by preventing viral replica and contamination by means of a precise marked RNA sequence and host components. Furthermore, pathologies and Covid-19 increase the global incidence of deaths, resulting in this contagion. Genomic editing using CRISPR/Cas to damage viral structures (in this case SARS-CoV-2) could be a protective method. Additionally, PAC-MAN in combination with CRISPR/Cas effectively destroys the particular RNA sequence to block viral reproduction. As a result, we believe that combining antiviral Pac-Man like CRISPR enzymes in human cells with the CRISPR/Cas system could be proved beneficial in battling SARS-CoV-2-caused worldwide contagions. This is a substitutive pandemic-prevention strategy that involves viral suppression to degrade the SARSCoV-2 target RNA structure.

Keywords: PAC-MAN; Oxidative Stress; Inflammation; Phagocytosis; Cytokines; Molecular Scissors

Introduction

Outbursts of Covid-19 are initiated by SARS-CoV-2. Humans may have been afflicted through the consumption of seafood from the indigenous marketplace in China as well as interaction to sick animals. At several cases, however, findings demonstrated that persons who had no prior history of come upon the seafood marketplace or being subjected to diseased animals in the market were afflicted as well. Moreover, the virus propagated throughout the community by wheezing, sneezing, and mist concentrate sprayer, resulting in a serious illness before it reaches the lungs via the nasal passages or mouth. Upper and lower respirational tracts of persons [1] are typically contaminated by SARS-CoV-2. Coronavirus invasion, on the other hand, modifies the balance between oxidants by creating reactive chemicals formed from O^2 (ROS) and oxidative stress $(OS)^2$ by altering host cell processes, resulting in a variety of aberrant conditions in the physique of human [2,3]. Furthermore, redox balance [4] could be disrupted by the frequent ingestion of high lipid food, thus it's possible that such foodstuffs induce OS,

which may act as a catalyst for pathological contamination. As a result, it's possible that OS shows a key part in SARSCoV-2 illnesses that causes severe acute respiratory syndrome and affect antioxidants signaling. Because there is no viable therapy for infectious SARSCoV-2, the only method to halt the contagion is to identify a conceivably operative antiviral strategic plan for Covid-19 [5]. As indications resembling Influenza are being generated by SARS-CoV-2, precise proof of identity of the sickness is critical for dropping the casualty rate. Real-time PCR can be used in the recognition of SARS-CoV-2 and WHO has certified it. Nevertheless, as it is an RNA virus, it changes promptly and may make contemporary investigative methods ineffectual in the forthcoming. Since there is presently no standard suppository or immunization for COVID-19, apposite identification is indispensable for its controlling. At present, only supportive handling methodologies are employed throughout the world. As a consequence, research and improvement for pertinent diagnostics, vaccines, and/or cures is moving at a hurried pace. The comprehensive wreckage instigated by SARS-CoV-2 obliges a more effectual controlling techniques that cover both the therapeutics as well as diagnostics aspects [6]. In order to obliterate the viral RNA as well as to constrain the viral replica in host cells, CRISPR/Cas might be the proficient, exceptional and all-inclusive tactic, effects in virus transmission control [7]. The existing study debates the growth of an antiviral protective methodology against SARS-CoV-2 by means of the CRISPR/Cas system to modify genes.

Covid19 and the production of pro-inflammatory cytokines

According to the data presented thus far, the Covid-19 contagion can cause a febrile immunologic reaction in the host. In an examination of Covid-19 sufferers, they have come across monocytes that were bigger than normal and undoubtedly recognized by accelerative dispersing, as well as a inimitable group of monocytes with substantial onward dispersion. Covid-19 contagion bases an excessive activation of monocytes/macrophages, resulting in too many inflammatory signals and, as a result, the commencement of acute respiratory distress syndrome (ARDS). In addition, monocytes and macrophages show a significant representation in the nonspecific immune response. Their conscription is decisive for pathogen recognition, opsonisation, and riddance; they are also essential in the dominion and disbursement of contagion, inflammation, and tissue injury, along with other immune cells. Macrophages demonstrate two types of polarization in reaction to ecological influences: the classic/pro-inflammatory/anti-tumor (M1) phenotype and the alternative/anti-inflammatory (M2) phenotype, both of which are deliberated very imperative for possessing an equilibrium in both proinflammatory and anti-inflammatory interleukins [8]. COVID-19 indications comprise pulmonic inflammation, fever, and toughness, which are initiated by the production of active IL1 controlled by toll-like receptors (TLR) when it take part with cytokine pro-inflammatories such as IL-1b and IL-6 via Covid-19 engendered inflammation [9].

CRISPR/Cas system

The Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) system has been modified from the CRISPR-associated (Cas) system of the prokaryotic "specific immunity" to be utilized as a unique and particular gene editing utensil for other species. CRISPR–Cas pathways are split into two primary groups, each of which is further partitioned into six main kinds (I–VI) and more than 19 subclasses. Presently, recombinant DNA technology-based examination makes it simple for scientists and technologists to identify the primary button of any infection and handle it appropriately. Many prokaryotes, such as archaea and bacteria, have the CRISPR/ Cas system, which confers "specific immune response" contrary to attacking genetic code. CRISPR/Cas is a recombinant DNA technology technique that aids in the recognition of selected genes in a variety of disorders [10]. They have also participated an important part in modifying and editing particular ribonucleic acid (RNA) sequences, in addition to deoxyribonucleic acid (DNA). RNA of ORF1a/b could be inactivated either by trimming it or by Cas13. Plentiful amount of guide RNAs, here, don't perform cleaving activity, but complement the sequences of guide RNAs in ORF1a/b; and thus generate prRNA, many mRNAs being involved in or number of pathways could be simply targeted by the processing of only one crRNAs through pre-crRNA by using the intrinsic capacity of Cas 13. (Figure 1) [11]. In prokaryotic classes with hereditary adaptive or specific immune response, In order to battle against foreign substances, it may act as DNA targeting being guided by RNA. The methods are divided into two categories: type I, III, and IV CRISPR/Cas methods, that combine complex having multi-effects with crRNA which results when an employed receptor muddles to added protein to discover the marked or selected sequence and then cut it. Type II/Cas9, type V/Cas12, and type VI/Cas13, on the flip side, necessitate a solitary multidomain Cas protein in conjunction with CRISPR RNA (crRNA) for participation. The CRISPR/Cas system's second class has proved critical for gene editing and investigative pointers for various illnesses [12]. CRISPR/Cas12a, CRISPR/Cas13a, and CRISPR/Cas13b, on the other hand, have recently been

used to develop a reliable diagnostic utensil for identifying bacterium and virus related toxicities in humans [13]. By changing gene sequences, molecular tool-based technology has recently been employed to contest numerous bacterium or virus related illnesses. As a result, we consider it might be a beneficial armament in the contest against SARS-CoV2- related contagion in the body [7].

Figure 1: Different target sites of CRISPR deadCas13 or CRISPR Cas13 on SARS-CoV-2 genome.

COVID-19 diagnosis using crispr-based applications

Following the global outbursts of the Covid-19 prevalent, there is an essential necessity for rapid and simple diagnostic methods [14]. CRISPR-based technologies may be able to solve this problem, as they have demonstrated considerable recognition efficacy in about 1 hour; however, they are currently pending FDA approval (FDA) [10]. The notion of "collateral cleavage activity" has been applied to CRISPR employing different nucleases such as Cas12a or Cas13. The CRISPR tool's Cas12a/Cas 13 nuclease is activated and in succeeding order to cleave crRNA (CRISPR RNA) and hence all the immediate units whether they are RNA or single stranded DNA undergo cleavage [15]. This characteristic has been exploited to paradigm fluorescently categorized ssDNA/RNA reporter probes that can perceive observable bands in a sideways flow test on a paper band, letting for the development of a unusual nucleic acid-based analytical tool [12]. The crRNA targeting viral RNA might trigger the Cas protein, instigating the reporter probes to be collaterally slashed and, as a result, the development of a positive band on the paper strip [16].

Human pathogenic viruses and the CRISPR/Cas system

In addition to human genome, CRISPR/Cas is such an exceptional system that can attack any double strand humanoid virus. CRISPR/Cas system has been shown to reduce the amount of viral toxicities in humanoid in the laboratories and in organisms itself models in several studies. CRISPR machinery has good antiviral stratagem counter to Human gamma herpes virus 4, Human alpha herpes virus, orthohepadnavirus, Human Polyomavirus 2, Arbovirus, and Herpes virus of swine, human immunodeficiency virus (HIV), hepatitis C virus (HCV), human cytomegalovirus (HCMV); Reticence of translation, virus duplication, or straight destruction of the viral genome are the most conceivable contrivances [17]. CRISPR/Cas is an antiviral technology that interrupts the HCV genome in direction to battle HCV-related contagions. In this scenario, previous research revealed that the Cas9 from Francisella novicida (FnCas9) had the ability to bind bacterial mRNA and cause viral gene suppression. As a result, the antiviral approach of the CRISPR/FnCas9 system, which targets RNA to contest HCV contagion in eukaryotic species, was irreplaceable [18]. HCV trans-

lation was heretofore repressed by preventing D11A/H969A (the catalytically dormant form of FnCas9), according to scientists [13]. As a result, the CRISPR/FnCas9 system does not require direct RNA dilapidation in the virus to block the translation of pathological protein. Otherwise, just attaching ribonuclease acid genome of HCV to Fcas9 is big enough to stop the virus from translating and duplicating. As a result, CRISPR/Cas being specified for the DNA viruses is slightly dissimilar from the CRISPR/Cas being specified for the RNA viruses [7].

CRISPR-cas based diagnostics and therapeutic tools have limitations

Because CRISPR-Cas techniques are effective, uncomplicated, and require inexpensive chassis, they may be used by healthcare personnel in resource-constrained settings [16]. These techniques' benefits are assisting in their acceptance in fundamental and basic and clinical research, as well as analytic and therapeutic improvement. Though these gears offer various advantages, they do have certain disadvantages, which are discussed below. There are several moral aspects to consider when using this technique in preclinical or clinical research [19]. Click or tap here to enter text. Resolving the multiple systematic constraints now linked with CRISPR/Cas9-mediated human germline modifying will need extensive research that should be broadly publicize. Furthermore, all key shareholders must be included in a public conversation on the dangers, advantages, and primary uses, which will eventually decide research primacies in this field [8].

CRISPR technology's off-target effect

The conveyance of the CRISPR system to the selected cells has proven to be the most difficult issue thus far. The CRISPR systems across the board target 3 - 5 incompatibilities of nucleic acids has been a source of worry, especially when it is used for investigative and therapeutic purposes. Effective distribution of the CRISPR/Cas protein apparatus is critical for reducing the unintended mutations inside the gene and guaranteeing that the tool reaches the appropriate cell or tissue [20]. Several researchers are working to overcome unintended mutation difficulties, either by formulating off-target revealing methods or by building CRISPR gears [14]. Off-target discovery approaches include using bioinformatics gears such as Cas OFFinder and gears such as SELEX, DISCOVER, Digenome-Seq, Guide-seq, and others. CRISPR instrument engineering comprises physical alterations to Cas proteins to improve selectivity for selected nucleic acids. Using a Staphylococcus aureus variant Cas protein (SaCas9) with a new mutation (Mut268) might lessen unintended mutation effects while retaining the protein's functioning. Cas9 nickase, a altered form of Cas9 that could produce nicks in merely single strand of dsDNA, was also found to limit the system's unexpected mutation effects [10]. It's unclear if changed creatures will be impacted permanently, or whether the rectification will be passed on to future generations. Additionally, while the qEva-CRISPR approach has some benefits, it cannot be utilized for a whole-genomic investigation, does not consent for the identification of all possible and unintentional off-target locations, and does not describe the changes found. During continuing trials, the protection and effectiveness assessments must be constantly maintained. The insertion of unexpected modifications to the genomic sequence is a possible danger of utilizing CRISPR, therefore enhancing tools for detecting uncommon mutations and estimating their potential consequences will be critical for upcoming medical development [12].

Inferences

CRISPR/Cas13d is a molecular biology and recombinant DNA technology that purposes with the great pliability and uniqueness in order to perform the activity against virus, constraining RNA virus mediated contagion. In SARS-CoV-2 infected persons, not only therapeutic-based application is needed but also measurement of being secured and success rate is also needed, and for this more research is required. If it substantiates to be efficacious, it might be organized as a weapon to avert SARSCoV-2-related sicknesses all over the world, succeeding the configuration of medical science's progress in knocking down or mortifying particular RNA sequences in SARS-CoV-2 and concomitant disorders.

Conflicts of Interest

None.

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