



Recombinant DNA Technology Approaches to Words the Vaccination or Treatment Hepatitis B

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Abstract

Recombinant DNA technology is a crucial method that involves separating and inserting a gene of interest into a specific vector. One important application of this technology is in combating Hepatitis B, a widespread infectious disease in humans, by developing effective vaccines and treatments. By using genetically engineered Hepatitis B surface antigens produced through recombinant DNA techniques in yeast cells, large-scale vaccine production becomes possible. This technology has led to successful and safe vaccines for preventing Hepatitis B infection, as well as therapeutic treatments for those already infected. Vaccination is the most effective way to control HBV infection, and recombinant DNA technology has played a significant role in its development. Moreover, nucleoside analog therapy can inhibit HBV DNA, while lenvovimab is expected to reduce serum HBsAg levels and enhance the HBV-specific immune response after HBsAg eradication, as shown in a phase 2 clinical trial.

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Introduction

Recombinant deoxyribonucleic acid (rDNA) technology and describe the importance of rDNA technology. It explains DNA sequencing and its methods, and explores micronetworks, micronetworks, and their complements. Generating rDNA is a multi-step process that involves the separation and insertion of the gene of interest into a particular vector. In microinjection, DNA is injected directly into See the nucleus of the cell undergoing transformation. In biological sciences, host cells are bombarded with high-speed microscopic particles, such as gold or tungsten particles coated with DNA. Restriction enzymes are enzymes that cut double- or single-stranded DNA at specific recognized nucleotide sequences, called restriction sites. These enzymes are very important components of rDNA technology. Polymerase chain reaction has become a standard tool in forensic science because it can multiply very small samples of DNA for many tests in a criminal laboratory [1]. Recombinant DNA (rDNA) is a DNA molecule is produced by Joining genetic information obtained from one species to an other host through recombinant DNA methods and is not otherwise found in nature normally. The rDNA technology is involved cutting and combining of DNA Segments from different sources and cloning

in a host cell that can express so called recombinant DNA [2]. A diverse group of human viruses that primarily infect liver cells form the human hepatitis virus. Of all human hepatitis viruses, only hepatitis B virus (HBV) and hepatitis C virus (HCV) cause acute and chronic infection and have clinical pathologies and outcomes. the same. Both viruses cause chronic inflammation, fibrosis, cirrhosis, and hepatocellular carcinoma, but HBV and HCV are two completely different viruses. While both viruses are transmitted by direct blood-to-blood contact, only HBV is transmitted vertically from mother to child (1). HBV infection during childhood carries a >90% risk of developing chronic hepatitis and accounts for the greatest number of chronic carriers, despite the availability of effective preventive vaccines. HBV belongs to the family Hepadnaviridae, a group of pararetroviruses that replicate by reverse transcription (2,3) and express viral proteins from their nuclear transcription substrate, covalent closed-loop DNA (cccDNA). HCV, on the other hand, is a positive-stranded RNA virus of the family Flaviviridae that does not have a stable gene form. Therefore, it must constantly replicate in order to survive, allowing for effective targeting by antiviral drugs. In addition, the positive-sense HCV genome is translated into a polyprotein that requires extensive processing to yield viral end protein products and thus provides several



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targets for antiviral drugs [3]. Human and creature life intensely depends on great wellbeing, and secure and proficient strategies to stay solid and combat different maladies. Since long time past times, different strategies have been presented to deliver drugs, drugs, antibodies, anti-microbials, etc to help in a solid life. A cutting edge, broadly utilized method that's picking up more notoriety among researchers all over the world nowadays is recombinant DNA innovation. Not at all like conventional approaches to overcoming wellbeing issues through solutions of the more seasoned eras and ordinary methods, hereditary building makes utilize of advanced strategies and approaches, such as atomic cloning and change, which are speedier and create more precise comes about. A innovation in which proteins are utilized to cut and glue DNA sequences intrigued to make a "recombinant DNA". The recombined DNA groupings can at that point be embedded into vectors, which transport the DNA to a appropriate have cell where it can be replicated or communicated. This is often progressive as the recombinant DNA can be controlled depending on the require and utilize, and can be made to meet numerous issues with ideal arrangements [4]. Recombination can also be introduced artificially as observed in 1972 when Paul Berg and his team became the first to construct recombinant DNA by inserting segments of lambda phage genes and the galactose operon of *Escherichia coli* into simian virus 40 DNA. Recombinant DNA is the rearrangement of DNA sequences of organisms often occurring naturally producing mutations and subsequent population diversity across species or involved in DNA repair mechanisms. Recombination provides solutions in food production, pharmaceuticals, diagnostics, therapeutics, biofuel, bioremediation, and, more recently, vaccine development. As seen in Figure 4, recombinant vaccine development paved the way for the production of subunit (e.g., protein, carbohydrate), conjugate, live recombinant vector (bacterial, viral), DNA, VLP, and more recently, mRNA vaccines [5]. A major scientific development that has significantly improved human existence is recombinant DNA technology. In recent years, it has created methods for medical uses such the treatment of cancer, genetic diseases, diabetes, and various plant maladies. especially fungal and virus resistance. Recombinant DNA technology has received widespread acclaim for its role in environmental cleanup (phytoremediation and microbial remediation) and for improving plant tolerance to a variety of damaging factors (drought, pests, and salt). Along with humans, it significantly improved microorganisms, plants, and other living things. For the sake of the development of recombinant DNA technology in the future, the challenges in improving products at the gene level occasionally provide significant problems that must be solved. For the sake of the development of recombinant DNA technology in the future, the challenges in improving products at the gene level occasionally provide significant problems that must be solved. There are substantial issues with production, particularly in the pharmaceutical industry. high-quality goods because the body rejects the gene modification. Growing a product isn't always a positive thing, though, since a number of factors could work against its success. Recombinant technology is helping to treat a number of diseases that are intractable under normal circumstances, but immune reactions make it challenging to get satisfying results [6].

Principles of Recombinant DNA

There are a few approaches to embeddings modern genetic data into chromosomes in cells and animals. At this time, the foremost engaging strategy is single duplicate quality addition at a characterized locus. This approach has various preferences,

with regard to reproducible transgene expression. Irregular inclusion transgenesis has been successfully utilized to test quality work in mouse models. It is by and large acknowledged that this requires a unconstrained chromosome break. Later NGS information recommend that the repair instrument takes after chromothripsis. In expansion to unintended quality disturbances owing to chromosome harm, the arbitrary addition of transgenes uncovered them to "position effects" in which their expression is controlled by neighboring qualities. In a perfect world, the insertion of columnist cDNAs within the genome comes about in single duplicate transgene inclusions in characterized loci in such a way that endogenous qualities are not disturbed, and correspondents are put beneath the control of particular endogenous promoters [7].

Applications of recombinant DNA technology

Recombinant DNA technology plays a crucial role in enhancing the quality of plants and animals, contributing to advancements in biotechnology. It has the potential to effectively treat currently incurable diseases. Furthermore, this method can be used to produce valuable low molecular weight functional groups or peptides in the future.

Insulin, a vital medicinal protein, has a rich history of development and use through recombinant DNA processing. Genetic engineering has further improved the production and recovery of this essential peptide, leading to a growing demand for environmentally friendly therapeutic proteins and reduced purification costs. Additionally, EPO shows promise as a preventive tool for kidney injury [8]. Researchers from all around the world are still influenced by the scientific development, subsequent study, and use of rDNA in a variety of fields, including the generation of vaccines, antibiotics, hormones, and in remote hybridization. The research conducted and written about by scientists and researchers is examined in this article. Scientific searches that take into account current patterns and data also highlight additional facets of recombinant DNA technology. Additionally, this essay investigates potential applications for rDNA is used in a variety of applications, including the production of antibiotics using *Acremonium chrysogenum* strains for rDNA, the treatment of diabetes using insulin analogs, the production of various hormones like human erythropoietin and gonadotropins using synthetic bacteria, among others [9].

Hepatitis B

Hepatitis B is universally quite possibly of the most widely recognized irresistible sickness in people, which is associated with critical dismalness and mortality. Hepatitis B virus (HBV) has infected approximately 2 billion people worldwide, and approximately 257 million people suffer from chronic HBV infections. An expected 887,000 people passed on in 2015 from intense or persistent results of hepatitis [10]. A viral infectious disease that is contagious everywhere is hepatitis B. The hepatitis B virus (HBV) is a chronic infection that affects about 300 million people. According to the prevalence in the community as determined by the detection of HBsAg, hepatitis B is typically divided into three groups of endemicity: High (8%), intermediate (2-7%), and low (2%) [11]. The human hepatitis B infection (HBV) is a significant human microorganism. An HBV infection can be acute or chronic, with chronic cases affecting more than 240 million people worldwide and resulting in cycles of liver inflammation and significant mortality from liver failure and hepatocellular carcinoma (HCC) and reviewed in. The life cycle of HBV is complicated. After entering hepatocytes, the somewhat

twofold abandoned virion DNA genome is changed over into viral covalently shut round DNA (cccDNA), which fills in as the transcriptional format. cccDNA is one target of the HBV regulatory HBx protein, is thought to be a cause of viral persistence, and is very stable (reviewed in. This brief overview aims to provide a summary of the functions of the HBV HBx protein that could contribute to the persistence of an HBV infection and thus be potential therapeutic targets for stopping chronic HBV replication. Albeit various HBx exercises that could influence tenacious HBV replication have been accounted for, we center around three HBx capabilities. We apologize to colleagues who have defined additional HBx activities that may also be crucial for persistent HBV replication but were unable to describe due to space constraints [12].

Hepatitis B approaches vaccination

Mouse monoclonal antibodies (MAbs) were developed and characterized specifically for HBsAg. One of these antibodies, called HBsAg, was used in the development of an immunocapture ELISA (IC-ELISA) as the capture antibody, while a biotin-labeled detection antibody was used. IC-ELISA was standardized and validated using experimental hepatitis B vaccine batches with different concentrations of HBsAg per dose, as well as commercial vaccines. To prepare the vaccine samples for testing, an alkaline solubilizer was used to remove the HBsAg from Algel-adjuvanted vaccines. The sensitivity of the IC-ELISA was determined to be 5 ng/ml, meaning it could detect HBsAg at concentrations as low as 5 ng/ml. Comparing the results obtained from the IC-ELISA and another method called AxSYM, a good correlation was observed between the estimated HBsAg values, except at higher concentrations where the IC-ELISA provided estimates closer to the actual values than AxSYM [13]. Despite the availability of prophylactic vaccines against hepatitis B for more than 3 decades, there are still more more than 2 billion people were infected, of which 240 million were chronic. Antiviral treatments Currently, the standard therapy for CHB (chronic hepatitis B) infection is peg interferon. α -interferon and nucleoside/tide analogues (NA), but none of them provide continuous antiviral protection reproduction As an alternative strategy, therapeutic vaccines for patients with CHB have been extensively studied has shown promising efficacy in dozens of preclinical and clinical studies. In this article we will consider current research into several therapeutic vaccines for the treatment of CHB, including protein vaccines, DNA-based vaccines, live vector-based vaccines, peptide-based vaccines and cell-based vaccines therapies These studies may provide clues to the development of new treatments for CHB infection [14]. As a result, efforts to create recombinant vaccines against hepatitis B were initially driven more by speculative local scientific and technical interests, such as pharmaceutical manufacturers' desire to keep up with the most recent production technologies. In any case, the new vaccines exceeded expectations by turning a huge profit, putting pharmaceutical companies on notice of the business opportunities that other vaccines of this kind might present. At the same time, the fact that a vaccine was one of the first novel medical products to come out of the new biotechnology sector helped policymakers believe that commercialization was a good way to improve public health and that businesses should be supported in this endeavor. That's what subsequently in 1994, the European Commission concluded while a joint endeavor between Pasteur Mérieux (replacement to Pasteur Vaccins) and Merck to disseminate the hepatitis B and other immunizations was hostile to serious and rejected different organizations from the market, this was offset by the

assumption that the Pasteur-Merck joint effort would speed up development in an area of "certifiable general wellbeing concern", thus ought to be permitted to go ahead (Commission of the European People group, In impact, the effective commercialisation of the hepatitis B antibodies justified the assumptions and interests that had informed arrangement on biomedicine and biotechnology since the late 1960s. At last, the advancement of the hepatitis B immunizations additionally throws light on the worldwide relations of the arising antibody development framework. This became increasingly two-tiered over time. In North America and Europe, the most recent biotechnologies were harnessed to create new significant expense recombinant antibodies which served the requests of business benefit as much as general wellbeing. In the interim, the general wellbeing needs of less rich nations were consigned to a second level of foundations and drives which depended, at first, on less expensive plasma-based creation innovations. A substantial transfer of recombinant hepatitis B vaccine technology from rich to poor countries occurred over time as a result of philanthropic efforts by non-profit organizations and the development of local manufacturing capabilities. However, there is still a problem with how the two levels of the vaccine innovation system interact with one another [15]. Biotechnology research has made significant progress in developing recombinant vaccines. However, the future of vaccine development is heading towards utilizing recombinant DNA technology and therapeutic vaccines to target specific diseases. This review article highlights the historical background of vaccines and emphasizes their crucial role in saving human lives from a wide range of potential diseases [16]. HBV immunization is widely accepted worldwide as part of routine vaccination programs, with recombinant vaccines used preventively. In certain situations, HBV immunoglobulins provide immediate protection. The duration and nature of HBV vaccine protection depend on various factors, including immunological and clinical factors. There are specific and comprehensive regulatory recommendations for the clinical development of HBV vaccines. Researchers are exploring various approaches to improve HBV vaccination, such as using different portions of HBsAg, increasing antigen dose, adjusting vaccination schedules, exploring alternative routes, and using new adjuvants. Therapeutic vaccination aims to activate humoral immunity and induce a multifunctional and multi-specific T cell response to effectively control the HBV virus [17]. The most effective method to control HBV infection is through vaccination against hepatitis B. The initial hepatitis B vaccine was developed by purifying HBsAg from the plasma of individuals without symptoms who carried the HBsAg. Subsequently, recombinant DNA technology allowed the creation of a recombinant hepatitis B vaccine. Administration of a three-dose vaccine series can provide long-lasting protection for over 30 years. The combined use of hepatitis B immunoglobulin and hepatitis B vaccine has significantly reduced the transmission of HBV from mother to child, resulting in almost no infections in children born to carrier mothers without the hepatitis B e antigen (HBeAg) and 5-10% infection rate in children of HBeAg-positive mothers. By the end of 2018, 189 countries had adopted universal hepatitis B vaccination programs, leading to a considerable decrease in the global prevalence of HBsAg in children under five years old, dropping from 4.7% in the pre-vaccine era to 1.3% in 2015. However, the implementation of universal hepatitis B vaccination faces challenges in certain regions, with many newborns not receiving the timely birth dose vaccine as a routine practice. Achieving optimal worldwide universal hepatitis B vaccination requires increased efforts to address social and eco-

conomic obstacles [16]. The improvement of safeguard immunizations against hepatitis B came about in surprising advances in decreasing HBV related liver illnesses. In any case, constant hepatitis B is as yet hard to control because of nonstop popular replication driven by the episomal cccDNA present in the cores of contaminated hepatocytes. Developing vaccines using structurally modified subunits to improve immunogenicity and/or altering antigen processing to alter the order in which epitopes are presented may provide a means of overcoming persistent viral infections or may enhance a vaccine made from native proteins. HBsAgS SVPs have been utilized as transporter stages for various antigenic arrangements to instigate against unfamiliar humoral and cell invulnerable reactions. Based on the HBsAgS backbone fused to a *P. falciparum* CS-polypeptide, one of the most advanced chimeric vaccines with a foreign antigenic sequence arrayed on a particulate carrier is available. For the plan of cutting edge immunizations with restorative abilities, definitions in view of antigen combinations, for example, combinations of HBsAgS SVPs and SVPs made out of the HBV nucleocapsid antigen (HBcAg), might permit the enlistment of wide CD4 and CD8 White blood cell reactions reasonable for helpful results. On the other hand, the appraisal of synergistic impacts between biochemically altered immunogens and adjuvant mixtures conceivably address a road for the age of upgraded immunizations what's more, conveyance stages, which might be appropriate for restorative applications to defeat established ongoing contaminations [18]. Vaccination against hepatitis B is the most effective strategy for controlling HBV infection. first licensed Hepatitis B vaccine was developed by purifying hepatitis B surface antigen (HBsAg) from plasma. Asymptomatic HBs antigen carrier. Then, through recombinant DNA technology, Recombinant hepatitis B vaccine. Three consecutive doses of the vaccine may provide longer-term protection 30 years and older The combination of hepatitis B immunoglobulin and hepatitis B vaccine is highly effective mother-to-child transmission of HBV has decreased, and carrier mothers rarely transmit HBV to their children. Hepatitis B e antigen (HBeAg)-negative and HBeAg-positive mothers have 5-10% infections in their children. From at the end of 2018, 189 countries introduced universal hepatitis B vaccination programs, with dramatic results. The global prevalence of HBsAg in children under 5 years of age has decreased significantly from his pre-vaccination pre-vaccination rate of 4.7%. 1.3% in 2015. However, hepatitis B vaccine dissemination has not yet been completed in some regions More than half of newborns are not routinely given suboptimal birth doses of vaccines infant. Optimal global hepatitis B vaccination needs more effort to overcome social problems and economic challenges [19]. Researcher was found that the recombinant DNA in vaccines for cancer hepatitis B and lassa and filo virus, preparation of antibiotics using *acremonium chrysogen* strains for rDNA, production of various hormones like gonadotropins, etc. And this technology is hybridisation for manipulation of chromosome and nuclear chromatin restructuring in plants and animals. further research and test is required to gain a better understanding the principles of rDNA Technology [20].

Treatment of Hepatitis B

As a DNA virus, hepatitis B virus (HBV) is a species of the genus Orthohepadnavirus, part of the hepadnaviruses. Viruses of the Viridae family. Hepatitis B is caused by HBV. Viral hepatitis caused by HBV is recognized as a serious public health challenge worldwide, causing dangerous outcomes such as cirrhosis and hepatocellular carcinoma. About 500 million people are currently infected with HBV, and the virus contributes to mortal-

ity from liver disease. About 1 million people are infected each year. Recently, there has been a great deal of attention and respect for the detection and pathogenesis of HBV. diagnostic system. Nano-based materials and techniques have received much attention in solving challenges related to DNA detection, especially his HBV. Diagnose [21]. Current treatments for the administration of CHB incorporate peginterferon (Stake IFN) and orally controlled nucleos(t)ide analogs (NAs). NAs are the most broadly picked option universally. For NAs, all territorial affiliations concur that first-line treatment ought to accompany an oral antiviral with a solid boundary to opposition: either entecavir, TDF, or TAF. Transient treatment with NAs is practical for those HBeAg-positive patients who experience seroconversion to against HBe during treatment. After HBeAg seroconversion happens, treatment ought to go on for no less than 1 year and, it is trusted, an additional 3 years to accomplish a dependable reaction whenever treatment is stopped. Treatment continuation for something like 3 years brings backslide rates down to under 30% and rushes the resulting loss of HBsAg. Higher backslide rates following treatment end happen among more established patients and those with HBV genotype C disease. The suggested treatment cutoff models for NAs in HBeAg-negative patients vary by district. Given the extremely high pace of backslide following treatment withdrawal, AASLD suggests that NAs be removed from HBeAg-negative patients solely after affirmation of the deficiency of HBsAg, regardless of seroconversion. Ongoing reports from Asian and European nations recommend that NAs might be halted in HBeAg-negative patients who have imperceptible HBV DNA at three unique times while the testing times are a half year separated, albeit the term of on-treatment HBV DNA imperceptibility remains significant. The infection stays latent, characterized as a HBV DNA level of 2,000 IU/ml and a typical ALT level, in roughly 50% of the patients at 3 years after treatment withdrawal. Treatment stopping isn't suggested for patients with cirrhosis, because of the endanger of dangerous hepatitis flares following virological backslide. Soon, fresher markers, like HBV RNA and HBcrAg, may guide treatment choices [22]. Nucleoside analog therapy can completely inhibit hepatitis B virus (HBV) DNA. Second, HBsAg plays a pivotal role in maintaining HBV-specific immune tolerance. The use of lenervimab is expected to decrease serum HBsAg levels and increase sustained virological response. In addition, a significant therapeutic effect by increasing the HBV-specific immune response after eradication of HBsAg is expected.5,6 A phase 2 clinical trial showed prevention of hepatitis B recurrence. in Hepatitis B seropositive liver transplant recipients who have been treated with lenervimab for 6 years. months after transplant. A phase 2 study with HCB patients receiving nuke is underway, involving 6 months of lenervimab administration (twice weekly for 2 months followed by weekly lenervimab for up to 6 months) and a follow-up period of 6 months. month; this may demonstrate long-term efficacy and safety data in the CHB population. The results of the phase 2 trial will provide insight into how lenervimab works in the treatment of chronic hepatitis B [24]. Regardless of viral concealment by nucleos(t)ide analogs, there are numerous boundaries to accomplish a "fix" of HBV disease. In the first place, HBV perseveres in the hepatocyte core through ceaseless recharging of the cccDNA pool, with a long half-life and the incorporated types of viral DNA. Second, HBV-infected hepatocytes cannot be cleared due to a defective immune response, particularly a defective CD8+ response and an ineffective innate immune response. To switch the equilibrium towards end of HBV disease, diminished reusing of the cccDNA repository, non-cytolytic and additionally

cytolytic cccDNA end and expanded non-contaminated hepatic cell division are required. In any case, even with the speculative accomplishment of cccDNA disposal, coordinated viral successions would in any case be available in hepatocytes, and accordingly keep up with the gamble for hepatocellular carcinoma advancement [23]. In any case, HBV is many times reactivated in the wake of halting nucleos(t)ide analogs since antivirals alone don't straightforwardly target covalently shut roundabout DNA, which is the layout for every viral Rna. Thusly, albeit at present accessible antiviral treatments accomplish concealment of HBV replication in most of patients, hepatitis B surface antigen (HBsAg) misfortune furthermore, seroconversion is seldom accomplished notwithstanding long haul antiviral treatment (HBsAg loss of not exactly 10% in 5 years). Different clinical preliminaries of specialists that interfere with the HBV life cycle in hepatocytes have been directed. Potential treatment methodologies and new specialists are arising as HBV fix. A blend of current and new enemy of HBV specialists might build the pace of HBsAg seroclearance; subsequently, advanced regimens should be approved. Preclinical and/or clinical trial findings as well as newly investigated therapeutic compounds are discussed in this section [25].

Conclusion

Recombinant DNA technology has been crucial in developing effective vaccines and treatments for Hepatitis B. The primary approach involves using genetically engineered Hepatitis B surface antigens to stimulate the body's immune response. These antigens are produced using recombinant DNA techniques in yeast cells, which allows for large-scale production of the vaccine. This technology has been successful in creating safe and potent vaccines to prevent Hepatitis B infection and also in developing therapeutic treatments for those already infected. The HbsAg was removed from Algel-adjuvanted vaccines by using an alkaline solubilizer in order to prepare the vaccine samples for testing. The first hepatitis B vaccine was created by purifying HbsAg from the plasma of asymptomatic individuals who were carriers of the HbsAg. Current treatments for the administration of CHB incorporate peginterferon (Stake IFN) and orally controlled nucleos(t)ide analogs (Nas). Nucleoside analog therapy has the potential to fully suppress hepatitis B virus (HBV) DNA. Additionally, HbsAg is crucial in sustaining specific immune tolerance to HBV.

References

- Khan FA. Recombinant DNA technology. In *Biotechnology Fundamentals*. CRC Press. 2018; 125-177.
- Duman H, Ulupinar P, Pişiren G, Kaymaz ZR, Karav S. *Principles and Applications of Recombinant Protein Production in Plants*. 2019.
- Hu J, Protzer U, Siddiqui A. Revisiting hepatitis B virus: challenges of curative therapies. *Journal of virology*. 2019; 93: 10-1128.
- Nair AM, Mary A, Yadav S. *A Meta-Review On Principles Of Recombinant Dna Technology*. 2021.
- Carascal MB, Pavon RDN, Rivera WL. Recent progress in recombinant influenza vaccine development toward heterosubtypic immune response. *Frontiers in Immunology*. 2022; 13: p.878943.
- Godse SA, Patil SM, Itape PT, Sarjerao V. *Recombinant DNA technology*. 2023.
- Lanigan TM, Kopera HC, Saunders TL. *Principles of genetic engineering*. *Genes*. 2020; 11: 291.
- Khushboo Singh, Yachana Mishra, Vijay Mishra, Sujit Bose, Manvendra Singh, Pallavi Nayak. *Development and Application of Recombinant DNA. Technology In Pharmaceutical Field*. 2019; 22.
- Carascal MB, Pavon RDN, Rivera WL. Recent progress in recombinant influenza vaccine development toward heterosubtypic immune response. *Frontiers in Immunology*. 2022; 13: p.878943.
- Ho JKT, Jeevan-Raj B, Netter HJ. Hepatitis B virus (HBV) subviral particles as protective vaccines and vaccine platforms. *Viruses*. 2020; 12: 126.
- Wolf JM, Simon D, Lunge VR. Hepatitis B virus genotypes in Brazil: Introduction and dissemination. *Infection, Genetics and Evolution*. 2021; 93: 104936.
- Medhat A, Arzumanyan A, Feitelson MA. Hepatitis B x antigen (HBx) is an important therapeutic target in the pathogenesis of hepatocellular carcinoma. *Oncotarget*. 2021; 12: 2421.
- Shanmugham R, Thirumeni N, Rao VS, Pitta V, Kasthuri S, et al. Immucapture Enzyme-Linked Immunosorbent Assay for Assessment of In Vitro Potency of Recombinant Hepatitis B Vaccines. *Clinical and Vaccine Immunology*. 2010; 17: 1252-1260.
- Li J, Bao M, Ge J, Ren S, Zhou T, et al. Research progress of therapeutic vaccines for treating chronic hepatitis B. *Human Vaccines & Immunotherapeutics*. 2017; 13: 986-997.
- Huzair F, Sturdy S. *Biotechnology and the transformation of vaccine innovation: The case of the hepatitis B vaccines 1968–2000*. *Studies in History and Philosophy of Science Part C: Studies in History and Philosophy of Biological and Biomedical Sciences*. 2017; 64: 11-21.
- Zakir F, Islam F, Jabeen A, Moni SS. *Vaccine development: a historical perspective*. *Biomedical Research*. 2019; 30: 452-455.
- Das S, Ramakrishnan K, Behera SK, Ganesapandian M, Xavier AS, et al. Hepatitis B vaccine and immunoglobulin: key concepts. *Journal of clinical and translational hepatology*. 2019; 7: 165.
- Ho JKT, Jeevan-Raj B, Netter HJ. Hepatitis B virus (HBV) subviral particles as protective vaccines and vaccine platforms. *Viruses*. 2020; 12: 126.
- Zhao H, Zhou X, Zhou YH. Hepatitis B vaccine development and implementation. *Human vaccines & immunotherapeutics*. 2020; 16: 1533-1544.
- Nair AM, Mary A, Yadav S. *A Meta-Review On Principles Of Recombinant Dna Technology*. 2021.
- Khosravi-Nejad F, Teimouri M, Jafari Marandi S, Shariati M. The highly sensitive impedimetric biosensor in label free approach for hepatitis B virus DNA detection based on tellurium doped ZnO nanowires. *Applied Physics A*. 2019; 125: 1-8.
- Nguyen MH, Wong G, Gane E, Kao JH, Dusheiko G. Hepatitis B virus: advances in prevention, diagnosis, and therapy. *Clinical microbiology reviews*. 2020; 33: 10-1128.
- Alexopoulou A, Vasilieva L, Karayiannis P. New approaches to the treatment of chronic hepatitis B. *Journal of Clinical Medicine*. 2020; 9: 3187.
- Lee HW, Park JY, Hong T, Park MS, Ahn SH. Efficacy of lenvima, a recombinant human immunoglobulin, in treatment of chronic hepatitis B virus infection. *Clinical Gastroenterology and Hepatology*. 2020; 18: 3043-3045.
- Lee HW, Lee JS, Ahn SH. Hepatitis B virus cure: targets and future therapies. *International journal of molecular sciences*. 2020; 22: 213.