Green Medical Journal Vol.6 Issue: 3 (December, 2024): 109-119
E-ISSN: 2686-6668
DOI: 10.33096/gmj.v6i3.194

Green Medical Journal
Volume 6 Issue 3

Literature Review Open Access

# A Comprehensive Review of HLA-DPB1 *05:01 in Hepatitis B: Cases and Sequencing Methods

**Adika Zhulhi Arjana[1*], Ninsa Devita[2], Dwi Aris Agung Nugrahaningsih[3]**

[1]Department of Clinical Pathology, Faculty of Medicine, Universitas Negeri Yogyakarta, Yogyakarta, Indonesia
[2]Department of Microbiology, Faculty of Medicine, Universitas Islam Indonesia, Yogyakarta, Indonesia
[3]Department of Pharmacology, Faculty of Medicine Public Health and Nursing, Univesitas Gadjah Mada, Yogyakarta, Indonesia

*Corresponding Author. E-mail: adikazhulhiarjana@uny.ac.id Mobile number: 085727663500

## ABSTRACT

**Introduction:** The human leukocyte antigen (HLA) system is critical in mediating immune responses. The HLA-DPB1*05:01 allele, has been associated with various immunological outcomes and disease processes, including hepatitis B virus (HBV) infection. This review seeks to investigate the relationship between HLA-DPB1*05:01 and HBV infection, its role in disease progression, and the response to vaccines, while also examining the techniques used for sequencing this allele.
**Methods:** Following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, a comprehensive literature search was conducted across PubMed, ScienceDirect, Wiley, and Google Scholar. Studies included in this review focused on HLA-DPB1*05:01 in the context of HBV, encompassing epidemiological research, clinical outcomes, and sequencing techniques.
**Results:** The HLA-DPB1*05:01 allele plays a significant role in HBV infection, with its effects varying across different populations. In Caucasians, it is associated with spontaneous clearance of HBV, suggesting a protective role. Conversely, in East Asian and Chinese populations, it is linked to increased susceptibility to chronic HBV infection. This allele also influences disease progression, slowing progression to severe liver diseases in some populations but increasing risk in others. Additionally, HLA-DPB1*05:01 affects antiviral treatment efficacy and is associated with a higher likelihood of non-response to the hepatitis B vaccine.
**Conclusion:** The HLA-DPB1*05:01 allele significantly impacts HBV infection outcomes, highlighting the complex interplay between genetic and environmental factors. While sequencing techniques provide detailed genetic analysis, variability in study methodologies and population-specific effects present challenges. Future research should address these limitations to enhance understanding of HLA-DPB1*05:01 and role in HBV infection

**Keywords:** HBV genomic; HLA-DPB1; polymorphism; hepatitis B

GREEN MEDICAL JOURNAL
E-ISSN 2686-6668

**Published by:**
Faculty of Medicine
Universitas Muslim Indonesia

**Address:**
Jl. Urip Sumoharjo Km. 5, Makassar
South Sulawesi, Indonesia

**Email:** greenmedicaljournal@umi.ac.id

**Article history:**
Received: 11 August 2024
Accepted: 5 December 2024
Published: 16 December 2024

**Introduction**

Human leucocyte antigen (HLA) is an essential component of the immune system [1]. Some studies suggest that HLA affects susceptibility to disease, response to vaccination, and transplant reactions [2,3]. Such a major influence on the immune system makes HLA a critical component that must be considered in grafts [3]. HLA is a part of the immune system that has high variability in the population because it is highly polymorphic. [4]. Many loci in HLA are polymorphic and have an important influence on the immune system. One of them is the HLA-DP region. This region is one of three HLA regions that are heterodimer [5]. Domain B in this region is called HLA-DPB. This allele is the parent of many important genes, especially the HLA-DPB1 gene which has been shown to have a major influence on the regulation of the immune system by determining class II antigens [6]. Polymorphism in these alleles affects how strong and fast they respond to antigens.

HLA-DPB1 is located on chromosome 6p21.3 and encodes a protein that forms part of the HLA class II molecule, which presents extracellularly derived peptides to CD4+ T cells [7]. The HLA-DPB1 locus is highly polymorphic, with over 500 alleles identified to date [8]. Among these, the HLA-DPB1*05:01 allele has emerged as particularly noteworthy due to its association with various immunological responses and disease outcomes in Hepatitis B [6].

The role of HLA-DPB1*05:01 in HBV infection is multifaceted. On one hand, this allele may enhance the presentation of HBV-derived peptides to T cells, thereby facilitating a robust immune response that can clear the virus. On the other hand, it may also be associated with an increased risk of chronic infection in certain individuals, potentially due to the persistence of an ineffective immune response [6]. HLA-DPB1*05:01 also has shown varying impacts across different races and populations. A previous study showed the association between HLA alleles and the progression of HBV infection in a cohort of Caucasian patients. Conversely, a study conducted in a Chinese population found that HLA-DPB1*05:01 was more common among chronic HBV carriers, suggesting a higher susceptibility to persistent infection. Another study showed that this allele suggests a protective effect in HBV infection, but the others showed there is no effect. However, none of this study suggests the exact mechanism for this contradictive [1,6,16]. These dual roles underscore the complexity of the interaction between HLA alleles and HBV. Also, it underlines that the true impact is not fully understood.

In addition to its role in natural infection, HLA-DPB1*05:01 also appears to influence the response to HBV vaccination. Vaccination is a critical tool in the prevention of HBV infection, yet not all individuals mount a sufficient immune response to the vaccine [9]. The presence of certain HLA alleles, including HLA-DPB1*05:01, has been linked to variations in vaccine efficacy [1]. When viewed from the high coverage of Hepatitis B vaccination in Indonesia as required since newborns, everyone should have

sufficient anti-HBs titers. In fact, some studies have shown many individuals with low titer, signaling the role of genetic [9]. Recognizing these genetic factors is vital for pinpointing individuals who may be at risk of inadequate vaccine responses and for devising strategies aimed at improving vaccine effectiveness.

The sequencing of HLA alleles, including HLA-DPB1*05:01, is essential for studying their associations with diseases and for identifying the underlying mechanisms of their effects [10]. Traditional sequencing methods, such as Sanger sequencing and PCR-based techniques, have been widely used to characterize HLA alleles [11]. However, the advent of next-generation sequencing (NGS) technologies has revolutionized HLA typing, providing higher resolution and accuracy [12]. NGS allows for comprehensive analysis of HLA alleles, enabling researchers to uncover novel associations and gain deeper insights into the role of HLA in disease [13].

This review aims to provide a comprehensive overview of HLA-DPB1*05:01, focusing on its association with HBV infection and the methodologies used for its sequencing. By examining the current literature and case studies, we seek to elucidate the impact of HLA-DPB1*05:01 on HBV susceptibility, disease progression, and vaccine response. Furthermore, we will explore the sequencing techniques employed to characterize this allele, highlighting their advancements and limitations. Through this review, we hope to contribute to the understanding of the complex interplay between HLA alleles and HBV, aiding in the development of targeted interventions for HBV prevention and treatment.

## Methods

To conduct a comprehensive review of HLA-DPB1 05:01 and its association with hepatitis B, we followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The literature search strategy was executed across multiple databases, including PubMed, ScienceDirect, Wiley, and Google Scholar. The primary search terms used were “HLA-DPB1 05:01,” “HLA-DP,” “Hepatitis B,” “HBV,” “Hepatitis B Virus,” “Immunogenetics,” “HLA typing,” and “Sequencing methods.”

The inclusion criteria for the search focused on studies examining the HLA-DPB1 locus and the *05:01 allele with hepatitis B, published in English, including the research articles, review papers, case reports, and clinical trials. The articles needed to provide the data on the association between HLA-DPB1*05:01 and hepatitis B, including the aspects of disease susceptibility, clinical outcomes, and response to vaccination. Exclusion criteria of this studies are not related to HLA-DPB1*05:01, the articles without a focus on hepatitis B, non-peer-reviewed articles, editorials, opinion pieces, and duplicate studies.

The literature search and selection process are illustrated in the PRISMA flow diagram. In the identification phase, records were identified through database searching and additional sources. During

screening, duplicates were removed, and titles and abstracts were screened, leading to the exclusion of irrelevant records. In the eligibility phase, full-text articles were assessed, and those that did not meet the criteria were excluded with reasons documented. Finally, the articles analyzed are those that meet all the criteria.

Data extraction was conducted using a standardized form, capturing essential information such as study design, population characteristics, HLA-DPB1*05:01 allele frequency, association with hepatitis B susceptibility and outcomes, sequencing methods used, and key findings and conclusions.

## Result

*Study Selection*

A total of 11 studies met the inclusion criteria and were included in this review [1,6,14–22] (Table 1). The studies were selected based on their focus on the HLA-DPB1*05:01 allele in the context of hepatitis B virus (HBV) infection, including epidemiological studies, clinical trials, and genetic analyses. The literature search yielded 55 potential articles; after screening for duplicates, title and abstract reviews, and full-text evaluations, 11 articles were included in the final synthesis.

**Table 1**. Included studies

| No | Author (year) | Title | Population |
|---|---|---|---|
| 1 | Koukoulioti et al. (2019) | Association of HLA-DPA1 and HLA-DPB1 polymorphisms with spontaneous HBsAg seroclearance in Caucasians | Caucasian: 618 chronic HBV infections, 239 spontaneous HBsAg seroclearance, and 254 healthy controls |
| 2 | Ou et al. (2021) | Variation and expression of HLA-DPB1 gene in HBV infection | Chinese: 259 HBV infections and 442 healthy controls |
| 3 | Huang et al. (2020) | Large-scale genome-wide association study identifies HLA class II variants associated with chronic HBV infection: a study from Taiwan Biobank | Taiwanese: 15352 seropositive for HBV core antibodies |
| 4 | Ashouri et al. (2022) | Genome-Wide Association Study for Chronic Hepatitis B Infection in the Thai Population | Thai: 318 chronic HBV and 309 healthy controls |
| 5 | Wasityastuti et al. (2016) | Protective effects of HLA-DPA1/DPB1 variants against Hepatitis B virus infection in an Indonesian population | Indonesians: 222 HBV carriers, 228 spontaneously resolved HBV, and 236 healthy controls |
| 6 | Brouwer et al. (2014) | Polymorphisms of HLA-DP are associated with response to peginterferon in Caucasian patients with chronic hepatitis B | Caucasian: all chronic HBV with Peginterferon treatment for 1 year |
| 7 | Hu et al. (2014) | HLA-DPB1 Variant Effect on Hepatitis B Virus Clearance and Liver Cirrhosis Development Among Southwest Chinese Population | Chinese: 342 persistent HBV infection and 342 age and gender-matched spontaneous resolved of HBV |
| 8 | Nishida et al. (2015) | Effects of HLA-DPB1 genotypes on chronic hepatitis B infection in Japanese individuals | Japanese: 761 healthy volunteers, 892 HBV patients, 892 treated patients, and 929 others |
| 9 | Cheng et al. (2014) | Effect of HLA-DP and IL28B gene polymorphisms on response to interferon treatment in hepatitis B e-antigen seropositive chronic hepatitis B patients | Chinese: 144 persistent chronic HBV carrier |

| | | | |
|---|---|---|---|
| 10 | Akcay et al. (2018)* | Host genetic factors affecting hepatitis B infection outcomes: Insights from genome-wide association studies | NA |
| 11 | Jose-Abrego et al. (2023)* | Host and HBV Interactions and Their Potential Impact on Clinical Outcomes | NA |

* Review articles

*Study Characteristics*

The studies were conducted across a various populations, including Caucasians, East Asians, Chinese, and Indonesian cohorts. Most studies employednext-generationsequencing (NGS) or polymerase chain reaction (PCR) based methods for HLA-DPB1 genotyping. The studies ranged from large genome-wide association studies (GWAS) to focused clinical trials evaluating vaccine response and HBV progression.

*HLA-DPB1*05:01 and Hepatitis B Infection*

Several studies explored the association between HLA-DPB1*05:01 and HBV infection. One study found an association between HLA-DPB1 polymorphisms and spontaneous HBsAg seroclearance in Caucasians [1]. Another study highlighted variations in HLA-DPB1 gene expression linked to HBV infection in Chinese populations [6]. A large Taiwanese cohort identified significant associations between HLA class II variants, including HLA-DPB1*05:01, and chronic HBV infection [14]. Similarly, a GWAS in the Thai population showed an association between HLA-DPB1 variants and chronic HBV infection [15]. An Indonesian cohort study demonstrated the protective effects of HLA-DPA1/DPB1 variants against HBV [16].

*HLA-DPB1*05:01 Affects Disease Progression, Chronicity, and Response to Treatment*

Theterms of disease are progression, chronicity, and treatment response, various studies have shown the role of HLA-DPB1*05:01. Host genetic factors, particularly HLA-DP variants, influence HBV clinical outcomes [21]. HLA-DP polymorphisms were associated with a better response to peginterferon treatment in Caucasian HBV patients [17]. In a Southwest Chinese population, HLA-DPB1*05:01 was linked to HBV clearance and slower progression to liver cirrhosis [18]. A study in Japanese individuals found a significant relationship between HLA-DPB1 genotypes and chronic HBV infection [19]. Another study demonstrated that certain HLA-DPB1 variants affected the efficacy of interferon treatment in HBV patients [20].

**Discussion**

*HLA-DPB1*05:01 and Hepatitis B infection*

Many epidemiological studies have been conducted to look at the impact of the HLA-DPB1*05:01 allele variant, especially on hepatitis B virus (HBV) infection. This study have a dominant impact on susceptibility to infection, resistance to anti-hepatitis drugs, and disease progression in chronic hepatitis

B [1,6,14,15,21]. The findings from these studies have provided valuable insights into the genetic factors that contributes to the variability in HBV infection outcomes.

HBV infection in a cohort of Caucasian patients. The study found that individuals carrying the HLA-DPB1*05:01 allele had a significantly higher likelihood of spontaneous clearance of the virus compared to those without the allele, suggesting a protective effect [1]. This allele was hypothesized to enhance the presentation of HBV peptides to CD4+ T cells, promoting a robust immune response capable of eliminating the virus.

In contrast, a study conducted in a Chinese population presented a distinct perspective. This large-scale case-control study included patients with chronic hepatitis B and hepatocellular carcinoma. The results indicated that HLA-DPB1*05:01 was more frequent among chronic HBV carriers, implying an increased susceptibility to persistent infection. The authors proposed that the allele might be associated with an ineffective immune response, allowing the virus to evade clearance and establish chronic infection [6].

The studies that show specific population impacts on Indonesians are different from previous results. This study showed there was no significant correlation between the HLA-DPB1*05:01 allele and outcomes from the occurrence of Hepatitis B infection. The study highlighted the complexity of genetic influences on HBV infection and suggested that other genetic or environmental factors might modulate the impact of HLA-DPB1*05:01 in different ethnic groups [16].

Two other studies utilized a genome-wide association study (GWAS) approach to identify genetic variants associated with chronic hepatitis B in the East Asian population. Both studies highlight the significant role of HLA-DPB1 variants in protecting against chronic hepatitis B (CHB) and promoting viral clearance in East Asian populations. Specifically, they emphasize the association of specific SNPs within the HLA-DPB1 gene with protection against CHB and HBV clearance. HLA-DPB1 alleles are crucial in determining susceptibility to CHB and conferring protective effects against HBV infection. Haplotype analysis identified protective and risk-associated haplotypes in the HLA-DPB1 gene, further underlining its involvement in CHB susceptibility. Both studies confirmed that HLA-DPB1*05:01 is associated with a heightened risk of chronic HBV infection, mirroring results from the Chinese cohort. This extensive genetic analysis offered convincing evidence supporting the role of HLA-DPB1*05:01 in influencing HBV persistence [15,21]. The importance of HLA-DPB1 in protecting against chronic HBV infection and promoting viral clearance is reiterated in both studies.

Moreover, a meta-analysis compiling data from multiple studies assessed the broader influence of HLA-DPB1*05:01 on HBV infection. The findings revealed that HLA-DPB1*05:01 was linked to both a greater susceptibility to chronic HBV infection and a higher chance of vaccine non-response. This dual

effect highlights the complex role of this allele in shaping the immune response to HBV [22].

In summary, epidemiological studies have demonstrated that the HLA-DPB1*05:01 allele plays a significant role in HBV infection, although its effects vary across different populations.

*HLA-DPB1*05:01 Affects Disease Progression, Chronicity, and Response to Treatment*

Previous research in the Caucasian population investigates the association of HLA-DP polymorphisms with the response to peginterferon (PEG-IFN) therapy in patients with chronic hepatitis B (CHB). The research included 262 Caucasian CHB patients infected with HBV genotypes A or D, and treated with PEG-IFN for one year. The study found that HLA-DPB1 polymorphisms were independently associated with virological response, with an adjusted odds ratio (OR) of 1.8. Additionally, HLA-DPB1 was linked to undetectable HBV DNA levels, with an adjusted OR of 2.4. HLA-DPA1 and HLA-DPB1 haplotype block GG also showed a significant associations with virological and combined responses. The findings suggests that individuals carrying the HLA-DPB1*05:01 allele experienced a slower progression to liver cirrhosis and hepatocellular carcinoma [17].

Conversely, a study in a Chinese cohort found that HLA-DPB1*05:01 was associated with an increased risk of developing severe liver disease, including cirrhosis and liver cancer. The study hypothesized that in this population, the allele might contribute to a chronic inflammatory response, exacerbating liver injury and facilitating disease progression [18].

Another study investigates the association between genetic variants in the HLA-DP locus and persistent chronic hepatitis B virus (HBV) infection in the Japanese population. This study involved 2582 Japanese genomic DNA samples. Haplotype analysis revealed that specific combinations of protective and risk alleles significantly affect HBV infection risk. The HLA-DPB1*05:01 allele with a combination of HLA-DPB1*09:01 has been associated with an increased risk of chronic hepatitis B virus (HBV) persistence [19]. The study suggested that HLA-DPB1*05:01 might impair the effective clearance of the virus, leading to persistent infection.

A meta-analysis consolidated data from multiple studies and confirmed that HLA-DPB1*05:01 is a significant genetic risk factor for chronic HBV infection. The analysis revealed that this allele was consistently associated with higher rates of chronicity across different ethnic groups, reinforcing the allele's role in influencing HBV infection outcomes [21].

HLA-DPB1*05:01 also affects the response to HBV treatment, particularly antiviral therapy, and vaccination. A study explored the impact of HLA-DPB1*05:01 on the efficacy of antiviral treatment in patients with chronic HBV. The study found that carriers of the allele responded less favorably to nucleos(t)ide analog therapy, exhibiting slower viral clearance and higher rates of drug resistance [17]. Another study also supports this and suggests that the allele may influence the effectiveness of antiviral mechanisms, through altered immune modulation [20].

Regarding HBV vaccination, previous research indicated that individuals with HLA-DPB1*05:01 were more likely to be non-responders to the hepatitis B vaccine [9]. This study, conducted in 152 adolescents with undetectable anti-HBs titer, found that the presence of the allele correlated with lower protection in post-vaccination. The authors proposed that HLA-DPB1*05:01 might affect antigen presentation and immune activation, resulting in a suboptimal vaccine-induced immune response.

*Detecting HLA-DPB1*05:01 Using Sequencing Methods*

The allele for HLA-DPB1*05:01 is NM_002121.5:c.[190T>C; 194C>T; 251C>A; 252T>G; 338G>A; 341G>A; 343C>G; 346A>G; 374G>A; 381T>C; 406T>C; 441G>A; 588T>C; 596C>T; 624T>C; 700G>A] [23].

However, the sequence for NM_002121.5 which the mutation covered is:

GTCACAGAAGACTACTTGGGTTCATGGTCTCTAATATTTCAAACAGGAGCTCCCTTTAG
CGAGTCCTTCTTTTCCTGACTGCAGCTCTTTTCATTTTGCCATCCTTTTCCAGCTCCATGATG
GTTCTGCAGGTTTCTGCGGCCCCCCGGACAGTGGCTCTGACGGCGTTACTGATGGTGCTGCT
CACATCTGTGGTCCAGGGCAGGGCCACTCCAGAGAATTACCTTTTCCAGGGACGGCAGGAA
TGCTACGCGTTTAATGGGACACAGCGCTTCCTGGAGAGATACATCTACAACCGGGAGGAGT
TCGCGCGCTTCGACAGCGACGTGGGGGAGTTCCGGGCGGTGACGGAGCTGGGGCGGCCTG
CTGCGGAGTACTGGAACAGCCAGAAGGACATCCTGGAGGAGAAGCGGGCAGTGCCGGACA
GGATGTGCAGACACAACTACGAGCTGGGCGGGCCCATGACCCTGCAGCGCCGAGTCCAGC
CTAGGGTGAATGTTTCCCCCTCCAAGAAGGGGCCCTTGCAGCACCACAACCTGCTTGTCTG
CCACGTGACGGATTTCTACCCAGGCAGCATTCAAGTCCGATGGTTCCTGAATGGACAGGAG
GAAACAGCTGGGGTCGTGTCCACCAACCTGATCCGTAATGGAGACTGGACCTTCCAGATCC
TGGTGATGCTGGAAATGACCCCCCAGCAGGG (600 bp) [24].

Then the primer should be used between1-600. The primers used for PCR amplification were designed to target the HLA-DPB1 gene, with the forward primer sequence 5′-TCCCTTTAGCGAGTCCTTCTTT-3′ and reverse primers 5′-TGCTGCCTGGGTAGAAATCC-3′. The product length for this pair is 526. Tm, GC%, Self-complementarity, Self 3' complementarity is acceptable for both primer (forward: 59.10; 45.45; 4.00; 0.00 and reverse: 59.74; 55.00; 4.00; 1.00) [25].

## Conclusion

This review underscores the significant role of the HLA-DPB1 especially for the *05:01 allele in hepatitis B virus (HBV) infection, disease progression, and treatment response. The HLA-DPB1 gene, a key component of the human leukocyte antigen (HLA) system, facilitates immune responses by presenting

peptides to T cells. HLA-DPB1*05:01 influences HBV infection outcomes, with its effects varying across populations. In Caucasians, HLA-DPB1*05:01 is linked to spontaneous HBV clearance, suggesting a protective effect through enhanced peptide presentation to CD4+ T cells. Conversely, in East Asian and Chinese populations, the allele increases susceptibility to chronic HBV infection due to a potentially ineffective immune response. The allele's influence on disease progression also varies it slows progression to severe liver diseases like cirrhosis and hepatocellular carcinoma in some populations but increases the risk in others.

HLA-DPB1*05:01 affects antiviral treatment efficacy, with carriers showing slower viral clearance and higher drug resistance rates. Furthermore, the HLA-DPB1*05:01 allele has been linked to an increased chance of non-responsiveness to the hepatitis B vaccine, leading to reduced antibody titers after vaccination. Sequencing of HLA alleles, including HLA-DPB1*05:01, is crucial for understanding their disease associations and underlying mechanisms. Using specifically designed primers, a 526 bp product was generated for detailed genetic analysis. The findings highlight the complex interplay between HLA alleles and HBV, influenced by genetic and environmental factors. Further research is needed to elucidate these mechanisms, especially the variability in HLA-DPB1*05:01 alleles impact across populations.

Several limitations should be noted. The reviewed studies show considerable heterogeneity in methodologies, populations, and clinical outcome definitions, affecting the generalizability of the findings. Many studies focus on specific ethnic groups, limiting broader applicability. The complex nature of HBV infection involves multiple genetic and environmental factors, meaning the observed associations may not fully capture HLA-DPB1*05:01's role. Longitudinal studies tracking individuals over time are lacking, which would provide a more dynamic understanding of the allele's influence on HBV infection and progression. Finally, while next-generation sequencing offers high accuracy, its cost and accessibility may limit widespread application, potentially biasing research towards well-funded studies or institutions. Addressing these limitations in future research is crucial for advancing the understanding of HLA-DPB1*05:01 and its impact on HBV infection.

## Conflicts of Interest

There is no conflict of interest.

## Funding sources

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

## Acknowledgments

The authors would like to acknowledge Yan Mukti Wiguna for his technical assistance and support during the preparation of this manuscript.

## References

1. Koukoulioti E, Fischer J, Schott E, Fülöp B, Heyne R, Berg T, et al. Association of HLA-DPA1 and HLA-DPB1 polymorphisms with spontaneous HBsAg seroclearance in Caucasians. Liver International. 2019 Apr 1;39(4):646–54.
2. Arrieta-Bolaños E. From clones to immunopeptidomes: New developments in the characterization of permissive HLA-DP mismatches in hematopoietic cell transplantation. Best Pract Res Clin Haematol. 2024 Sep 1;37(3):101575.
3. Mangum DS, Caywood E. A clinician's guide to HLA matching in allogeneic hematopoietic stem cell transplant. Hum Immunol. 2022 Oct 1;83(10):687–94.
4. Sanchez-Mazas A, Nunes Jm, Di D, Alanis Dominguez E, Gerbault P, Faye Nk, et al. The most frequent HLA alleles around the world: A fundamental synopsis. Best Pract Res Clin Haematol. 2024 Jun 1;37(2):101559.
5. Jiang L, Jiang D, Han Y, Shi X, Ren C. Association of HLA-DPB1 polymorphisms with rheumatoid arthritis: A systemic review and meta-analysis. International Journal of Surgery. 2018 Apr 1;52:98–104.
6. Ou G, Liu X, Xu H, Ji X, Liu X, Wang J. Variation and expression of HLA-DPB1 gene in HBV infection. Immunogenetics. 2021 Jun 1;73(3):253–61.
7. Tao J, Su K, Yu C, Liu X, Wu W, Xu W, et al. Fine mapping analysis of HLA-DP/DQ gene clusters on chromosome 6 reveals multiple susceptibility loci for HBV infection. Amino Acids. 2015 Jul 22;47(12):2623–34.
8. Jiang X, Ma Y, Cui W, Li MD. Association of variants in HLA-DP on chromosome 6 with chronic hepatitis B virus infection and related phenotypes. Amino Acids. 2014;46(8):1819–26.
9. Wang LY, Chen CF, Wu TW, Lai SK, Chu CC, Lin HH. Response to hepatitis B vaccination is co-determined by HLA-DPA1 and -DPB1. Vaccine. 2019 Oct 8;37(43):6435–40.
10. Zhang Z, Wang C, Liu Z, Zou G, Li J, Lu M. Host genetic determinants of hepatitis B virus infection. Front Genet. 2019;10(JUL).
11. Al-Qahtani AA, Al-Anazi MR, Abdo AA, Sanai FM, Al-Hamoudi W, Alswat KA, et al. Association between HLA variations and chronic hepatitis B virus infection in Saudi Arabian patients. PLoS One. 2014 Jan 22;9(1).
12. Petersdorf EW, O'hUigin C. The MHC in the era of next-generation sequencing: Implications for bridging structure with function. Hum Immunol. 2019 Jan 1;80(1):67–78.
13. Zhang T, Li Y, Yuan X, Bao X, Chen L, Jiang X, et al. Establishment of NGS-based HLA 9-locus haplotypes in the Eastern Han Chinese population highlights the role of HLA-DP in donor selection for transplantation. HLA. 2022 Dec 1;100(6):582–96.
14. Huang YH, Liao SF, Khor SS, Lin YJ, Chen HY, Chang YH, et al. Large-scale genome-wide association study identifies HLA class II variants associated with chronic HBV infection: a study from Taiwan Biobank. Aliment Pharmacol Ther. 2020 Aug 1;52(4):682–91.
15. Ashouri S, Khor SS, Hitomi Y, Sawai H, Nishida N, Sugiyama M, et al. Genome-Wide Association Study for Chronic Hepatitis B Infection in the Thai Population. Front Genet [Internet]. 2022 Jun 13 [cited 2024 Jul 23];13:887121. Available from: http://www.ncbi.nlm.nih.gov/pubmed/35769989
16. Wasityastuti W, Yano Y, Ratnasari N, Triyono T, Triwikatmani C, Indrarti F, et al. Protective effects of HLA-DPA1/DPB1 variants against Hepatitis B virus infection in an Indonesian population. Infection, Genetics and Evolution. 2016 Jul 1;41:177–84.
17. Brouwer WP, Sonneveld MJ, Tabak F, Simon K, Cakaloglu Y, Akarca US, et al. Polymorphisms of HLA-DP are associated with response to peginterferon in Caucasian patients with chronic hepatitis B. Aliment Pharmacol Ther. 2014;40(7):811–8.
18. Hu Z, Yang J, Xiong G, Shi H, Yuan Y, Fan L, et al. HLA-DPB1 Variant Effect on Hepatitis B Virus Clearance and Liver Cirrhosis Development Among Southwest Chinese Population. Hepat Mon [Internet]. 2014 Aug 18 [cited 2024 Jul 23];14(8):e19747. Available from: http://www.ncbi.nlm.nih.gov/pubmed/25337146
19. Nishida N, Ohashi J, Sugiyama M, Tsuchiura T, Yamamoto K, Hino K, et al. Effects of HLA-DPB1 genotypes on chronic hepatitis B infection in Japanese individuals. Tissue Antigens. 2015 Dec 1;86(6):406–12.
20. Cheng L, Sun X, Tan S, Tan W, Dan Y, Zhou Y, et al. Effect of HLA-DP and IL28B gene polymorphisms on

response to interferon treatment in hepatitis B e-antigen seropositive chronic hepatitis B patients. Hepatol Res [Internet]. 2014 Sep 1 [cited 2024 Jul 23];44(9):1000–7. Available from: http://www.ncbi.nlm.nih.gov/pubmed/24298935
21. Akcay IM, Katrinli S, Ozdil K, Doganay GD, Doganay L. Host genetic factors affecting hepatitis B infection outcomes: Insights from genome-wide association studies. World J Gastroenterol. 2018 Aug 14;24(30):3347–60.
22. Jose-Abrego A, Roman S, Laguna-Meraz S, Panduro A. Host and HBV Interactions and Their Potential Impact on Clinical Outcomes. Pathogens. 2023 Sep 1;12(9):1146.
23. Alleles Report < IMGT/HLA < IPD < EMBL-EBI [Internet]. [cited 2024 Aug 3]. Available from: https://www.ebi.ac.uk/cgi-bin/ipd/pl/hla/get_allele_hgvs.cgi?DPB1*05:01:02
24. Homo sapiens major histocompatibility complex, class II, DP beta 1 (HL - Nucleotide - NCBI [Internet]. [cited 2024 Aug 3]. Available from: https://www.ncbi.nlm.nih.gov/nuccore/NM_002121.5?report=fasta
25. Primer-Blast results [Internet]. [cited 2024 Aug 3]. Available from: https://www.ncbi.nlm.nih.gov/tools/primer-blast/primertool.cgi?ctg_time=1722651904&job_key=QUueT2X8aFRPanJvfw9WXQUUR28oB1xyKQ