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COVID-19 Host GenomeDB: A Comprehensive Database Related to COVID-19 Host Genetics

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Abstract: The world is currently faced with a pandemic of coronavirus disease 2019 (COVID-19). Several genome-wide and exome-wide studies (GWAS and EWAS) have been performed to identify the variability in the host genetic constitution that likely underlines the inter-individual variabilities in COVID-19 severity and clinical manifestation. Due to the magnitude of the articles available, creating a list of host-specific genetic variants and genes associated with COVID-19 can be both time-consuming and extremely challenging for COVID-19 researchers. To this end, the COVID-19 Host Genome database was built. This is currently the only dedicated, free-to-use database that deals solely with COVID-19 host-specific genetic variants and genes. HyperText Markup language (HTML), Cascading Style Sheets (CSS), Hypertext Preprocessor (PHP), and My Structured Query Language (MySQL) server (version 5.7.38) were used to develop the website, storage, and extraction of the data. So far, 787 genetic variants from 63 previously published articles were collected. The tabular data are hyperlinked to the original articles and the users can download all data from the database. COVID-19 Host GenomeDB is being revised constantly every month, and can benefit the research community studying the genetic variants to improve COVID-19 treatment and prevention strategies.

Keywords: COVID-19 database; association studies; genetic variants and genes

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1. Introduction

Worldwide, coronavirus disease 2019 (COVID-19) spread extensively and resulted in serious health consequences and huge economic problems, with 536,590,224 confirmed cases and 63,16,655 deaths reported, as stated by the World Health Organization (WHO) on 15 June 2022 (https://covid19.who.int/, accessed on 15 June 2022). Several Genome-Wide and Exome-Wide Association Studies (GWAS and EWAS) have been performed to identify the genetic variants associated with the disease. The data generated by these association studies can be utilized by researchers to optimize COVID-19 therapeutics. Several databases have been created to outline the GWAS data, which may or may not be specific to a disease (Table 1). Among these, GWAS Central [1], GWAS Catalog [2,3], and Phenotype-Genotype Integrator (PheGenI) [4] databases give an overview of GWAS data without being specific to a disease. Amyotrophic Lateral Sclerosis online Database (ALSoD) [5], EyeDiseases [6], Type 2 diabetes genetic association database (T2DGADB) [7], Analysis of Breast Cancer GWAS (ABC-GWAS) [8], Epilepsy Genetic Association Database (epiGAD) [9], GenomicsDB [10], and Parkinson's disease genome-wide association study (PD GWAS) locus browser [11] are some databases that give an insight to GWAS details that are specific to diseases such as brain, eye, diabetes, cancer, and neurological disease.

Table 1. Databases that give an overview of Genome-Wide Association Study (GWAS) data. These databases may or may not be specific to a disease. If the database is specific to a disease, then the disease on which this database focused is mentioned in the "Disease" column. A link to this database is also mentioned in the table.

S.No.	Database	Disease-Specific (Yes/No)	Disease	Web Address
1	GWAS Central	No	All	https://www.gwascentral.org/ (accessed on 14 July 2022)
2	GWAS Catalog	No	All	https://www.ebi.ac.uk/gwas/ (accessed on 14 July 2022)
3	PhenGenI (Phenotype-Genotype Integrator)	No	All	https://www.ncbi.nlm.nih.gov/gap/phegeni (accessed on 14 July 2022)
4	ALSoD (Amyotrophic Lateral Sclerosis online Database)	Yes	Amyotrophic Lateral Sclerosis (ALS)	https://alsod.ac.uk/ (accessed on 14 July 2022)
5	EyeDiseases	Yes	Eye	https://eyediseases.bio-data.cn/ (accessed on 14 July 2022)
6	T2DGADB (Type 2 diabetes genetic association database)	Yes	Type 2 Diabetes	http://allie.dbcls.jp/pair/T2DGADB;type+2+diabetes+genetic+association+database.html (accessed on 14 July 2022)
7	ABC-GWAS (Analysis of Breast Cancer GWAS)	Yes	Breast Cancer	http://education.knoweng.org/abc-gwas/ (accessed on 14 July 2022)
8	epiGAD (Epilepsy Genetic Association Database)	Yes	Epilepsy	https://www.epigad.org/ (accessed on 14 July 2022)
9	GenomicsDB	Yes	Alzheimer's Disease	https://www.niagads.org/genomics/ (accessed on 14 July 2022)
10	PD GWAS (Parkinson's disease genome-wide association study) locus browser	Yes	Parkinson's Disease	https://pdgenetics.shinyapps.io/GWASBrowser/ (accessed on 14 July 2022)

With the rapid rise of COVID-19, several genome-wide and exome-wide studies have been published to identify the host genetic variants associated with the disease. Creating a list of genetic variants related to COVID-19 from the previously published articles can be time-consuming, labor-intensive, and extremely challenging for the researchers involved in COVID-19-related research. To this end, we have developed the first, dedicated COVID-19 Host genome database: GenomeDB (http://covid.gwas.genomemapster.com, accessed on 15 July 2022). This is currently the only database specifically designed to store and share the host-specific genetic variants and genes involved in COVID-19. The COVID-19 Host GenomeDB is a publicly or readily available database that is simple to use, has an easily navigable graphical user interface, with original articles connected through hyperlinks. This database can be easily reviewed and downloaded around the world. Scientists, researchers, clinicians, students, and other users can make use of this database to list all the host-specific genetic variants and genes linked to COVID-19, and also to identify the population in which the study was performed. The data for the database comes from a systematic literature survey through Google Scholar and PubMed. HyperText Markup language (HTML), Cascading Style Sheets (CSS), Hypertext Preprocessor (PHP), and My Structured Query Language (MySQL) server (version 5.7.38) were used to develop the website and to store and fetch the data. The COVID-19 Host GenomeDB contains the relevant data on COVID-19 host-specific genetic variants and genes. The database results contain ten fields, and each column represents a serial number, reference single nucleotide polymorphism cluster ID or chromosome position, gene, title, ID (PubMed reference number), link, population, odd ratio, p-value, and comment in a table format.

2. Materials and Methods

2.1. Data Acquisition

COVID-19 Host GenomeDB is a composite and free-to-use database. A systematic literature survey was performed to identify the host-specific genetic variants and genes involved in COVID-19. Overall, over two months, 787 genetic variants from 63 articles were collected from previously published articles for COVID-19. The host-specific genetic variants and genes involved in COVID-19 and other relevant information related to articles were collected from Google Scholar and PubMed ranging from 1 January 2000, to 31 December 2021. "(((COVID-19) AND (Genome-wide association study)) OR (GWAS)) AND (Host)" was the all-fields search term used to collect the previously published articles. This database contains the relevant data on COVID-19 host-specific genetic variants and genes, where each field represents the data on the serial number, reference single nucleotide polymorphism cluster ID or chromosome position, gene, title, ID (PubMed reference number), link, population, odd ratio, *p*-value, and comment, respectively. The chromosome position is mentioned if the reference single nucleotide polymorphism cluster ID is not available.

2.2. Database Structure

The relevant information on the host-specific genetic variants and genes involved in COVID-19 from previously published articles was collected and entered into Microsoft Excel. The worksheet containing information in Microsoft Excel (.xlsx) format was converted to comma-separated values (.csv) format and uploaded to the MySQL server (version 5.7.38). A MySQL server was used to store, manage, and fetch the collected data based on query terms from the database. Therefore, without modifying the already existing data, the data fields and the content can be extended on-demand to the table in the database using the PHP scripting language. The collected information was organized in a table. To develop a website for the COVID-19 Host GenomeDB database, HTML, CSS, and PHP languages were used.

2.3. Search Methodology

On the main page of COVID-19 Host GenomeDB (Figure 1), a search method-based strategy is employed in the search box by reference single nucleotide polymorphism cluster ID, gene, ID, or population to fetch the information on host-specific genetic variants and genes involved in COVID-19. Users provide input (attribute `name`="look") to the search box on the main page of the website; this input is transferred to the PHP script of the search page. On the search page, the "`mysqli_connect()`" function is used to connect to the MySQL server. The "`if`" statement is executed if the conditions are satisfied, i.e. if the user input is not null and declared using the "`isset()`" function. If the condition is true, then the SQL `SELECT` statement inside the if statement gets executed. The "`SELECT`" statement selects all the fields "`FROM`" the table (gwas_content), and the "`WHERE`" clause with the "`LIKE`" operator is used if the input term matches the exact pattern in multiple columns such as "rsID", "Gene", "ID", `OR` "Population". When the input term matches any four of the columns in the MySQL table, then the matched rows are filtered and fetched. These fetched rows are placed in the variable ($result). The fetched result row data is put up in a table format. The "`while`" loop is used to create a loop to loop through results. Lastly, the "`mysqli_close`'' function is used to close the server connection. If the user input does not match any of the columns, then only the table header is displayed with no result data being fetched. Figure 2 shows the basic workflow and strategy used for the requested query search word in the search box. The output table of the result page from query search words gives information on the serial number, reference single nucleotide polymorphism cluster ID or chromosome position, gene, title, ID, link, population, odd ratio, *p*-value, and comment.

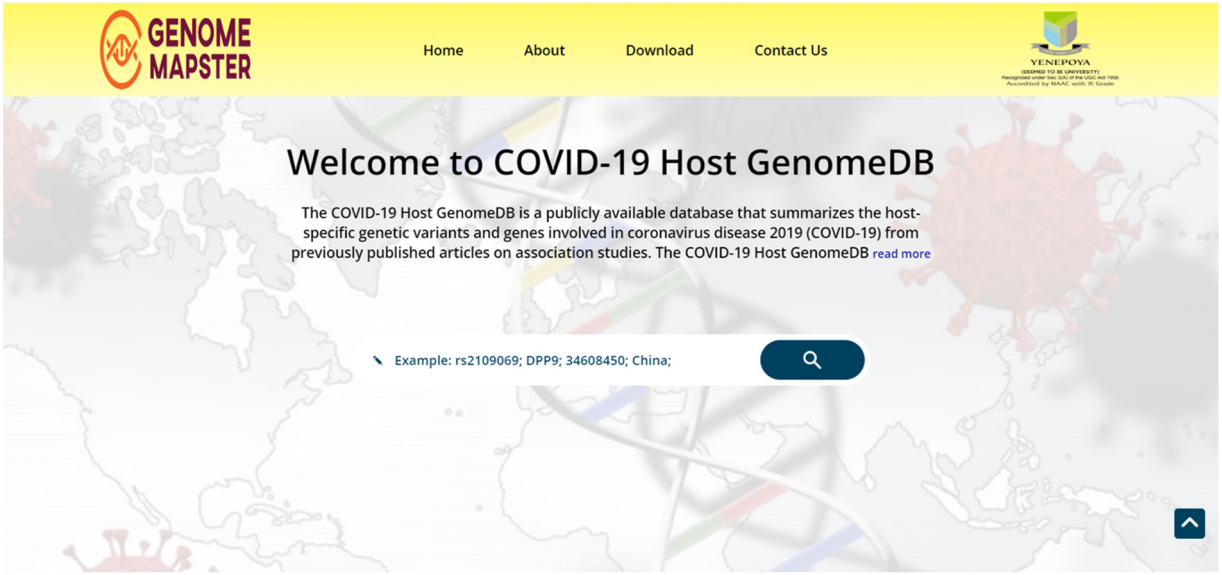


Figure 1. The snapshot of the main page of COVID-19 Host GenomeDB. This website contains four sections: home, about, download, and contact us. In the search box, users search by the reference single nucleotide polymorphism cluster ID, gene, ID (reference number of the article), or population.

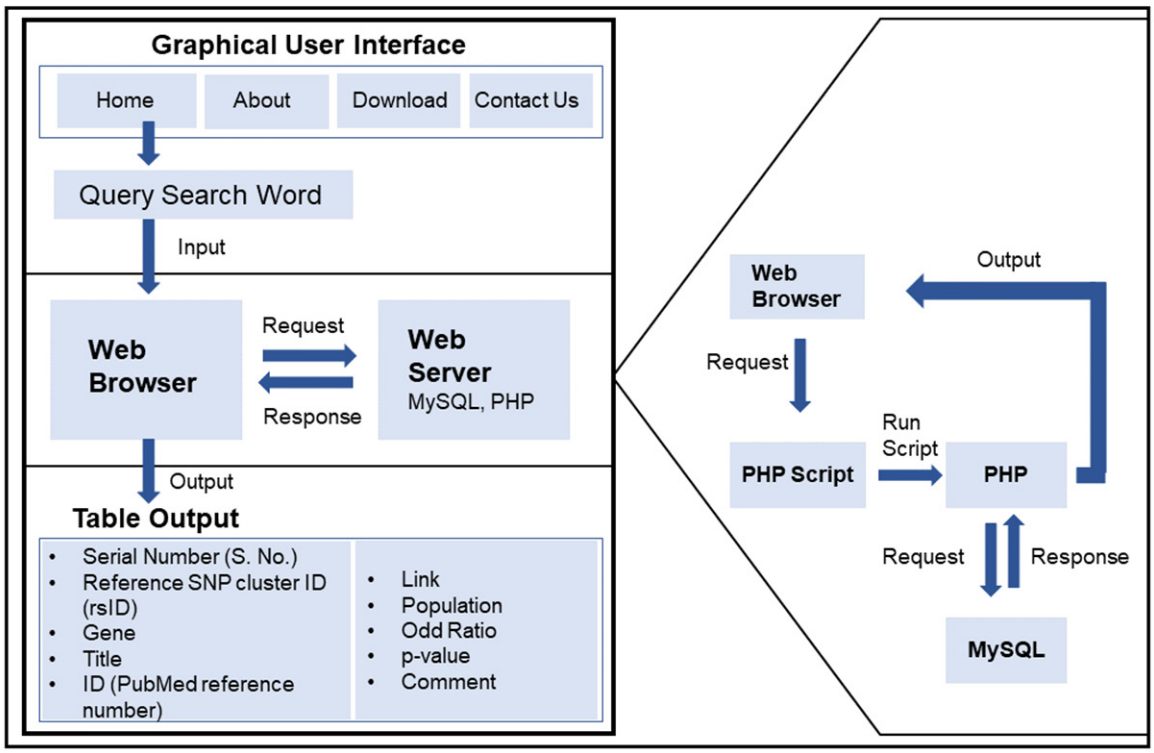
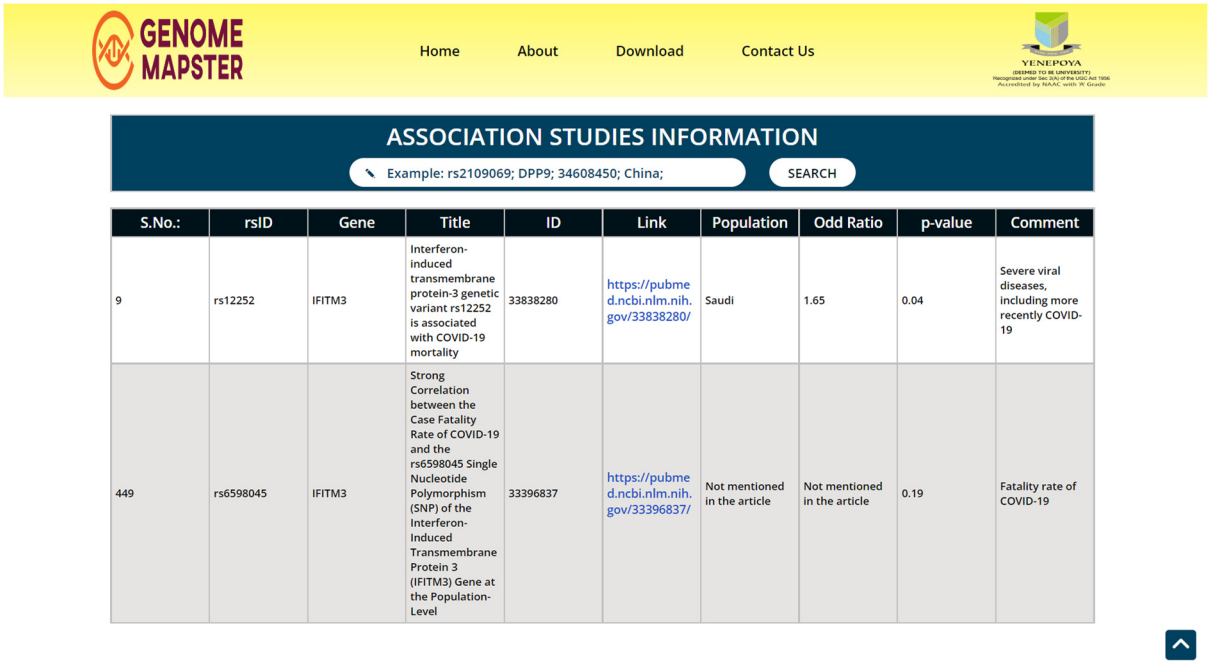


Figure 2. The basic workflow of the COVID-19 Host GenomeDB database. The user interface contains four sections: home, about, download, and contact us. On the main page, users search by reference single nucleotide polymorphism cluster ID, gene, ID, or population. The search word input is transferred to the Hypertext Preprocessor (PHP) script and matched fields containing all the information are fetched and shown in table format from the My Structured Query Language (MySQL) server.

3. Results

3.1. User Interface

COVID-19 Host GenomicDB gives information on host-specific genetic variants and genes involved in COVID-19 from the previously published articles on association studies to users. Figure 1 is the snapshot of the main page of COVID-19 Host GenomeDB. The user interface contains four sections: home, about, download, and contact us. The home section is the main page of this website, where users simply search by the reference single nucleotide polymorphism cluster ID, gene, ID (reference number of the article), or population in the search box. Based on the search query words, serial number (S.No.), reference single nucleotide polymorphism cluster ID (rsID) or chromosome position, the gene, title, ID, link, population, odd ratio, p-value, and comment are fetched in tabular format. For more information for users, the links are hyperlinked and directed to the original articles. For instance, if the users want to search by gene name, e.g., "*IFITM3 (Interferon-induced transmembrane protein 3)*", the results are fetched in table format containing all the information based on the search query word (Figure 3). The about section talks about this database. In the download section, the whole table is displayed and the users can freely download and extract detailed information on host-specific genetic variants and genes involved in COVID-19 and other relevant information related to articles in Microsoft Excel (.xls) format. The contact us section allows the user to get in touch with the author for any queries, feedback/comments, any assistance, or to note issues.



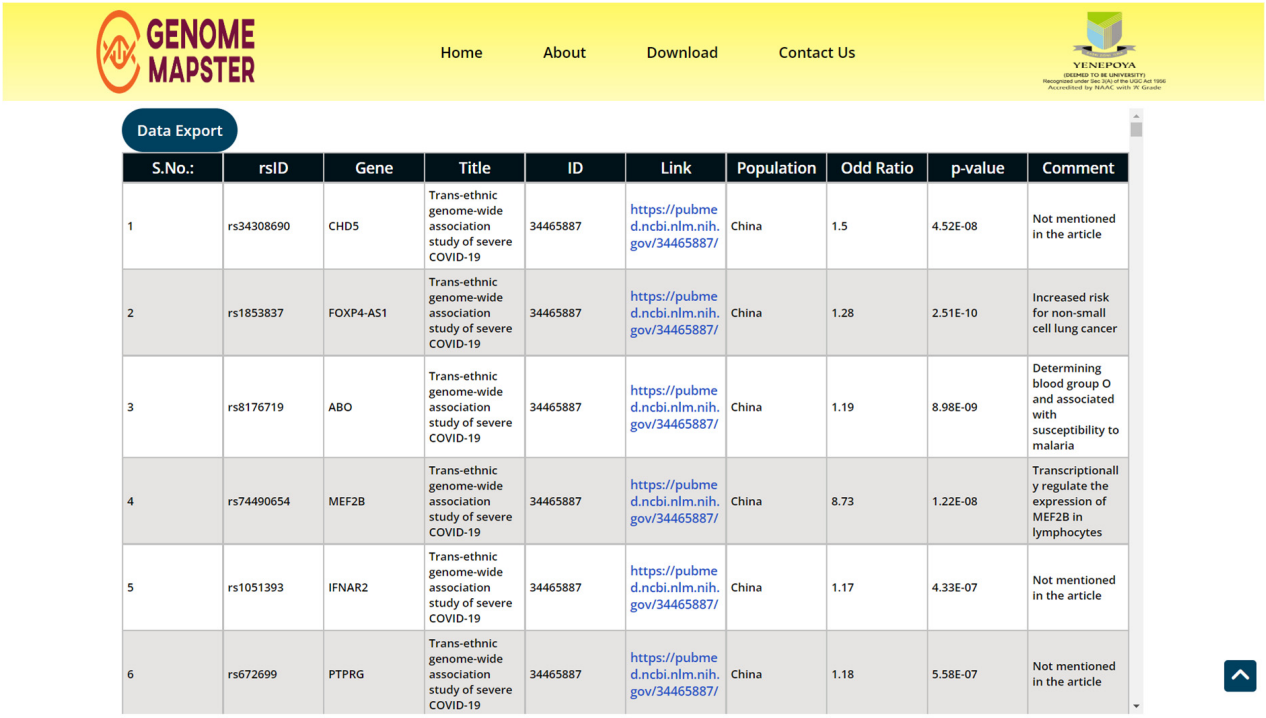
S.No.:	rsID	Gene	Title	ID	Link	Population	Odd Ratio	p-value	Comment
9	rs12252	IFITM3	Interferon-induced transmembrane protein-3 genetic variant rs12252 is associated with COVID-19 mortality	33838280	https://pubmed.ncbi.nlm.nih.gov/33838280/	Saudi	1.65	0.04	Severe viral diseases, including more recently COVID-19
449	rs6598045	IFITM3	Strong Correlation between the Case Fatality Rate of COVID-19 and the rs6598045 Single Nucleotide Polymorphism (SNP) of the Interferon-Induced Transmembrane Protein 3 (IFITM3) Gene at the Population-Level	33396837	https://pubmed.ncbi.nlm.nih.gov/33396837/	Not mentioned in the article	Not mentioned in the article	0.19	Fatality rate of COVID-19

Figure 3. The snapshot of the results page, which fetches all the information in a table format based on the gene name, e.g., "*IFITM3 (Interferon-induced transmembrane protein 3)*," as a search word.

3.2. Output Information

COVID-19 Host GenomeDB database summarizes the host-specific genetic variants and genes involved in COVID-19. It comprised 787 genetic variants extracted from previously published articles for COVID-19. The systematic literature survey (Google Scholar and PubMed) was performed to collect the host-specific genetic variants and genes involved in COVID-19 and other relevant information related to articles. The download page and results page give the relevant information in table format containing ten fields (Figure 4). Each field represents S. No., rsID or chromosome position, gene, title, ID, link, population, odd ratio, p-value, and comment, respectively. The S.No. is a unique identification number in ascending order given to each row of the table. The rsID is a unique identification num-

ber to identify the Single Nucleotide Polymorphisms (SNPs) for COVID-19. If rsID is not available, then the chromosome position is displayed. Each rsID represents a set of genes; the gene symbol was placed in the column named "Gene". The title of the article describes the headings of an experiment or research performed by scientists or research scholars and about the article. The PubMed database issued a unique identification number to the article that was put up in the field named "ID". The "Link" section contains a hyperlink to the original article. The "Population" column describes the population among which an association study was performed. The odd ratio and p-value mentioned in the article for the association study were also noted. The "Comment" section gives a brief note on the functionality of these variants. Scientists, researchers, clinicians, students, and other users can make use of this database in their studies by referring to or downloading the host-specific genetic variants and genes involved in COVID-19.



S.No.:	rsID	Gene	Title	ID	Link	Population	Odd Ratio	p-value	Comment
1	rs34308690	CHD5	Trans-ethnic genome-wide association study of severe COVID-19	34465887	https://pubmed.ncbi.nlm.nih.gov/34465887/	China	1.5	4.52E-08	Not mentioned in the article
2	rs1853837	FOXP4-AS1	Trans-ethnic genome-wide association study of severe COVID-19	34465887	https://pubmed.ncbi.nlm.nih.gov/34465887/	China	1.28	2.51E-10	Increased risk for non-small cell lung cancer
3	rs8176719	ABO	Trans-ethnic genome-wide association study of severe COVID-19	34465887	https://pubmed.ncbi.nlm.nih.gov/34465887/	China	1.19	8.98E-09	Determining blood group O and associated with susceptibility to malaria
4	rs74490654	MEF2B	Trans-ethnic genome-wide association study of severe COVID-19	34465887	https://pubmed.ncbi.nlm.nih.gov/34465887/	China	8.73	1.22E-08	Transcriptionally regulate the expression of MEF2B in lymphocytes
5	rs1051393	IFNAR2	Trans-ethnic genome-wide association study of severe COVID-19	34465887	https://pubmed.ncbi.nlm.nih.gov/34465887/	China	1.17	4.33E-07	Not mentioned in the article
6	rs672699	PTPRG	Trans-ethnic genome-wide association study of severe COVID-19	34465887	https://pubmed.ncbi.nlm.nih.gov/34465887/	China	1.18	5.58E-07	Not mentioned in the article

Figure 4. Snapshot of the download page containing ten fields in table format. This page gives detailed information on host-specific genetic variants (reference single nucleotide polymorphism cluster ID/chromosome position) and genes involved in COVID-19, and other relevant information such as a serial number, title, ID, link, population, odd ratio, *p*-value, and comment.

4. Discussion

There are many databases that give information on association studies from the previously published articles or other databases. Some databases are made with or without disease-specific information. GWAS Central, GWAS Catalog, and PheGenI databases give an outline of GWAS data [1–4]. All these databases are not specific to a disease and are free to use. ALSoD, EyeDiseases, T2DGADB, ABC-GWAS, epiGAD, GenomicsDB, and PD GWAS locus browser are a few of the databases that give an insight into GWAS details that are specific to diseases such as ALS, eye, type 2 diabetes, breast cancer, epilepsy, Alzheimer's Disease, and Parkinson's disease, respectively [5–11]. All the disease-specific databases are embedded with other tools and are free to use except the T2DGADB database, which is only for commercial end-users. There has been no database specially designed for COVID-19. Our database, COVID-19 Host GenomeDB, is the first, unique, and publicly available database designed for host-specific genetic variations and genes on COVID-19 disease from already published articles on case-control-based association studies. This database provides an easy-to-search option and uniquely performs a search based on the

population among which the study was performed. This database provides an excellent user interface and with one click a whole data table can be downloaded.

The ALSoD database gathers data on ALS-related genetic variations and genes. Data for this database is obtained from a literature survey or by direct submission [5]. The EyeDiseases database incorporates multi-omics data and analyzes eye illnesses. To collect eye disease-related information on variants and genes, PubMed, Online Mendelian Inheritance in Man (OMIM), GWAS Catalog, and Gene Expression Omnibus (GEO) are used [6]. The T2DGADB database gives details on type 2 diabetes-related genetic variants and genes from previously reported association articles. Human Genomic Epidemology (HuGE) Navigator is used to collect the list of articles [7]. The ABC-GWAS database collects the genetic variants of breast cancer individuals who were positive for estrogen receptors through association studies. This database collects data from the Encyclopedia of DNA Elements (ENCODE) and the Cancer Genome Atlas TCGA [8]. The epiGAD database collects information on genetic association studies related to epilepsy by the literature survey using PubMed, Google Scholar, ISI Web of Science, and HuGE Navigator [9]. The GenomicsDB database finds, fetches, evaluates, and shares files from the National Institute of Aging Genetics of Alzheimer's Disease Data Storage Site (NIAGADS), and gives an overview of Alzheimer's GWAS data. The data collected from NIAGADS have been incorporated with GWAS summary statistics, meta-analysis results by Alzheimer's Disease Sequencing Project's (ADSP), and the GWAS Catalog [10]. The PD GWAS locus browser provides a platform to collect the Parkinson's disease-appropriate genetic variants and genes. PubMed is used to collect the data [11]. The COVID-19 Host GenomeDB database summarizes the COVID-19 host-specific genetic variants and genes from previously published association articles. The data come through Google Scholar and PubMed.

The ALSoD database used the ASP.NET framework incorporated with Perl, JavaScript, Extensible Markup Language (XML), Transact-SQL (T-SQL), Visual Basic. NET (VB.NET), and C# to write a program. The Microsoft.NET platform is utilized and the user-interface interactive website was created using Microsoft Visual Web Developer 2008 Express Edition. To maintain the database, Microsoft SQL Server 2008 is used [5]. In the EyeDiseases database, data are stored and managed using PostgreSQL. The front-end elements were built using Vue (2.6.11). The complete website was set up on the CentOS operating system [6]. The T2DGADB web interfaces were developed based on HTML, JavaScript, and Java Server Pages (JSP) languages. It operates on CentOS (version 4.7) and Apache-Tomcat (version 6.0.18), and a MySQL server was used to store data [7]. The ABC-GWAS database works on any platform, and HTML, R, Python, and JavaScript languages were used to develop this database [8]. GenomicsDB uses PostgreSQL v.9.5 to query and mine data. The Genomics Unified Schema version 4 (GUS4) is used to organize the data. Overall, the website was built using Web Development Kit system strategies (WDK) [10]. R Shiny package was used to develop the PD GWAS locus browser web page [11]. The COVID-19 Host GenomeDB database provides a good user interface and is simple to use. Our website was created using the easiest programming languages, such as HTML, CSS, PHP, and MySQL server (version 5.7.38), and a popular Relational Database Management System (RDMS) is used to store and fetch the data for the database.

The host's genetic makeup plays a key role in the severity of COVID-19. COVID-19 Host GenomeDB was developed to give a detailed overview on host-specific genetic variants and genes related to COVID-19 disease. It is a simple, unique, and free-to-use database. We aim to give an overview list of COVID-19 host-specific genetic variants and genes from previously published articles on association studies. To collect the data, the systematic literature survey was performed using Google Scholar and PubMed. To this end, 787 genetic variants were collected from 63 previously published articles on association studies for COVID-19. HTML, CSS, PHP, and MySQL server (version 5.7.38) were used to develop the website and to store and fetch the data for the database.

The details present in COVID-19 Host GenomeDB can be utilized by researchers studying COVID-19 to enhance disease detectability, therapy, and prevention. This database can

be used by scientists, researchers, clinicians, students, and other users who are interested in COVID-19 host genetics research. Obtaining information from previously published articles can be a time-consuming and labor-intensive task. By using this database, researchers can look for all the host-specific genetic variants and genes linked with COVID-19, as well as the population in which association studies were conducted. Researchers can utilize the genetic variants to make improvements in COVID-19 treatment and prevention strategies. COVID-19 Host GenomeDB can be of benefit to the research community in personalized medicine and to study the impact of genes on people's diverse reactions towards drugs.

In our database, the data collected on host-specific genetic variants and genes involved in COVID-19 are quite small; to overcome this, our team scheduled a revision of the database every month. We did not add a column on the analysis details; instead, the "Link" column is included which provides hyperlinks to the original articles. We included all the genes or the closest gene that showed variation in genetic variants. This database does not include a predefined p-value cut-off; instead, we listed all the p-values mentioned in the study. These are the few limitations of COVID-19 Host GenomeDB.

5. Conclusions

COVID-19 Host GenomeDB (http://covid.gwas.genomemapster.com, accessed on 15 July 2022) is a publicly available database with an easy-to-use interface that is specific to COVID-19 disease, and that gives information on host-specific genetic variations and genes. The main objective of this database is to summarize COVID-19 host-specific genetic variants and genes from previously published articles on association studies. This database can be useful for scientists, researchers, clinicians, students, and other users who are interested in COVID-19 host genetic research to find all the COVID-19-associated host-specific genetic variations and genes.

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Data Availability Statement: COVID-19 Host GenomeDB is easily and freely accessible at http://covid.gwas.genomemapster.com (accessed on 14 June 2022). SNPs curated here have come from published articles. Genome Mapster is not responsible for any mistakes in the functionality of curated SNPs. The supplementary data section contains all the additional files created in the duration of the study. Get in touch with the corresponding author of COVID-19 Host GenomeDB or send emails to das.ranajit@gmail.com with any queries, feedback/ comments, any assistance, or to notice issues.

Conflicts of Interest: The authors declare no conflict of interest.

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