



Development of a Genome-phenome Browser for Rice Cultivars

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/IJPSS/2023/v35i143045

Open Peer Review History:

This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: <https://www.sdiarticle5.com/review-history/100237>

Original Research Article

Received: 09/03/2023

Accepted: 13/05/2023

Published: 05/06/2023

ABSTRACT

With the advent of modern sequencing techniques, the genome study of Rice has become more precise and effective. Modern bioinformatics tools have contributed a lot to the functional genomics of Rice. Worldwide researches are being carried out to understand the biology of rice better. Biological experimental information needs to be inferred more precisely so that further progress can be made. In this study, a comprehensive analysis is undertaken on functionally validated and characterized rice genes which are found to affect the phenotypes of rice. A database and browser have been developed with the help of information available across literatures which will be used to identify genes responsible for affecting morphological, physiological and resistance or tolerance traits. Such detailed analysis will also provide the annotation of genes that are functionally characterized. It will also help to understand how these genes affect the traits useful for Rice breeding.

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Keywords: Database; functional genomics; genome browser; phenotype; rice (*Oryza sativa*).

1. INTRODUCTION

A major chunk of the world's population regularly consumes rice in their diet. Inevitable expansion in global population and climate change has made the demand for higher yield and better quality rice imperative. So, As a result, developing new rice varieties which increase yield and ensure quality is a daunting task. The generation of huge data of rice genome sequence through sequencing technology has made it possible to extract a wealth of data about the variety of genes and alleles that can help to improve beneficial agronomic features. Several researches have been carried out to find the variation in rice. Phenotype analysis leads to a better understanding of genes and their interaction with the environment. This will improve the introduction of new varieties which will be withstanding more biotic and abiotic stresses. Genome-wide Association Studies (GWAS) help to study phenotype features by identifying causal genes and variants it creates. Many researchers have made rice functional genomics achieve a great height during the past two decades. Because rice is a popular food crop and a model plant, functional genomics research findings must be used to improve rice breeding. A comprehensive analysis of the functionally validated rice genes could give detailed information on the natural variation of Rice to collect and analyse phenotypes within the context of a particular species, phenotype ontologies were created. These ontologies have recently been extended with formal class definitions that can be used to combine phenotypic data and make it possible to compare traits among various species directly. A database of rice variation is needed to record and gather various genes- and specific effects. According to Rice Variation Map [1], around 1479 rice accessions were sequenced to identify 6551358 single nucleotide polymorphisms (SNPs) and 1214627 insertions/deletions (INDELs). All INDEL/SNP genotypes can be accessed and downloaded from online. SNPs, and INDELs can be searched for using gene names, genomic areas, SNP/INDEL identifiers, and gene annotation keywords. There are many genome browsers of Rice for specific purposes which enable the study of rice genes and their functions precisely. There is no complete phenotypic browser that would allow for extensive annotation of rice phenotypes in the context of mutations, quantitative trait loci, and

strains that are utilised as models for the biology of Rice and diseases. This kind of browser is required to find out the genetic background of a given phenotype. This could help researchers to integrate genotypes and phenotypes of rice. There are many rice genome browser Post Rice Genome Annotation project progress has been built to uncover the functional diversity of alleles for agriculturally relevant genes which have been obtained from functional genomics researches. We have gathered data on functionally validated rice genes across scientific literatures. Genetic and phenotype information is compiled from this literature. The data is combined in different categories. In this study, our aim is to provide information on rice gene function to study phenotypes characters due to the effect of various genes in Rice. To accomplish this, a comprehensive search was attempted to gather articles related to functional genomics of rice and prepare a list of genes which are functionally characterized. The information gathered on functionally characterized and validated genes of Rice was compiled to make a new database and finally, a browser is developed. Same genes are found to affect multiple traits. The position of the genes in the genome along with the objective of the study are also compiled. A deep analysis of the functionally characterized and validated genes will help to understand variation which offers a useful additional resource for identifying novel gene functions as well as allelic variants that particularly interact with the genetic makeup and/or environment or alleles showing minor effect on phenotype, especially for characteristics related to plant adaptation. Ohyanag H, et al. [2] developed OryzaGenome, a Genome Diversity Database of Wild Oryza Species. This resource can serve as an excellent genotype-phenotype association resource for analyzing rice functional and structural evolution, and the associated diversity of the Oryza genus. Two variant viewers are implemented: SNP Viewer as a conventional genome browser interface and Variant Table as a text-based browser for precise inspection of each variant one by one. Portable VCF (variant call format) file or tab-delimited file download is also available. Rice Stress-Resistant SNP database [3] (<http://bioinformatics.fafu.edu.cn/RSRS>) mainly focuses on SNPs specific to biotic and abiotic stress-resistant ability in rice, and presents them in a unified web resource platform. Yao W. et al. [4] built comprehensive and accurate dataset of ~2800 functionally characterized rice genes and

~5000 members of different gene families by integrating data from available databases and reviewing every publication on rice functional genomic studies. The dataset accounts for 19.2% of the 39 045 annotated protein-coding rice genes, which provides the most exhaustive archive for investigating the functions of rice genes. They also constructed 214 gene interaction networks based on 1841 connections between 1310 genes. The largest network with 762 genes indicated that pleiotropic genes linked different biological pathways. Increasing degree of conservation of the flowering pathway was observed among more closely related plants, implying substantial value of rice genes for future dissection of flowering regulation in other crops. Yan J. et al. [5] developed SnpReady for Rice (SR4R), an Integrative SNP Resource for Genomic Breeding and Population Research in Rice. SR4R presents four reference SNP panels, including 2,097,405 hapmapSNPs after data filtration and genotype imputation, 156,502 tagSNPs selected from linkage disequilibrium-based redundancy removal, 1180 fixedSNPs selected from genes exhibiting selective sweep signatures, and 38 barcodeSNPs selected from DNA fingerprinting simulation. SR4R thus offers a highly efficient rice variation map that combines reduced SNP redundancy with extensive data describing the genetic diversity of rice populations. In addition, SR4R provides rice researchers with a web interface that enables them to browse all four SNP panels, use online toolkits, as well as retrieve the original data and scripts for a variety of population genetics analyses on local computers.

2. MATERIALS AND METHODS

The categories of information on functionally validated rice genes that have been derived from literatures have been listed in Table 1. The descriptions of the phenotypes in each of the articles were used to annotate functionally characterised genes. The phenotypes related to every gene were divided into two categories: "major category" and "minor category". Within each relevant category, genes related to multiple characters were counted. Information gathered from corresponding articles have been divided into specific categories as shown in Table 2. These specific categories are used to make columns in our database. An entity relationship diagram is used to design the database. ER diagram (Fig. 1) helps to identify entities, attributes and their relationship exists among entities. In our database, some of the major

entities identified are genes, Protein, wet lab analysis, resistance etc., and their relationship with each other. Entity relationship model is represented by ER Diagram. Entities are represented by rectangular box. Attributes are presented by ellipses. In this study, the entities chosen are Protein, Gene, Stress, Marker, Wet lab analysis, expression analysis, resistance . All these entities are related to each other through relation which have been represented by Diamond Box. Every entity has one unique primary key. Like Gene Id is the primary key of gene table. Entities among them different degree of relationship. The degree of relationship may be different. One gene can have one to one relationship with protein and this one to one relationship between entities are indicated with number 1. Similarly, One gene can show multiple types of resistance and there exists one to many relationship with gene and resistance entities. One to Many relationship is indicated by N. Genes which translate into protein and their effect on phenotype have been understood by going through the results in the corresponding literature. The variation found in the number of genes which are functionally validated among the various classes most likely reflects the agronomic importance of each characteristic and the research interests of specific researchers instead of the exact number of genes associated with each character. Transgenic techniques like , knockdown, and knockdown/ overexpression were more frequently used for functional study of genes in case of "resistance or tolerance" than for genes in case of "morphological trait" and "physiological trait." The difficulty in identifying mutant and natural populations for characters associated with tolerance or resistance in mutant and normal populations may result in this difference. Overexpression analysis was used to characterise the major numbers of genes in several categories "cold," "drought," and "salinity" under the major category "resistance or tolerance".

2.1 Database and Web Tool

All data of the Rice genes which are functionally validated were compiled to create a database. The database is consisting of a Gene information table and a genome-phenome viewer. GBrowse [6] is used for the purpose of the Genome viewer. Interactive web pages have been developed to see Gene information table on the desired click. The gene information will be displayed in a separate window when the user will choose to see the gene details in GBrowse.

The gene details link has been included in a balloon which will be reflected when user will point the cursor to the desired gene in the GBrowse. A web tool shows the phenotype for a specific gene under a particular experiment. Several phenotypic attributes related to genes have been incorporated along with genomic information. Phenotypic information under different stress conditions has been shown in the browser. The creation of an integrated PheGen database [7] has made it possible to further study GWAS results in the context of the genome and link them to characteristics of SNP, gene, and eQTL data. These data are easily accessible in a user-friendly format made available to the scientific community who are interested to look into genetic association results in more depth. This is achieved by including functionalities to download data tables, personalise the view, and dynamically browse features of the genomic sequence. Web tools help to understand disease pathways and biology by providing the interconnection between the genetic variants with many phenotypes. RPAN [8] database is used to search and analyze the rice pan-genome obtained from 3KRG. RPAN is a database that contains general information about 3010 accessions of rice, such as sequences,

expression data, gene annotations and genes from the rice pan-genome. RPAN also includes a variety of search and visualization features. PhenoScanner [9] is a curated library of results from extensive genetic association research that are readily accessible to all. This programme performs "phenome scans," or the comparison of genetic variations with a broad range of phenotypes, to enhance knowledge of biological processes and disease pathways. Similarly, a genome-phenome browser shows the phenotype for a specific gene under a particular experiment. Several phenotypic attributes related to genes have been incorporated along with genomic information. Phenotypic information under different stress conditions has been shown in browser. For the purpose of phenome browser development GBrowse genome browser has been used. Through the customization facility, GBrowse is configured to visualize the phenotype data. Rice annotated data is used which is added in GBrowse. Annotation tracks in the Genome Browser are comprised of files in line-oriented format. Every line in the file defines a track display characteristic or a data item within the track. There are three types of lines in annotation files: browser lines, track lines, and data lines.

Table 1. Different categories of information for rice genes

Particulars of Gene Information	Remarks
Gene	Name of the gene
Gene Symbol	Abbreviated Gene Name
Major	Major character
Minor	Minor character
Chromosome	No. of chromosome where gene lies
Start	Start of gene on the Chromosome
End	End of the gene on the chromosome
Locus ID	Locus id of the gene
Isolation	Method of isolation
Objective	Phenotypes studied in each of the research articles
Reference	Digital Object Identifier (doi)

Table 2. Minor characters studied in literature classified under each of the major characters

Character Major	Character Minor
Morphological	Dwarf
	Culm Leaf
	Seed
	Shoot seedling
	Panicle flower
	root

Character Major	Character Minor
Physiological traits	Eating quality Flowering Germination dormancy Sterility Lethality Source activity
Resistance	Bacterial Blight Resistance Blast Resistance Lodging resistance
Tolerance	Cold tolerance Drought tolerance Salinity tolerance Sub mergence tolerance

Table 3. Broad categorization of data found from literatures

Gene name	Gene Id	Gene sequence	Genomic position	Protein ID	Protein structure
Protein sequence	Expression pattern	Gene function	Growth analysis	Northern blot analysis	Southern blot analysis
Hormonal sensitivity	Stress response	Transcriptional analysis	PCR	Biochemical analysis	Metal concentration
Enzyme activity	Pest resistance	Chemical treatment	Over expression	QTL	cDNA analysis
Physiochemical properties	Starch biosynthesis	Chlorophyll biosynthesis	Herbicide resistance	Weed resistance	Transgenic lines
Agricultural traits	Mycorrhiza formation	Nutrient deficiency	SSR	SNPs	DGE

*PCR = Polymerase Cahin Reaction, QTL = Quantative Trait Loci, SSR= Single Sequece Repeat, DGE= Differential gene Expression Analysis , cDNA= complementary DNA

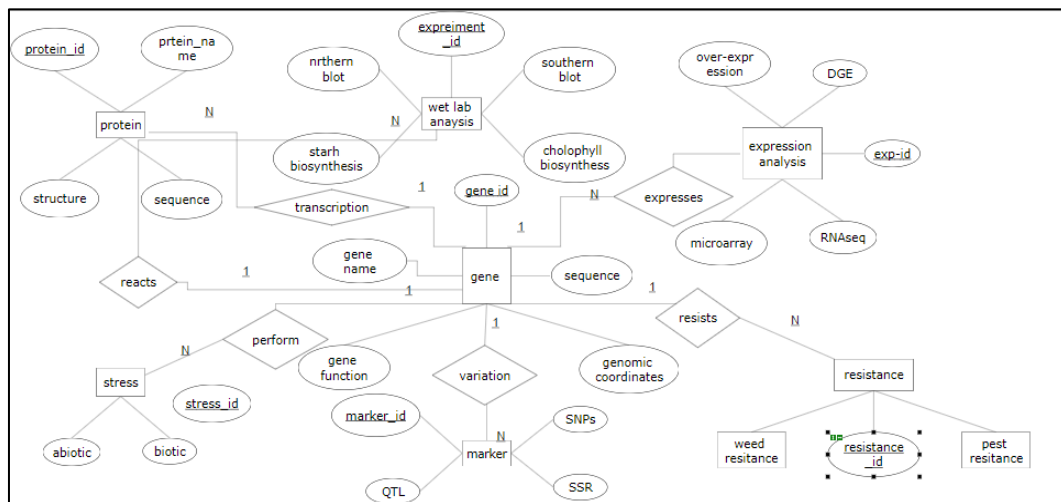
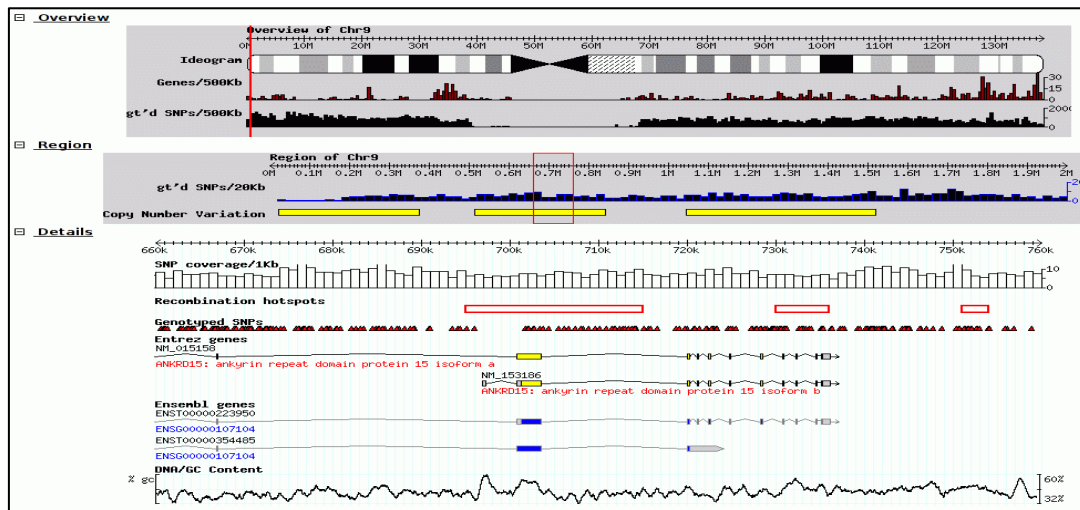
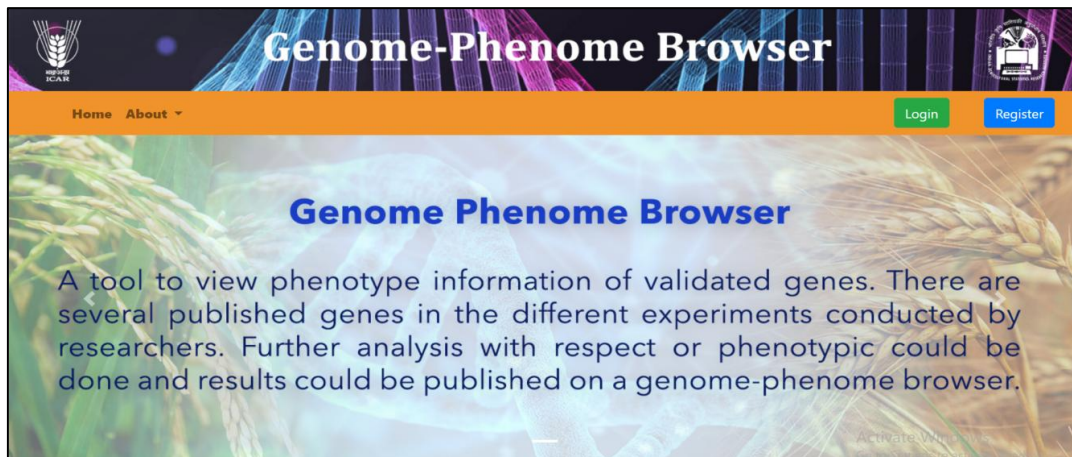


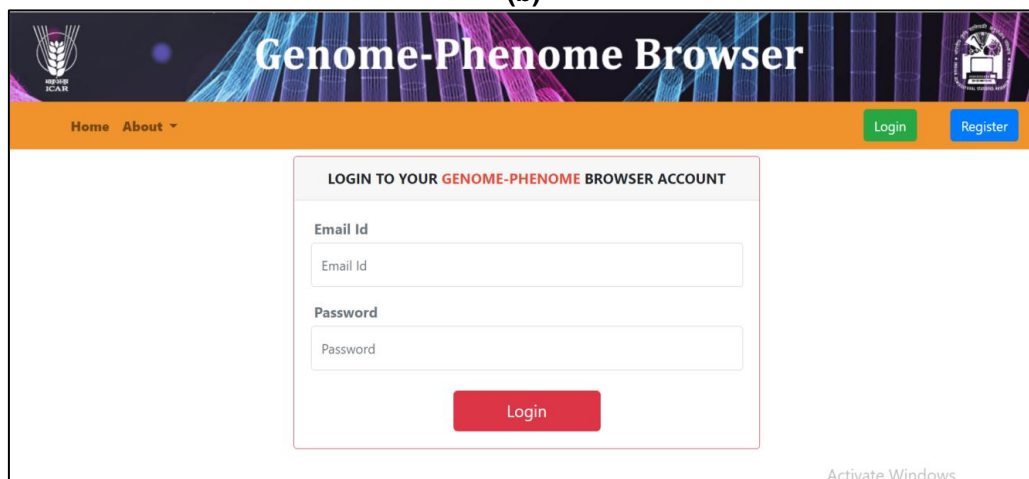
Fig. 1. ER diagram from different categories of information which will be used to develop database



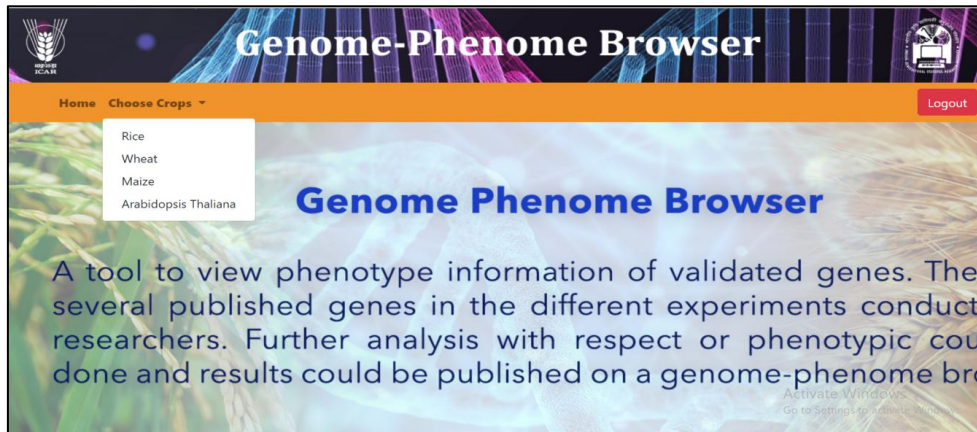
(a)



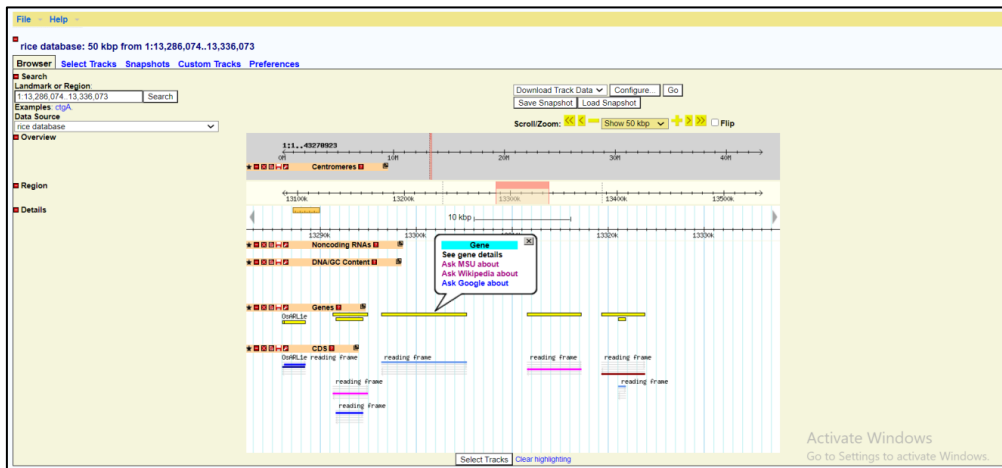
(b)



(c)



(d)



(e)

Genome-phenome information of Rice Genes

Sr. No	Locus Id	Gene Name	Gene Symbol	Chromosome	Genomic Position	Protein Expression	Expression Values	Protein Structure	Protein Sequence	Growth Analysis	DOI
1	Osl1g0293000	Elicitor	ELS	1	10705422-10708091	ELS is Preferentially Expressed in the Developing Panicle and in the Roots11*	View	MPEVSAKGTTSKKGFKAVTKTKQCKEGRKGRKRCREESYSNYKVLKQVHPDTGSSKAMSIMNSFVTD	Dwarfism, Fertility, Germination rate, Flowering time, affects root development	10.1016/j.jipph.2011.05.020	

(f)

Fig. 2. Overview genome-phenome browser. A) GUI of GBrowse B)Home page of the Genome-phenome browser C)Login page where user has to login for accessing the browser D)After login use can choose desired crop, in this study Rice is used E) for chosen crop GBrowse will appear along with all the genomic details including the validated genes that have been used in this study, yellow bar represent the gene F) gene details consists of the genome –phenome phenotype information’s of the particular gene

3. RESULTS AND DISCUSSION

In this study, we have a list of rice genes which are functionally characterized and validated. The information contains the Gene name, Gene symbol, Major characteristics including Morphological traits, physiological traits, resistance or tolerance, methods of isolation, doi etc. All these information helps to better understand the phenotypes and how it is affected by genes. A genome browser is a graphical user interface for visualizing genomic data obtained from a biological database. The genome browser shows the biological data in a user-friendly format. It generally takes very huge datasets, such as whole genome FASTA files, and exhibits them in a way that users can understand the information contained within. A comprehensive database of functionally characterized rice Genes is developed. This database consists of two types of information one is genome information and other phenotype exhibited by the gene. Genome Browser GBrowse has been configured for Rice Annotation data. All the genomic information gathered on functionally characterized genes of Rice have been displayed in GBrowse. GBrowse displays biological information in different coordinates of the genes. It contains several information like genomic position of genes, locus ids, positions of the genes in the chromosomes, SNPs, Flanking regions, copy number variations etc. Further information on specific genes that how it is functionally affecting different traits can be viewed on the desired click. It leads to a detailed information table comprising of all the information on the validated rice genes compiled in the database extracted from the literatures. In the table, data regarding the phenotypes of the validated genes will be displayed. All the data gathered on functionally validated rice genes from corresponding literature have been summarized and will be reflected on the new window in the browser. The database was created in MySQL. MySQL is a popular relational database management system. GBrowse is configured to fetch data from a database which enables GBrowse to integrate phenotypes and provide a channel to search, browse, retrieve and analyze genomic as well as phenotype data of queried genes.

4. CONCLUSION

It is concluded that all the data gathered on functionally validated rice genes from corresponding literature have been summarized

and will be reflected on the new window in the browser. The database was created in MySQL. MySQL is a popular relational database management system. GBrowse is configured to fetch data from a database which enables GBrowse to integrate phenotypes and provide a channel to search, browse, retrieve and analyze genomic as well as phenotype data of queried genes.

STUDY AREA / SAMPLE COLLECTION

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ACKNOWLEDGEMENT

I would like to convey my sincere gratitude to Division of Bioinformatics, ICAR- Indian Agricultural Statistics Research Institute and Indian Agricultural Research Institute for facilitating the research lab and other research facilities during the tenure of this study.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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Peer-review history:

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