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Insilico Techniques Utilized in Malaria Research

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Abstract:

Malaria causes most of the deaths among all the parasitic diseases. Malaria belongs to neglected tropical diseases class and NTDs affects around 1 billion people mostly living in rural areas and having low income. Drug resistance in parasitic diseases is a major threat to the researchers working in the synthesis of malarial drugs. Bioinformatics approach is useful in malaria research and malarial drug design. In the present work, malarial databases such as MARA, PhenoPlasm, PlasmoDB etc and tools suchas MaGnET, Malaria tools etc have been discussed. This review article provides upto date information regarding the various malarial databases and tools utilized in malarial research work.

Keywords:

Malaria, Database, Tools, Insilico, Parasite.

Introduction:

In the year of 1880, Charles Louis discovered parasites which cause malaria in humans. Malaria is caused by *Plasmodium species* and near about five plasmodium species have the capability to cause malaria in human beings. Around 200 millions of people every year are infected each year and lots of people die every year due to malaria. It is a serious problem in India and in African countries[1]. According to WHO report, in 2017, there are 219 million cases of malaria have been reported which have caused around 435 000 deaths all over the world. Some of the symptoms in malaria include fever, headache, vomiting and sometimes shivering also found. Malaria is commonly seen in tropical and subtropical countries. It has been founded that

Plasmodium falciparam is most deadly malaria parasite. In India, malaria cases are reported more in rural areas. Moreover, young children are getting affected than adults. Plasmodium affects humans in various stages and it is shown in figure1. Antimalarial drugs such as quinolines and artemisinins are very important component of malaria control programmes [2].

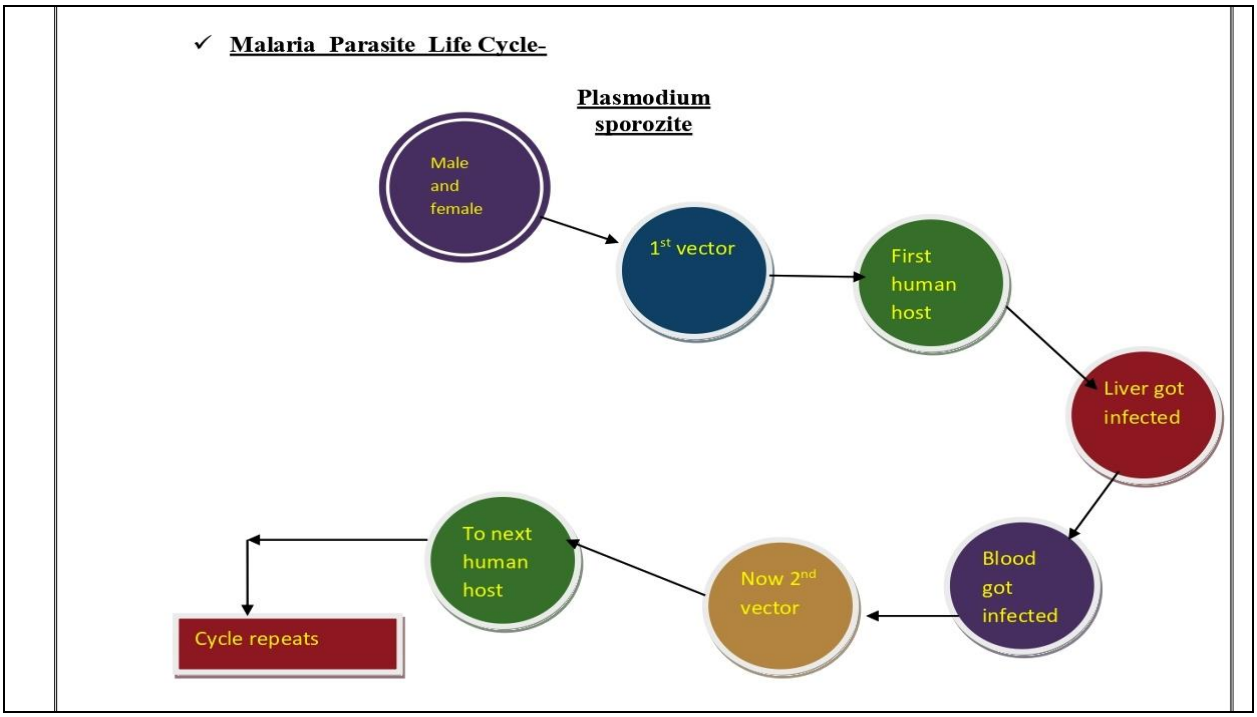

Fig1: Representing the malaria parasite life cycle.

Wellcome Genome Trust, Melinda gates foundation and the Drugs for neglected diseases initiative have taken major initiatives for the malarial research. Bioinformatics tool are used in research of malaria and are very helpful in saving lives[3]. With the help of bioinformatics tools like Gene Ontolgy (go) database, Next generation sequence method and MaGnET (Malaria Genome Exploration Tool) which is a software tool that provides a graphic displays for different database, genomic locations of genes, mRNA expression can easily be done with the help of these software tools. There are various factors by which malaria is being controlled which is shown in figure2.

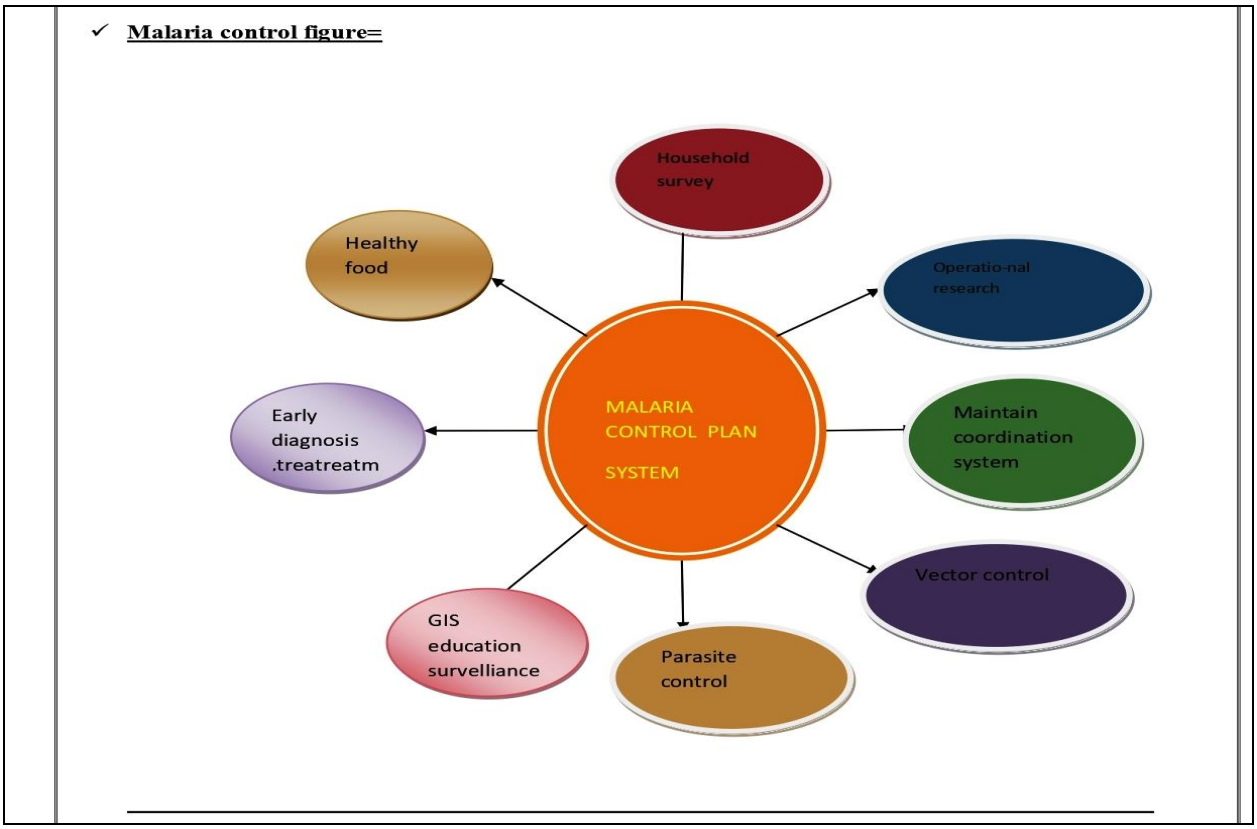

Fig 2: Showing the malaria control plan.

Chloroquine and sulfadoxine-pyrimethamine (SP) which anti malarial drugs have shown resistance[4]. Parasitic drugs are being depleted because of the increasing drug resistance. Moreover, old drugs are not being replaced due to negligence. There are various factors such as epigenetics, drug efflux, DNA damage repair, cell death inhibition, epithelial mesenchymal transition, drug target aleration and drug inactivation[5]. At present, there is no proper vaccination for malaria. This triggers the progression of more robust drugs which are useful in the treatment of malaria. Computer aided drug design is a powerful weapon for malarial scientists. In this study, we have focused on malarial databases and tools which will be extremely useful for parasite researchers.

Materials and methods:

Tools used in malarial research:

1. MaGnET: It is an exploration tool which provides the genomic data of *Plasmodium falciparum*. It provides new graphical displays for expression of mRNA, gene positioning, and

interaction of two proteins molecule [6]. It operates with Java and Mysql. With the help of MaGnET, genome display as well as expression of mRNA of *P. falciparum.* MaGnET programming gets affected by the presence of YETI.

2. Malaria Threat Map: This map allows user friendly data of different countries. It contains three datasets which includes vector insecticide resistance, parasite gene deletions and parasite drug resistance [7]. The data is available in many languages and various filters are there to select subsets of data (Fig 3). The map is further linked with WHO guidance.

Fig 3: Represents the Malaria Threat Map Tool.

3. Magic-BLAST: Magic-BLAST is a RNA seq tool for studying big as well as short reads. It uses various methods to optimize scores of spiced alignment. The capability of Magic- BLAST depends upon its capability to find non coding regions on RNA datasets from NGS datasets. It can read upto 250 bases. Moreover, another advantage of Magic-BLAST can accept a FASTQ file as input [8,9].

4. **WWARN Explorer:** The WWARN Explorer is useful in clinical trials. It visualizes the data obtained from the trail studies of antimalarial resistance studies in various countries of the world (Fig 4). It shows the data from 198 clinical studies and 19 pharmacology studies. With the help

of thi tool, we can study place, time range and anti malarial drugs. This tool can be used for the comparative studies for different patients [10].

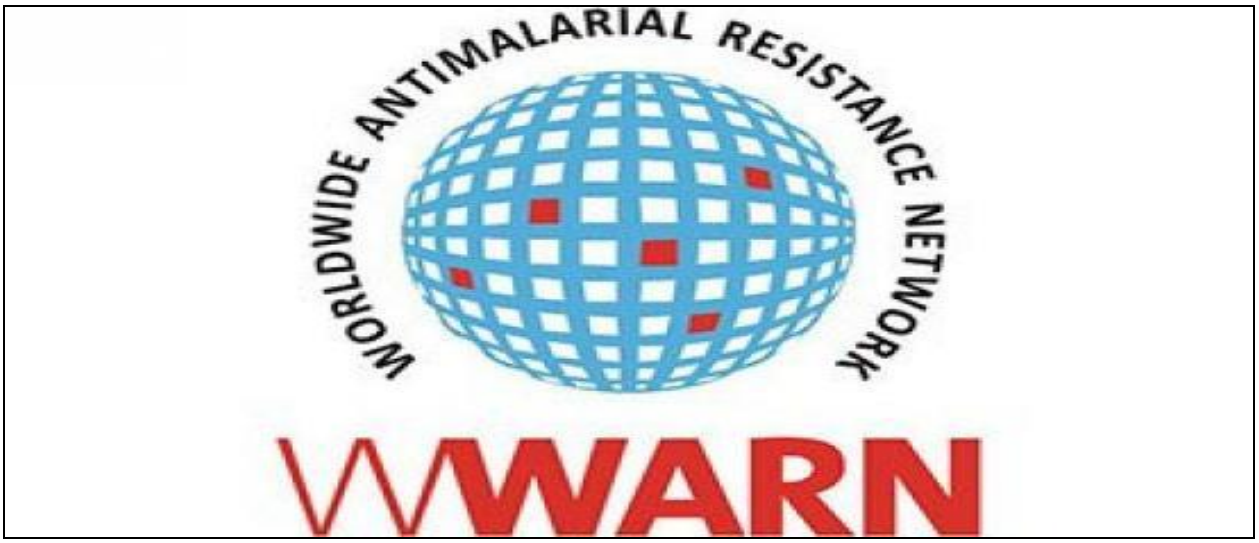

Fig 4: Represents the WWARN Tool.

5. IDOMAL: IDOMAL is a tool for malarial ontology. It became these days cautioned to apply ontologies as an efficient tool to beautify the impact of IT tools in vector biology and malaria entomology [11]. This may be done through building databases and/or decision help structures pushed by means of extensive-ranging ontologies that comply with commonplace and established policies. In a simplified instance, a given biomedical ontology might provide the definition of the term "translation", list its synonym "protein synthesis", and also include its determine (e.G. Organic procedure, metabolic technique, gene expression, and many others) and phases (Initiation, elongation, termination, tRNA aminoacylation).

Different databases used for malaria research:

1. MARA (Mapping Malaria Risk in Africa): It was started in 1996 with the aim of generating danger maps of malaria in South African countries. It became installation as a non-institutional Pan-African effort within the spirit of an open collaboration. It receives financial help from bill and Melinda gates foundation. It is an open access website where malaria predominance data is being studied (Fig: 5). Rare data obtained from the plasmodium species can also be studied with the help of MARA.

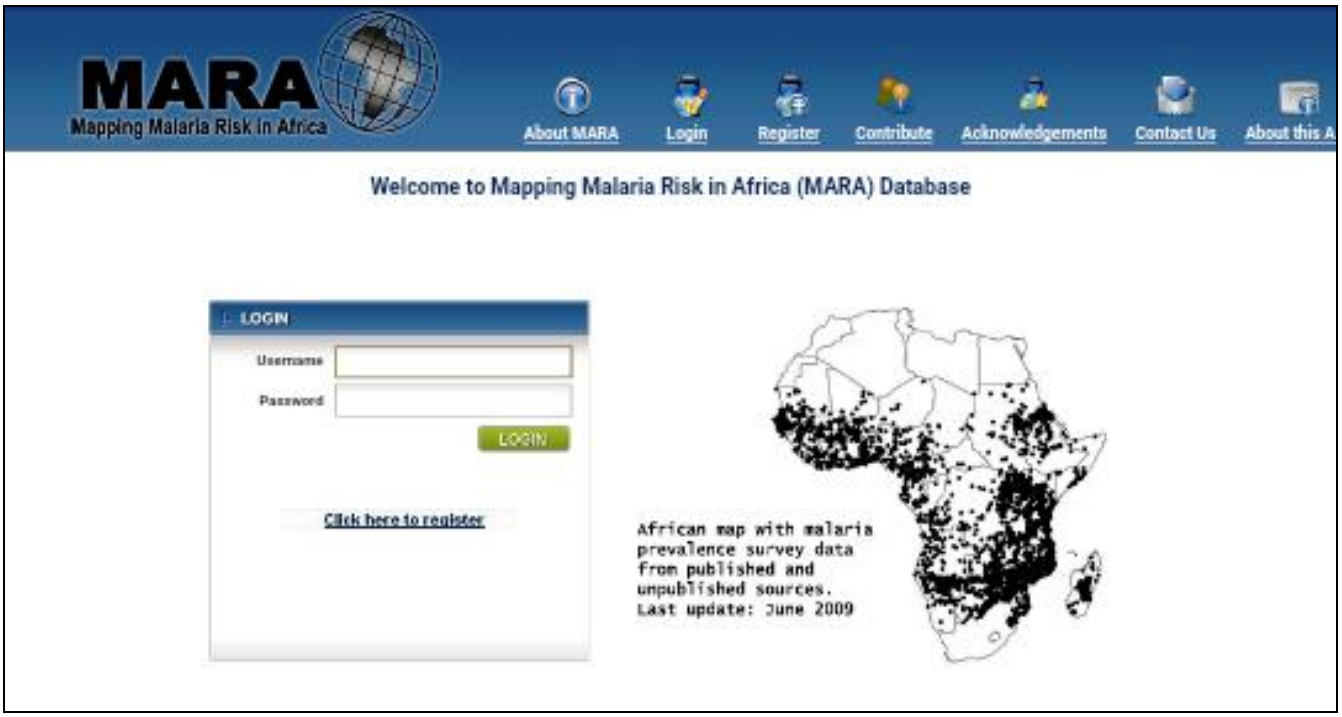

Fig 5: Represents the MARA database.

2. PhenoPlasm: This database objective is to assemble a complete series of dependent phenotyping data from attempts to knock out Plasmodium genes. It is curated by Theo Sanderson. A primary portion of the data in this website comes from the Rodent Malaria genetically modified parasites database, the Adams lab saturation display screen in P. Falciparum and from PlasmoGEMGenome facts come from GeneDB via PlasmoDB. In phenoplasm database, immunofluorescence pictures from the malaria metabolic pathways can be studied [12]. PhenoPlasm is a database where different plasmodium genes are present according to species and genera and function of different genes can be studied easily. It is also helpful for finding various plasmodium genes responsible for malaria (fig:6).

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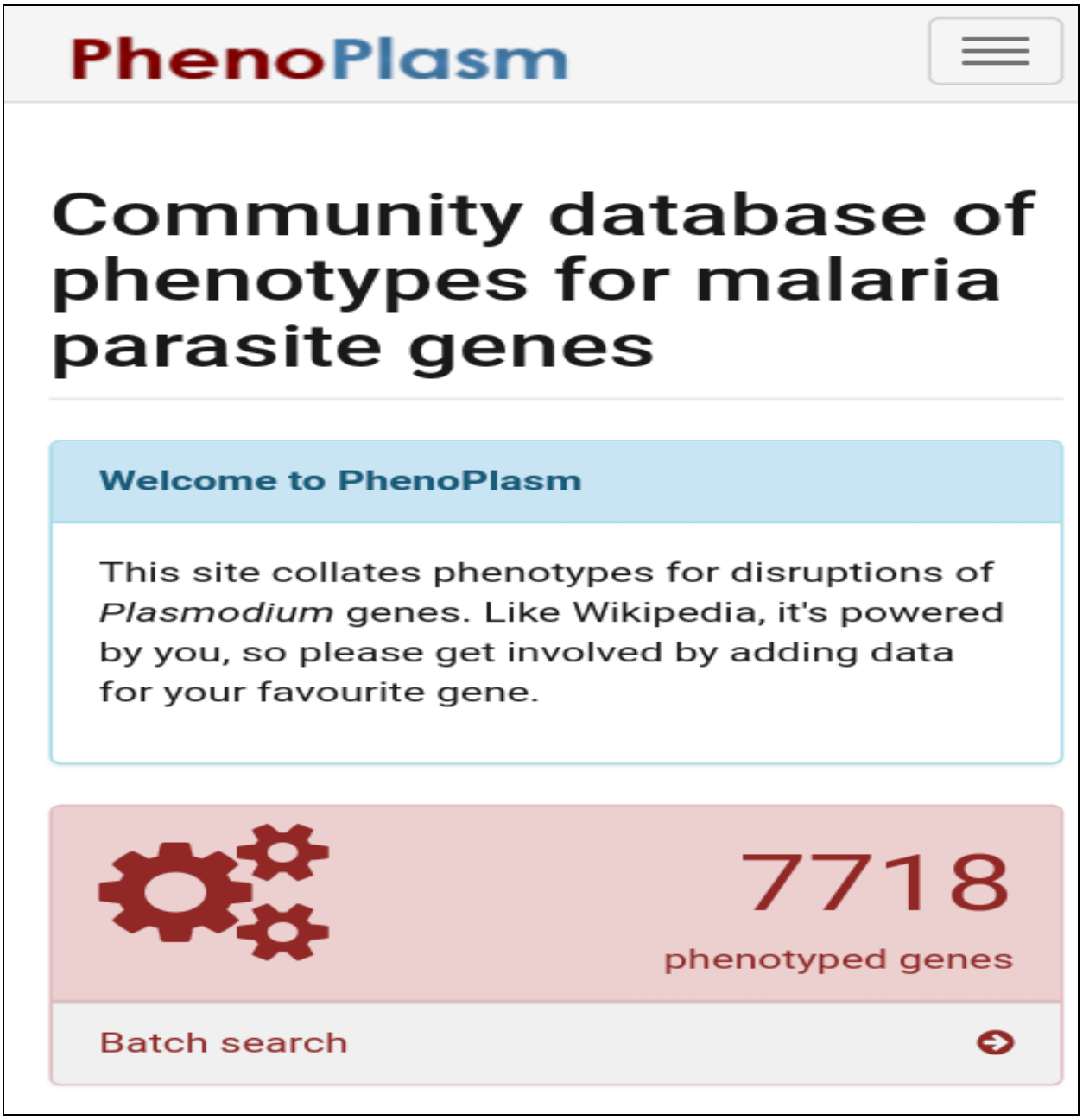

Fig 6: Represents the phenoplasm database.

3. Global Database: The global database on antimalarial drug efficacy and resistance became initiated in 2000 to centralize information and facilitate reporting at the repute of antimalarial drug efficacy in malaria endemic countries. It contains data from therapeutic studies and various

studies on the markers for malarial drug resistance studies. This database includes molecular markers associated with artemisinin, piperaquine and chloroquine resistance [13].

4. Drugbank: Database contains 9591 drug entries which include 2037 FDA-permitted small molecule capsules, 241 FDA-permitted biotech capsules, 96 nutraceuticals and over 6000 experimental drugs and 4270 non-redundant protein sequences. In case of malaria there are different drugs available which can cure malaria and they differ from each other by physical and chemical properties (Fig: 6). The drugs that are utilized in the management of malaria such as mefloquine, quinine sulfate, primaguine phosphate etc. Drug bank is extremely useful in studying the physicochemical properties of the drug and mechanism of action of drugs by which malaria is treated [14].

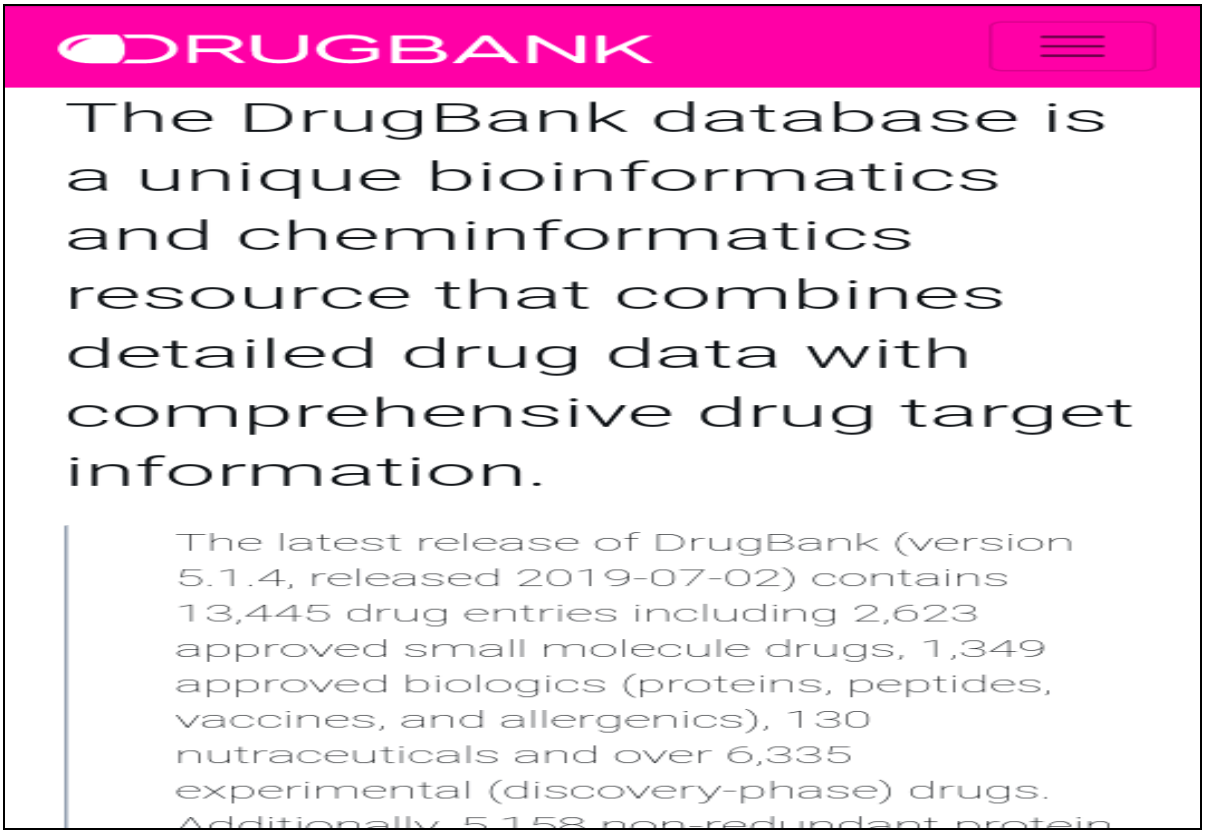

Fig 6: Represents the Drugbank database.

5. NCBI: NCBI stands for national centre for biotechnology information. It is a part of national library of medicine USA. It was founded in 1988 by Claude Pepper. It is linked with different

databases such as DDBJ, EMBL and Swissprot. According to the data available for malaria in NCBI, there are 6243 genes and 579221 proteins in NCBI. A total of 34 malarial databases are available in NCBI (Fig: 7). Moreover, with the help of NCBI, *plasmodium vivax and plasmodium falciparum* genes and their functions can also be studied [15].

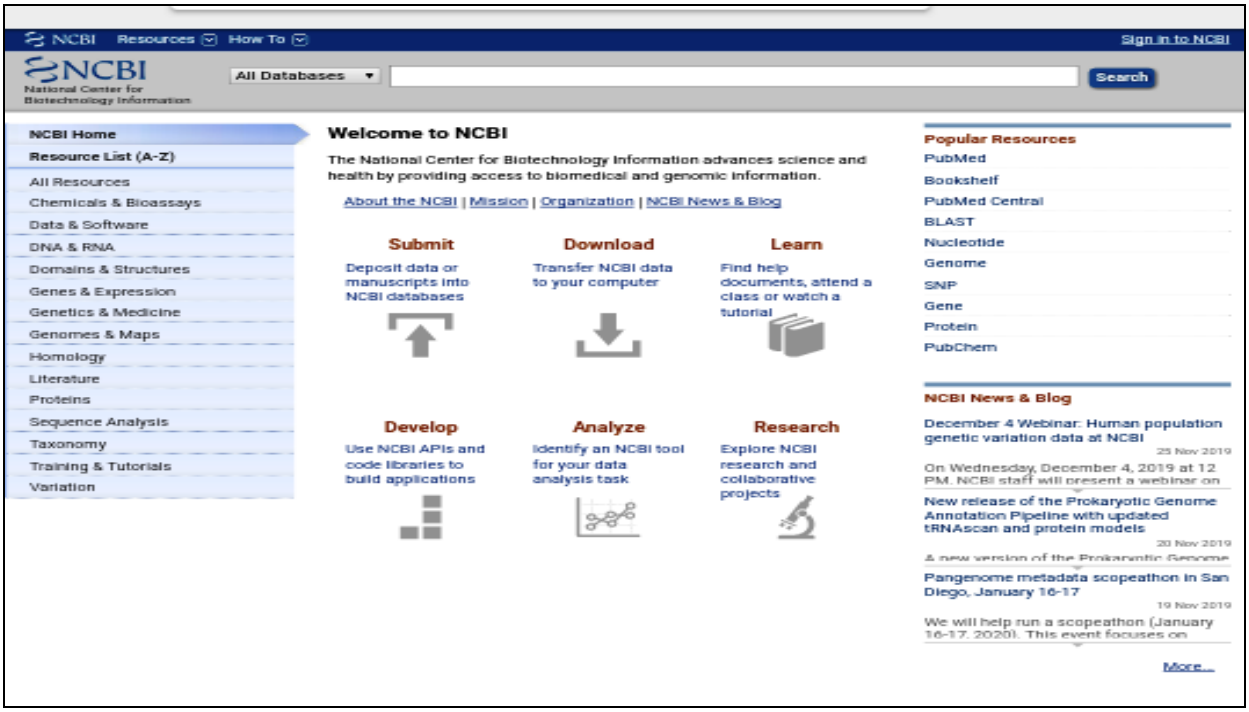

Fig 7: Represents the NCBI database.

6. PlasmoDB: PlasmoDB is a database for studying the genomics of Plasmodium species. With the help of this database, we can study the gene models, annotation, genomic location, orthology and synteny, taxonomy, phenotype, transcriptomics and pathways of the malarial species[16]. Apart from these details, it also provides SNP (single nucleotide polymorphism) data, EST (Expressed sequence tag) data and ORF (open reading frame) data (Fig: 8).

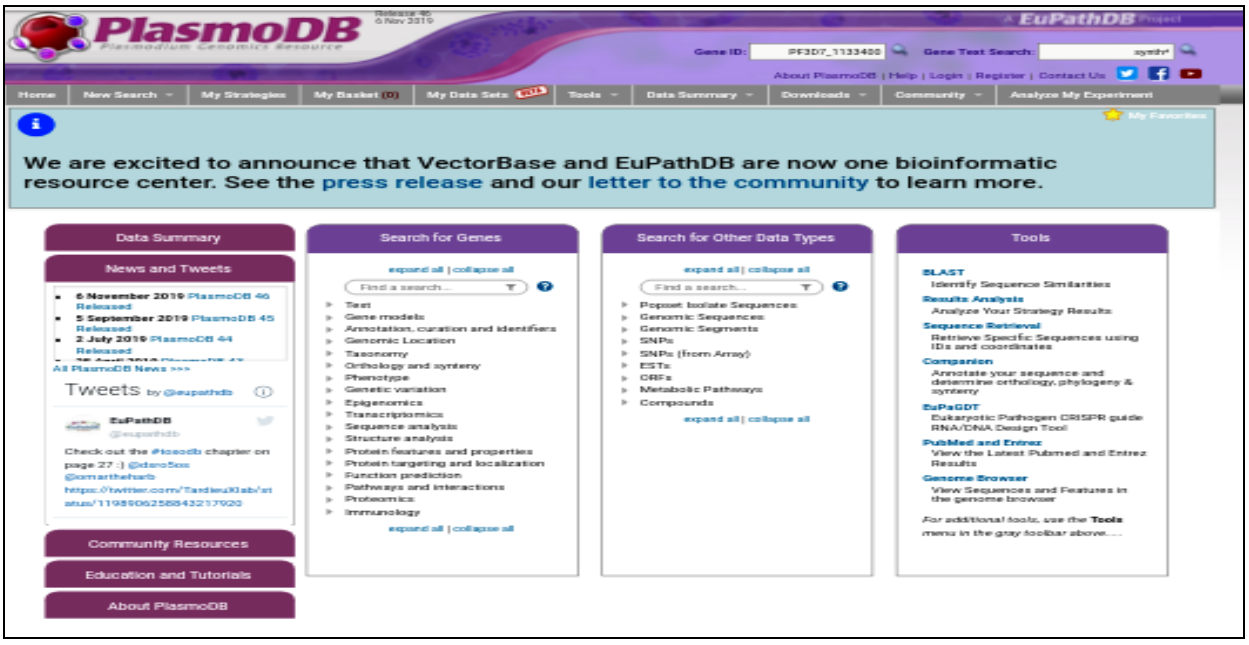

Fig 8: Represents the PlasmoDB database.

7. KEGG: KEGG is a database of Kyoto university. With the help of KEGG database, malaria genes and malaria genome (Eg: *Anopheles gambiae*, African malaria mosquito) can be analyzed in detail. Moreover, malarial enzymes (PFAPG; malaria aspartic hemoglobinase) can also be studied with the help of KEGG [17,18]. DBGET is a integrated database retrieval system in KEGG. KEGG is a useful database for studying the genetic disorders[19-21] (Fig: 9).

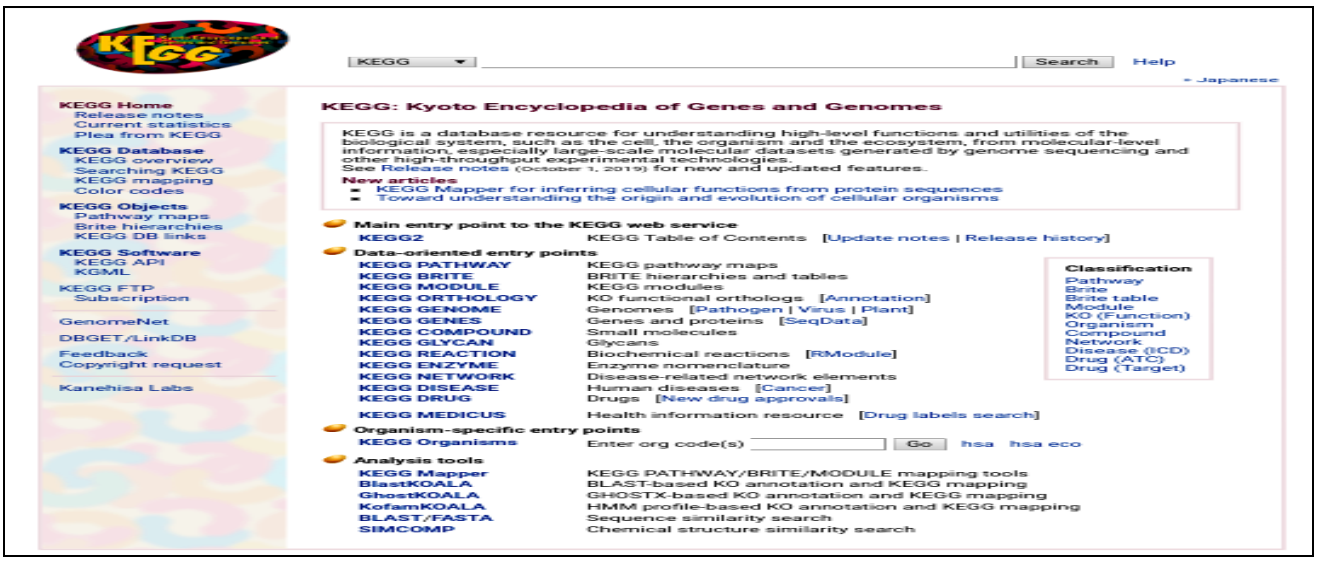

Fig 9: Represents the KEGG database.

Summary of different databases and tools are discussed in Table1.

Year of the Establishment	**Web Resource name**	**Description**	**Website/ Useful paper link**
2017	Malaria Threat Map	WHO Global Database	https://www.who.int/malaria/maps/threats-about/en/
2007	MaGnET	Results into 3D structure	https://bmcsystbiol.biomedcentral.com/articles/10.1186/1752-0509-1-S1-P32
2015	WWARN Explorer	Clinical studies	https://www.wwarn.org/tracking-resistance/wwarn-xplorer
2017	PhenoPlasm database	Identify malarial genes	www.phenoPlasm.org
1988	NCBI	Useful in the fundamental research work	https://www.ncbi.nlm.nih.gov/
1995	KEGG	Metabolic pathways	https://www.genome.jp/kegg/
2009	PlasmoDB	SNP and ORF data	https://plasmodb.org/plasmo/
2006	Drugbank	FDA approved drug molecules	https://www.drugbank.ca/
1996	MARA database	Mapping Malaria Risk in Africa	https://www.mara-database.org/login.html

Table 1. Showing the different databases and tools used in the malarial research.

Conclusion:

In the present work, it primarily focused on the tools and databases that are utilized for malarial research work. The tools and databases can be utilized for the gene information, enzymes utilized in the metabolic activities of the malaria, SNP data, drug resistance studies and drug target interactions. Malaria is a serious public health hazard in developing countries. Moreover, drug resistance is a big threat in the parasite world. Research is required in this area to combat drug resistance. With help of CADD, the researchers can screen the potent drug molecules from the databases. The authors sincerely hope that the work will be extremely useful to those who are working in parasite biology.

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Conflict of interest: The authors declare that they have no conflict of interest.

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