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Computational Tools and Databases Utilized in HIV Research

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Abstract:

HIV is a pandemic which has spread across the world. Millions of people suffer from HIV and lose their lives because of this deadly virus. Computational tools have already helped in the discovery of HIV-1 integrase inhibitors, the best example in this regards is Ritonavir. It is a highly active anti-retro viral drug which was discovered with the help of CADD. Bioinformatics is the science of managing and analyzing huge amount of biological data with the help of advanced computing tools and software programmes. Biological databases provides potential and useful drug targets associated with the HIV drug resistance. HIV drugs such as Doravirine, rilpivirine, nevirapine, atazanavir, lopinavir etc have shown resistance. Drug resistance creates problem with the patients undergoing HIV treatment. Moreover, the high cost associated with the drug discovery in HIV compels scientists to undergo a cheaper and effective treatment for HIV and Computer aided drug design is the solution for this problem. In this review article, an updated information about various tools and databases used for HIV research have been discussed. Moreover, the databases and tools of HIV will provide important drug target and phylogenetic information that can be used for designing the anti-HIV drugs.

Keywords:

HIV, Databases, Bioinformatics, CADD, retrovirus, Immunodeficiency

Introduction:

HIV stands for human immuno deficiency virus which when infects the human being hampers the immune system by attacking T-helper cells or the CD4 cells. According to a report from WHO, there are around 37.9 million people are suffering from HIV across the world with Africa leading the list [1,2]. HIV virus belongs to the retrovirus class and it has leads to HIV infections and after some years, it becomes AIDS. AIDS stands for acquired immune deficiency syndrome

ISSN: 0971-1260

Vol-22-Issue-17-September-2019

and the main reasons by person suffers from HIV are unprotected sex, infected needles, during pregnancy from the mother to the foetus, from infected mothers milk to the new born child and during delivery from infected mother [3]. HAART (highly active antiretroviral therapy) and ART (Anti-retro viral) therapies are given to patients undergoing HIV treatment. HIV virus mechanism is still not known clearly because the virus undergoes rapid genetic changes. There are various genes in HIV virus such as Env, Gag, Pol, Tat, Rev, Nef, Vif, Vpr, and Vpu which plays an important role in pathogenicity. Reverse transcriptase is an important target for creating anti-viral drugs [4,5]. There are two types of HIV types have been reported which are HIV1 and HIV2. HIV1 causes more serious infections and more people get affected around the world than HIV2. It causes more than twenty plus infections or HIV related cancers. The signs of HIV illness develop within five to ten years and antiretroviral drugs are given to HIV patients. Antiviral drugs interferers with the HIV virus replication process and thus minimizes the virus load in the patients blood [6].

The commonly used drugs to treat HIV are as under: incase of integrase inhibitors, the drugs used are bictegravir, dolutegravir, elvitegravir and altegravir. Moreover, incase of nucleotide reverse transcriptase inhibitors, the commonly used drugs are abacavir, emtricitabine, Lamivudine and zidovudine. Sometimes in the HIV treatment, combined therapies are being used suchas Trizivir, it consists of abacavir, lamivudine, and zidovudin and combivir consists of lamivudine and zidovudine [7,8]. One more class of inhibitors used to treat HIV is protease inhibitors. Atazanavir, lopinavir, ritonavir and tipranavir are the major protease inhibitors used to treat HIV. Drug resistance is observed in the cases of reverse transcriptase inhibitors [9]. At present, there is no medicine which can cure 100% HIV effects. So, the researchers need to focus on potential drug targets which have the ability to treat HIV effects [10]. This triggers the progression of more anti viral drugs which are useful in the treatment of HIV. CADD (computer aided drug design is a powerful tool for scientists who are working in HIV drug design. In this study, we have focused on HIV databases and tools which will be extremely useful for HIV researchers.

ISSN: 0971-1260

Vol-22-Issue-17-September-2019

Materials and methods:

HIV DATABASES

1. HIV Drug resistance database: It is a drug resistance database maintained by Stanford university, USA. The data is publically available. It has a query pages that includes genotype treatment which retrieves the sequences from person receiving selected HIV drugs and also treatments from virus with specific mutations as well [11]. HIV drug resistance database contains data from the clinical trials. In this two important databases are majorly used in genetic research of HIV are HIV Sequence database and other one is Almos, it was developed by division of AIDS and NIH [12]. It also contains all coding proteins, sequence annotations and uses tools, programs for analysis (Fig 1). This database generates various tools such as Pept Gen, Pep Map , Motif Scan, Alignment Slicer and HIV Genome Browser.

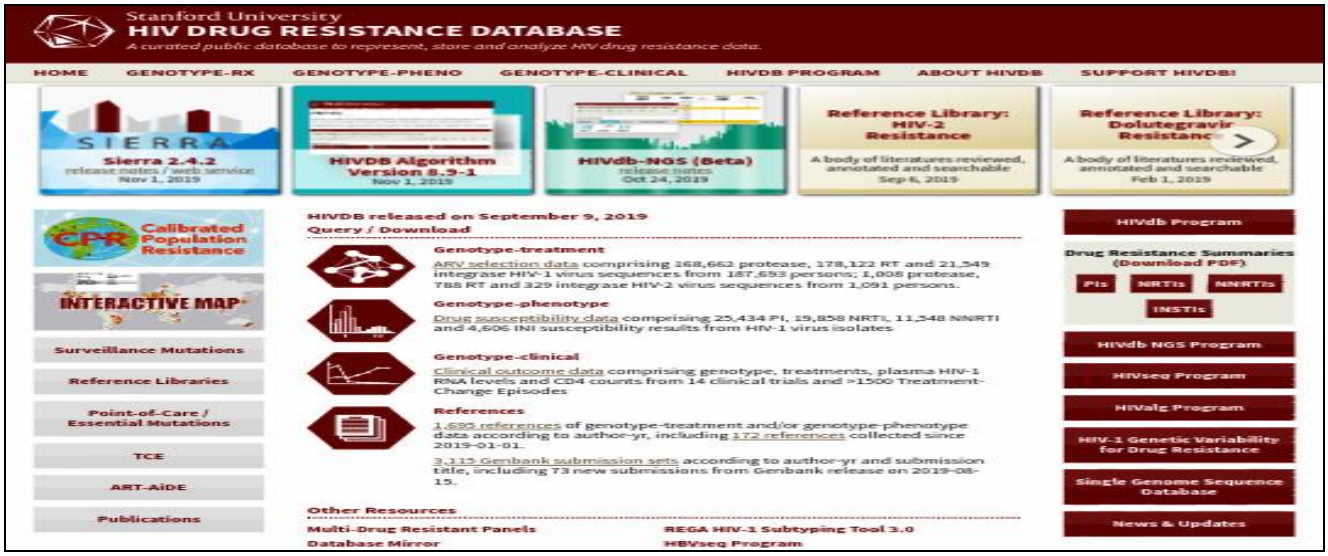

Fig1: Representing the HIV Drug resistance database.

2. HIV Molecular Immunology Database: HIV Molecular Immunology Database is an annotated, collection of HIV-1cytotoxic and Helper T cell epitopes and even antibody binding sites. Moreover it was founded in 1995 by Bettle Korber and the funding for this database is done by National Institute of allergy and infectious diseases [13]. This database includes data of

ISSN: 0971-1260

Vol-22-Issue-17-September-2019

cross reactivity, TCR usage and various immune responses. Moreover, it includes data for human leucocyte antigen for various T cell epitopes (Fig 2). This database contains epitopes of well defined HIV epitopes.

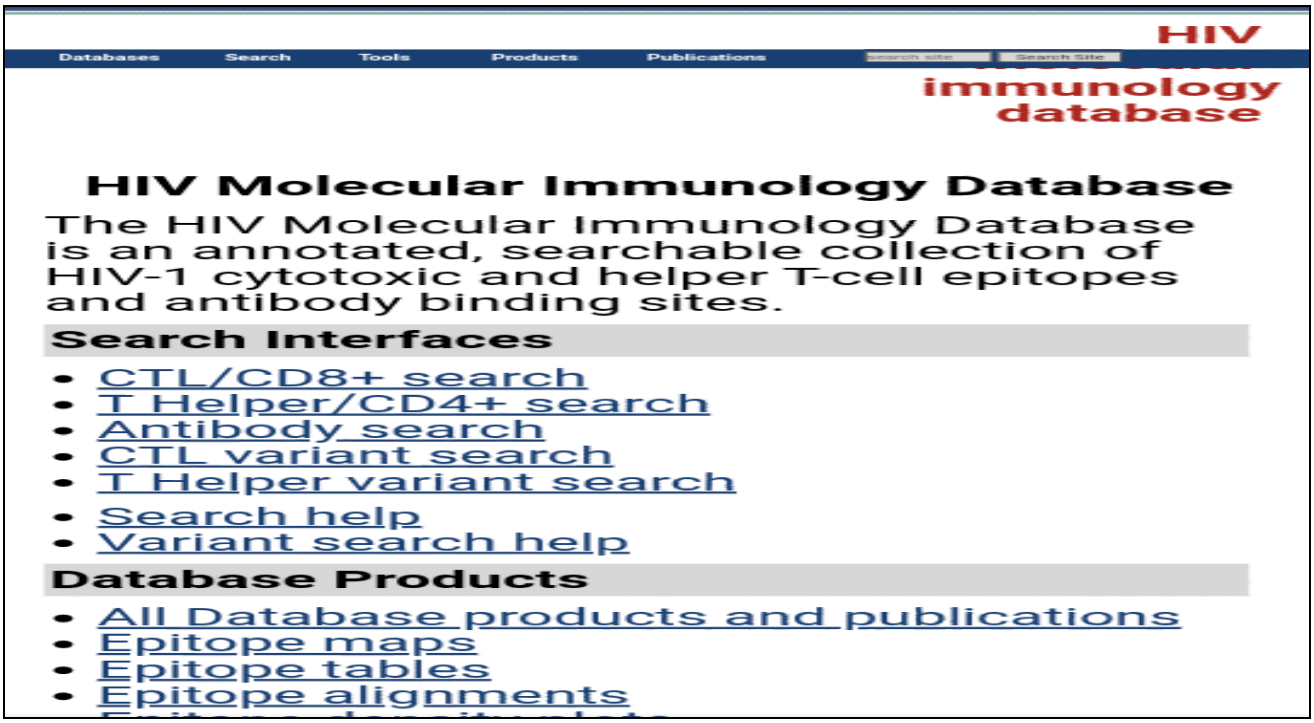

Fig2: Representing the HIV Molecular Immunology Database.

3. Vaccine Trial Database: This database is supported by non govt. organization. It plays an important role in the areas of biomedical innovation, vaccines and antibodies. The major aim of this database is on discovering the antibodies (Fig 3). Vaccines play an important role in maintaining the immunity of a person and helps in preventing the diseases.

ISSN: 0971-1260

Vol-22-Issue-17-September-2019

Fig3: Representing the Vaccine Trial Database.

4. UNAIDS: It is a WHO database which primarily works on HIV and AIDS. It also focuses on HIV virus impact and the risks associated with the HIV (Fig 4). According to the data accessed by the UNAIDS in 2018, there are around 37.9 million people living with HIV in this world and because of AIDS in 2018, 770000 deaths occurred due to AIDS related illness. UNAIDS has a

ISSN: 0971-1260

Vol-22-Issue-17-September-2019

vision to eradicate AIDS by 2030. UNAIDS also provides the statistical data regarding HIV and spreads the information through the world [14,15].

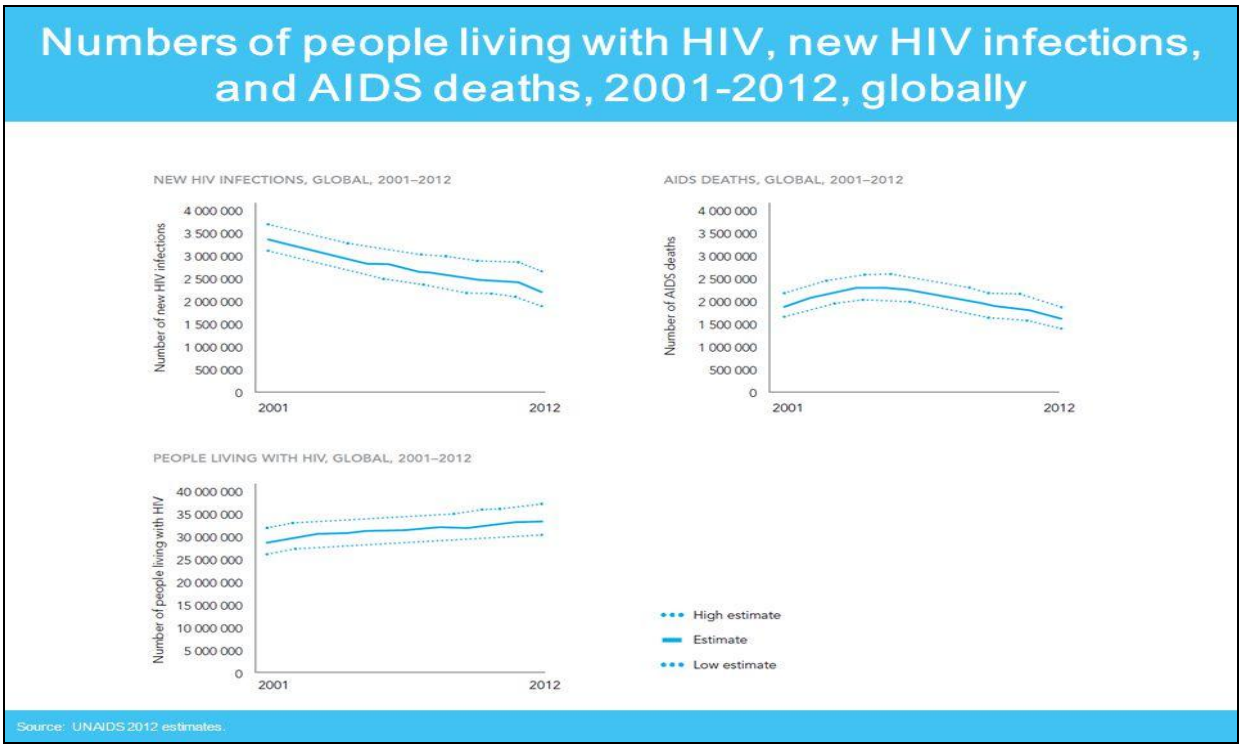

Fig4: Representing the UNAIDS Database.

5. HIV/AIDS Surveillance database: It was founded in 1987. The HIV/AIDS Surveillance Database gives information regarding HIV and a powerful tool for HIV research. The data in the database provides user friendly data and can be downloaded in .pdf or .csv file. The main objective of HIV/AIDS Surveillance database is to gather and spread information regarding HIV. Moreover, it calculates the AIDS mortality levels and finds how many people are getting affected by AIDS [16]. The other databases are discussed in table 1.

ISSN: 0971-1260

Vol-22-Issue-17-September-2019

Fig5: Representing the HIV/AIDS Surveillance database.

Summary of significant databases are discussed in Table1.

Database name	**Description**	**Website/ Useful paper link**
1. ACTG (aids clinical trials group)	Clinical trial database (funded by US Dept. of health services)	https://actgnetwork.org/HIV-databases-links
2. I – Base	Upto date information regarding HIV	http://i-base.info/
3. HIVbio	Human Immunodeficiency Virus (HIV) life cycle and infection	http://crdd.osdd.net/raghava/hivbio/index.html

ISSN: 0971-1260

Vol-22-Issue-17-September-2019

4. AIDSinfo	HIV treatment and prevention clinical trials	https://aidsinfo.nih.gov/
5. NCBI	Useful in the fundamental research work regarding HIV genes.	https://www.ncbi.nlm.nih.gov/
6. HIV Sequence Database	•HIV Sequence Database •HIV Molecular Immunology Database •HIV Vaccine Trials Database	https://www.hiv.lanl.gov/content/index
7. Centers for Diseases Control and Prevention (CDC) database	Disease prevention and control of HIV	https://www.cdc.gov/
8. Drugbank	FDA approved drug Molecules for the HIV treatment	https://www.drugbank.ca/
9. `HIV mutation browser	Mutation data on HIV	http://hivmut.org/index.php?page=home

Table 1. Showing the different databases utilized in the HIV research.

ISSN: 0971-1260

Vol-22-Issue-17-September-2019

Tools for HIV Database

1. Align multi tool: This tool aligns sequences and also changes the alignment and renaming the proteins. Align multi tool has alignment slicer that slices the sequences vertically (Fig 6). Moreover, consensus marker provides consensus to the alignment in align multi tool [17]. Other parameters suchas HIV/SIV subtype, custom list, similarity and sequence are included in this tool.

Fig6: Representing the Align multi tool.

2. Gene Cutter tool: With the help of gene cutter tool, we can extract the protein and alignments of HIV virus. It is also useful in extracting the gene from the set of nucleotide alignments [18]. Moreover, it aligns the reference genomic sequences and slices the various sequences into genes (Fig 7). The input sequences studied in this database are HIV1, HIV2 and SIV and options included in the database are Gag-Pol, Gag, p17, p7, p1, p2, p6, Pol CDS, p51, p15, Vif CDS.

ISSN: 0971-1260

Vol-22-Issue-17-September-2019

Fig7: Representing the Gene Cutter tool.

3. Annotate Tree: This tool is useful in studying the phylogenetic relationship. Phylogenetic relationship tells about the evolutionary relationship between the sequences (Fig 8). Annotate tree creates the pictorial diagram and shows the figure based upon the Newick format. It generates phylogram or circular tree [19].

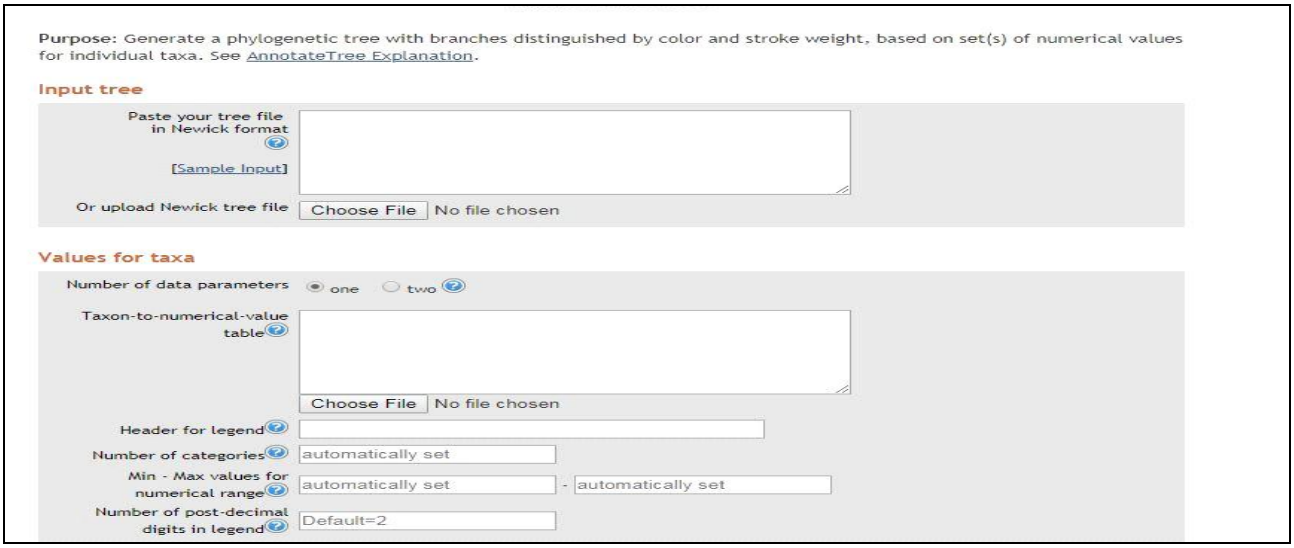

Fig8: Representing the Annotate tree tool.

ISSN: 0971-1260

Vol-22-Issue-17-September-2019

4. Rainbow Tree: Rainbow tree exhibits different colors for different branches of phylogenetic tree. Phylogenetic tree is divided into two types that are rooted and unrooted tree . Rooted tree is a phylogenetic tree which shows the common ancestor and unrooted tree is phylogenetic tree which doesn't show the common ancestor in the final phylogenetic diagram [20,21]. The input used in the Rainbow tree is Newick file format (Fig 9).

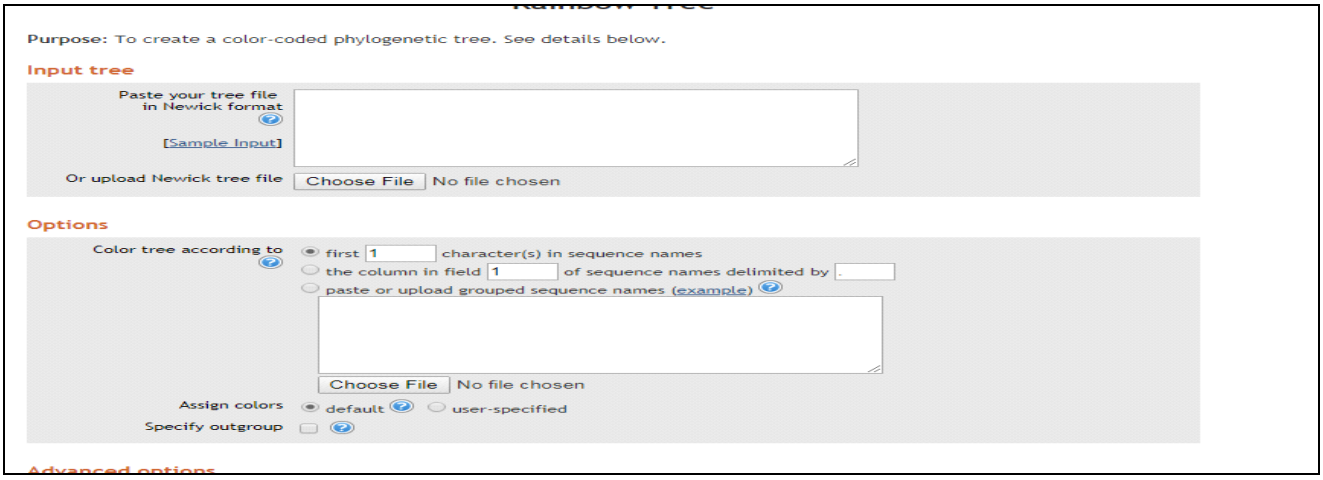

Fig9: Representing the Rainbow tree tool.

5. Epigraph tool suite: This tool generates epigraphs which can be used for vaccine design. The various parameters used in this tool are vaccine sequence names and epitope length (Fig 10). Epigraphs are the synthetic set of amino acids joined by peptide bond that make the most of epitope coverage of sequence of protein.

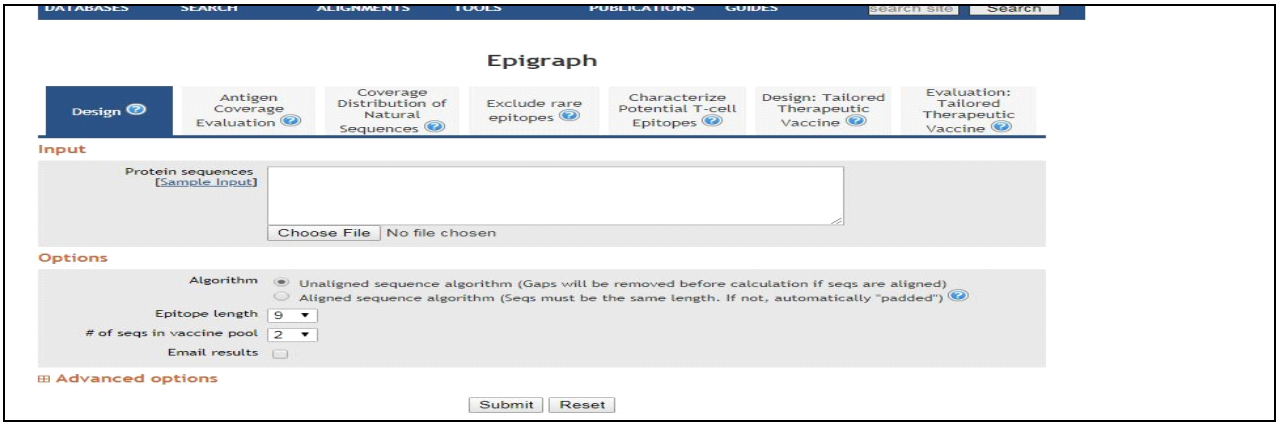

Fig10: Representing the Epigraph tool suit.

ISSN: 0971-1260

Vol-22-Issue-17-September-2019

Conclusion:

In the present work, the authors primarily focused on the tools and databases that are utilized for HIV research work. The tools and databases can be utilized for the gene information, symptoms, SNP data, drug resistance studies and drug target interactions. HIV is a serious public health hazard in developing countries especially in African countries. Therefore, drug resistance in HIV is a big threat to the HIV researchers as well as to the patients. Moreover, research is required in this area to combat drug resistance in HIV. With help of CADD, the researchers can screen the potent drug molecules from the HIV databases and tools. The authors sincerely hope that it 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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ISSN: 0971-1260

Vol-22-Issue-17-September-2019

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ISSN: 0971-1260

Vol-22-Issue-17-September-2019

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