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13. ABSTRACT (Maximum 200 Words)
In response to the potential use of viruses as biological weapons, we have established the Viral Biological-threat Bioinformatics Resource (VBBR) that collects, catalogs, annotates, and analyzes genetic information related to potential viral threats. This work expands upon available knowledge of virus replication, pathogenicity, and virus-host interactions on the basis of individual protein domains, individual genes, and whole genomes. To date, we have constructed a genome and gene sequence database that has been populated with the sequence information for viruses currently listed on the NIH and CDC priority pathogen list. We have also developed a variety of analytical and visualization tools that aid in the analysis of the genomic information coded for by these viruses. Finally, the information developed as a result of this work has been made available to the scientific community through a (currently access-controlled) web site (http://vbbr.genome.uab.edu) that supports research efforts to develop environmental detectors, diagnostics, antiviral compounds, new vaccines, and animal models in support of biodefense research goals.

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INTRODUCTION:

In response to the potential use of viruses as biological weapons, we have established the Viral Biological-threat Bioinformatics Resource (VBBR) that collects, catalogs, annotates, and analyzes genetic information related to potential viral threats. This work expands upon available knowledge of virus replication, pathogenicity, and virus-host interactions on the basis of individual protein domains, individual genes, and whole genomes. This information has been made available to the scientific community to support current research efforts to develop environmental detectors, diagnostics, antiviral compounds, new vaccines, and animal models.

Specifically we are:

1. developing a relational database that supports the data storage, annotation, analysis, and information exchange goals of this proposal;

2. developing a world-wide web site that will allow all information and analytical results compiled and generated by this work to be publicized to the scientific community, providing rapid access to specific information as required by an individual researcher;

3. collecting existing gene and genomic sequences for viral threat agents and importing them into the database for subsequent annotation and analysis;

4. providing computer-automated and human-directed annotation to confirm and update existing biological information in the sequence records for all sequences; and

5. performing a variety of analyses on genome and gene sequences to provide additional information on their structure, function, and evolution.

BODY:

Substantial progress has been made in accomplishing many of the tasks outlined in the original statement of work. Accomplishments extend to database construction, data population, development and implementation of analytical and visualization tools, and publication of all available information on a web site. The accomplishments are listed below, itemized according to the original statement of work and task list.

Task 1. **To develop a relational database that will support the data storage, annotation, analysis, and information exchange goals of this proposal. (Months 1-6)**

- The database has been created based on our previous work on poxviruses and has been updated and refined to better support a wider range of virus threats. An overview of the database schema is provided in figure 1.

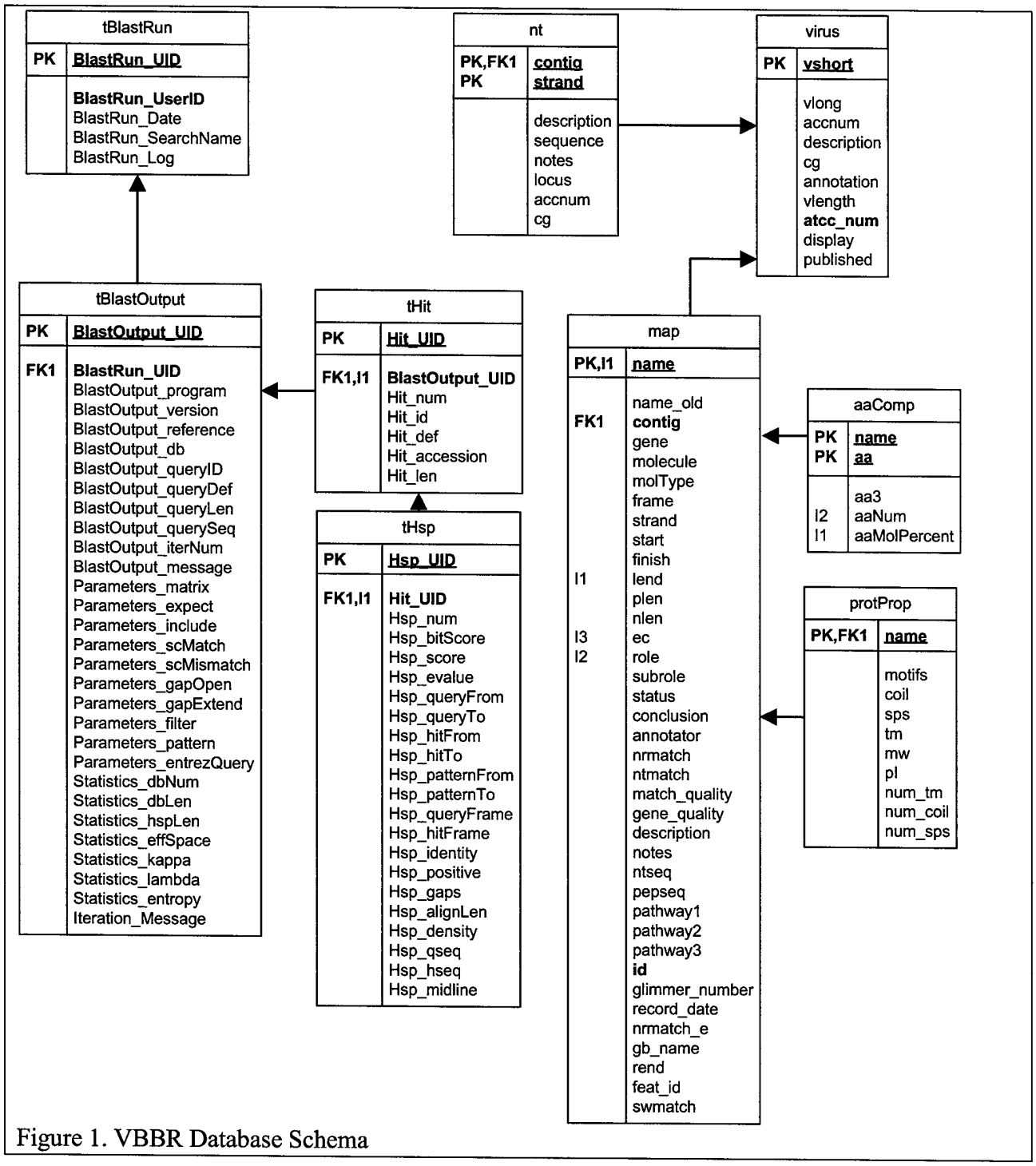


Figure 1. VBBR Database Schema

Task 2. **To develop a world-wide web site that will allow all information and analytical results compiled and generated by this work to be publicized to the scientific community, providing rapid access to specific information as required by an individual researcher. This web site will also provide the necessary security and access controls to ensure that only individuals and groups as designated by the granting agency (USAMRMC) can utilize these resources. (Months 1-12)**

- The web site has been established and is accessible at the url: http://vbbr.genome.uab.edu.
- Login to the web site requires registration. Following registration, a user account is established, and access is secured via a username/password. To register, a user needs to

logon to the following web page: https://btd.genome.uab.edu/register/register.asp using the following credentials: Username: genuab; Password: $mgbf2003 and fill out the form. The user will be vetted for access and when approved will then be notified via Email when the account is established.

- The home page for the VBBR web site is shown below in figure 2.

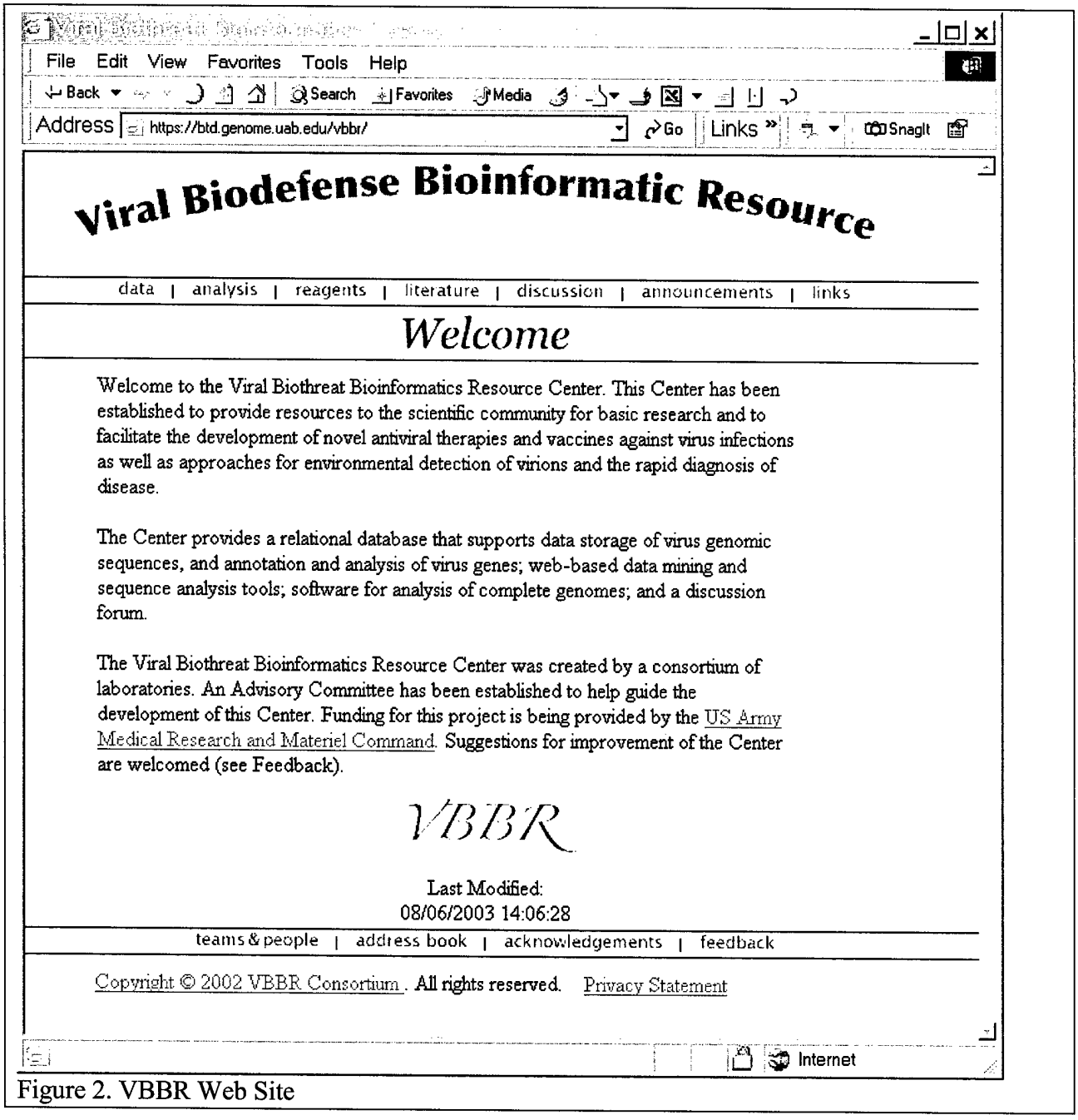


Figure 2. VBBR Web Site

Task 3. **To collect existing gene and genomic sequences for viral threat agents and import them into the database for subsequent annotation and analysis (Months 1-24).**

a. We will obtain existing gene and genomic sequences for all viruses that potentially could be used as agents of biological warfare or terror. The

information collected will include the corresponding descriptive annotation provided with the sequences.

- An automated parser has been developed (XSeq Exchange) that can parse XML-formatted GenBank sequence records and their annotation and load that information into the VBBR database. This application will greatly enhance our ability to add new viral genomes to the VBBR database. The database schema for the parser is shown below in figure 3.

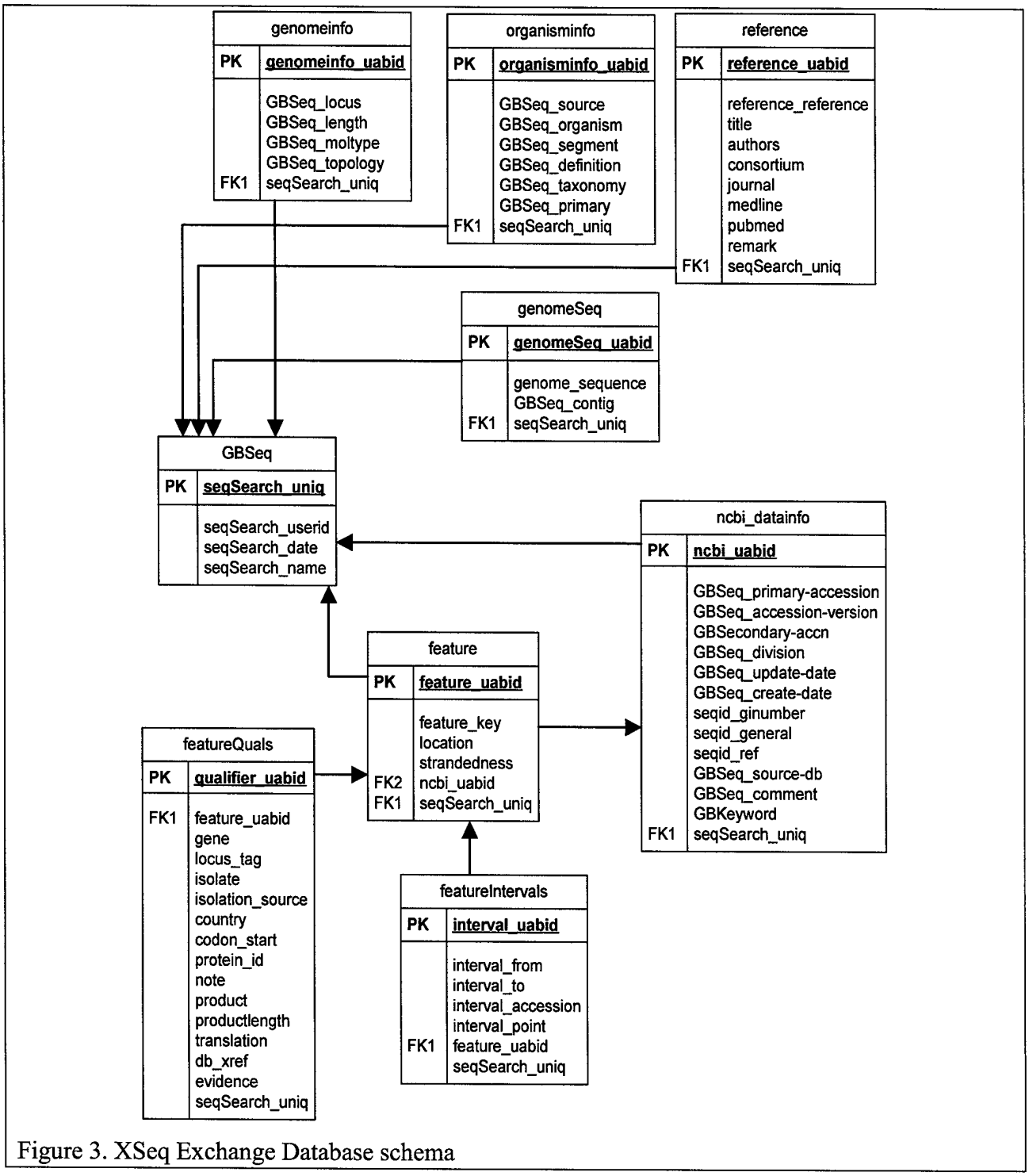
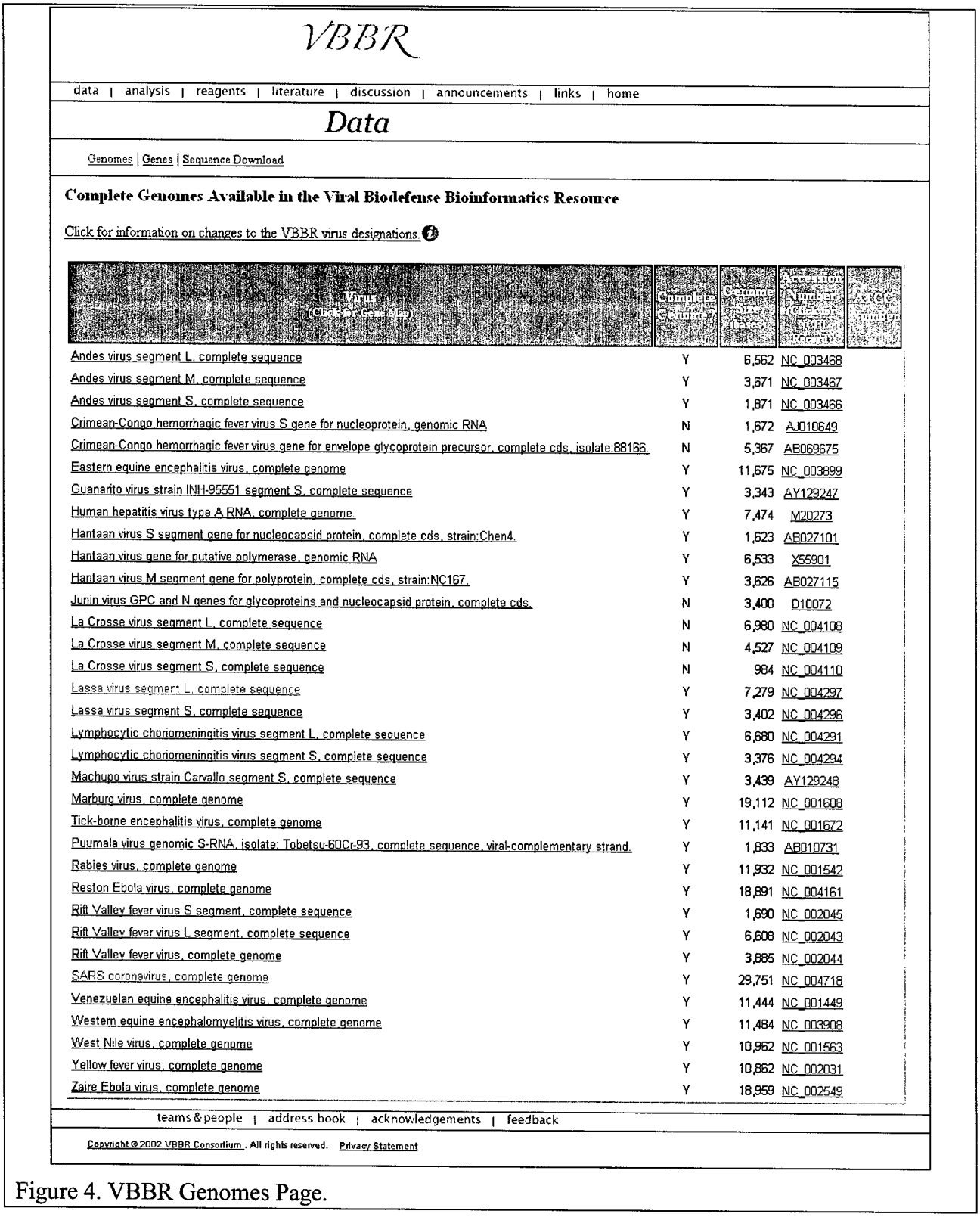


Figure 3. XSeq Exchange Database schema

- The genome and gene database is currently populated with most of the viruses currently on the NIAID A-C priority pathogen list. These are shown on the genomes page of the VBBR web site as displayed in figure 4.



VBBR

data | analysis | reagents | literature | discussion | announcements | links | home

Data

Genomes | Genes | Sequence Download

Complete Genomes Available in the Viral Biodefense Bioinformatics Resource

Click for information on changes to the VBBR virus designations

Virus (Click for Gene Data)	Complete Genome	Genome Size	Accession Number (Click for Genome Record)	Notes
Andes virus segment L, complete sequence	Y	6,562	NC_003468	
Andes virus segment M, complete sequence	Y	3,671	NC_003467	
Andes virus segment S, complete sequence	Y	1,871	NC_003466	
Crimean-Congo hemorrhagic fever virus S gene for nucleoprotein, genomic RNA	N	1,672	AJ010649	
Crimean-Congo hemorrhagic fever virus gene for envelope glycoprotein precursor, complete cds, isolate:88166.	N	5,367	AB069675	
Eastern equine encephalitis virus, complete genome	Y	11,675	NC_003899	
Guanarito virus strain INH-95551 segment S, complete sequence	Y	3,343	AY129247	
Human hepatitis virus type A RNA, complete genome.	Y	7,474	M20273	
Hantaan virus S segment gene for nucleocapsid protein, complete cds, strain:Chen4.	Y	1,623	AB027101	
Hantaan virus gene for putative polymerase, genomic RNA	Y	6,533	X55901	
Hantaan virus M segment gene for polyprotein, complete cds, strain:NC167.	Y	3,626	AB027115	
Junin virus GPC and N genes for glycoproteins and nucleocapsid protein, complete cds.	N	3,400	D10072	
La Crosse virus segment L, complete sequence	N	6,980	NC_004108	
La Crosse virus segment M, complete sequence	N	4,527	NC_004109	
La Crosse virus segment S, complete sequence	N	984	NC_004110	
Lassa virus segment L, complete sequence	Y	7,279	NC_004297	
Lassa virus segment S, complete sequence	Y	3,402	NC_004296	
Lymphocytic choriomeningitis virus segment L, complete sequence	Y	6,680	NC_004291	
Lymphocytic choriomeningitis virus segment S, complete sequence	Y	3,376	NC_004294	
Machupo virus strain Carvallo segment S, complete sequence	Y	3,439	AY129248	
Marburg virus, complete genome	Y	19,112	NC_001608	
Tick-borne encephalitis virus, complete genome	Y	11,141	NC_001672	
Puumala virus genomic S-RNA, isolate: Tobetsu-60Cr-93, complete sequence, viral-complementary strand.	Y	1,833	AB010731	
Rabies virus, complete genome	Y	11,932	NC_001542	
Reston Ebola virus, complete genome	Y	18,891	NC_004161	
Rift Valley fever virus S segment, complete sequence	Y	1,690	NC_002045	
Rift Valley fever virus L segment, complete sequence	Y	6,608	NC_002043	
Rift Valley fever virus, complete genome	Y	3,885	NC_002044	
SARS coronavirus, complete genome	Y	29,751	NC_004718	
Venezuelan equine encephalitis virus, complete genome	Y	11,444	NC_001449	
Western equine encephalomyelitis virus, complete genome	Y	11,484	NC_003908	
West Nile virus, complete genome	Y	10,962	NC_001563	
Yellow fever virus, complete genome	Y	10,862	NC_002031	
Zaire Ebola virus, complete genome	Y	18,959	NC_002549	

teams & people | address book | acknowledgements | feedback

Figure 4. VBBR Genomes Page.

b. We will also collect and provide the references for publications in the scientific literature that describe studies on the structure and function of orthopoxvirus genes and genomes. We will link this information on our web site to the appropriate gene records in our database.

- Not yet done. Tasked for year 2.

c. We will initially obtain viral sequence from public databases such as GenBank. We will also obtain unpublished sequence information through inquires and interactions with other scientists that have been initiated by our collaborators.

- Not yet done. Tasked for year 2.

Task 4. **To provide computer-automated and human-directed annotation to confirm and update existing biological information in the sequence records for existing as well as newly obtained sequences. (Months 6-24)**

- Computer-automated annotation has been completed for the viruses listed in figure 4. Human directed annotation is tasked for year 2. An example annotation record is shown in figure 5.

Task 5. **To perform a variety of analyses on genome and gene sequences to provide additional information on their structure, function, and evolution. (Months 6-24)**

- Initial computer-aided analysis has been completed. Additional analyses tasked for year 2.

Task 6. **To provide through the web site, a set of analytical and visualization tools that will allow users of this resource to mine the data for useful information, to perform comparative analyses between these and other viruses, and to better visualize and assess the significance of their results. (Months 6-24)**

- Currently available analytical and visualization tools include:
  a. Genome map visualization (Figure 6.)
  b. Genome protein gene ortholog comparisons
  c. Gene synteny visualization (Figure 7.)
  d. BLAST similarity searches
  e. BLAST search parsing and database storage
  f. Java-based Visualization of BLAST search results (Figure 8.)
- A new database and web server has been installed and is now supporting all VBBR resources. This new server provides added security and has greatly increased performance of the VBBR web site.
- Development of additional analytical and visualization tools are tasked for year 2. These will include tools for creation and visualization of multiple sequence comparisons and tools for the inference and visualization of evolutionary trees.

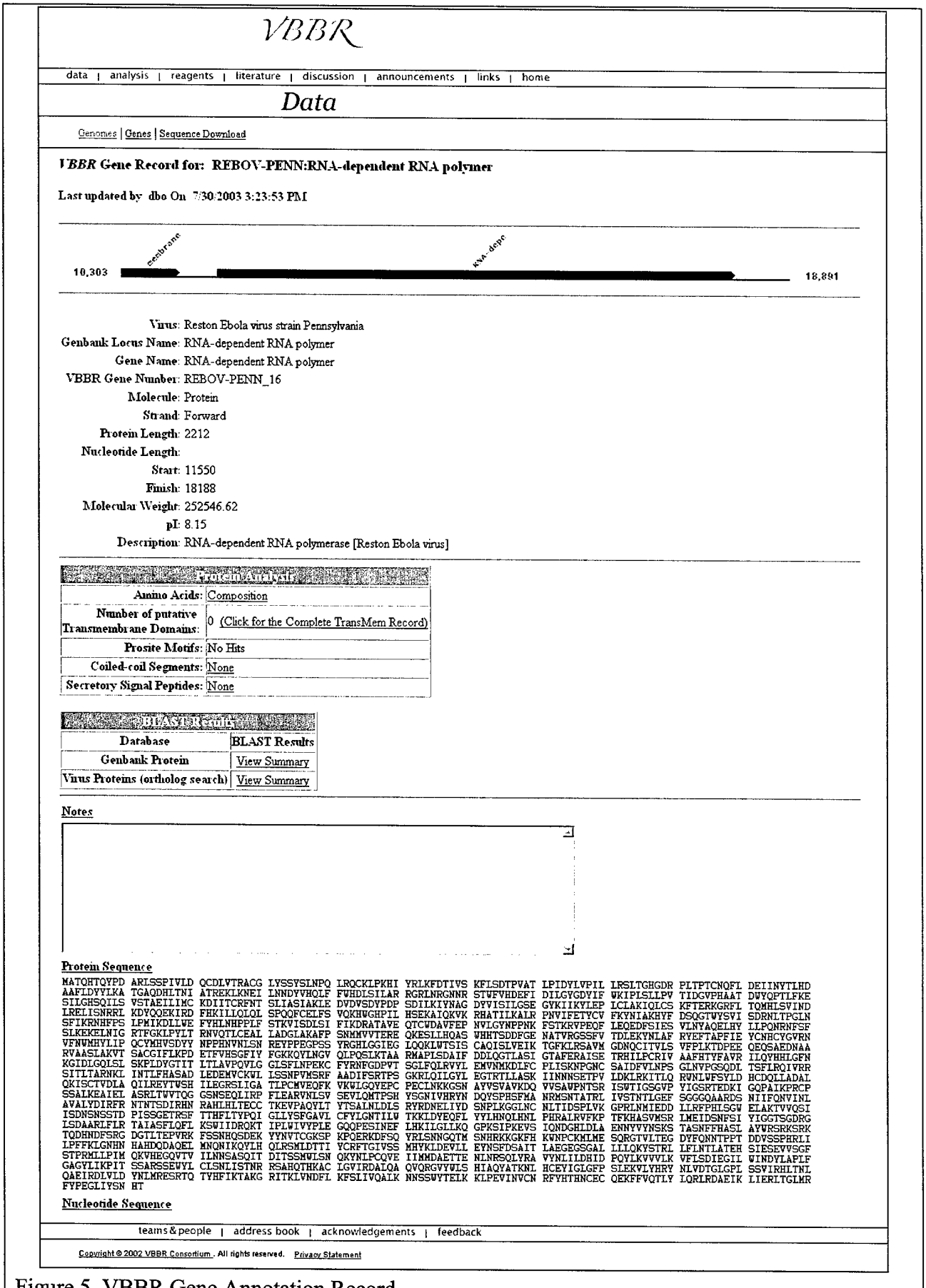


Figure 5. VBBR Gene Annotation Record.

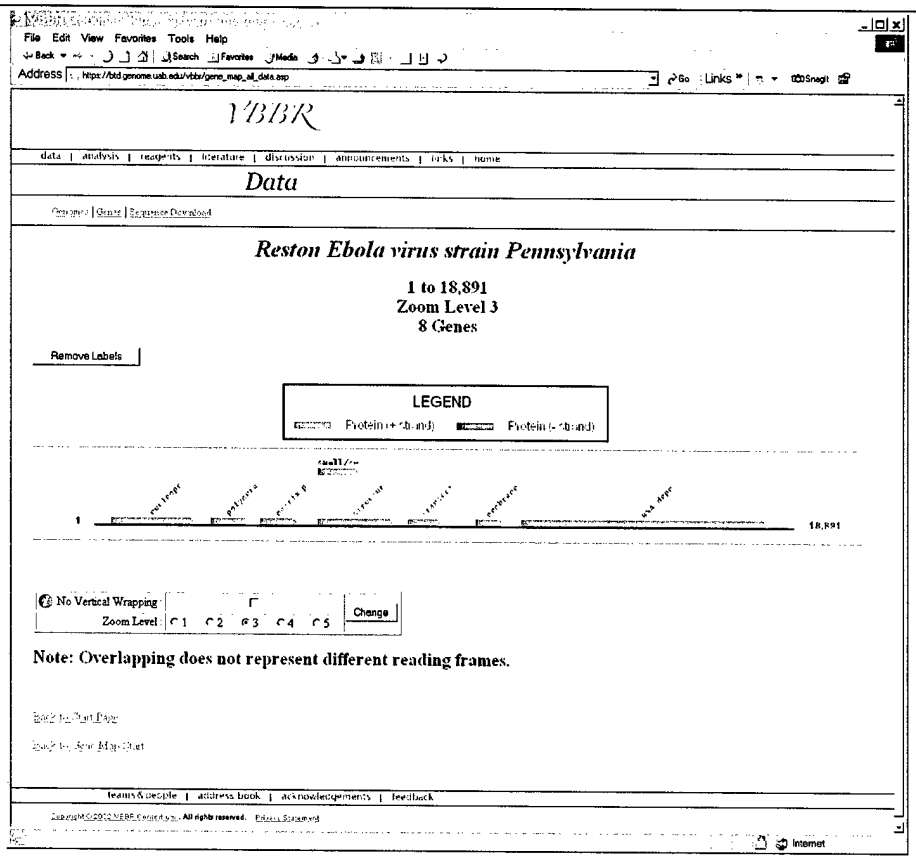


Figure 6. VBBR Genome Map.

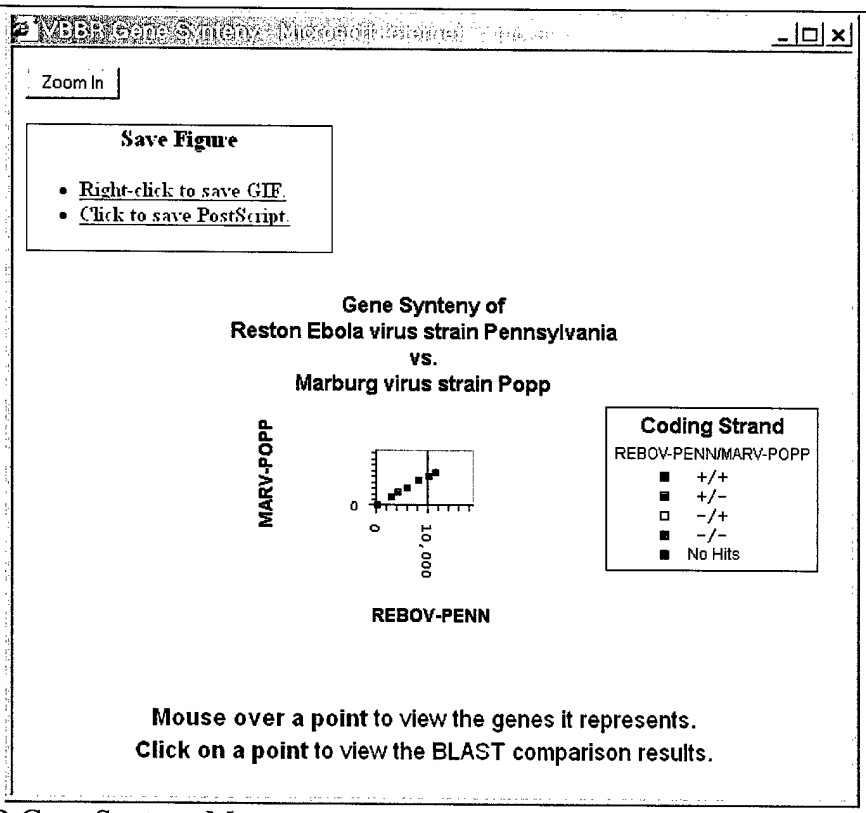


Figure 7. VBBR Gene Synteny Map.

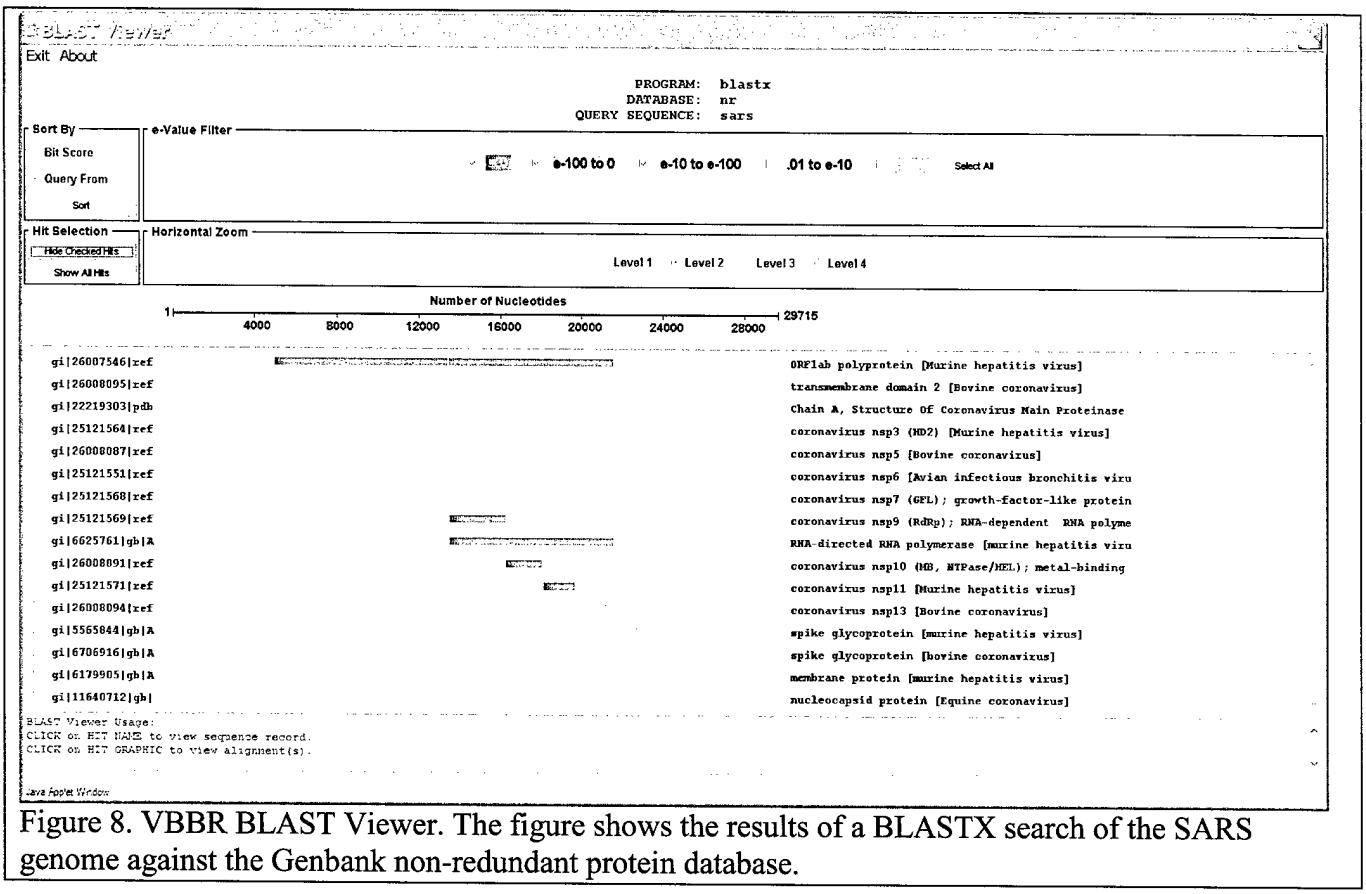


Figure 8. VBBR BLAST Viewer. The figure shows the results of a BLASTX search of the SARS genome against the Genbank non-redundant protein database.

KEY RESEARCH ACCOMPLISHMENTS:

- Establishment of the VBBR Database
- Establishment of the VBBR Web Site
- Development of the XSeq Exchange GenBank sequence parser
- Population of the VBBR database with virus genomic information
- Computational annotation of virus genes
- Implementation of analytical and visualization tools for BLAST searches
- Implementation of analytical and visualization tools for genome ortholog comparisons

REPORTABLE OUTCOMES:

Informatics:

- VBBR Database
- VBBR Web site (http://vbbr.genome.uab.edu)
- VBBR analytical and visualization tools

Presentations:

- USAMRIID/WRAIR/LANL/UAB Workshop, August 11, 2003 WRAIR
- USAMRMC Bioinformatics Workshop, November 4, 2003 (Poster)

Funding proposals submitted extending this work:

- NIH/NIAID Proposal in response to the RFP: NIH-NIAID-DMID-04-34, "Bioinformatics Resource Centers for Biodefense and Emerging/Re-emerging Infectious Diseases"

CONCLUSIONS:

Development of the Viral Biological-threat Bioinformatics Resource (VBBR) has substantially followed the original task list and essentially all tasks proposed for year 1 have been accomplished. The result is a Bioinformatics Resource Center that can now begin to support the needs of basic and applied biodefense research directed at gaining a better understanding of the pathogenesis, evolution, and overall biology of viral pathogens as well as support the development of detectors, diagnostics, antivirals, and vaccines. Future work will follow the original task list and is aimed at providing human-curated gene records along with additional analytical and visualization tools that can better support understanding the role of individual genes in virus pathogenicity.

REFERENCES:

None other than the VBBR web site.

APPENDICES:

None