VectorBase: a home for invertebrate vectors of human pathogens

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ABSTRACT

VectorBase (http://www.vectorbase.org/) is a web-accessible data repository for information about invertebrate vectors of human pathogens. VectorBase annotates and maintains vector genomes providing an integrated resource for the research community. Currently, VectorBase contains genome information for two organisms: Anopheles gambiae, a vector for the Plasmodium protozoan agent causing malaria, and Aedes aegypti, a vector for the flaviviral agents causing Yellow fever and Dengue fever.

INTRODUCTION

Even before the completion of the human genome a number of laboratories initiated projects to sequence the genomes of important human pathogens: Plasmodium, Trypanosome and Leishmania species (1–3). The aim of these projects was to better understand the biology of the pathogen through its genome, with the goal of identifying new therapeutics and thus shorten the time from therapeutic lead to marketable product, a notoriously slow process. A more holistic approach to improving our understanding of these pathogens needs to include intermediary vectors where they exist. Over the past few years the cost of genome sequencing has fallen dramatically making it feasible to sequence the genomes of vectors and complete our knowledge of the triumvirate of species involved in many parasitic diseases.

VectorBase is funded by the National Institute of Allergy and Infectious disease (NIAID) as part of a group of Bioinformatics Resource Centres (BRCs) (http://www.brc-central.org/) aiming to provide web-based resources to the scientific community for organisms considered to be causing or transmitting emerging or re-emerging infectious disease. Parallel to this, NIAID has funded a number of genome projects of important vector species that are destined to be housed within the VectorBase system (Table 1).

VectorBase is involved in all the stages of genome analysis: first-pass annotation of new genome sequences in collaboration with the sequencers, re-annotation of existing genome sequences and submission of these data sets to the public nucleotide databanks.

VectorBase acts as the repository for the genome and predicted gene set providing web access for browsing and data mining capability. VectorBase participates in teaching workshops (supporters include WHO-TDR, MR4, EMBO and BioMalPar) and has undertaken ‘hands-on’ demonstrations at international meetings. VectorBase strives to improve

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the accuracy and scope of the annotations, expanding controlled vocabularies for the vectors and incorporating new data types (expression, population and variation data).

RESULTS

Data storage

VectorBase uses the Genome Model Organism Database (GMOD) construction set for the storage of genome sequence and annotations. The GMOD CHADO schema facilitates the rapid incorporation of diverse data types, e.g. literature, controlled vocabularies and good inter-operability with the manual annotation effort, using Apollo, as well as the Ensembl system. For web display and access to the genome data and annotation, VectorBase utilises the Ensembl database schema, API and web code (4).

Genome browsing and data mining

The Ensembl system provides a good model for handling genomic data from a number of species in a consistent and unified manner and a highly sophisticated set of interlinked web pages.

Entry points into the genome are through text searches of gene names, symbols and descriptions, pairwise similarity searches and from cross-references in the public nucleotide and protein databanks.

The VectorBase website contains standard Ensembl style gene and transcript pages. Gene pages contain information about the prediction including gene orthologue and protein features (signal peptides, trans-membrane domains, InterPro domains). Gene Ontology (GO) codes and Enzyme Classification (EC) numbers are assigned where possible.

Batch file downloads are available for both the raw sequence data (fasta files of genomic sequence, including repeat masked sequence and ESTs) and the annotation (GFF3 files or a MySQL dump for use with the Ensembl API).

Batch searching capabilities are handled by the powerful data mining tool BioMart (5) and through two spreadsheets, AnoXcel and AegyXcel (6) that contain gene based information about the presence of signal peptides, trans-membrane domains, protein domains and the best similarity with yeast, Drosophila and human.

Annotation

The two genomes currently available through VectorBase are good examples of the multiple roles undertaken by the group.

Anopheles gambiae annotation

The A. gambiae PEST genome was published in 2002 (7) with a genome size of 260 Mb and ~14 000 genes. The predicted gene set has been reviewed and updated several times since publication. This process involves a blend of automated evidence-based gene prediction (8) and manual approaches. Manual appraisal of gene models is firstly targeted to regions of interest from the community and regions for which we are aware that automated approaches fail. A manual re-annotation of chromosome arm 2L is finished. Manually appraised gene models are highlighted for the user as a separate track on the genome browser.

Aedes aegypti annotation

The A. aegypti Liverpool strain was sequenced and assembled by The Institute of Genomic Research (TIGR) and the Broad Institute. Aedes has a large genome size of 1.3 Gb and a predicted gene complement of ~16 000 genes. This represents the first-pass annotation of the genome using automated approaches. Improvements in quality will be achieved by manual efforts and enhancements to the evidence-based automated gene predictions.

Sequence comparisons between Anopheles and Aedes

The presence of two related mosquito genomes in VectorBase allows for comparative analysis to identify conserved regions between the genomes. This can be useful in verifying, and correcting, gene models and for studying gene family expansions. Translated BLAT (9) similarities between the two mosquito species and with Drosophila have been identified. Figure 1 shows a view of an orthologous locus between the two mosquito genomes and highlights the expanded intron size in A. aegypti and related higher repeat content.

Use of Distributed Annotation System (DAS) in VectorBase

The DAS protocol (10) allows community researchers to integrate and display their data sets in the genome browser window. This is especially powerful with alternative sets of gene predictions. As an example, the Anopheles browser contains DAS tracks for alternate EST based gene predictions from AnoEST (11), an independent re-annotation effort by Li et al. (12) and predictions based on mass spectrometry data (13).

Microarray data

Microarray data exists for both Anopheles and Aedes and array probes from both species are mapped to the genome. These alignments are displayed in the browser and queries can be made against these via BioMart. Concise expression summaries for probes and genes are made available as experiments are published.
FUTURE DIRECTIONS

At least four new arthropod vector genomes will soon be incorporated into VectorBase: the mosquito *Culex pipiens quinquefasciatus*, the tick *Ixodes scapularis*, the kissing bug *Rhodnius prolixus* and the human body louse, *Pediculus humanus* (see Table 1 for more details). Furthermore, the genomes of two molecular forms of *A. gambiae* (the S and M forms which are considered to be incipient or possibly distinct species) will soon be completed and integrated into VectorBase. We will continue to re-annotate the existing mosquito genomes to improve gene prediction drawing more on manual/community annotation and comparative analysis with additional arthropod genomes.

The increased importance of manual/community annotation is being addressed by the development of a CHADO-based database for tracking internal VectorBase manual annotation and submissions from the community.

Other material of interest to the vector community is being incorporated, including the newly developed controlled vocabulary of mosquito anatomy (http://obo.sourceforge.net/detail.cgi?mosquito_anatomy) and other vector-related ontologies.

VectorBase is an ongoing project and the scope and usability of the site are improving rapidly. The coming year will see a significant expansion in the number of vector genomes housed.

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