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Nematode.net: a tool for navigating sequences from parasitic and free-living nematodes

Todd Wylie^{*1}, John C. Martin¹, Michael Dante¹,
Makedonka Dautova Mitreva¹, Sandra W. Clifton¹, Asif Chinwalla¹,
Robert H. Waterston^{1,2}, Richard K. Wilson¹ and James P. McCarter^{1,3}

¹ The Genome Sequencing Center, Washington University School of Medicine, St Louis, MO 63108, USA, ² Department of Genome Sciences, University of Washington, 1705 NE Pacific Street, Seattle, WA 98195, USA and ³ Divergence Inc., 893 North Warson Road, St Louis, MO 63141, USA

*To whom correspondence should be addressed. Tel: +1 314 286 1114; Fax: +1 314 286 1810; Email: twylie@watson.wustl.edu

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ABSTRACT

Nematode.net (www.nematode.net) is a web-accessible resource for investigating gene sequences from nematode genomes. The database is an outgrowth of the parasitic nematode EST project at Washington University's Genome Sequencing Center (GSC), St Louis. A sister project at the University of Edinburgh and the Sanger Institute is also underway.

More than 295 000 ESTs have been generated from >30 nematodes other than *Caenorhabditis elegans* including key parasites of humans, animals and plants. Nematode.net currently provides NemaGene EST cluster consensus sequence, enhanced online BLAST search tools, functional classifications of cluster sequences and comprehensive information concerning the ongoing generation of nematode genome data. The long-term goal of nematode.net is to provide the scientific community with the highest quality sequence information and tools for studying these diverse species.

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INTRODUCTION

Nematodes or roundworms are members of an ancient phylum that accounts for perhaps four out of every five individual animals in the world (1). Parasitic nematodes infect nearly half the world's human population, resulting in significant morbidity and mortality. Nematodes also parasitize livestock and companion animals and cause over 80 billion dollars in crop damage annually (2,3). Nematode.net is a specialty database that makes accessible the rapidly expanding nucleotide sequence data and related resources from species across this phylum to target audiences including human/mammalian parasitologists, plant nematologists, *Caenorhabditis elegans* biologists and other scientists.

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SEQUENCES FROM PARASITIC NEMATODES

Following the completion of the first fully sequenced animal genome, the nematode *C.elegans* (4), increasing efforts have been made to rapidly generate and make public gene sequences from parasitic nematodes of medical and economic importance as a route toward research on new anthelmintic drugs, vaccines, safe pesticides and resistant plants. Initiatives have primarily utilized expressed sequence tags (ESTs), focusing first on the filarial worms responsible for elephantiasis and river blindness (5,6). A collaboration is currently underway involving the Genome Sequencing Center (GSC) at Washington University in St Louis, the Wellcome Trust Sanger Institute, the University of Edinburgh and dozens of participating parasitologists to extend EST-based gene discovery to more than 30 nematode species (7,8). To date, over 295 000 ESTs have been generated from nematodes beyond *C.elegans*, with nearly 220 000 of these sequences provided by the GSC (Table 1).

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View this table: [Table 1. Nematode EST projects by species](#)

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NemaGene CLUSTERS AND NemaBLAST SEARCHES

While GSC-generated ESTs are immediately deposited in GenBank's database of ESTs (dbEST), no such repository exists for nematode EST cluster consensus sequences, nor are tailored BLAST searches easily performed. Nematode.net began in 2000 by providing these services. NemaGene clustering improves upon EST data by reducing data redundancy, increasing transcript length and improving base accuracy. The NemaGene method uses the Phred/Phrap/Consed suite of analysis programs (10), together with internal supplemental scripts, and has the advantage that clusters can be edited when necessary and tracked by name through multiple builds (11). Clusters can be searched on the nematode.net website by EST name, putative identity and individual contig or cluster name (Fig. 1). Cluster entries provide EST membership with NCBI links, as well as SWIR non-redundant protein database, Sanger Centre and *C.elegans* (Wormpep) homology. Cluster information and sequences can also be downloaded by FTP. NemaGene clusters have so far been generated for 15 species (Table 1). Both NemaGene clusters and individual ESTs can be searched for sequence identity using the online NemaBLAST tool, which utilizes a local WU-BLAST server (12) (<http://blast.wustl.edu>). Searches can be performed on ESTs from specific species, clades, stages and libraries, in any combination desired by the user.



Figure 1. A NemaGene Cluster Search query response showing constituents of consensus sequence by contig.

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FUNCTIONAL CLASSIFICATIONS AND OTHER FEATURES

Nematode.net provides the user with two avenues to explore the putative function of NemaGene clusters. Both are based on extrapolation from homology and must be regarded as providing only a starting hypothesis in studying function. Cluster sequences were used to search the Interpro protein domain database (13) (www.ebi.ac.uk/interpro) with InterProScan. Based on the presence of conserved domains, clusters were then mapped

onto the Gene Ontology (GO) classification scheme (14) (www.geneontology.org). GO biological, molecular and cellular classifications are provided at nematode.net with the AmiGO interface. NemaGene clusters have also been mapped to the Kyoto Encyclopedia of Genes and Genomes (KEGG) database of biochemical pathways using enzyme commission (EC)

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numbers as the basis for putative assignment (15) (www.genome.ad.jp/kegg). Additional useful features of nematode.net include summaries of sequence status for all nematode species, cDNA library descriptions, project specifics, >300 organized nematology links and a trace viewer that allows users to examine raw sequence data. Nematode.net is also used to manage requests for clones generated by the project. Since 1999, 377 clones and dozens of plates have been provided to 37 investigators in 14 countries.

SITE AND DATABASE DESIGN

The Nematode.net interface was constructed using the Dreamweaver MX web development application in combination with a Perl CGI/DBI database interface. The GUI-based Dreamweaver MX editor was chosen for HTML design due to ease of use, ability to make rapid site-wide modifications and project tracking features. HTML pages written under Dreamweaver MX are sourced by a GSC Perl module, which has proved to be fast, extensible, and useful for recycling previously written code. Relational databases were initially built in MySQL and are now being replaced by a single, more efficient Oracle database.

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FUTURE DIRECTIONS

Nematode.net is a work in progress with the long-term goal of providing the nematology community with useful, consistent and lasting integrated databases and tools. With over 29 000 unique users in the past year, nematode.net is already providing a useful service, but improvements are envisioned in three areas. First, the site's current databases will be extended to include almost all available nematode species and sequences, expedited by further automation of clustering algorithms. Second, nematode.net will become more closely integrated with the *C.elegans* database Wormbase (16) (www.wormbase.org) and Nembase (www.nematodes.org), a site maintained by our collaborators at the University of Edinburgh that also provides tools for investigating nematode sequences (8). Plans for Wormbase integration include the layering of non-*C.elegans* nematode gene sequences over *C.elegans* homologs using the Distributed Annotation System (DAS) method (17). Currently, 9894 *C.elegans* genes have strong homologs in other nematodes (BLAST score of <1e-20). *C.elegans* information will continue to reside only at Wormbase. Third, in collaboration with Nembase, additional features for navigating nematode sequences will be made available. Databases covering all nematodes will include: postulated amino acid translations of EST clusters; protein domains connected to Pfam (18) and Interpro including new nematode-specific domains; genes with homologs in *C.elegans* where RNA interference phenotype information is available (19); proteins with predicted signal peptide sequences; and codon usage tables for each species. Other possible additions include the integration of whole-genome information for parasitic nematode species (e.g. *Brugia malayi*) as such data become available.

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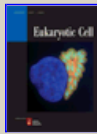
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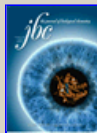
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