WEB WATCH

World Wide Worms

Wormbase (www.wormbase.org) is the database of choice for the *Caenorhabditis elegans* community, but although it has been around for a while, there have recently been some valuable improvements.

Whether you are a worm aficionado or a novice you will probably like the RNAi phenotype search facility. You can find information on an RNAi phenotype for a specific gene from the sequence report pages, which also provide standard genomic information, such as genomic neighbourhood and predicted splice sites. You can also search for RNAi results by phenotype, as the RNAi data is subdivided into four categories: maternal, embryonic, as well as general and specific postembryonic phenotypes. In these groupings, you can search for general morphology defects or for more specific phenotypes, such as uncoordinated movement.

There is also a comprehensive set of gene expression pages that include images of *lacZ* expression, and the curators especially encourage *C. elegans* researchers to send in their GFP expression data. Expression patterns can be searched by gene, cell type, cell group or life stage, and each expressing cell is linked to the cell pedigree browser. A link to the *C. elegans* Atlas, which will contain a series of diagrams and micrographs, is planned in the near future.

Wormbase lacks sufficient protein information, but new protein pages are planned. You can already search for protein family motifs and some links to **WormPD** are provided. Eventually, Wormbase will include new data sets from microarray studies, the **ORFeome** project, yeast two-hybrid screens and transposon knockouts, as well as **polymorphism** information and more sequence data from other nematodes, such as *C. briggsae*.

Magdalena Skipper

HUMAN GENETICS

Tall stories from unused data

In genome-wide studies of human complex disease, supplementary phenotypic data — such as height and weight — are routinely collected from study participants but are often not used. Now, two papers show the usefulness of these data for investigating the genetic architecture of human complex traits by identifying — in previously studied population groups — quantitative trait loci (QTL) that affect adult stature. Hirschhorn *et al.* also investigate a problem that haunts complex-disease linkage studies — non-replication of linkage between different study populations.

Adult stature is a relatively straightforward complex trait to study. It can be measured easily and accurately; it does not fluctuate throughout life and so can be ascertained with a single measurement (unlike weight); and its inheritance has a strong genetic component. Clinically, it might be a risk factor for some diseases, and understanding its underlying genetics could inform future research into short-stature syndromes. Despite this, little has been known of its genetics, until now.

To look for stature QTL, Perola *et al.* carried out genome-wide marker scans on 614 individuals from 247 Finnish families, who had been recruited into five genetic studies on other complex traits, such as hypertension and migraine. Analysis of the pooled genotypic data from these scans revealed two QTL, on 7q and 9p, showing linkage to stature. Hirschhorn *et al.* studied 2,327 individuals from four regions — Finland, western Finland, southern Sweden and Quebec, Canada — who had been recruited into studies of type 2 diabetes and coronary heart disease. These authors analysed genotypic data from each population group independently to minimize the effects of environmental variation. They found evidence of linkage to stature at 6q, 7q, 12p and 13q, although each QTL was population-group specific in the samples they studied. Remarkably, the 7q QTL identified in the Swedish group overlapped with that detected in the Finnish population by Perola *et al.*, indicating the significance of this locus.

These results prompted Hirschhorn *et al.* to investigate potential sources of variation — such as population-specific effects or sampling variation — that could cause this non-replication of linkage between their study groups. The authors opted to study sampling-variation effects predominantly because analysing population-specific effects ideally requires the identification of causal variants (to detect, for example, founder effects on allele frequencies and linkage disequilibrium). They did this by analysing 400 simulated data sets in which the presence of a moderate QTL (expected to give a LOD

score of 1.4) was assumed. They found that although this QTL gave a strong signal (a LOD score of >3.0) in some simulated scans, it was almost undetectable in others. The authors believe that these findings make interpreting negative-replication results “somewhat difficult”, but suggest that larger sample sizes might help to combat this problem.

Of course, identifying the variants that underlie these QTL would help to clarify these results. With two candidate genes to hand, *ESR1* and *VDR* at 6q and 12p, respectively, Hirschhorn *et al.* are now working towards this goal. Although the 7q QTL reported by both studies at present covers too large an interval for candidate-gene searching, the availability of finished chromosome 7 sequence in the near future, together with new SNP data, promise to provide the required tools to narrow down this QTL.

Jane Alfred

References and links

ORIGINAL RESEARCH PAPERS Hirschhorn, J. N. *et al.* Genomewide linkage analysis of stature in multiple populations reveals several regions with evidence of linkage to adult height. *Am. J. Hum. Genet.* **69**, 106–116 (2001) | Perola, M. *et al.* Quantitative-trait-locus analysis of body-mass index and of stature, by combined analysis of genome scans of five Finnish study groups. *Am. J. Hum. Genet.* **69**, 117–123 (2001)
WEB SITES Hirschhorn data set | Perola data set