Question 13

A user has identified an interesting phenotype in a mouse model and has been able to narrow down the critical region for the responsible gene to approximately 0.5 cM. How does one find the mouse genes in this region?

Ensembl provides a mouse genome browser, similar to the one available for humans. It is being updated with the latest mouse genome sequence assemblies and, at the time of writing, displays the MGSC version 3 assembly of the mouse genome, with sequence data from February 2002. The sequence is estimated to cover 96% of mouse euchromatic DNA, and Ensembl has predicted that it contains over 22,000 genes. Start at the Ensembl mouse home page, at http://www.ensembl.org/Mus_musculus/. Choose *Marker* from the pull-down menu, type the marker name 'RH114718' in the adjacent box, and press *Lookup*. Click either of the resulting links to view more details about this radiation hybrid marker. *RH114718* has been mapped to a single position on chromosome 19 and is also known as *MGI:102447, MTH1904* and *D19MIT109* (Fig. 13.1). Click on the chromosomal position to view the genomic context of the marker (Fig. 13.2).

The *Overview* section of Fig. 13.2 shows a region of 1 Mb of chromosome 19 centered around the marker, labeled D19MIT109 in this view. More than 30 mouse genes are predicted in this region, some already known and some new. The *Detailed View* at the bottom of the page is a zoomed-in display of the region around the marker. To get a better view of the genes and transcripts in this region, zoom out on the bottom view by clicking on the longest bar in the zoom control (closest to the minus sign). The *Detailed View* will now show the same region of chromosome 19 as the overview, but with many additional features (Fig. 13.3). The splice patterns of the genes and gene predictions are shown, as are regions of homology between the genome and other proteins and mRNAs. Pointing the computer mouse at any feature allows the user to open a small menu that links to additional descriptions.

Consider the new gene indicated by the red arrow in Fig. 13.3. To view general information about this gene, hold the computer mouse over the gene graphic and select *Transcript Information* from the pop-up menu. The *GeneView* window (Fig. 13.4) provides a description of this gene, as well as a link to the *GeneView* window for the putative human ortholog (Fig. 13.4, *Homology Matches* section). To view the database sequences that align with the predicted exons of the new mouse gene, place the computer mouse pointer over the gene in the *Detailed View* (Fig. 13.3, arrow) and select *Supporting evidence* from the pop-up menu. Fig. 13.5 depicts the mRNA and protein sequences that align with exons in the new gene. Click on any of the green boxes to see the alignment of the database sequence with the new transcript.

The zoomed-out *Detailed View* also provides links to computed regions of orthology between the mouse and human genomes (Fig. 13.3, pink bars). As the mouse genome assembly and annotation lag behind those of the human, it may also be useful to view the human genes in an orthologous region of the genome.

UCSC also provides a mouse genome browser and the BLAT search tool for use with the latest mouse genome sequence assemblies. The links are available from the UCSC genome browser home page, at http://genome.ucsc.edu/. Mouse genome analysis tools developed at the NCBI, including a mouse Map Viewer and mouse BLAST pages, are available from http://www.ncbi.nlm.nih.gov/genome/guide/mouse/.
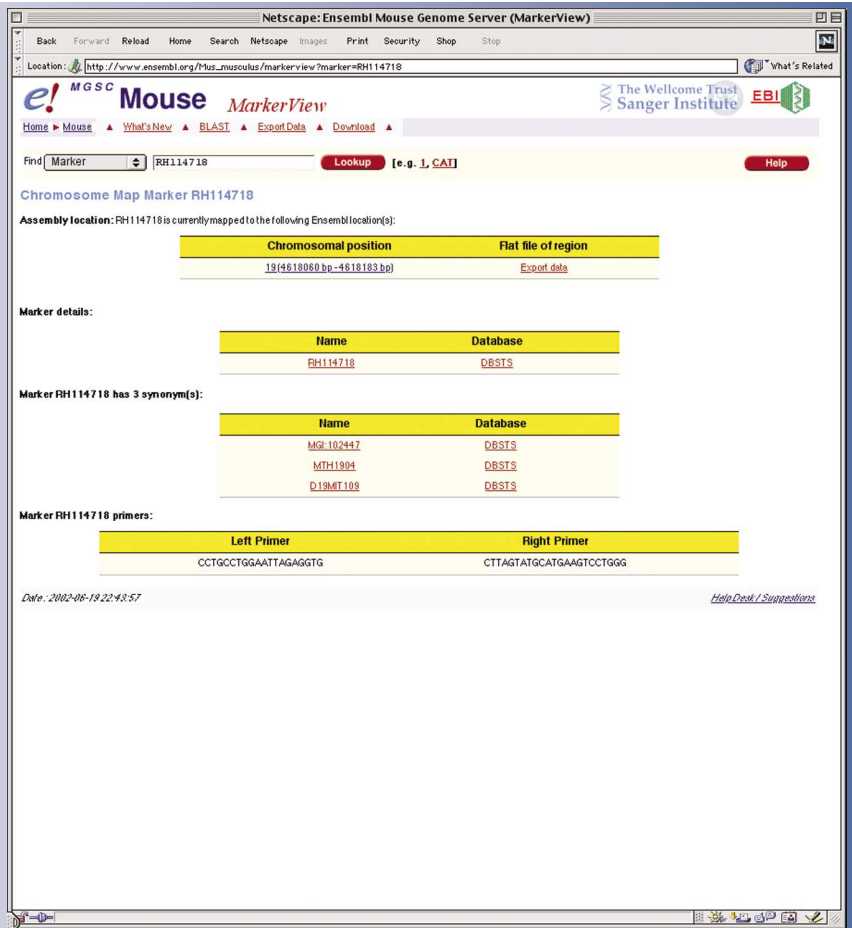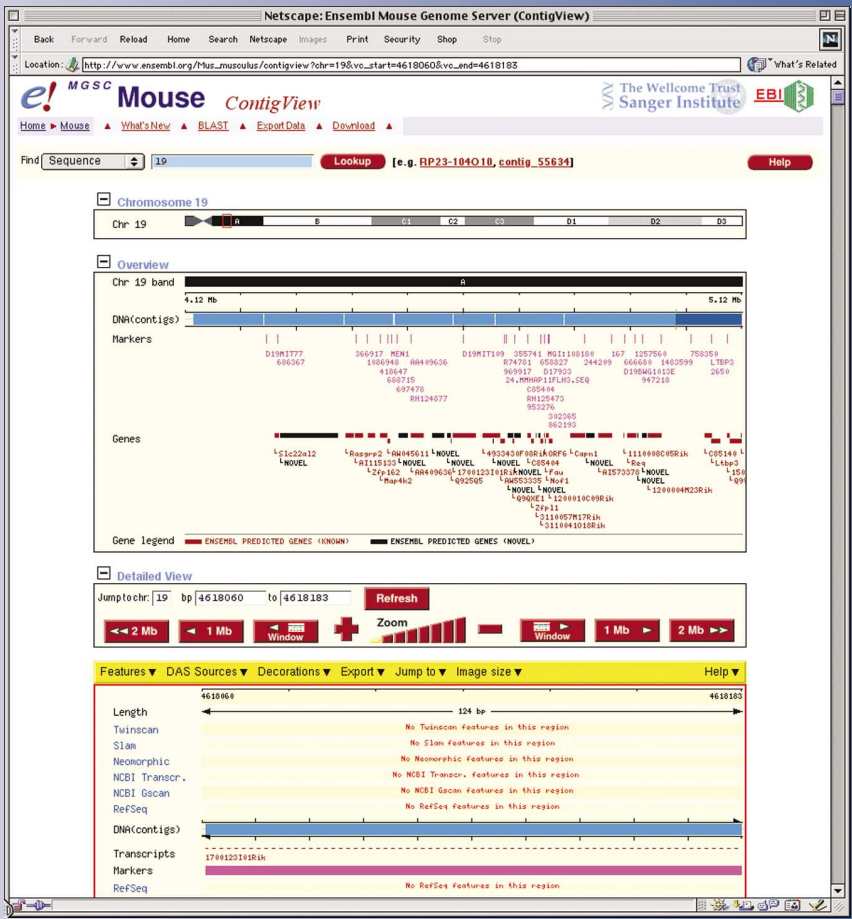
Figure 13.1

Figure 13.2

Figure 13.3

Figure 13.4

Figure 13.5