

## Question 12

### How does a user find characterized mouse mutants corresponding to human genes?

doi:10.1038/ng977

The NCBI provides a set of maps that show chromosomal regions homologous between mouse and human. This resource can be accessed directly at <http://www.ncbi.nlm.nih.gov/Homology/>. For this example using a known, mapped human gene, however, it is easier to start the search from the LocusLink entry for tyrosinase. The LocusLink<sup>10</sup> query page can be found at <http://www.ncbi.nlm.nih.gov/LocusLink/>. Select *Human* from the *Organism* pull-down menu, enter 'tyrosinase' into the *Query* box and click *Go*. To view the entry for tyrosinase (*TYR*), click on its LocusLink ID, 7299.

On the resulting page (Fig. 12.1), links to the mouse homology maps are in the section of the LocusLink summary page marked *Relationships*. In this case, there are four maps available for *TYR* showing mouse alignments: *NCBI vs MGD* aligns the current NCBI assembly of the human genome with the MGD (Mouse Genome Database<sup>21</sup>, at The Jackson Laboratory) genetic map, *UCSC vs. MGD* aligns the current UCSC genome assembly with the MGD genetic map, *NCBI vs. EST-based RH Map* aligns the NCBI assembly with the Whitehead–MRC RH map, and *UCSC vs. Hudson et al.* aligns the 7 October 2001 UCSC assembly with the Whitehead–MRC RH Map<sup>22</sup>. The *Hs* and *Mm* links adjacent to each map name show the mouse–human homology map with the master chromosome as human or mouse, respectively. Click on the *Hs* link next to the *NCBI vs. MGD* map.

The resulting mouse–human map shows the mouse genes that are the likely orthologs of human genes on human chromosome 11 (Fig. 12.2). Depending on the browser being used, one may have to click the *View as text* box to obtain the output; the resulting output will appear in text format, slightly different from what is shown in Fig. 12.2. Chromosomal locations of the mouse genes are shown, where known. The green circles link to the UniSTS entry for each locus; those on the left link to the human UniSTS entry, whereas those on the right link to the mouse UniSTS entry. The cytogenetic positions are hyperlinked to either the human or mouse Map Viewer, as appropriate. Gene symbols are linked to LocusLink<sup>10</sup>. The tyrosinase gene, highlighted in pink, maps to mouse chromosome 7 at 44 cM, a piece of information that will be needed in the next step.

The mouse models themselves are described at the Mouse Genome Informatics site at the Jackson Laboratory. Go to the Mouse Genome Informatics home page, at <http://www.informatics.jax.org/>, and use the *Query Forms* pull-down menu

to select *Linkage Maps*. On the resulting page, customize the search to find the region around the mouse gene *Tyr*. Under *Chromosome*, set the number to 7; then set the chromosomal region to between 40 and 48 cM.

Many of the uncloned mouse mutants are not mapped in high-resolution crosses, and many are carried out with a small number of mice relative to another easy-to-score phenotype for another mouse mutant that maps to the same chromosome. It is thus necessary to be lenient in looking for potential uncloned mouse mutants ( $\pm 4$  cM relative to the location). In this case, as the NCBI data tells us that the gene is at 44 cM, the region from 40 to 48 cM should be searched.

Further down the page (Fig. 12.3), under *Markers*, set *Include DNA segments* to *No* to reduce the number of markers shown. Do include *syntenic markers*, which are DNA markers and mutant alleles linked to chromosome 7 that have not been finely mapped but that may be associated with a phenotype of interest relative to *TYR*. Under *Comparative Maps*, *Show homologs from species*, choose *human (Homo sapiens)*. Select *Show all markers*. Use the default setting for all other options, and hit *Retrieve*.

The gene *Tyr* is found on page 2 of the output, at 44 cm (Fig. 12.4). The mouse chromosome is shown schematically on the left and expands as one moves to the right. In the rightmost columns are the names of the mouse markers in a particular region in blue and, if there is a corresponding human ortholog, the name of that ortholog in black. Some of the displayed mouse markers are genes, some are STSs, some are recessive mutants (all small letters) and some are dominant alleles (initial capital letter). At the bottom of the page are syntenic markers, those which have been mapped to chromosome 7 but not to an exact position.

Clicking the blue *Tyr* link at 44 cm opens up a summary of the *Genes, Markers, and Phenotypes* for that gene (Fig. 12.5). Of particular interest in this case are the phenotypic alleles. There are 99 mouse strains with mutations in the *Tyr* gene.

Users can also view chromosomal regions that are homologous between mouse and human by using Ensembl's *SyntenView*, available from the *ContigView* by clicking the *Jump to →syntenview* link (Fig. 1.14, center yellow bar).

Figure 12.1

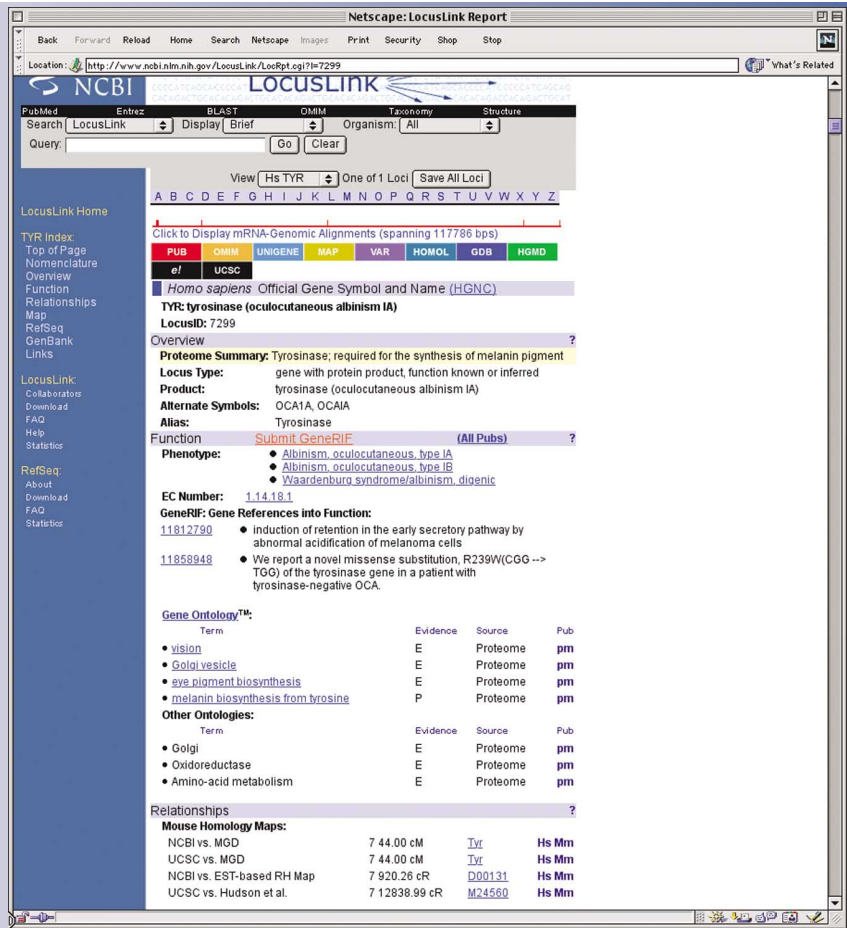
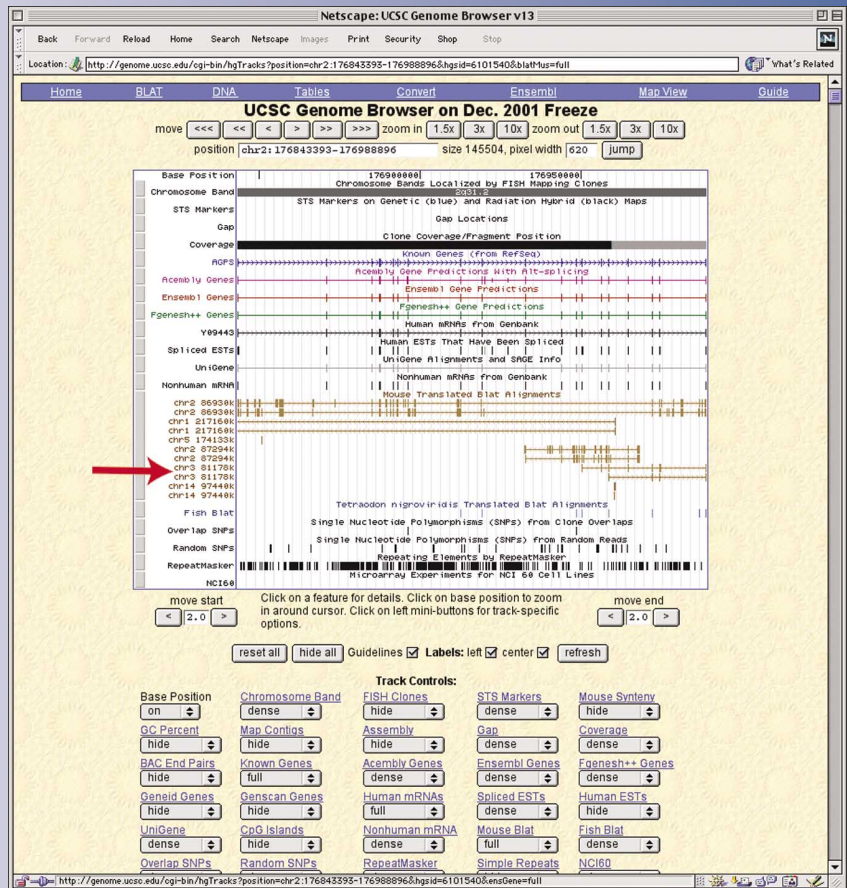


Figure 12.2



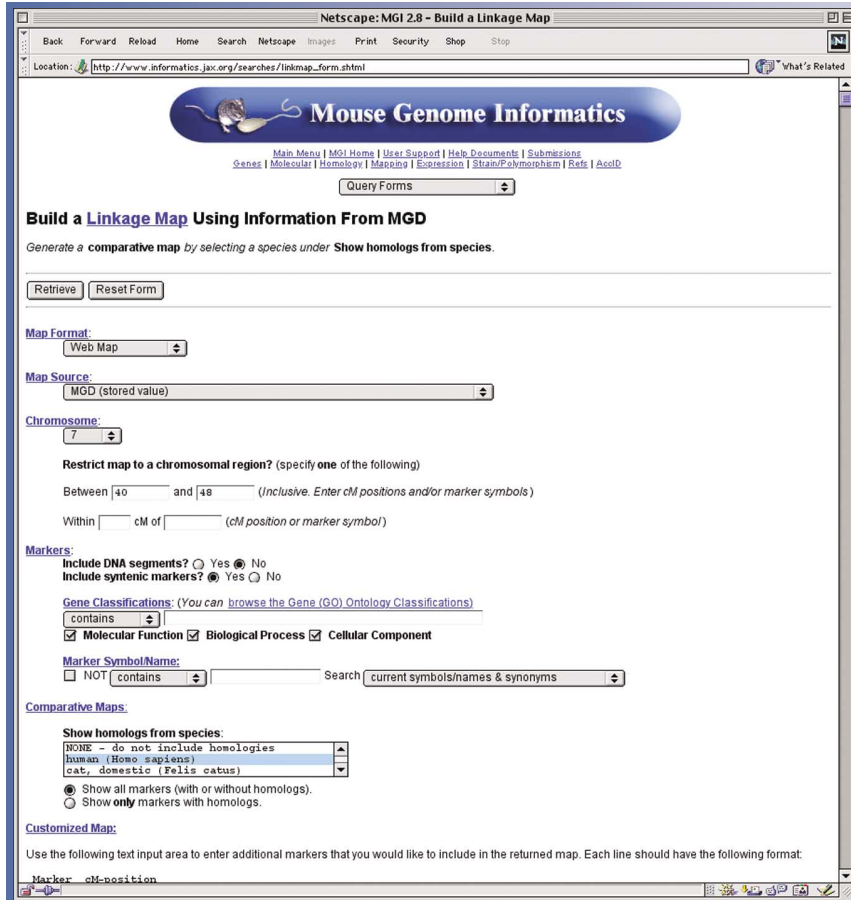


Figure 12.3

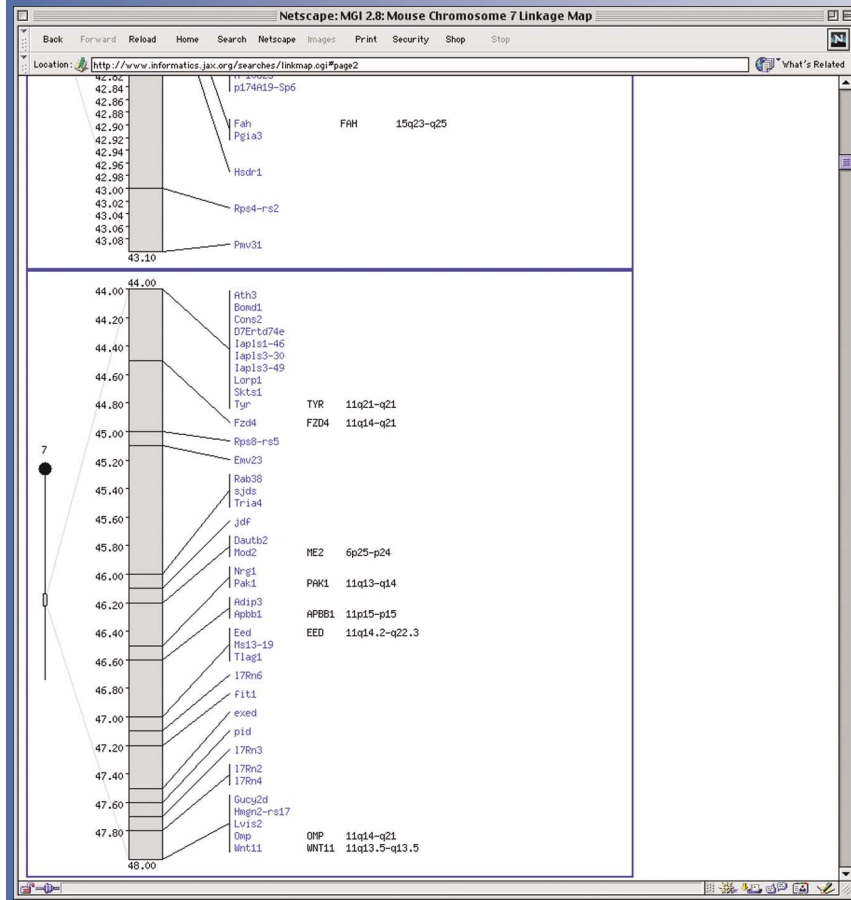


Figure 12.4

Figure 12.5



## **A User's Guide to the Human Genome**

T G Wolfsberg, K A Wetterstrand, M S Guyer, F S Collins & A D Baxevanis

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Figure 12.2

Human Gene	Human Location	Mouse Gene	Mouse Location	
11q13	<i>ART29 *</i>	7	Art2a	49
11q13	<i>CCND1 *</i>	7	Ccnd1	72.3
11q13	<i>FGF3 *</i>	7	Fgf3	72.4
11q13	<i>ALDH3B1 *</i>		1700001N19Rik	
11q13	<i>TM7SF2 *</i>		3110041O18Rik	
11q13	<i>MGC10871 *</i>		4921506I22Rik	
11q14.2-q22.3	EED	7	Ecd	47
11q14-q21	FZD4	7	Fzd4	44.5
11cen-q22.3	ME3		1700020C08Rik	
11q14.1	HSPC138		0610007P06Rik	
11q14.3-q21	NAALAD2		Naalad2	
11q14.2	CHORDC1		Chordc1	
11q14.3	PTD012		4931406C07Rik	
11q14.3	PANX1		Panx1	
11q21	MRE11A	9	Mre11a	
11q21	FUT4	9	Fut4	3
11q14.3	HSPC148		0610040D20Rik	
11q22	MTMR2		Mtmr2	
11q14.2-q21	NOX4		Nox4	
11q14-q21	TYR	7	Tyr	44
11q14.1-q14.3	CTSC	7	Ctsc	
11q14	<i>CAPN5 *</i>		Capn5	
11q14	<i>PRCP *</i>		2510048K03Rik	
11q23	PVRL1		Pvrl1	
11q22.1	USP2		Usp2	
11q21	<i>GPR72 *</i>	9	Gpr83	2
11q22.3-q23	THY1	9	Thy1	26
11q23.3	MCAM	9	Mcam	
11q23.3	CBL	9	Cbl	26
11q22.3	SCDGF-B	9	1110003109Rik	
11q22.1	FLJ11756	9	4432416O06Rik	
11q22.1	MGC2714	9	3110001A18Rik	
11q22.3	MMP13	9	Mmp13	
11q22.3	MMP12	9	Mmp12	1
11q22.3	MMP3	9	Mmp3	
11q22.3	MMP8	9	Mmp8	
11q22.3	MMP20	9	Mmp20	
11q21-q22	MMP7	9	Mmp7	1
11q22	BIRC2	9	Birc2	
11q22	BIRC3	9	Birc3	
11q13	YAP1	9	Yap	
11q21-q22	TRPC6	9	Trpp6	1
11q22-q23	PGR	9	Pgr	
11q22.2-q22.3	CASP4	9	Casp11	
11q23	CASP1	9	Casp1	1
11q22	GRIA4	9	Gria4	8
11q22	AASDHPPT		2810407B07Rik	
11q23.1	HSNOV1		1500009K05Rik	
11q22	<i>FDX1 *</i>		Fdx1	
11q22	<i>KPNA4 *</i>		Kpna4	
11q22.3-q23.1	ACAT1	9	Acat1	30
11q22-q23	NPAT	9	Npat	30
11q22-q23	ATM	9	Atm	30
11q22-q23	DDX10	9	Ddx10	
11q23	RDX	9	Rdx	
11q22	FDX1	9	Fdx1	
11q23.1	POU2AF1	9	Pou2af1	
11q23	BTG4	9	Btg4	
11q22.3-q23.1	CRYAB	9	Cryab	29
11q22-q23	HSPB2	9	Hspb2	
11q23.1-q23.2	TMM8B	9	Tmm8b	
11q22.2-q22.3	IL18	9	Il18	29
11q22	TEX12	9	Tex12	
11q22.2-q22.3	DTS	9	Dts	