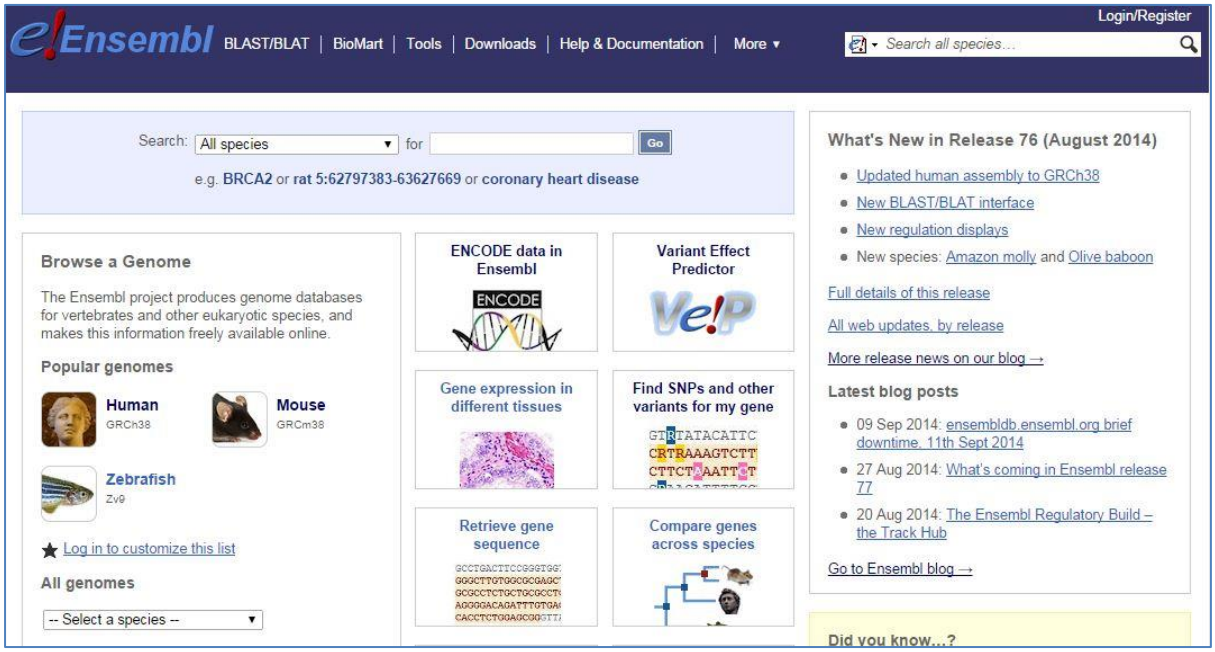
Tutorial: Ensembl walkthrough

In this tutorial you will walk through Ensembl using an example. You will explore the human ***ABCD1*** (ATP-binding cassette, sub-family D (ALD), member 1) gene.

The protein encoded by this gene is likely involved in the peroxisomal transport or catabolism of very long chain fatty acids (VLCFAs). Mutations in the *ABCD1* gene can cause **Adrenoleukodystrophy**, a rare X-linked disorder that causes a range of clinical phenotypes, often leading to a vegetative state and/or death (see also http://en.wikipedia.org/wiki/Adrenoleukodystrophy).

Go to the Ensembl homepage (http://www.ensembl.org/).

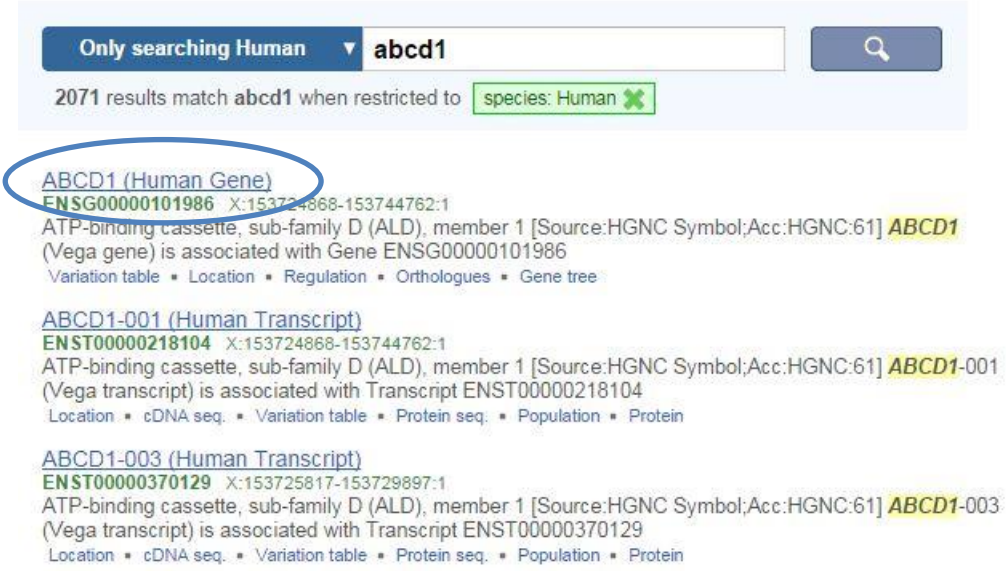


Searching

First of all, let's search for the human *ABCD1* gene.

Select 'Search: Human' and type 'abcd1' in the 'for' text box.
Click [Go].

The search result shows an *ABCD1* gene and several transcripts (splice variants).



Click on 'ABCD1 (Human Gene)' (the first hit)

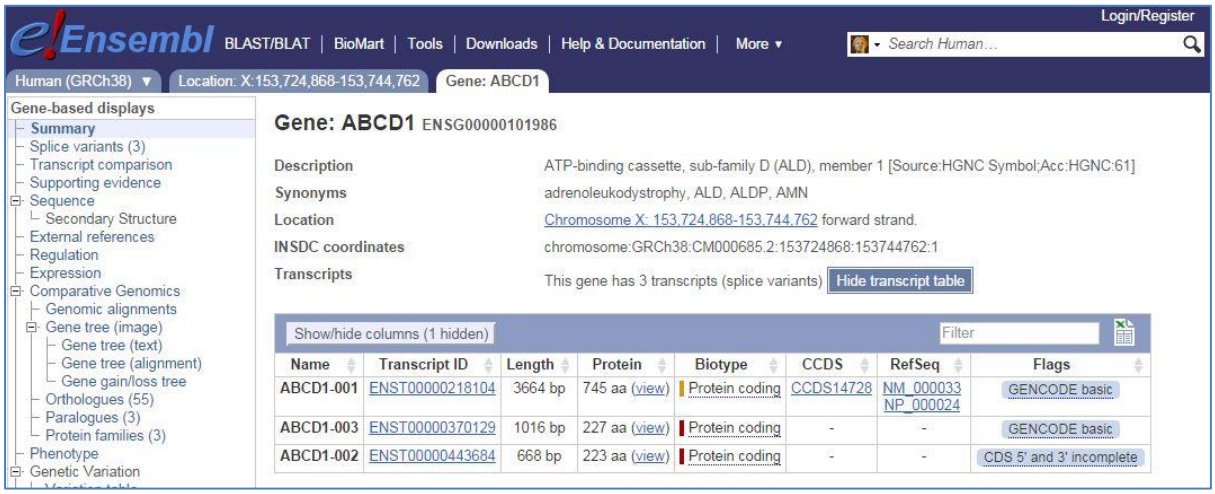
This leads us to the 'Gene summary' page under the 'Gene' tab.

The Gene tab

Pages (also called 'views') in Ensembl are organised under a number of tabs, i.e. 'Species', 'Location', 'Gene', 'Transcript', 'Variation' and 'Regulation'. The various available pages under each tab are listed in the left-hand side menu.

The 'Gene Summary' page shows general information about the *ABCD1* gene and the transcripts that have been annotated for it as part of the GENCODE gene set (http://www.gencodegenes.org/).. Note the information icon (*i*) next to 'Gene summary' that opens up a help page, as well as the legend at the bottom of the graphical display.

Click [Show transcript table].



You can customise the table by clicking on 'Show/hide columns'. For example, turn on the UniProt matches, and turn off the Flags.

The graphical display (as depicted below) shows the same three transcripts as the table. You can click on a transcript to learn more about it.

Protein-coding transcripts are gold or red. Gold transcripts are identical between the Ensembl and Havana projects, thus reflect a high standard. Red transcripts have either been annotated by Ensembl or Havana. In this case, ABCD1-002 and ABCD1-003 have been annotated by Havana.

Boxes and lines in the transcripts represent exons and introns, respectively. Empty boxes represent untranslated regions (UTRs), while filled boxes represent the coding sequence (CDS).

Summary – ABCD1 Transcripts

- There are three transcripts, all protein coding
- ABCD1-001 is gold, a symbol of high quality

The *ABCD1* gene is located on the forward strand of the genome. This can be seen from the arrows next to the transcript names, which indicate the direction of transcription and from the fact that the transcript models are shown above the blue bar that represents the genome. Transcripts located on the reverse strand are shown below the blue bar.

Click on 'Sequence' in the side menu.

Marked-up sequence

Download sequence | BLAST this sequence

Key

Exons | ABCD1 exons | All exons in this region

```
>chromosome:GRCh38:X:153724268:153745362:1
CCTCGTCGATGGGCCGGGGAGCCTCCGCGGTCCCGGAGCCCAGCCCGGCGCGCGGAGCCC
GCTCACCGAGTTTCCCACAGTCAACGTGCAGGCCCCGCCGCAGCAACAGAACTCTCCCAC
AGCAGCCCCGGCCCCGCCCCTCATACCGCGGCCGGAAACCGGAAGCGCCCGCCGGGCACC
GCCCACCAGCCCTCGCGAGGCCCCGGAGGCTCCGCCCACCTCCGCTTCCCACCCCGCCCC
GGAGCGGAGGGCCGGCGCTCCGAGCGGGAGAGGAAGAGGCGCCTCGGGCTCCGGGCGAGC
AGGGCGGGGTGGAGCGAGCACGCGGGCGGGGCGGGGCGGGGCTTTGTCGGGCCGGCGAGG
GCCGCTTCTCTAGTCCGCGCGGCCGTCCCACGTCTCTGTGGTGCGGGAGGGGCCCCGCCG
AGGGGCGAGAACGGGAGGTGGGGGTGTGGGCGGGCCCCGCCGAGGGGCGAGAACAGGGTG
GGGCTCCCGCGCCCGGACTCCGCCCCTCGCCCCTCCTCCGCCTCCTCCCCTTCCCCCGAC
TCGCCCCTGGGGAAGAGTGGGTGGGGATTCTGGGCCGGTGGAGGAGTCACTGTCGCTTCA
GCCAGGCTGCGGAGCGGACGGACGCGCCTGGTGCCCCGGGGAGGGGCGCCACCGGGGGAG
GAGGAGGAGGAGAAGGTGGAGAGGAAGAGACGCCCCCTCTGCCCGAGACCTCTCAAGGCC
CTGACCTCAGGGGCCAGGGCACTGACAGGACAGGAGAGCCAAGTTCCTCCACTTGGGCTG
CCCGAAGAGGCCGCGACCCTGGAGGGCCCTGAGCCCACCGCACCAGGGGCCCCAGCACCA
CCCCGGGGGCCTAAAGCGACAGTCTCAGGGGCCATCGCAAGGTTTCCAGTTGCCTAGACA
ACAGGCCCAGGGTCAGAGCAACAATCCTTCCAGCCACCTGCCTCAACTGCTGCCCCAGGC
ACCAGCCCCAGTCCCTACGCGGCAGCCAGCCCAGGTGACATGCCGGTGCTCTCCAGGCCC
CGGCCCTGGCGGGGGAACACGCTGAAGCGCACGGCCGTGCTCCTGGCCCTCGCGGCCTAT
GGAGCCCACAAAGTCTACCCCTTGGTGCGCCAGTGCCTGGCCCCGGCCAGGGGTCTTCAG
```

Exon from neighbouring gene (BCAP31)

ABCD1 Exon

On the 'Sequence' page the sequence of the *ABCD1* gene plus 600 bp upstream and downstream is shown. Exon sequences belonging to the *ABCD1* gene are shown in red letters on a peach background, while exons belonging to other genes are shown in black letters on a peach background. All possible exon sequence is shown, across all the transcripts.

Almost all graphical displays in Ensembl can be configured. This is done using the [Configure this page] button.

Click [Configure this page] in the side menu.

A pop-up window lists all display options.

Summary – Gene Sequence

- All exons are highlighted, for all genes in the region
- ABCD1 exons are in bold letters

Let's find out more about *ABCD1.*

Click on External References in the side menu.

This shows matches to the Ensembl gene in other projects and databases. A table that links Ensembl transcripts to UniProt and RefSeq identifiers is found at the bottom of the page.

The following database identifiers correspond to the transcripts of this gene:

Filter

Transcript ID	CCDS	UniProtKB/ Swiss-Prot	RefSeq peptide	RefSeq mRNA	Vega transcript	UniProtKB/ TrEMBL
ENST00000218104	CCDS14728.1	P33897	NP_000024.2	NM_000033.3	OTTHUMT00000061041	
ENST00000370129					OTTHUMT00000061043	A6NEP8
ENST00000443684					OTTHUMT00000061042	

This is similar to what we saw in the Transcript table, but has more information.

Click on 'Phenotype' in the side menu.

On the 'Phenotype' page phenotypes that have been associated with the *ABCD1* gene as well as with variants associated with the *ABCD1* gene are shown.

Phenotype

List of phenotype(s) associated with the gene ENSG00000101986

Filter

Phenotype	Source	Locations
Adrenoleukodystrophy, X-Linked	DDG2P	View on Karyotype
ADRENOLEUKODYSTROPHY	OMIMGENE	View on Karyotype
CADDS	Orphanet	View on Karyotype
ADRENOMYELONEUROPATHY	Orphanet	View on Karyotype
X-linked cerebral adrenoleukodystrophy	Orphanet	View on Karyotype

Phenotypes associated with the gene from variation annotations

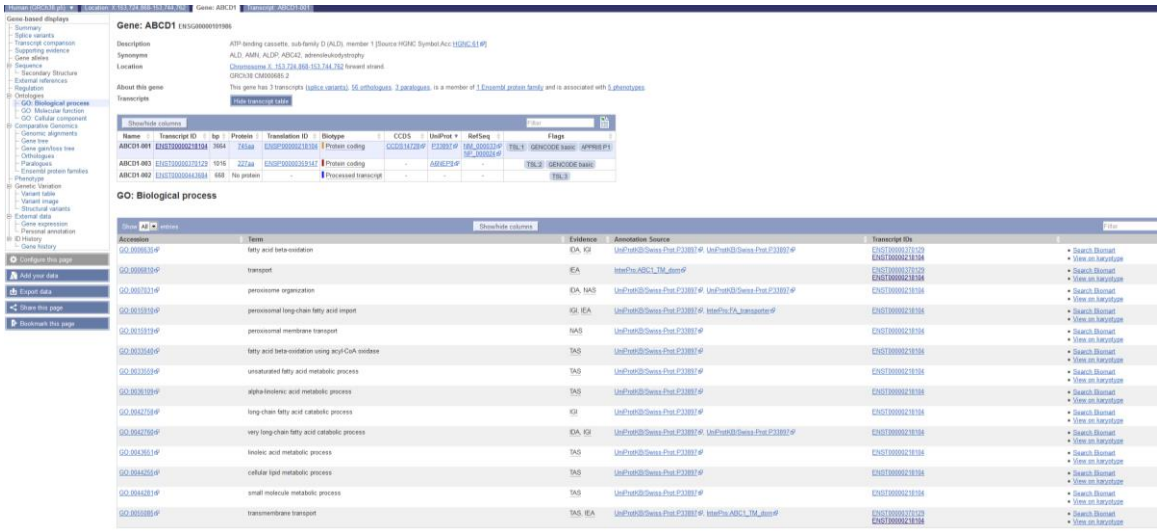
Show 10 entries

Filter

Number of variants	Show/hide details	Phenotype	Locations	Biomart	Source(s)
475	Show	ALL variations with a phenotype annotation			-
1	Show	ADRENOLEUKODYSTROPHY	View on Karyotype	-	OMIM
1	Show	ADRENOMYELONEUROPATHY	View on Karyotype	-	OMIM
410	Show	Annotated by HGMD but no phenotype description is publicly available	-	-	HGMD-PUBLIC
1	Show	COSMIC:tumour_site:NS	View on Karyotype	View list in BioMart	COSMIC
2	Show	COSMIC:tumour_site:autonomic_ganglia	View on Karyotype	View list in BioMart	COSMIC
4	Show	COSMIC:tumour_site:breast	View on Karyotype	View list in BioMart	COSMIC
1	Show	COSMIC:tumour_site:central_nervous_system	View on Karyotype	View list in BioMart	COSMIC
19	Show	COSMIC:tumour_site:endometrium	View on Karyotype	View list in BioMart	COSMIC
3	Show	COSMIC:tumour_site:haematopoietic_and_lymphoid_tissue	View on Karyotype	View list in BioMart	COSMIC

Click on 'GO: Biological process' in the side menu.

Gene Ontology (GO) terms (http://www.geneontology.org) associate proteins to biological process, molecular function and cellular component terms.



The 'biological process' terms indicate that the ABCD1 protein plays a role in fatty acid transport and catabolism.
The 'cellular component' terms indicate the ABCD1 protein is located in the peroxisomal membrane.

Click on 'ENST00000218104' in the transcript table at the top of the page.

This leads us to the 'Transcript summary' page under the 'Transcript' tab.

The Transcript tab

Note that, because we have moved from the 'Gene' tab to the 'Transcript' tab, the side menu has changed and now shows links to pages with information about this specific splice variant.

Click on 'Sequence - Exons' in the side menu.

On the 'Exons' page the sequence of the unspliced transcript is shown. The coding sequence (CDS) is shown in black, untranslated regions (UTRs) in purple, introns in blue and flanking sequences in green. By default only a small part of the introns and the flanking sequences is shown, but this can be changed on the configuration page.

Exons

Download sequence | BLAST this sequence

Key

Exons/Introns | Flanking sequence | Intron sequence | Translated sequence | UTR

Show All entries | Show/hide columns | Filter

No.	Exon / Intron	Start	End	Start Phase	End Phase	Length	Sequence
	5' upstream sequence						.....ggaagagtgggtggggattctgggcggtggaggagtcactgtcgcttca
1	ENSE00000868271	153,724,868	153,726,166	-	0	1,299	GCCAGGCTGCGGAGCGGACGGACGCGCCTGGTGCCCCGGGGAGGGGCGCCACCGGGGGAG GAGGAGGAGGAGAAGGTGGAGAGGAAGAGACGCCCCCTCTGCCCGAGACCTCTCAAGGCC CTGACCTCAGGGGCCAGGGCACTGACAGGACAGGAGAGCCAAGTTCCTCCACTTGGGCTG CCCGAAGAGGCCGCGACCCTGGAGGGCCCTGAGCCCACCGCACCAGGGGCCCCAGCACCA CCCCGGGGGCCTAAAGCGACAGTCTCAGGGGCCATCGCAAGGTTTCCAGTTGCCTAGACA ACAGGCCCAGGGTCAGAGCAACAATCCTTCCAGCCACCTGCCTCAACTGCTGCCCCAGGC ACCAGCCCCAGTCCCTACGCGGCAGCCAGCCCAGGTGACATGCCGGTGCTCTCCAGGCCC CGGCCCTGGCGGGGGAACACGCTGAAGCGCACGGCCGTGCTCCTGGCCCTCGCGGCCTAT GGAGCCCACAAAGTCTACCCCTTGGTGCGCCAGTGCCTGGCCCCGGCCAGGGGTCTTCAG GCGCCCGCCGGGGAGCCCACGCAGGAGGCCTCCGGGGTCGCGGCGGCCAAAGCTGGCATG AACCGGGTATTCCTGCAGCGGCTCCTGTGGCTCCTGCGGCTGCTGTTCCCCCGGGTCCTG TGCCGGGAGACGGGGCTGCTGGCCCTGCACTCGGCCGCCTTGGTGAGCCGCACCTTCCTG TCGGTGTATGTGGCCCGCCTGGACGGAAGGCTGGCCCGCTGCATCGTCCGCAAGGACCCG CGGGCTTTTGGCTGGCAGCTGCTGCAGTGGCTCCTCATCGCCCTCCCTGCTACCTTCGTC AACAGTGCCATCCGTTACCTGGAGGGCCAACTGGCCCTGTCGTTCCGCAGCCGTCTGGTG GCCCACGCCTACCGCCTCTACTTCTCCCAGCAGACCTACTACCGGGTCAGCAACATGGAC GGGCGGCTTCGCAACCCTGACCAGTCTCTGACGGAGGACGTGGTGGCCTTTGCGGCCTCT GTGGCCCACCTCTACTCCAACCTGACCAAGCCACTCCTGGACGTGGCTGTGACTTCCTAC ACCCTGCTTCGGGCGGCCCGCTCCCGTGGAGCCGGCACAGCCTGGCCCTCGGCCATCGCC GGCCTCGTGGTGTTCCTCACGGCCAACGTGCTGCGGGCCTTCTCGCCCAAGTTCGGGGAG CTGGTGGCAGAGGAGGCGCGGCGGAAGGGGGAGCTGCGCTACATGCACTCGCGTGTGGTG GCCAACTCGGAGGAGATCGCCTTCTATGGGGGCCATGAG
	Intron 1-2	153,726,167	153,729,231			3,065	gtggggcaggttggggtgccgggca.....tctctgtgtctgtcacccccccgcag

Click on 'External References - General identifiers' in the side menu.

On the 'General identifiers' page cross-references to other databases are shown that contain entries that correspond to the ENST00000218104 sequence.

General identifiers

This transcript corresponds to the following database identifiers:

Show All entries Filter

External database	Database identifier
CCDS	CCDS14728.1 [view all locations]
European Nucleotide Archive	BC015541 [align] [view all locations] BC025358 [align] [view all locations] U52111 [align] [view all locations] Z21876 [align] [view all locations] Z31006 [align] [view all locations] Z31007 [align] [view all locations] Z31008 [align] [view all locations] Z31009 [align] [view all locations] Z31010 [align] [view all locations] Z31348 [align] [view all locations]
HGNC transcript name	ABCD1-001 ATP-binding cassette, sub-family D (ALD), member 1 [view all locations]
Havana translation	OTTHUMP00000025960 [view all locations]
Human Protein Atlas	HPA035214 [view all locations] HPA035214 [view all locations]
INSDC protein ID	AAH15541.1 [align] [view all locations] AAH25358.1 [align] [view all locations] CAA79922.1 [align] [view all locations] CAA83230.1 [align] [view all locations]
RefSeq mRNA	NM_000033.3 [align] [view all locations]
RefSeq peptide	NP_000024.2 [Target %id: 100; Query %id: 100] [align] ATP-binding cassette sub-family D member 1 [view all locations]
UCSC Stable ID	uc004fif.2 [view all locations]
UniParc	UPI0000000DF5 [view all locations]
UniProtKB/Swiss-Prot	P33897 [align] ATP-binding cassette sub-family D member 1 [view all locations]

For example, ENST00000218104 matches the P33897 protein sequence in the UniProtKB/Swiss-Prot database (http://www.uniprot.org/) and the NP_000024.2 protein and NM_000033.3 mRNA sequence in the RefSeq database (http://www.ncbi.nlm.nih.gov/refseq/).

Let's have a look at the region on the chromosome, and neighbouring genes.

Click on the 'Location' tab.

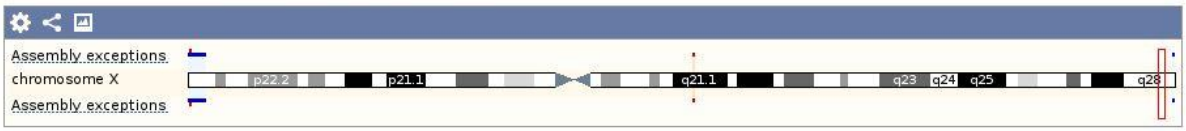
This leads us to the 'Region in detail' page under the 'Location' tab.

The Location tab

The 'Region in detail' page shows the genomic neighbourhood of the *ABCD1* gene. It consists of three parts.

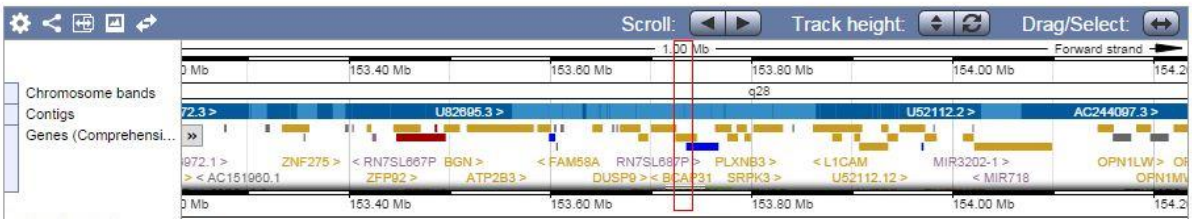
First, the complete chromosome.

Chromosome X: 153,724,868-153,744,762



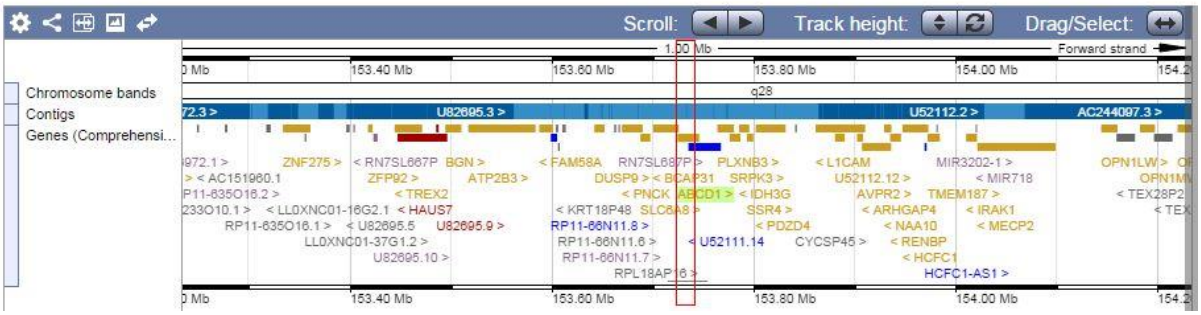
Second, the 1 Mb region around the gene of interest.

Region in detail



Drag down the bottom to reveal *ABCD1*.

Region in detail



This display is scrollable. Either use the ‘Scroll’ arrows click and drag the image in the same way as Google Maps. Zoom in by clicking the ‘Drag/Select’ icon, selecting the region of interest with your mouse and subsequently clicking ‘Jump to region’ in the resulting pop-up.

Third, the region of interest. In our case this is the *ABCD1* gene.

By default, the data tracks drawn are:

- 38 way GERP elements (the ‘constrained elements’, which are regions of high conservation based on comparison of sequence across 38 species)
- Human cDNAs (cDNA sequences aligned to the genome)
- CCDS set (transcripts in the Consensus Coding Sequence Set)
- Genes (GENCODE)
- Contigs (the genome)
- 1KG-All-common (Variants from the 1000 Genomes project with population frequency >1%)
- All phenotype-associated variants
- 1000 Genomes High Quality Structural Variants
- MultiCell regulatory features (sequences that may be involved in gene regulation)
- %GC (reflects GC content vs AT)

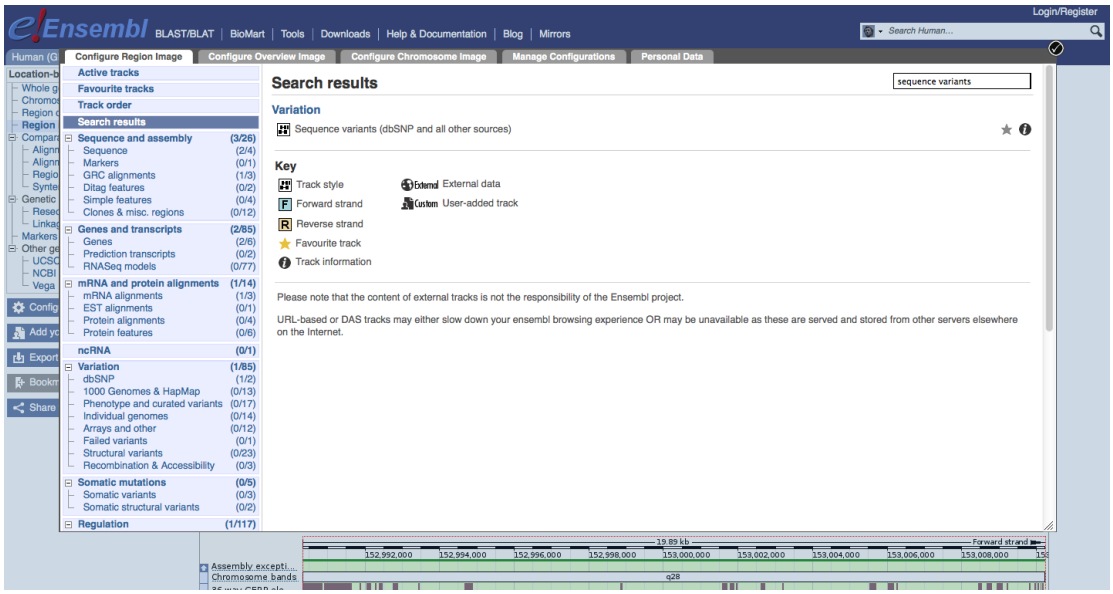
There are several ways to navigate this display:

- zoom in and out by using the [+/-] slider
- zoom in by drawing a box around the region of interest and subsequently clicking ‘Jump to region’ in the resulting pop-up
- moving up- and downstream with the single and double arrows next to the [+/-] slider.
- going to a particular region by changing the coordinates in the ‘Location’ text box or by searching for a gene using the ‘Gene’ text box (which has auto completion)

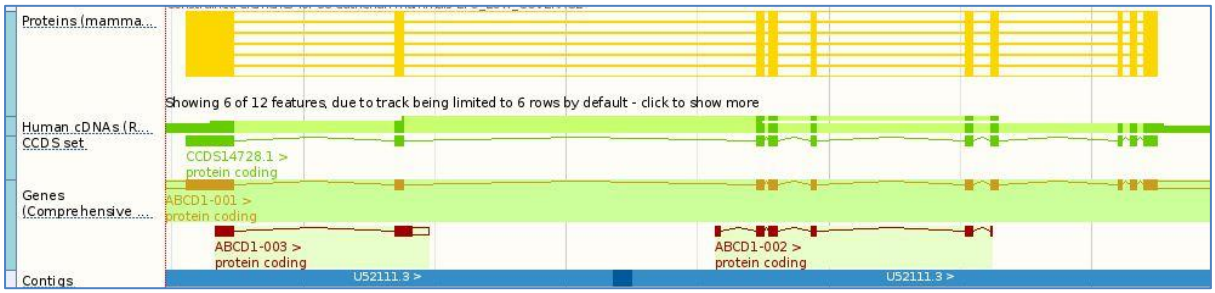
Datasets (or tracks) can be added to the display using [Configure this page]. On the configuration page all available tracks are grouped in the left-hand menu. It is also possible to search for tracks using the ‘Find a track’ text box.

For example, to add protein alignments from UniProt to the display:

- Click [Configure this page] in the side menu.
- Type 'UniProt in the 'Find a track' text box.
- Select 'Proteins (mammal) from UniProt'. Choose 'Normal'.
- Click (✓).



A new track, 'UniProt (mammals)', has now been added to the display.



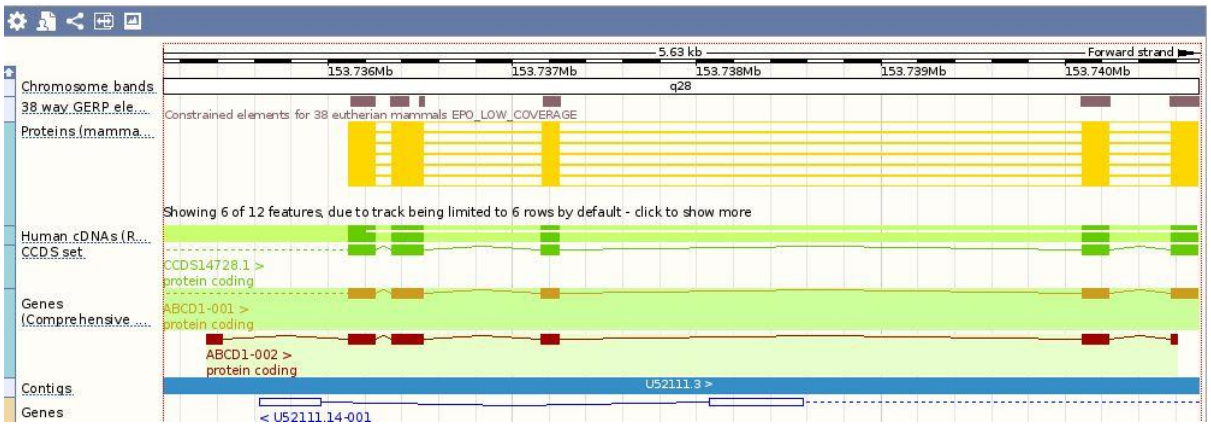
To turn the added track off again:

- Hover over the track name.
- Click on the 'Turn track off' icon (x) in the pop-up.

Tracks can be moved by clicking on the bar in front of the track name and dragging the track to the desired location.

To zoom in, you can click and drag your mouse around a region.

- Zoom in to ABCD1-002



At the top of the display (circled in the image above) several icons are shown, some of which can also be found on other displays:

- Configure this image: add/delete tracks (same as [Configure this page] button in the side menu).
- Manage your custom tracks: add your own data (same as [Add your data] button in the side menu)
- Share this image: create a URL that can be shared with others without the need to tell them how to configure the page
- Resize this image: resize the image
- Export this image: export the image in various formats (PDF, PNG etc.)