

# Lab 4: Polymorphisms and Mutations

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## Part 1: Using the UCSC Genome Browser to Visualize Polymorphisms and Mutations

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In this lab, we will use the UCSC Genome Browser to visualize polymorphisms in the HLA-A and H2A proteins. By the end of this lab, you will have a better idea of sequence conservation and how conservation differs across proteins.

### Exploring HLA-A

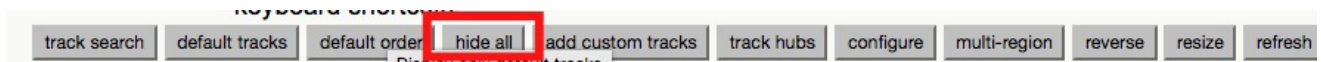
First, we will learn a little bit about the HLA-A gene.

1. To access the UCSC Genome Browser, go to [UCSC Genome Browser](#).
2. Click on 'Genome Browser', highlighted in red in the image.

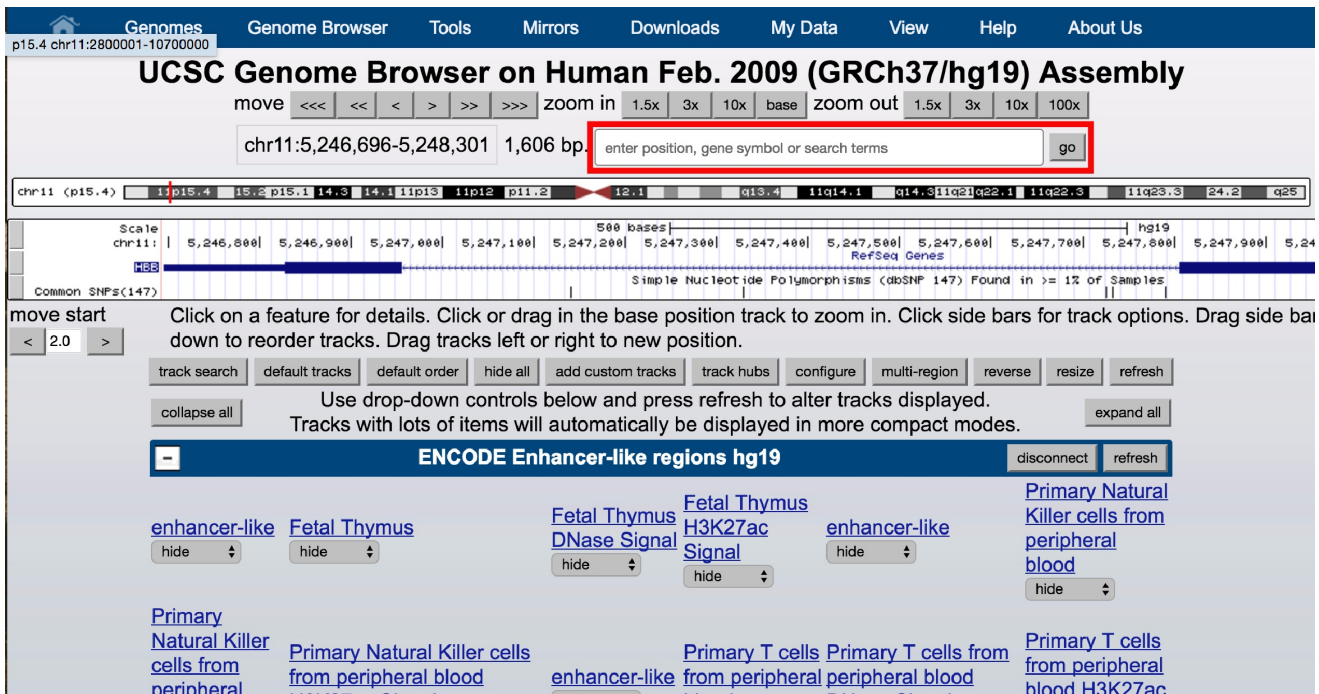


The image shows the UCSC Genome Browser homepage. At the top, there is a navigation bar with links: Genomes, **Genome Browser**, Tools, Mirrors, **Downloads**, My Data, Help, and About Us. Below the navigation bar is a large blue graphic of a DNA double helix. To the right of the graphic is a section titled "Our tools" with a list of tools: Genome Browser, BLAT, Table Browser, Variant Annotation Integrator, Data Integrator, **Gene Sorter**, Genome Browser in a Box (GBiB), In-Silico PCR, LiftOver, and VisiGene. The "Gene Sorter" tool is highlighted with a red box.

- To reset the view and hide unused tracks, click the **hide all** button below the viewer.

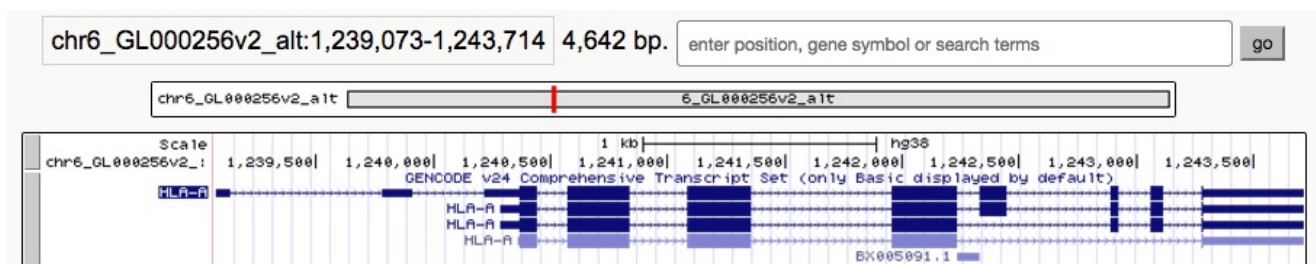


- Type in **HLA-A** in the search bar, highlighted in red.



The image shows the UCSC Genome Browser on Human Feb. 2009 (GRCh37/hg19) Assembly. The search bar is highlighted in red and contains the text "HLA-A". Below the search bar, the browser displays a genomic track for chromosome 11 (p15.4). The track shows various genomic features, including RefSeq Genes, Simple Nucleotide Polymorphisms (dbSNP), and ENCODE Enhancer-like regions. The "hide all" button is visible below the track. The "Known Genes" section is visible at the bottom, showing a list of genes with "Fetal Thymus" and "Primary Natural Killer cells from peripheral blood" as the first options.

- In the resulting list of **Known Genes**, click on the first option. This should redirect you back to the browser.



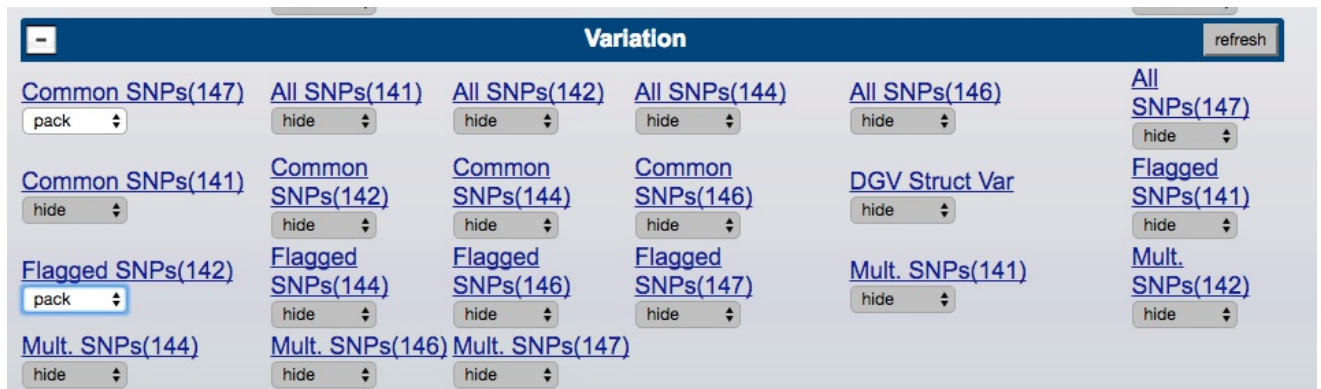
6. In the HLA-A track, click on the label for HLA-A. This should redirect you to a new screen. Given the information on this screen, answer the following questions.

## Questions: Exploring HLA-A

1. What does 'HLA' stand for? **Note:** You may of to use external resources to find this.
2. What is the location (chromosome and position) of HLA-A?
3. How long is the gene?
4. State the locations of three largest exons for HLA-A.
5. What important roles does HLA-A? **Note:** If this page does not provide enough information on the HLA-A gene, google to find more information.
6. Name two diseases associated with this gene. Explain briefly what these diseases are.

Now, let's navigate back to the browser to explore variation of HLA-A.

1. Scroll down to track options, below the visualization.
2. Navigate to the Variation section.
3. Toggle 'Common SNPs' and 'Flagged SNPs' to 'squish', as shown in the image.



4. Scroll back up to the visualization to view HLA-A and associated SNPs.

## Questions: HLA-A SNP Density

1. Zoom out to see the whole HLA-A gene. In what areas to you see the highest density of SNPs? Is there any reasoning behind this SNP distribution?
2. Zoom in to HLA-A and click on any SNP. This should take you to a new page.

## Questions: HLA-A SNP Search

1. What is a SNP?
2. What is a common SNP? A flagged SNP?
3. Let's get more information on the specific SNP you clicked on. What is the reference allele for this SNP?
4. What, if any, is the **Function** of this SNP? What does this function mean?

## Exploring H2A.

Now, we will explore H2A.

1. Type in **H2A** in the search bar.
2. In the resulting list of **Known Genes**, click on the **second** option,

called HIST3H2A. This should redirect you back to the browser.

3. In the H2A track, click on the label for H2A. This should redirect you to a new screen. Given the information on this screen, answer the following questions.

## Questions: Exploring H2A

1. What does 'H2A' stand for? **Note:** You may of to use external resources to find this.
2. What is the location (chromosome and position) of H2A?
3. How long is the gene?
4. State the locations of three largest exons for H2A.
5. What important roles does H2A? **Note:** If this page does not provide enough information on the H2A gene, google to find more information.
6. Name two diseases associated with this gene. Explain briefly what these diseases are.

Now, let's navigate back to the browser to explore variation of H2A. Make sure that Common SNPs and Flagged SNPs are still being displayed.

## Questions: H2A SNP Density

1. Zoom out to see the whole H2A gene. In what areas, if any, to you see the highest density of SNPs?
2. How does the SNP distribution in H2A compare to the distribution of HLA-A? Are there any reasons you can think of for why these distributions may differ?