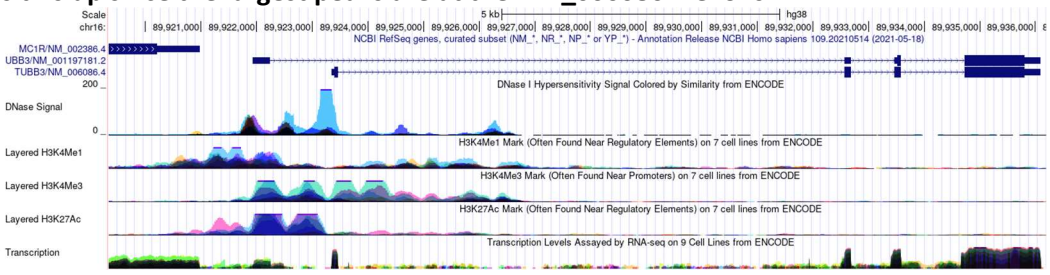
UCSC

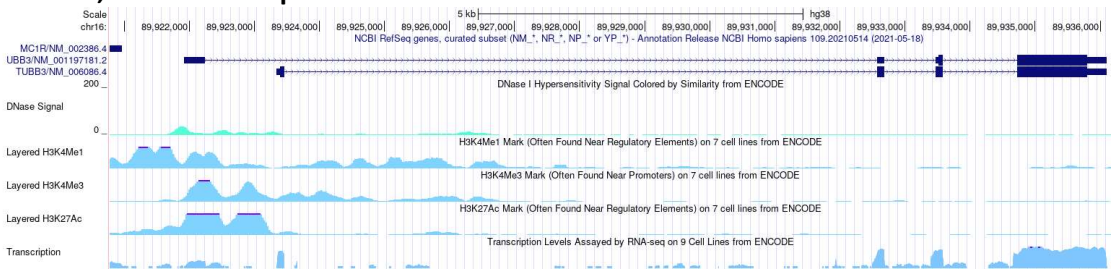
Find the human TUBB3 gene using the UCSC Genome Browser (hg38). Turn on the Encode Regulation track and NCBI RefSeq genes. In a few sentences, describe what you see at the TUBB3 locus in terms of the Encode Regulation tracks.

H3K4Me1 and H3K27Ac marks usually suggest enhancer and regulatory activity. H3K4Me3 marks are usually found near promoters, and DNase peaks usually indicate promoters or other regulatory regions since they are sensitive to being cut. These tracks indicate both transcripts for *TUBB3* are likely, but NM_006086.4 much more so than NM_001197181.2. The transcription track backs this up since the largest peaks are at the NM_006086.4 exons.



Configure each Encode track to only show data for the HUVEC cell line. What is the HUVEC cell line? Based on the Encode tracks, do you think this gene is expressed in the HUVEC cell line?

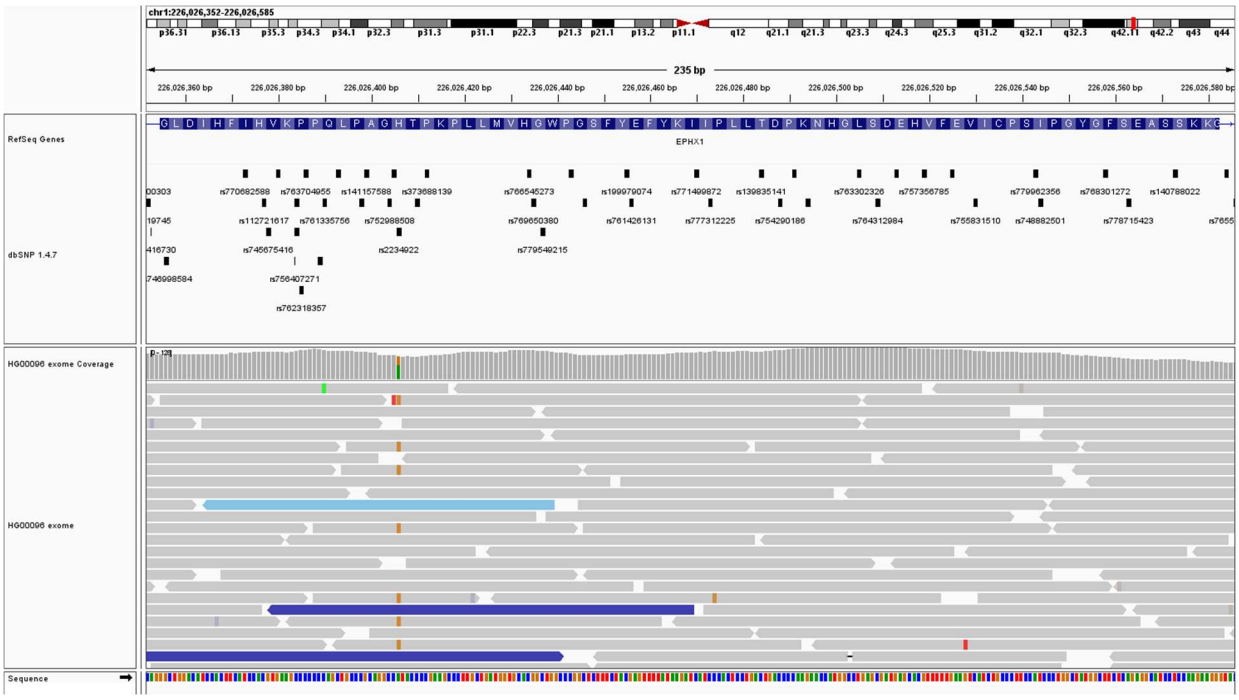
HUVEC cells are umbilical vein endothelial cells from a blood vessel tissue. The TUBB3 gene is likely expressed in these cells since there are large transcription peaks, as well as H3K4Me1, H3K4Me3, and H3K27Ac peaks.



IGV

1. Using IGV for hg19, load dbSNP 1.4.7 or newer and an exome sequencing track from the 1000 Genomes project. Go to the EPHX1 gene and zoom in on the exon #4.
   a. How many SNPs overlap this exon and what are the SNP IDs?
   There are 44 SNPs (rs746998584, rs770682588, rs112721617, rs745675416, rs769262345, , rs764460024, rs756407271, rs762318357, rs775238551, rs773821078, rs761335756, rs755378466, rs141157588, rs763704955, rs754199890, rs55784606, rs141157588, rs752988508, rs22234922, rs761017131, rs373688139, rs766545273, rs769650380, rs779549215, rs147296174, rs144904318, rs140788022, rs778715423, rs768301272, rs748882501, rs779962356, rs755831510, rs371520880, rs757356785, rs151050888, rs764312984, rs763302326, rs376877493, rs765684911, rs754290186, rs139835141, rs777312225, rs771499872, rs761426131)

b. At which SNP(s) in part a does this individual appear to be heterozygous? What is the sequence count for each nucleotide at this(these) position(s)
rs2234922 A: 57, G: 34



2. Using IGV, load the Firehose (TCGA) data from January 28, 2016 for OV-TP (ovarian cancer) using hg19. The following four genes have been shown to be associated with CNV in some forms of ovarian cancer: PKN2, GRXCR1, PRKN (or PARK2), and PPIAL4A. In a table, qualitatively evaluate the CNV summary (minus germline) in each gene's region. Repeat but for Firehose (TCGA) data for BRCA-TP (breast cancer). Add CNV summaries for part b as another column in the same table

Most BRCA-TP patients did not have an increase or decrease in copy number for each gene whereas the opposite was true for OV-TP patients.

Gene	OV-TP	BRCA-TP	Summary
PKN2	Red: 50%, Blue: 23%	Red: 14%, Blue: 32%	OV-TP: increase in copy number for half the patients CN for BRCA-TP: 54% no change, but 32% had a decrease
GRXCR1	Red: 30%, Blue: 45%	Red: 12%, Blue: 30%	OV-TP: decrease in copy number for 45% but increase in 30% BRCA-TP: 58% no change, but 30% had a decrease
PRKN	Red: 17%, Blue: 64%	Red: 13%, Blue: 36%	OV-TP: decrease in copy number for 64% BRCA-TP: 51% no change, but 36% had a decrease
PPIAL4A	Red: 60%, Blue: 2%	Red: 28%, Blue: 3%	OV-TP: increase in copy number for 60% BRCA-TP: 69% no change, but 28% had an increase

OTHER

Find the human CACNA1A gene in NCBI ClinVar. Filter to limit results to Variation type: Deletion.

a. How many total variations are listed after filtering?

118

b. How many variants from part a are pathogenic?

64

c. Find the CACNA1A gene in Ensembl and look for structural variants. How many structural variant entries can you find from the excel table?

1154

d. Find the CACNA1A gene in the NCBI Variation Viewer. Filter for dbVar and CNV. How many total CNVs?

0

e. What is the most typical pathogenic condition for the CACNA1A gene variation from ClinVar?

Epileptic encephalopathy, early infantile, 42, Episodic ataxia type 2

f. What clinical treatment options are available?

Anti-epileptic medications such as Sulthiame