

Exercises for the Genome Variation Server (Version 2, 2007)

You can choose to do these using the questions as your only guide—or see the following pages for the step-by-step checklist to finding these answers.

1) Find the number of individuals in the HapMap-JPT population that are homozygote for the rare allele (at a minimum frequency of 20%) of one nonsynonymous SNP located in the coding region of the ABO gene. What are their genotypes?

Skills: search by gene name, using SNP filter parameters, viewing genotype display data.

2) Browsing to the ABO gene location, determine if there are any other SNPs with at least an r-squared value of 0.6 paired with the SNP at position 135121293 in the HapMap-JPT population.

Skills: search by browsing chromosome, using color coding for LD plot parameters, viewing linkage disequilibrium display data.

3) Search the pga candidate gene ABO to find the rsID for the SNP at position 135121293 and its minor allele frequency in all populations (for PGA data). Study the SNP further in the dbSNP record.

Skills: search by pga candidate genes, viewing SNP summary display data.

4) Determine tag SNPs for genotyping variations with a minor allele frequency of greater than 20% in the ABO gene for both the PGA European and PGA African populations.


Skills: determining tag SNPs, merging population data, working with parameters.

GVS Exercises, version 2.0. Correspond to the data available in August 2007

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Step-by-Step checklist/instructions for the GVS introduction exercises

1.) Find the number of individuals in the HapMap-JPT population that are homozygote for the rare allele (at a minimum frequency of 20%) of one nonsynonymous SNP located in the coding region of the ABO gene. What are their genotypes?

Step	Action	
1	Go to the GVS homepage: http://gvs.gs.washington.edu/GVS	
2	Click on the “Gene Name” button in the “search database by” section.	
3	In the resulting window, type in “abo” in the text box labeled “gene name” (leaving the “Beyond Your Target” boxes empty) and click “Search.”	
4	Check the HapMap-JPT (Japanese) population data source in the “Select Population” table. Note: <i>Make sure to uncheck other checked populations. The “PGA-EUROPEAN-PANEL” population will be checked by default and checking another population will not uncheck it.</i>	
5	In the “Set up parameters for display and analysis” table, type in “20” for the “Allele Frequency Cutoff (%)” box (in the “Filtering SNPs” row). Change the “Output SNPs By” menu to “Chromosome Position.” Leave all other parameter choices as default.	
6	Click the “display genotypes” button (green) at bottom of the page.	
7	In the resulting browser window, click the “open graphical display of genotypes” link. Scroll down to bottom of the graphic display window and look at color legend. The color for homozygote-rare allele is <u>yellow</u> . The color for SNP function in a coding-nonsynonymous region is <u>red</u> .	
8	Scroll back up to view the graphic. There are <u>5</u> SNP(s) listed here that are coding nonsynonymous based on the color-code. We’ll look at the first listed. The first coding nonsynonymous SNP number is at location <u>135121293</u> .	
9	Viewing the column of the SNP(s) we’ve chosen , there are <u>three</u> individuals that have the box color for the homozygote-rare allele. The individual designations are <u>1411:5204</u> , <u>1411:5219</u> and <u>1411:5236</u> .	
10	Bring the text/table data display window (by clicking the “open table display of genotypes” link from step 7) to your view and look for the SNP(s) listed that you found in step 8 (hint: the same color-code for SNP function applies here as it does in the graphic display). Find the individual(s) you determined in step 9. Their genotype is T/T.	

2) Browsing to the ABO gene location, determine if there are any other SNPs with at least an r-squared value of 0.6 paired with the SNP at position 135121293 in the HapMap-JPT population.

Step	Action	✓
1	Go to the GVS homepage: http://gvs.gs.washington.edu/GVS	
2	Click on the “Browse” button in the “search data by” section.	
3	In the resulting page of chromosome icons, click on the last block in “Chromosome 9.” <i>Each block represents 10mb, from exercise 1 you know that ABO is in this region.</i>	
4	A map of the chromosome will open. You should see the ABO gene icon at around 135,000,000bp. Use the inside left and right arrows to walk to the left or right if you need to move short distances.	
5	Click on the ABO gene icon.	
6	Check the HapMap-JPT (Japanese) population data source in the “Select Population” table. Note: <i>Make sure to uncheck other checked populations. The “PGA-EUROPEAN-PANEL” population will be checked by default and checking another population will not uncheck it.</i>	
7	In the “Set up parameters for display and analysis” table, type in “0.6” in the “LD Minimum (0.0-1.0)” box (in the “Color-Coding For LD Plot” row). Change the “Output SNPs By” menu to “Chromosome Position.” Leave all other parameter choices as default.	
8	Click the “display linkage disequilibrium” button (green) at bottom of the page.	
9	In the resulting browser window, click the “open graphical display of genotypes” link. Scroll down to bottom of the graphic display window and look at color legend. The color for the lowest value is <u>blue</u> (in this case that value is 0.6). The color for the highest value (1.0) is <u>red</u> .	
10	View the LD Plot in the graphic display. There are <u>25</u> SNPs which have a r-squared value greater than 0.6 paired with SNP 135121293. Note: <i>To determine this, find the second diagonal row (down left to right) of the LD plot (this is the row for SNP 135121293). Count the colored boxes in that row. These are SNPs that have at least a 0.6 r-squared value paired with SNP 135121293).</i>	

3. Search the pga candidate gene ABO to find the rs ID for the SNP at position 135121293 and its minor allele frequency in all populations (for PGA data). Study the SNP further in the dbSNP record.

Step	Action	✓
1	Go to the GVS homepage: http://gvs.gs.washington.edu/GVS	
2	Click on the “pga” button in the “search candidate gene” section.	
3	In the resulting new page, under the section “Load pga Genes,” choose “abo” from the pull down menu in the “select gene” row. Leave “select population” as “all.”	
4	Leave all parameters in the “Set up parameters for display and analysis” section as default.	
5	Click the “display SNP summary” button (green) at bottom of the page.	
6	Look for SNP 135121293. The rs ID is <u>rs8176740</u> and the alleles are A/T, the minor allele is <u>A</u> with a frequency of <u>21%</u> .	
7	To do further study of this SNP, click the link of the rs ID. This will open a new window for the rs record in dbSNP of this SNP.	

4. Determine tag SNPs for genotyping variations with a minor allele frequency of greater than 20% in the ABO gene (include upstream and downstream regions) for both the PGA European and PGA African populations.

Step	Action	✓
1	Go to the GVS homepage: http:// gvs.gs.washington.edu/GVS	
2	Click on the “Gene Name” button in the “search data by” section.	
3	In the resulting window, type in “abo” in the text box labeled “gene name,” type in “1500” for upstream and “1000” for downstream boxes and click “Search.”	
4	In the “Select Data Set(s)” section, check off both “PGA-EUROPEAN-PANEL” and “PGA-AFRICAN-PANEL” data sets.	
5	In the parameters selection box choose these options for the following parameter sections. For “Merging Data Sets” select “B – Combined samples with common variations” ^{**} For “Filtering SNPs” section, type “20” into the “Allele Frequency Cutoff (%)” box. Leave all other parameters as default.	
6	Click the “display tag snps” button in the “Display Results” section.	
7	Since we have chosen two populations and have merged the data by combining samples (either choice “B” or “C”), we have invoked the “MultiPop algorithm.” A new window will appear with three links. The first link will be tables of tag SNPs. The next two links are graphic representations of tag SNPs from the two different populations you choose. Click the first “open table display of tag SNPs” link.	
8	The first table on the new window will be the “Multiple-Population Tag SNPs” chosen by the MultiPop algorithm. How many of these multiple-population tag SNPs are there? 30 (<i>hint: number is in table heading</i>). These tag SNPs will cover variation in both populations. Below this table will be a table of tag SNPs and bins for each of the two populations. How many bins are in these two populations? European: 12 African 24 (<i>hint: bins are numbered</i>).	
9	Spend a little time, if desired, to try out different population data set and merging options to see how these affect results. For example, you could try using the “A” merge choice in step 5, or the two different populations suggested in the step 5 note.	

*** Since these data sets are from two different geographic regions, they do not contain common samples (individuals) and thus selection “A – common samples with combined variations” would return no data. Both selections B and C combine samples (no need for common individuals), so either would work in this case.*