Online Genetic Variation Databases

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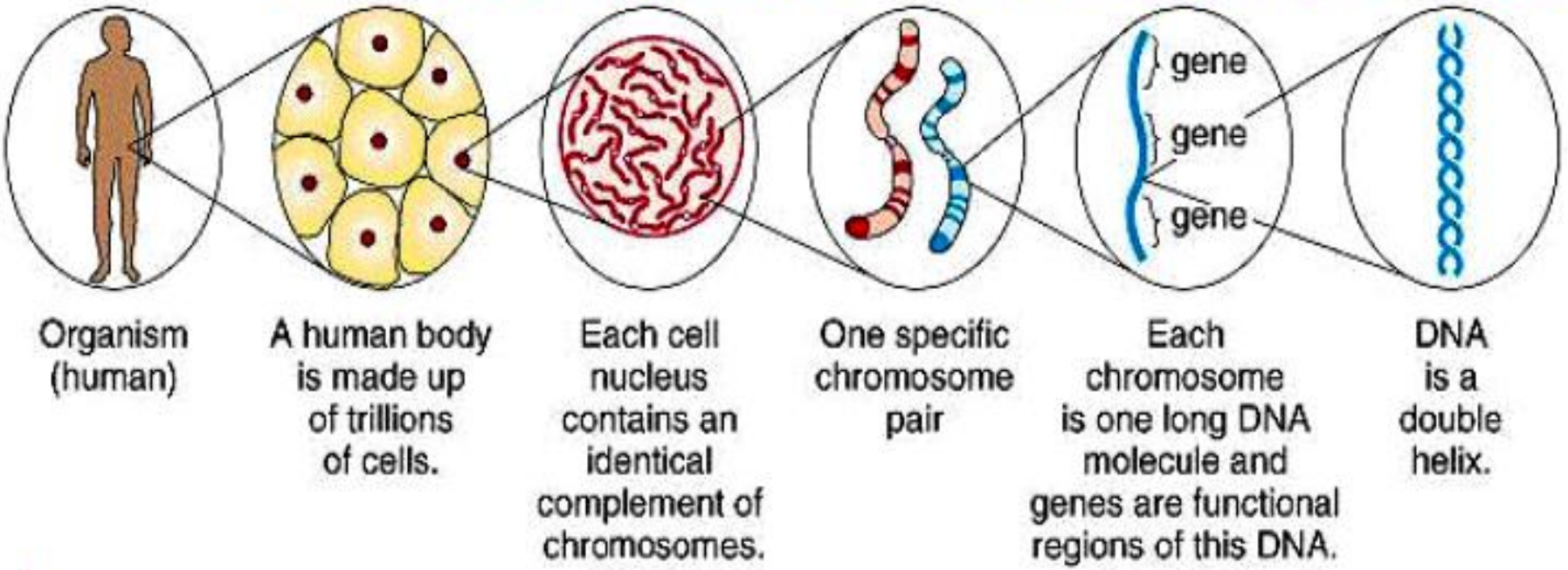
University of Thessaly, Larissa
November 2011

Genetics

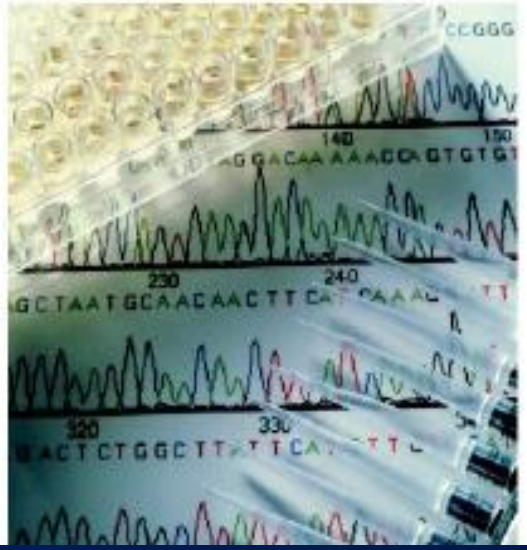
Scientific study of how physical, biochemical, and behavioral traits are transmitted from parents to their offspring. In essence, the science of heredity.

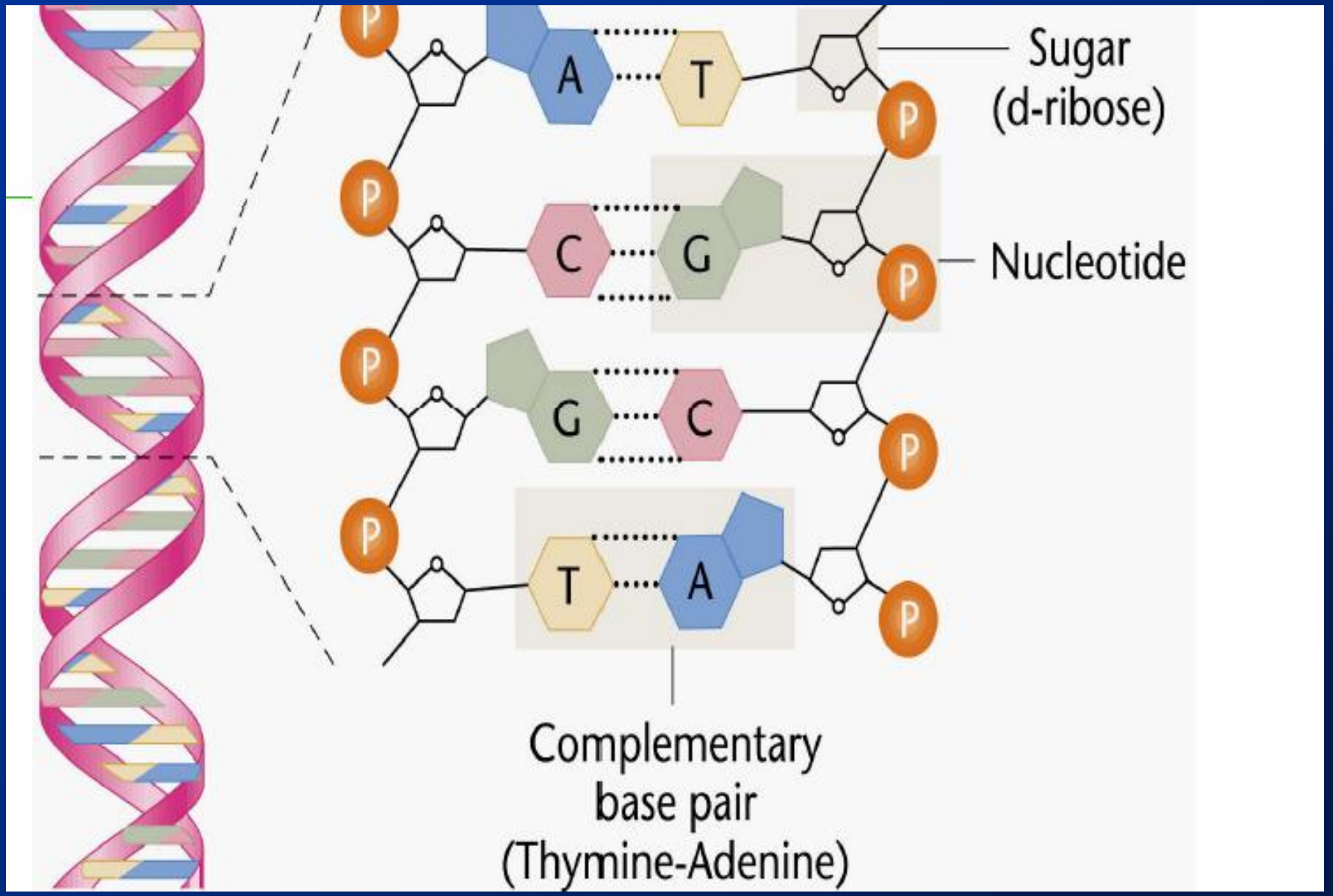


Genetic information contained in DNA

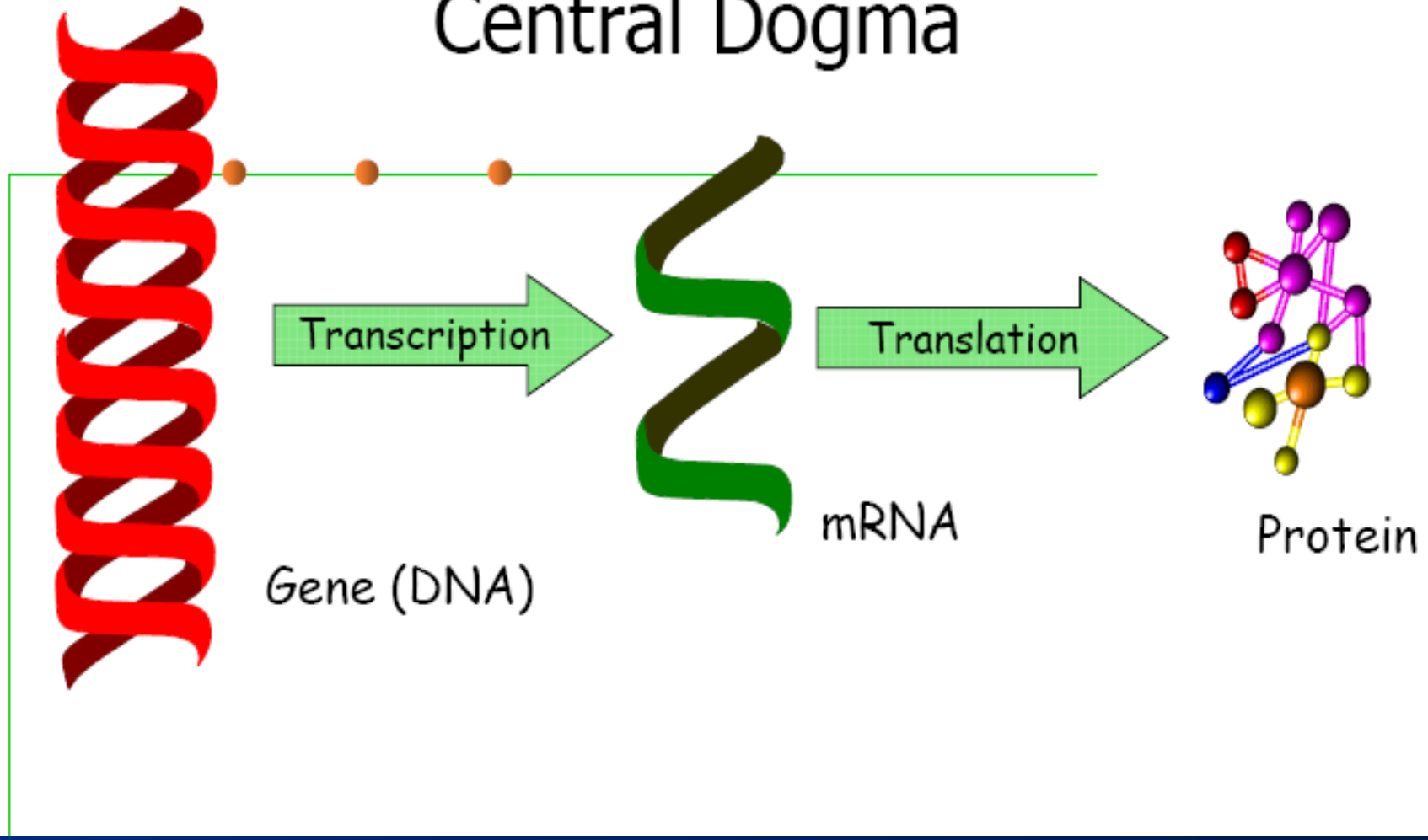
DNA is composed of nucleotides

A gene is a unique sequence of nucleotides

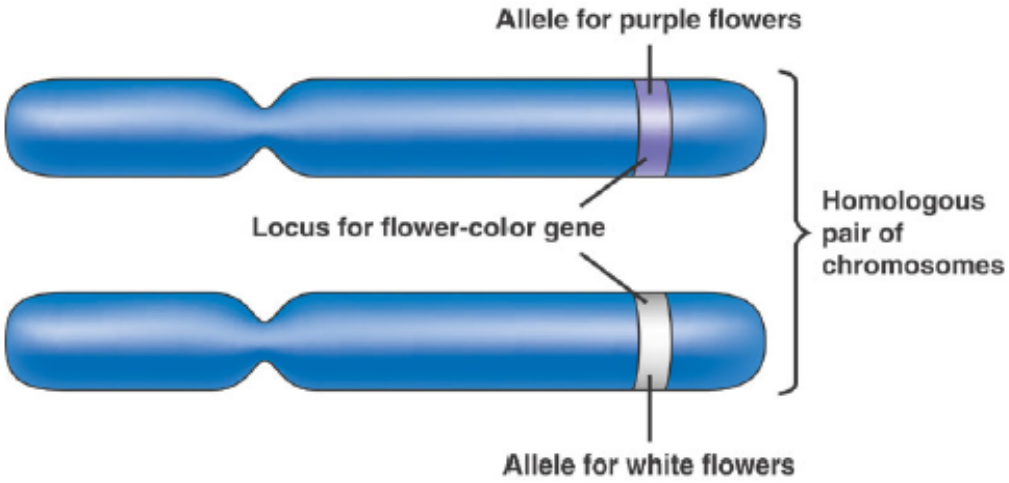



A
T
C
G
G
C
T
A
P
Sugar
(d-ribose)
Nucleotide
Complementary
base pair
(Thymine-Adenine)

Central Dogma



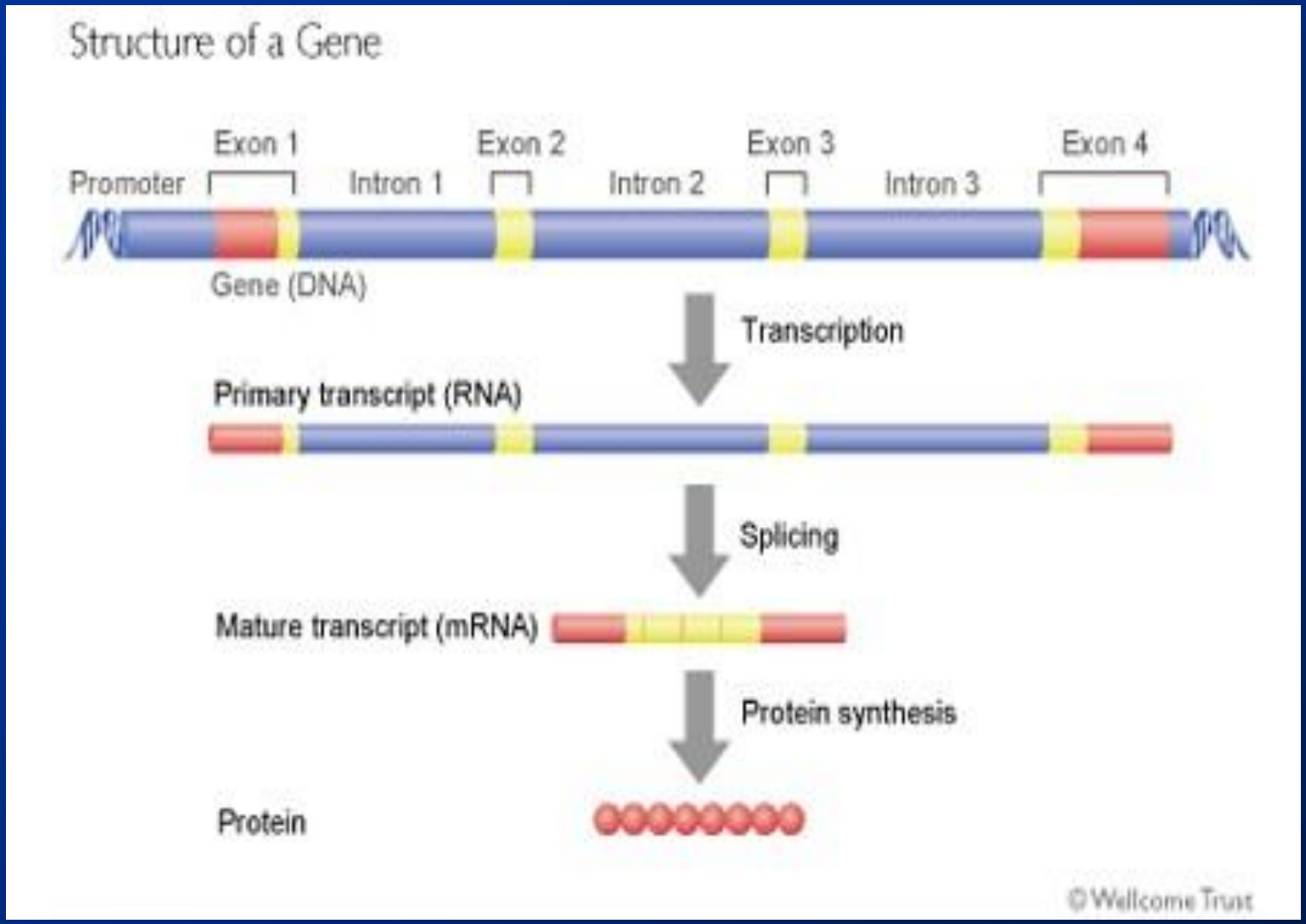
Some Genetic Terms



- Genes are instructions for producing a trait
- Locus is the spot each genes has on a chromosome
- Diploid cells have two genes (a gene pair) for each trait, each on a homologous chromosome
- Alleles are various molecular forms of a gene encoding for the same trait (i.e. flower color)

Τι είναι γονίδιο

- Βασική μονάδα κληρονομικότητας
- Ακολουθία βάσεων η οποία μεταφέρει την πληροφορία που απαιτείται για να δημιουργηθεί μια συγκεκριμένη πρωτεΐνη
- Ένα γονίδιο κωδικοποιεί μια πρωτεΐνη ή ένα μόριο RNA


Structure of a Gene
Exon 1
Exon 2
Exon 3
Exon 4
Promoter
Intron 1
Intron 2
Intron 3
Gene (DNA)
Transcription
Primary transcript (RNA)
Splicing
Mature transcript (mRNA)
Protein synthesis
Protein
© Wellcome Trust

HUMAN INDIVIDUALITY

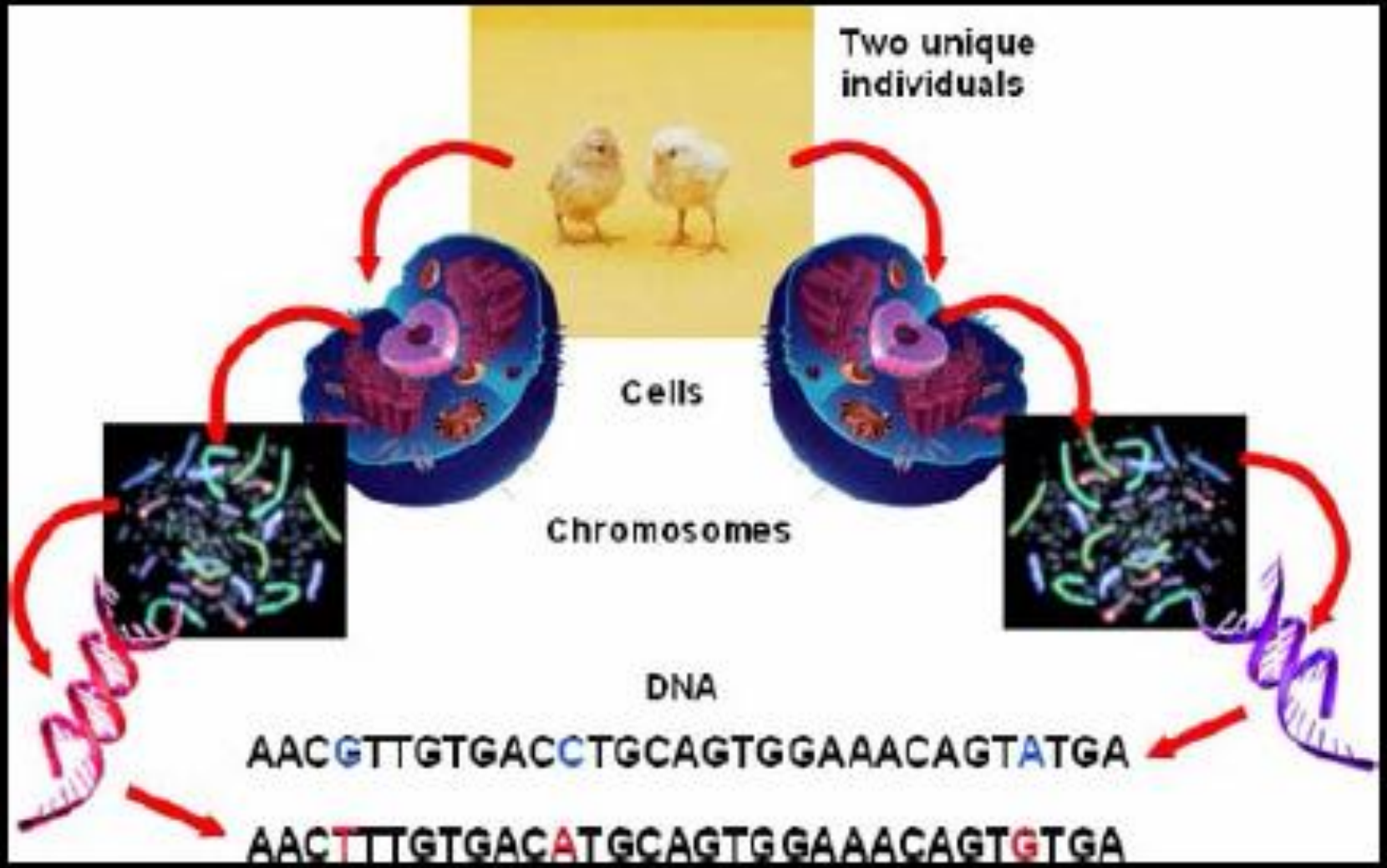
The Sanger Centre

DNA sequence of all human beings is 99.9% identical

- Our DNAs differ by 0.1%.
- Does it make a difference ? Yes

0.1% difference translates into 3 million separate "spelling" differences in a genome of 3 billion bases

Small variations in genotype can make big differences to phenotype (1.24%)

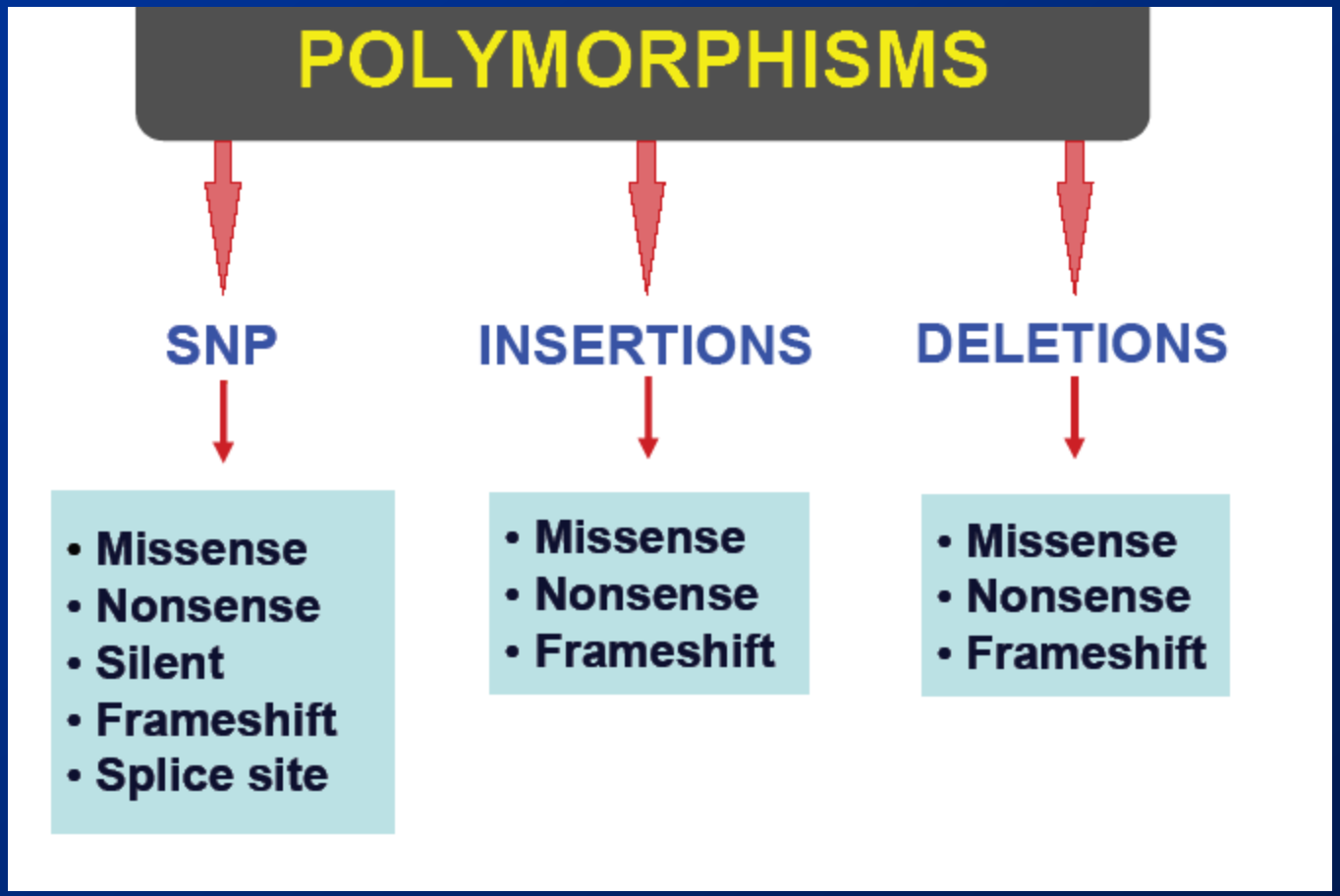

Two unique individuals
Cells
Chromosomes
DNA
AACGTTGTGACCTGCAGTGGAAACAGTATGA
AACTTTGTGACATGCAGTGGAAACAGTGTGA

definitions

- Polymorphism : a variation in nucleotide sequence at a given position in the genome, seen in the population at a frequency of 1% or higher

- Mutation : a change in nucleotide sequence which can occur in germ line cells or somatic cells. In germ line cells, mutations can be passed on to offspring who inherit the mutation. Mutations generally have a frequency of less than 1% in the population.

- Allele : the specific variant (nucleotide) of a polymorphism at a single locus on a chromosome; for example A, C, G or T


POLYMORPHISMS
SNP
INSERTIONS
DELETIONS
• Missense
• Nonsense
• Silent
• Frameshift
• Splice site
• Missense
• Nonsense
• Frameshift
• Missense
• Nonsense
• Frameshift

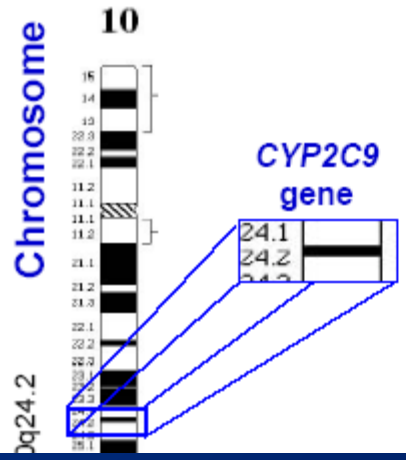
Single nucleotide polymorphisms (SNP)

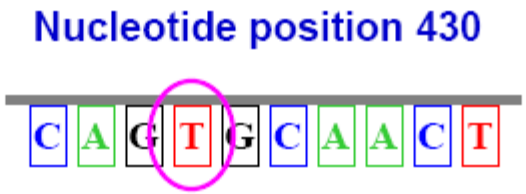
……..G G **T** A A C T T G ……

……..G G **C** A A C T T G ……

- **Most common, Incidence 1 per 300 - 600bp**

Example:

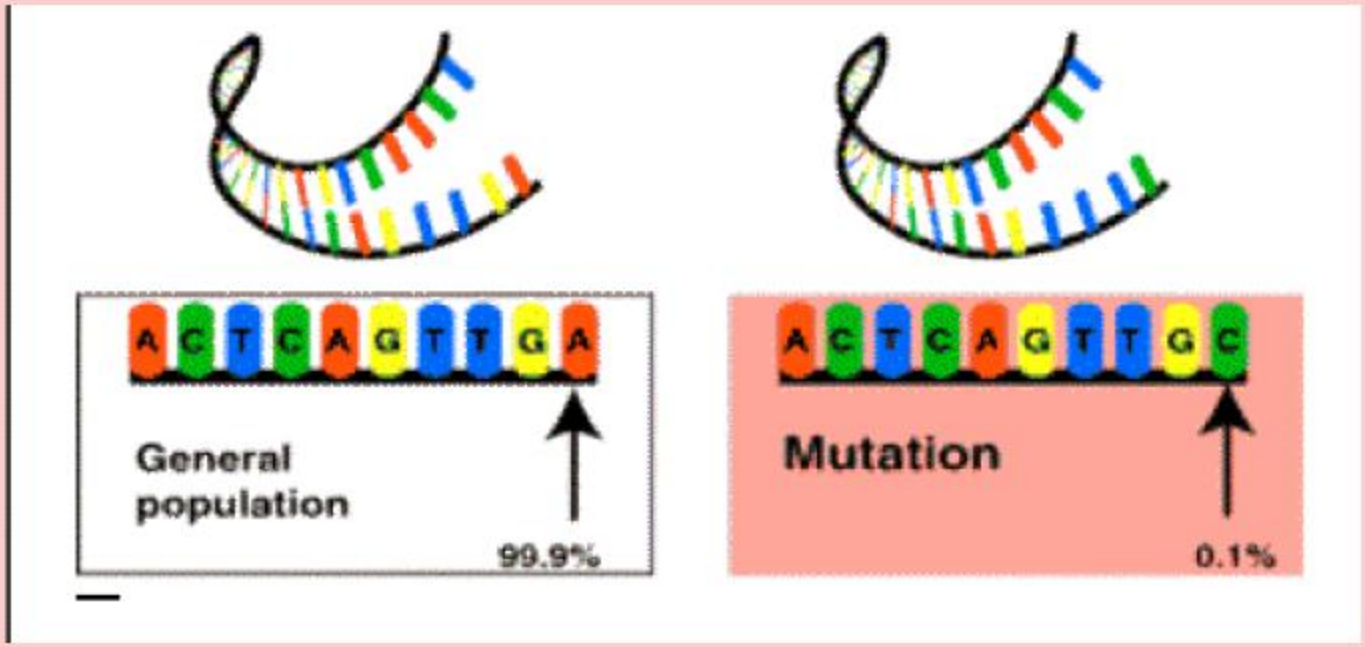




CYP2C9*2

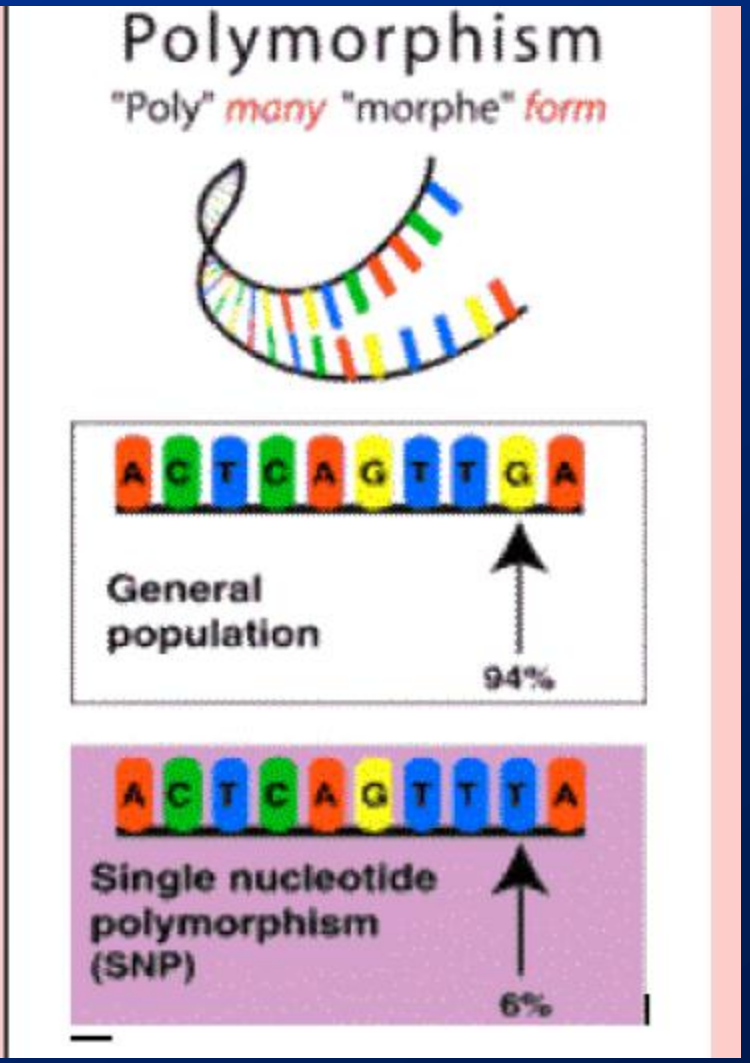
Decreased enzyme activity

Mutation


A C T C A G T T G A
General population
99.9%
A C T C A G T T G C
Mutation
0.1%

SNPs

(pronounced snips)



Mendelian Traits in Humans

Recessive phenotype: Albinism

Dominant phenotype: Achondroplasia

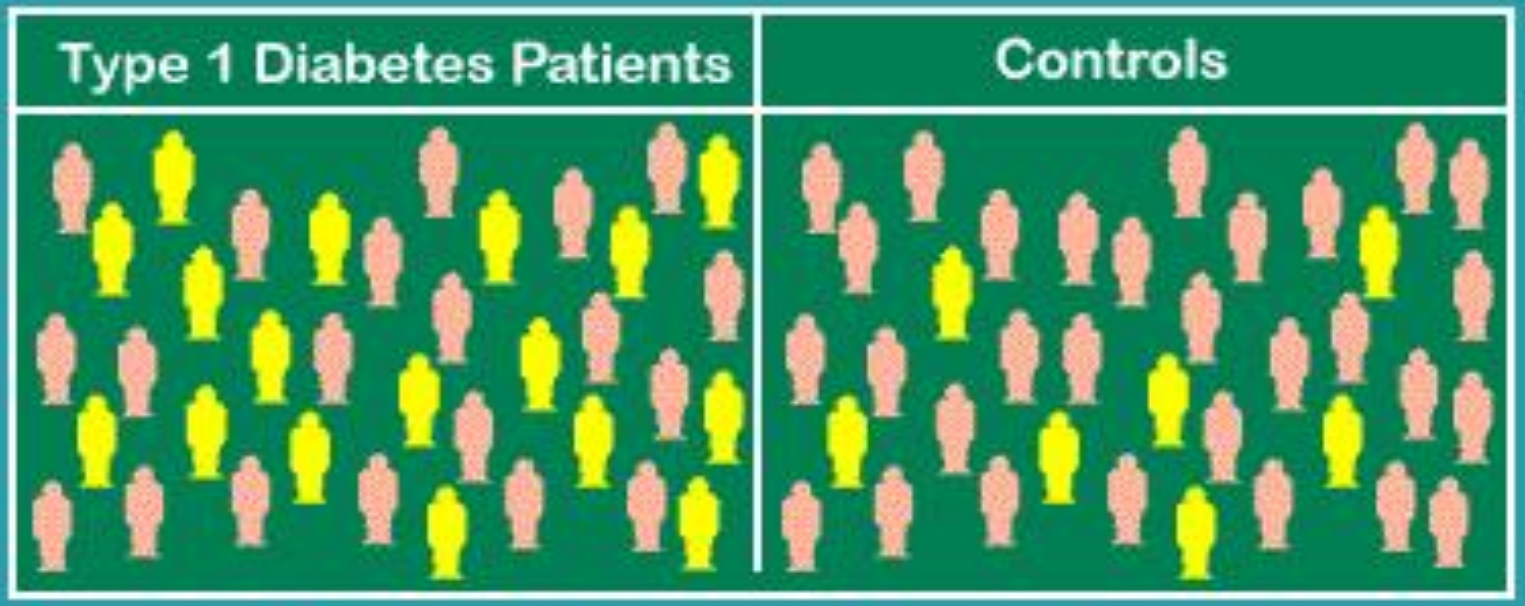
- However, common Multifactorial disorders result from polymorphisms in multiple genes, often coupled with environmental causes. The complicated bases of these diseases make them difficult to study and to treat. Heart disorder, diabetes and cancer are examples of this type of disorder.

- **SNPs may fall within coding sequences of genes, non-coding regions of genes, or in the intergenic regions between genes. SNPs within a coding sequence will not necessarily change the aminoacid sequence of the protein that is produced, due to degeneracy of the genetic code. A SNP in which both forms lead to the same polypeptide sequence is termed *synonymous* - if a different polypeptide sequence is produced they are *non-synonymous*.**

- **Variations in the DNA sequences of humans can affect how humans develop diseases and respond to pathogens, chemicals, drugs, vaccines, and other agents. However, their greatest importance in biomedical research is for comparing regions of the genome between cohorts (such as with matched cohorts with and without a disease).**

- **Genetic association studies**

Association Studies



Genotype	Type 1	Controls	Total
HLA DR4	17	7	24
NON-HLA DR4	20	30	50
	37	37	

$X^2_{.05} = 5.377$

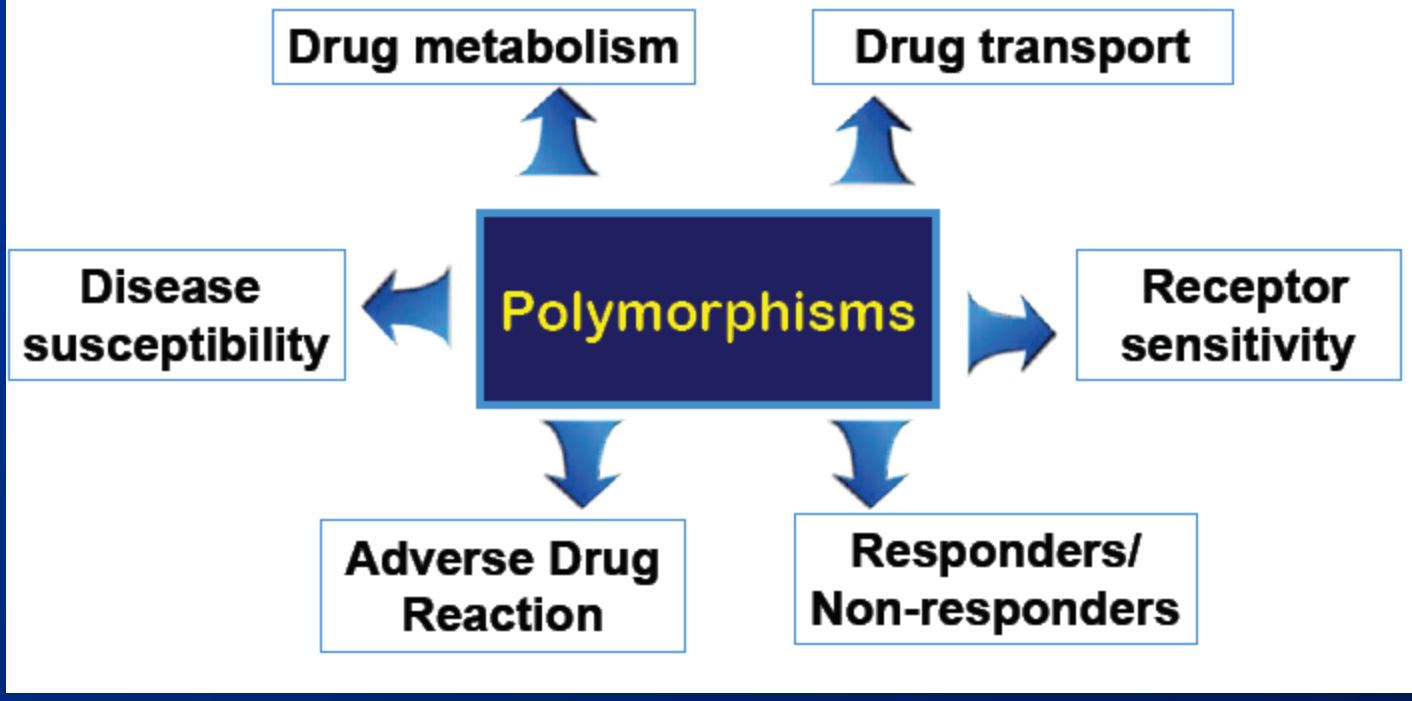
$p < 0.025$

Odds Ratio: 3.6
95% CI = 1.3 to 10.4

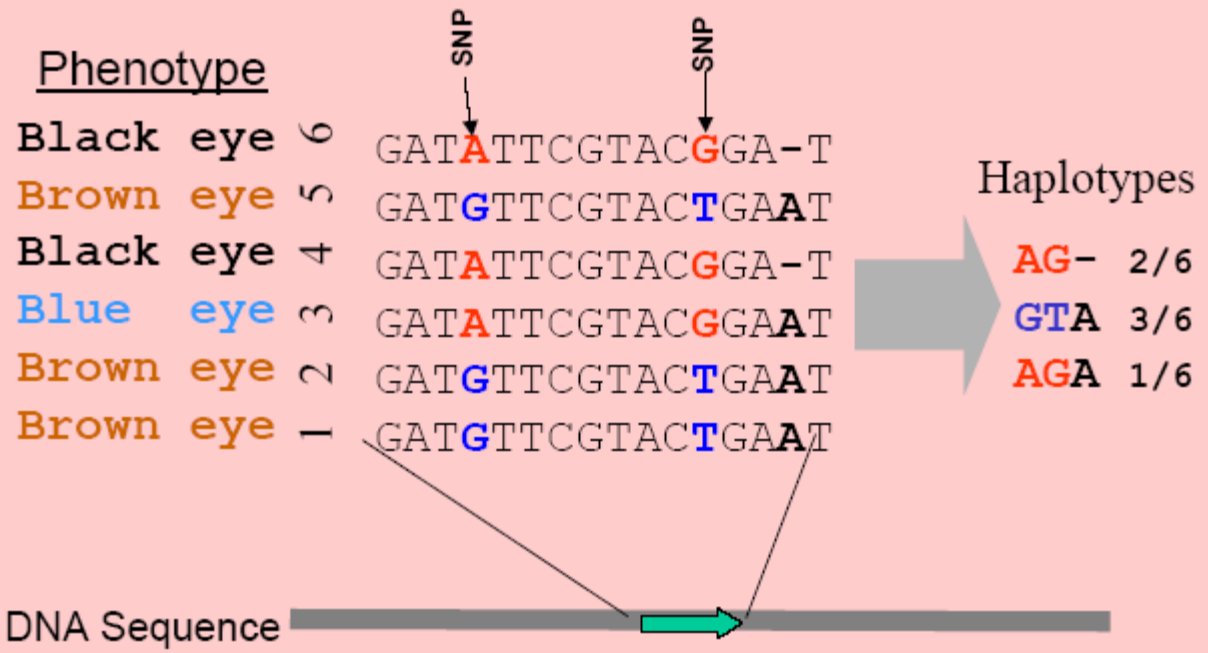
= HLA DR4

= non-HLA DR4

Consequences of polymorphisms



From SNP to Haplotype

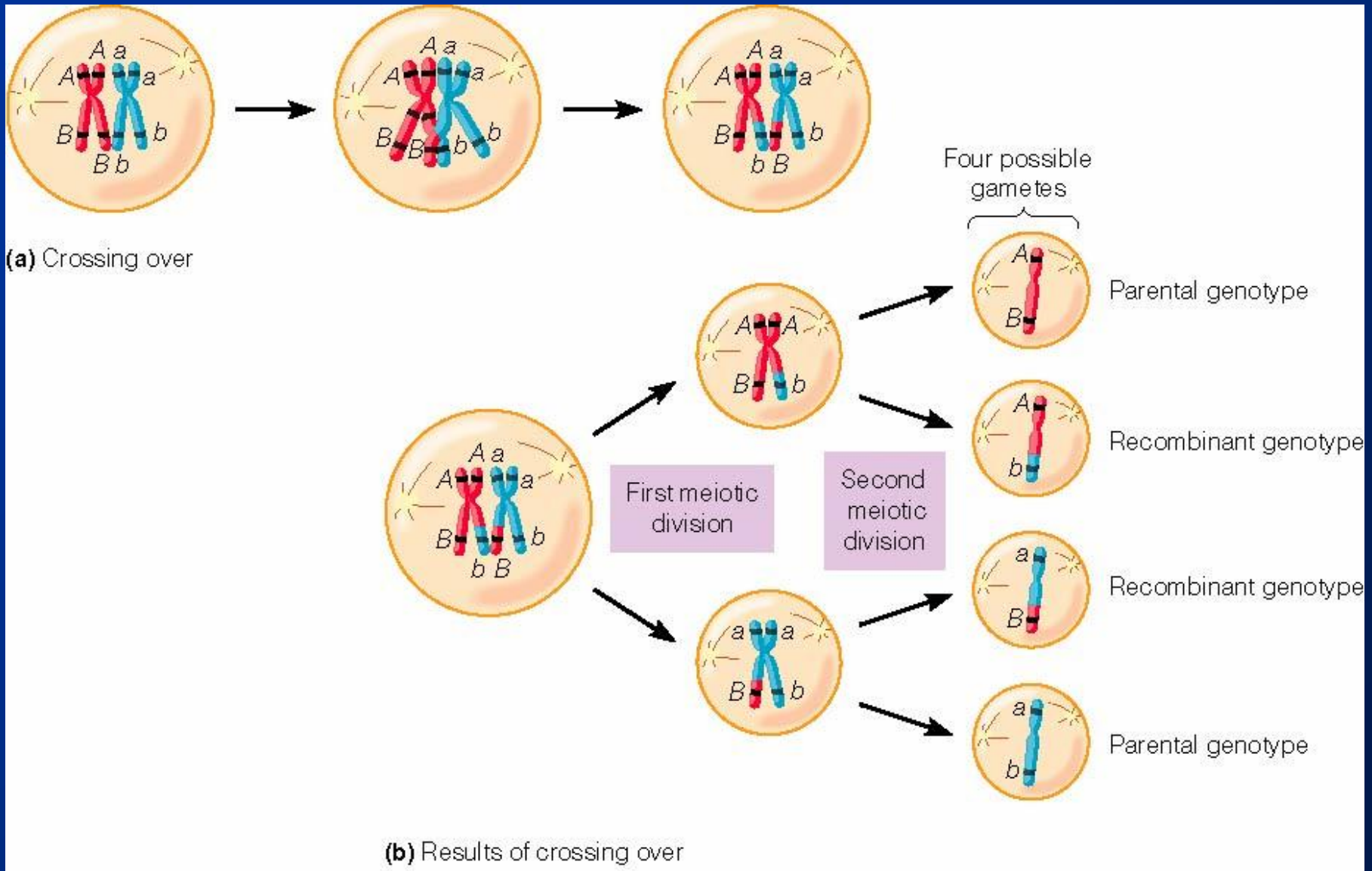


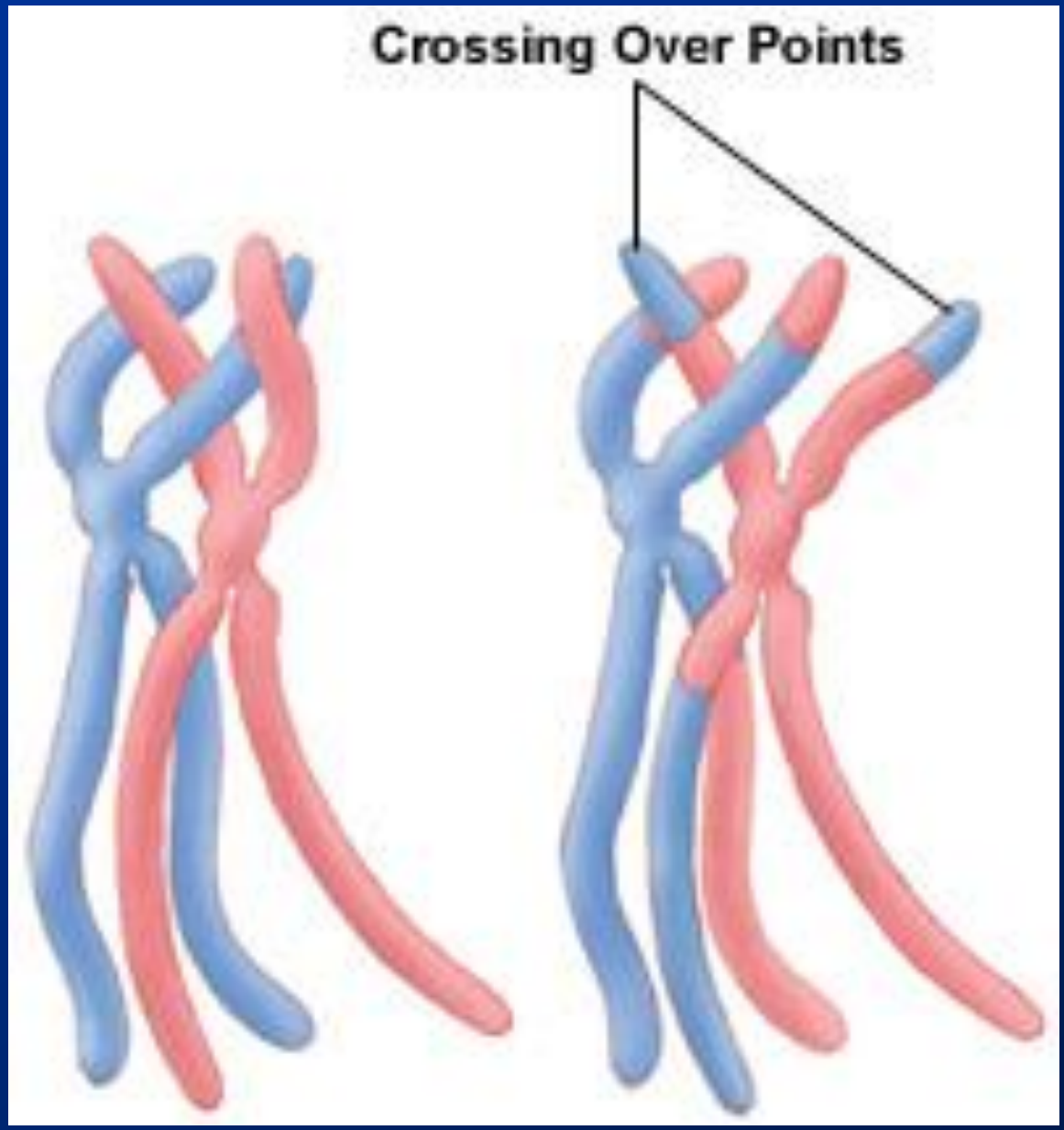
- Haplotype : the combination of two or more alleles at physically neighbouring positions within the genome

Haplotype

- Haplotype: A set of closely linked genetic markers present on one chromosome which tend to be inherited together (not easily separable by recombination).

Set of SNP polymorphisms: a SNP haplotype

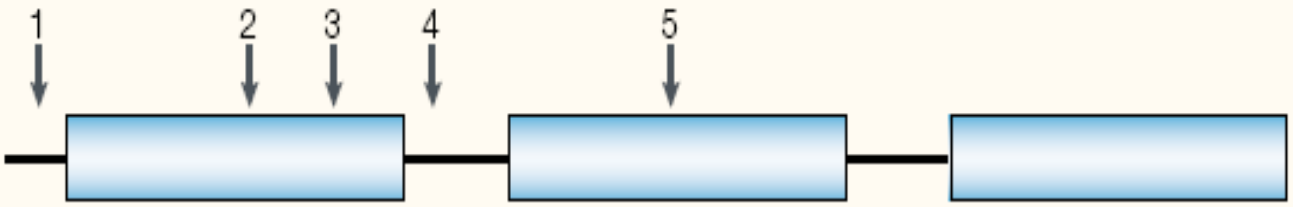



Crossing Over Points

Linkage disequilibrium

- The occurrence together on the same chromosome of specific alleles at closely linked loci more frequently than would be expected by chance. Because linkage disequilibrium is a function of the distance between loci, it can be used to help infer the order of genes on chromosomes.

- LD metrics: D, r^2, LOD



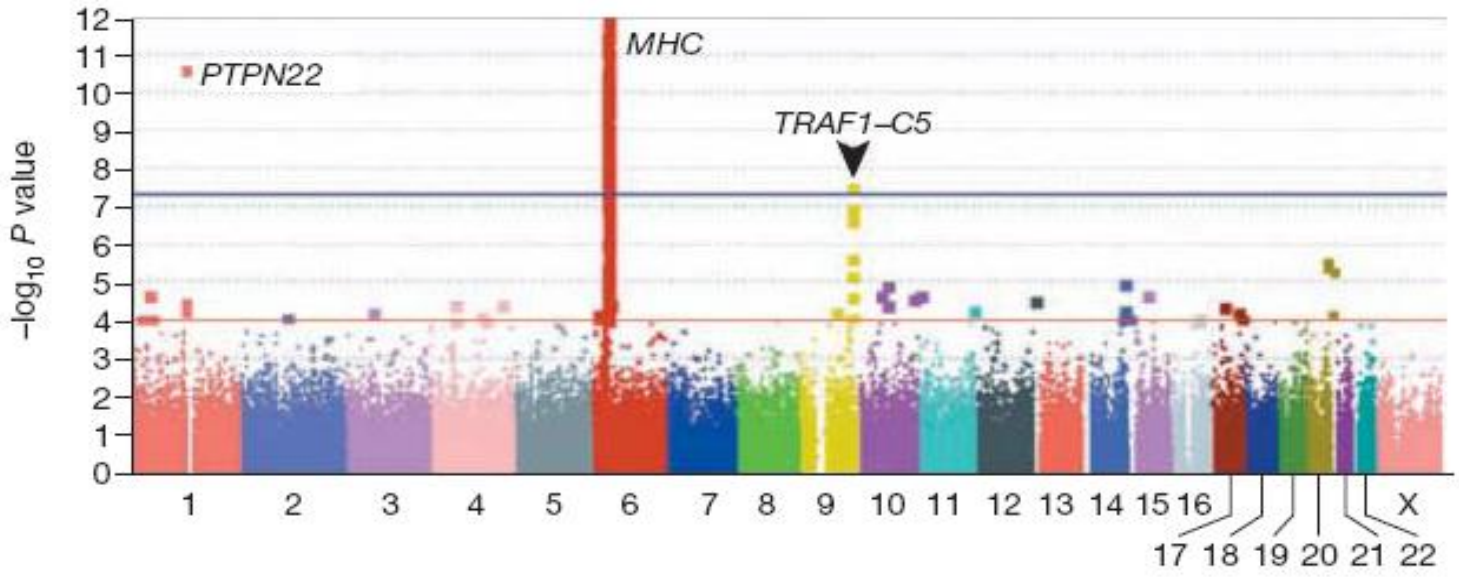
SNP1	C/T	Promoter
SNP2	A/G	Non-synonymous
SNP3	A/T	Synonymous
SNP4	T/G	Deep intronic
SNP5	A/C	Non-synonymous

Two major haplotypes SNPs 1–4			
SNP1	SNP2	SNP3	SNP4
C	A	A	T
T	G	T	G

Figure 1 | **Haplotypes and linkage disequilibrium in single-nucleotide-polymorphism selection.** Single-nucleotide polymorphisms (SNPs) 1–4 are in linkage disequilibrium and form two common haplotypes, which can be characterized by any of the variants. Therefore, it is only necessary to determine the genotype of one of the SNPs to capture the information about all four SNPs. SNP5 is not in linkage disequilibrium with SNPs 1–4 and is not part of the haplotype, but it might still contribute independently to the risk of the phenotype.

Genome wide association studies

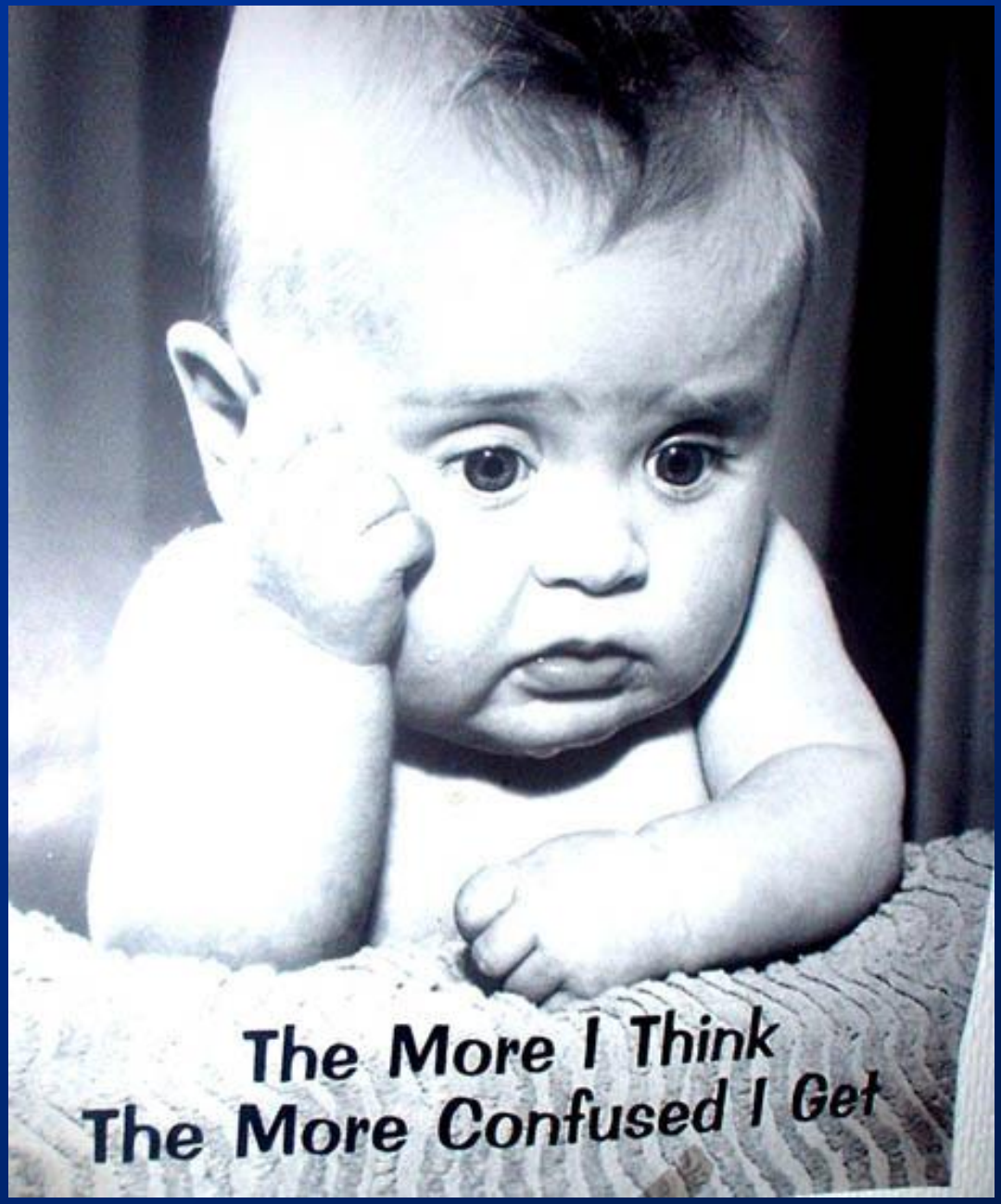
Figure 3. Genome-wide Association Findings in Rheumatoid Arthritis



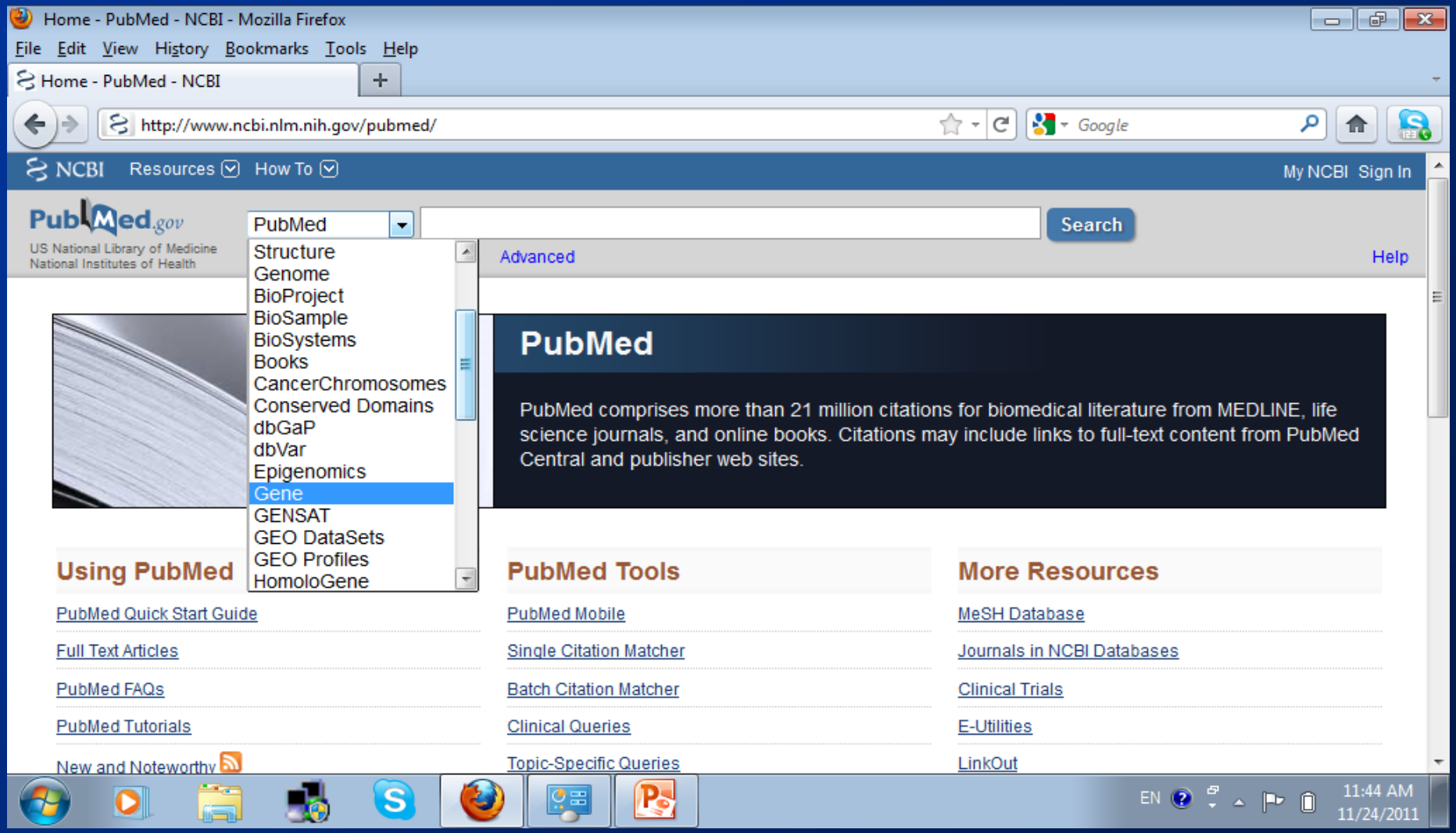
Genome-wide association studies assume a priori hypotheses about candidate genes or regions that might be associated with disease; rather, they test single-nucleotide polymorphisms (SNPs) throughout the genome for possible evidence of genetic susceptibility. Associations plotted as $-\log_{10} P$ values for a genome-wide association study in 1522 cases with rheumatoid arthritis and 1850 controls, showing single data points for SNPs with $P < 10^{-4}$ (lower horizontal red line) for 22 autosomes and the X chromosome. The predefined level of significance, at 5×10^{-8} is shown with a horizontal blue line. SNPs at *PTPN22* on chromosome 1, the major histocompatibility comples (MHC) on chromosome 6, and the *TRAF1-C5* locus on chromosome 9 exceed this threshold. Reproduced with permission from Plenge et al.[47]

Overview

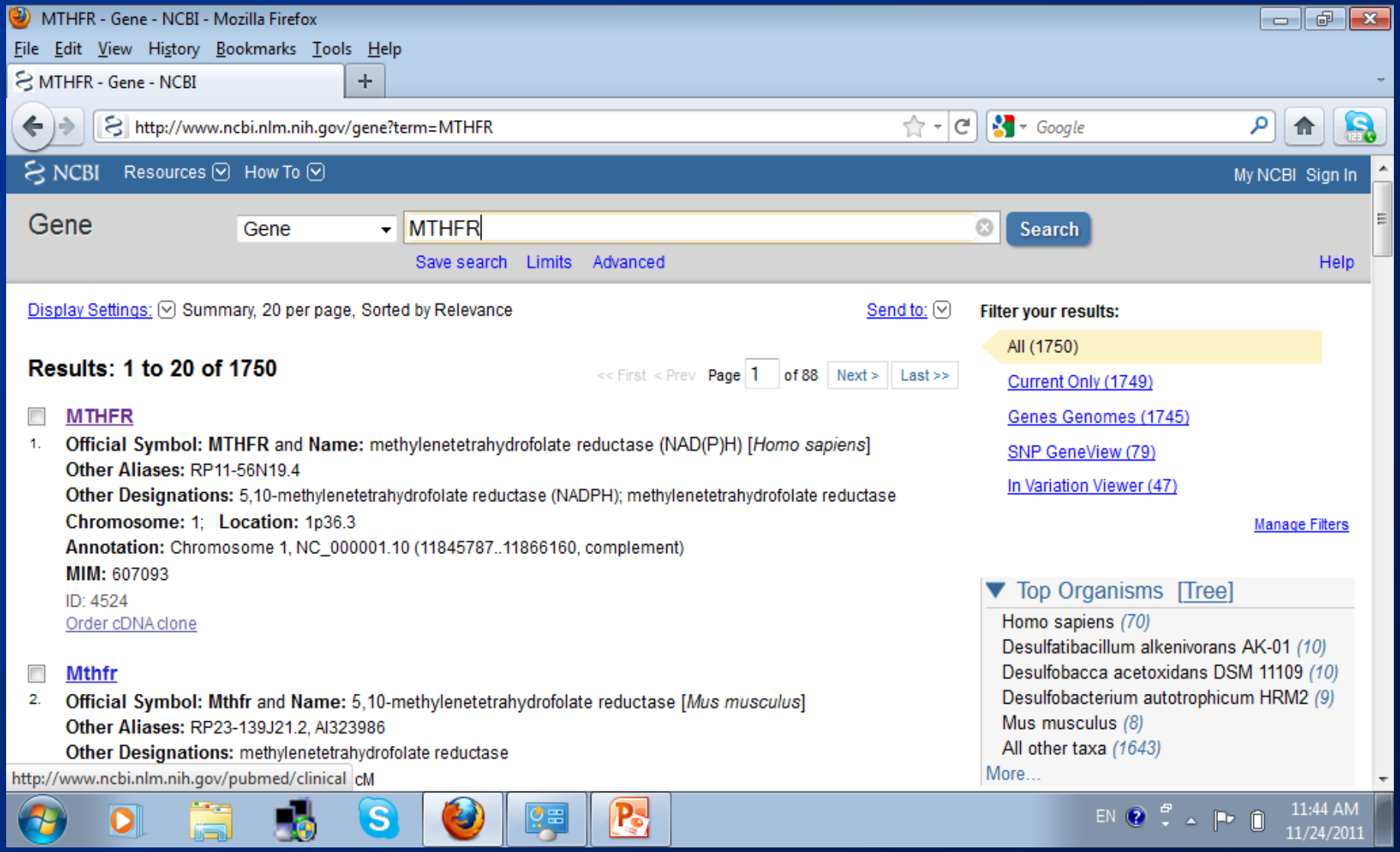
- Gene
- Polymorphism
- Mutation
- Genetic association studies
- Haplotype
- Linkage disequilibrium
- Genome-wide association studies


The More I Think
The More Confused I Get

Example: MTHFR gene. Go to PubMed (www.pubmed.com) and type MTHFR and search GENE



Click MTHFR for Homo Sapiens



Available information regarding :Summary, Genomic regions, transcripts, Genomic context, Bibliography, Interactions, General gene information General protein information, Reference Sequences, Related Sequences

MTHFR methylenetetrahydrofolate reductase (NAD(P)H) [Homo sapiens] - Gene - NCBI - Mozilla Firefox

File Edit View History Bookmarks Tools Help

MTHFR methylenetetrahydrofolate redu...

http://www.ncbi.nlm.nih.gov/gene/4524

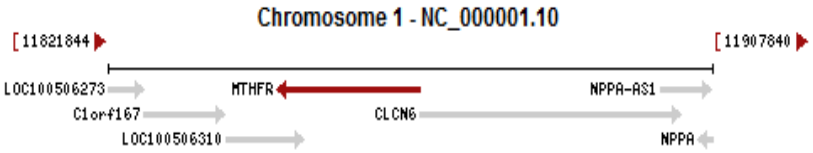
Google

Genomic context

Location: 1p36.3

See MTHFR in Epigenomics, MapViewer

Sequence: Chromosome: 1; NC_000001.10 (11845787..11866160, complement)

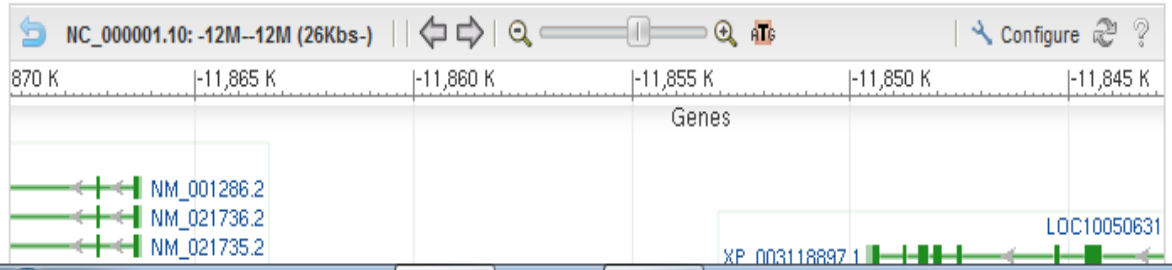


Genomic regions, transcripts, and products

Genomic Sequence NC_000001 chromosome 1 reference GRCh37.p5 Prim

Go to reference sequence details

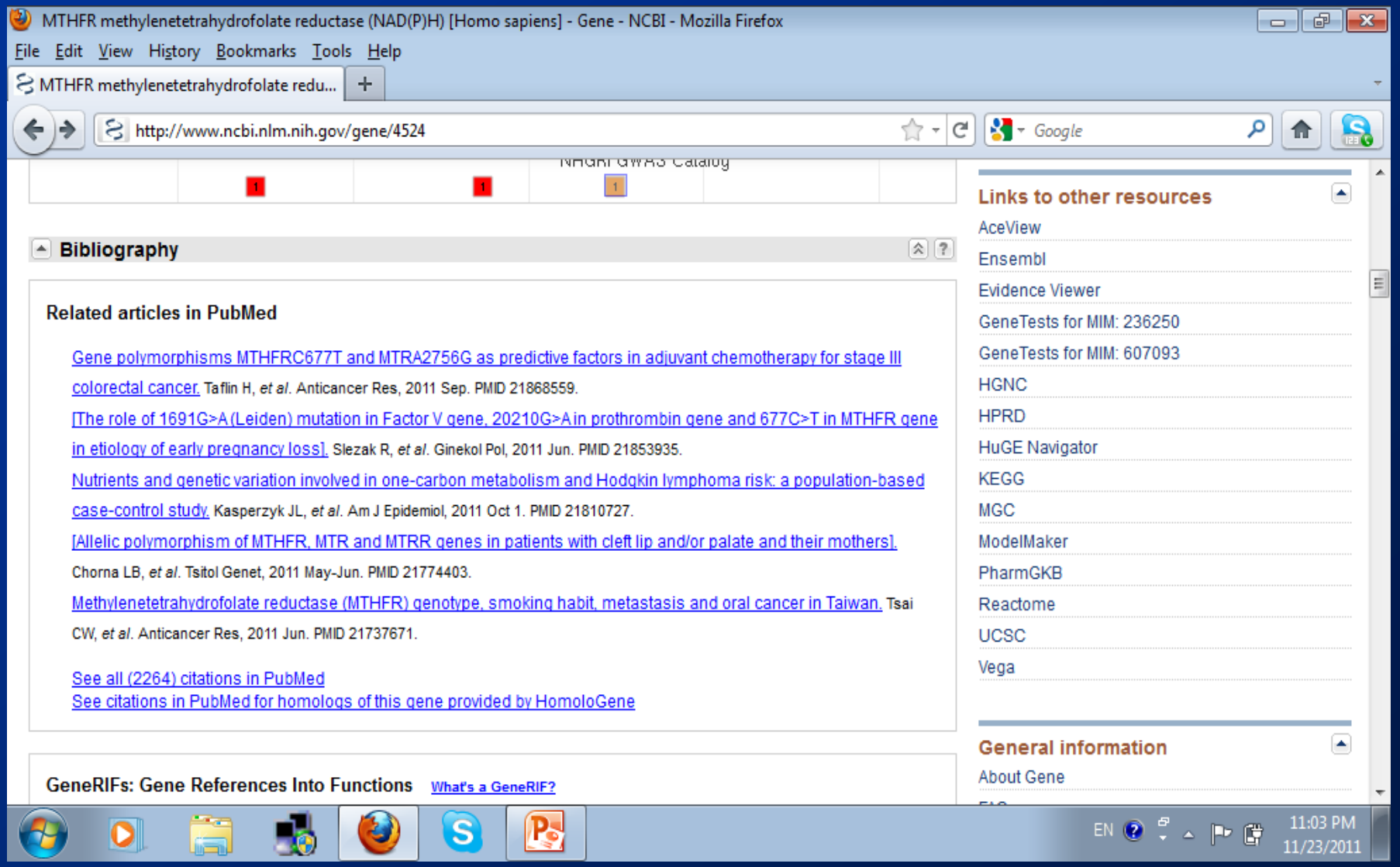
Go to nucleotide Graphics FASTA GenBank



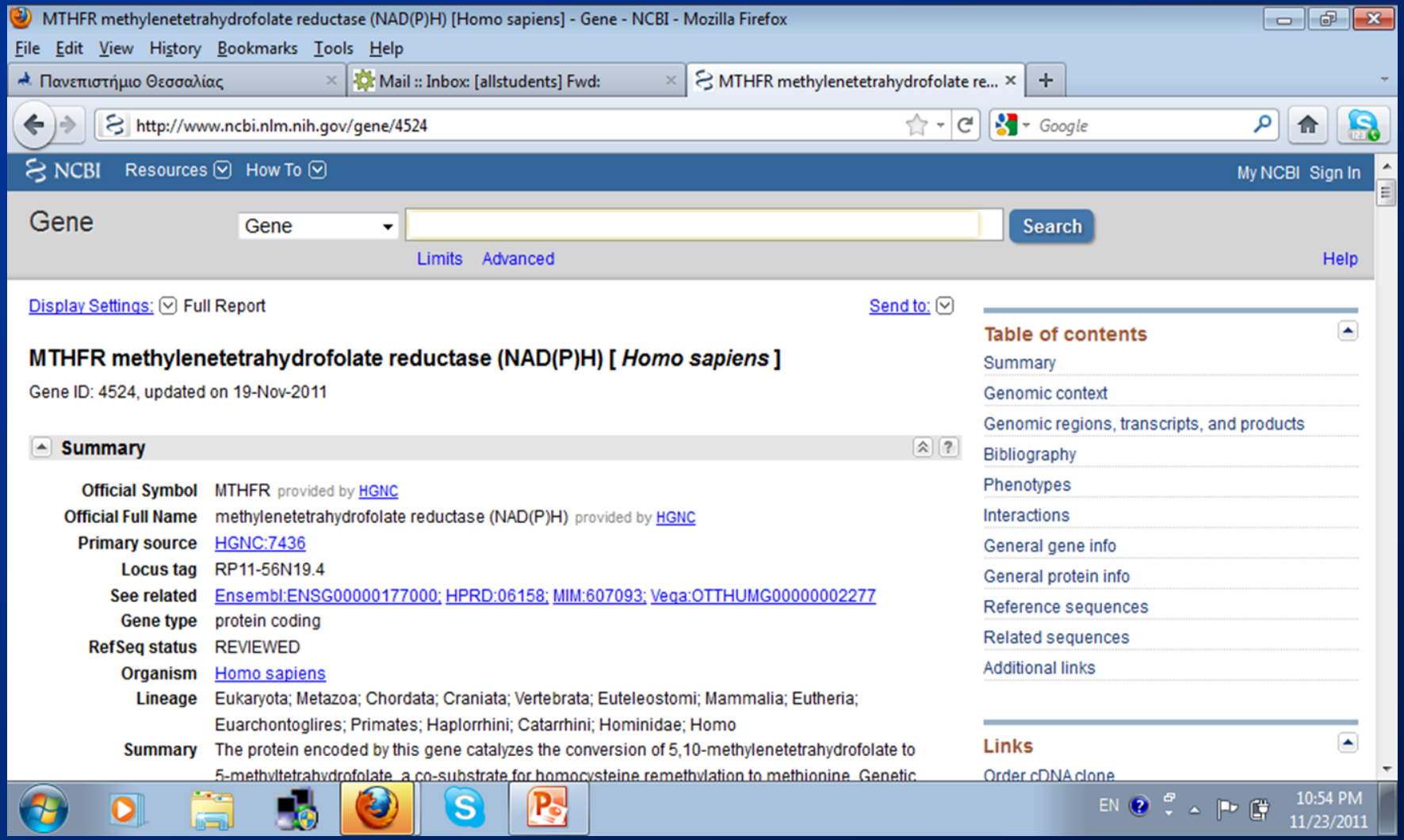
- Books
- CCDS
- Conserved Domains
- dbVar
- EST
- Full text in PMC
- Genome
- GEO Profiles
- HomoloGene
- Map Viewer
- Nucleotide
- OMIM
- Probe
- Protein
- PubChem Compound
- PubChem Substance
- PubMed
- PubMed (GeneRIF)
- PubMed (OMIM)
- RefSeq Proteins

EN 11:04 PM 11/23/2011

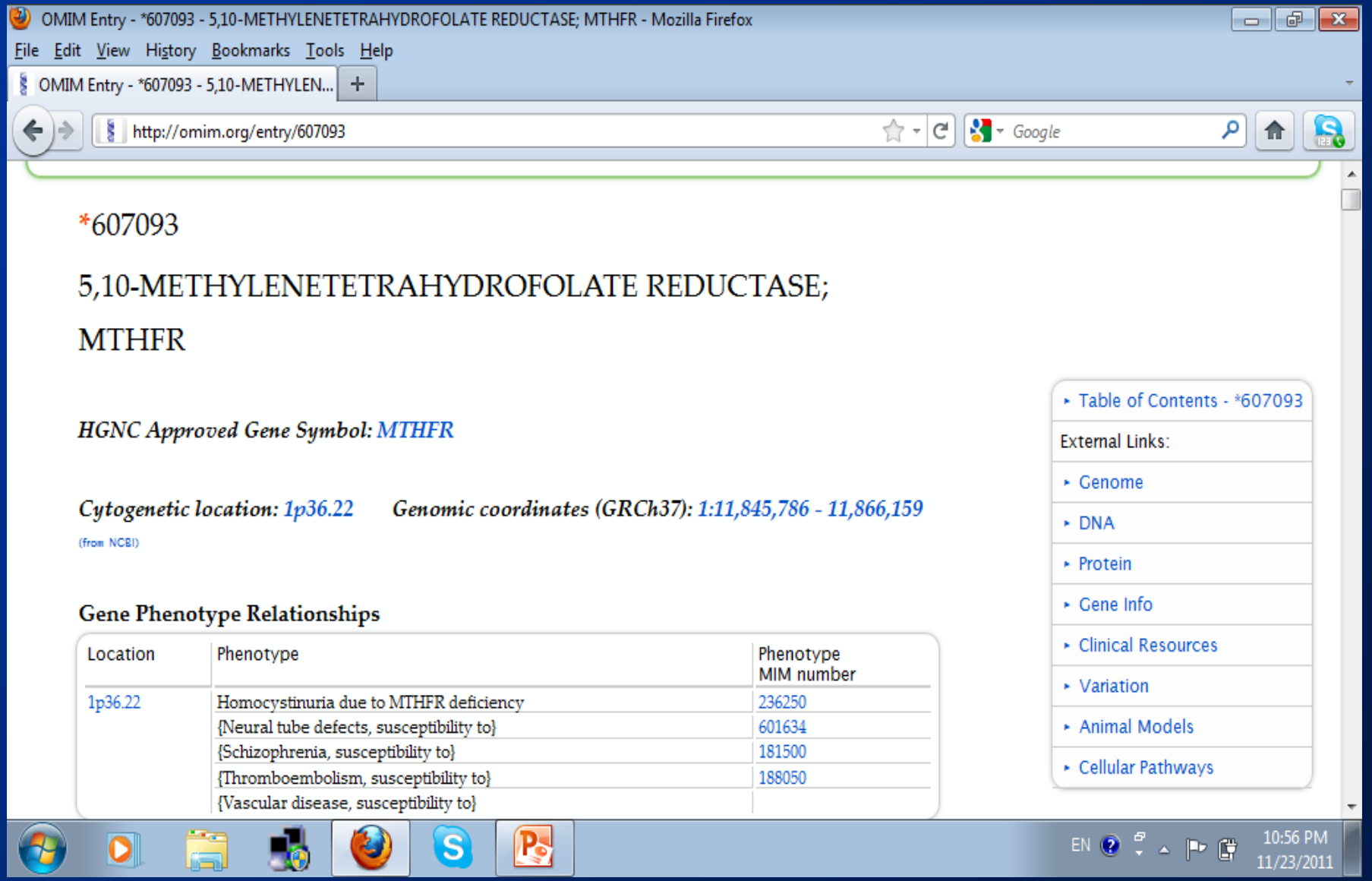
Have a look to the references from PubMed…and how the gene and its SNPs are named in the literature…



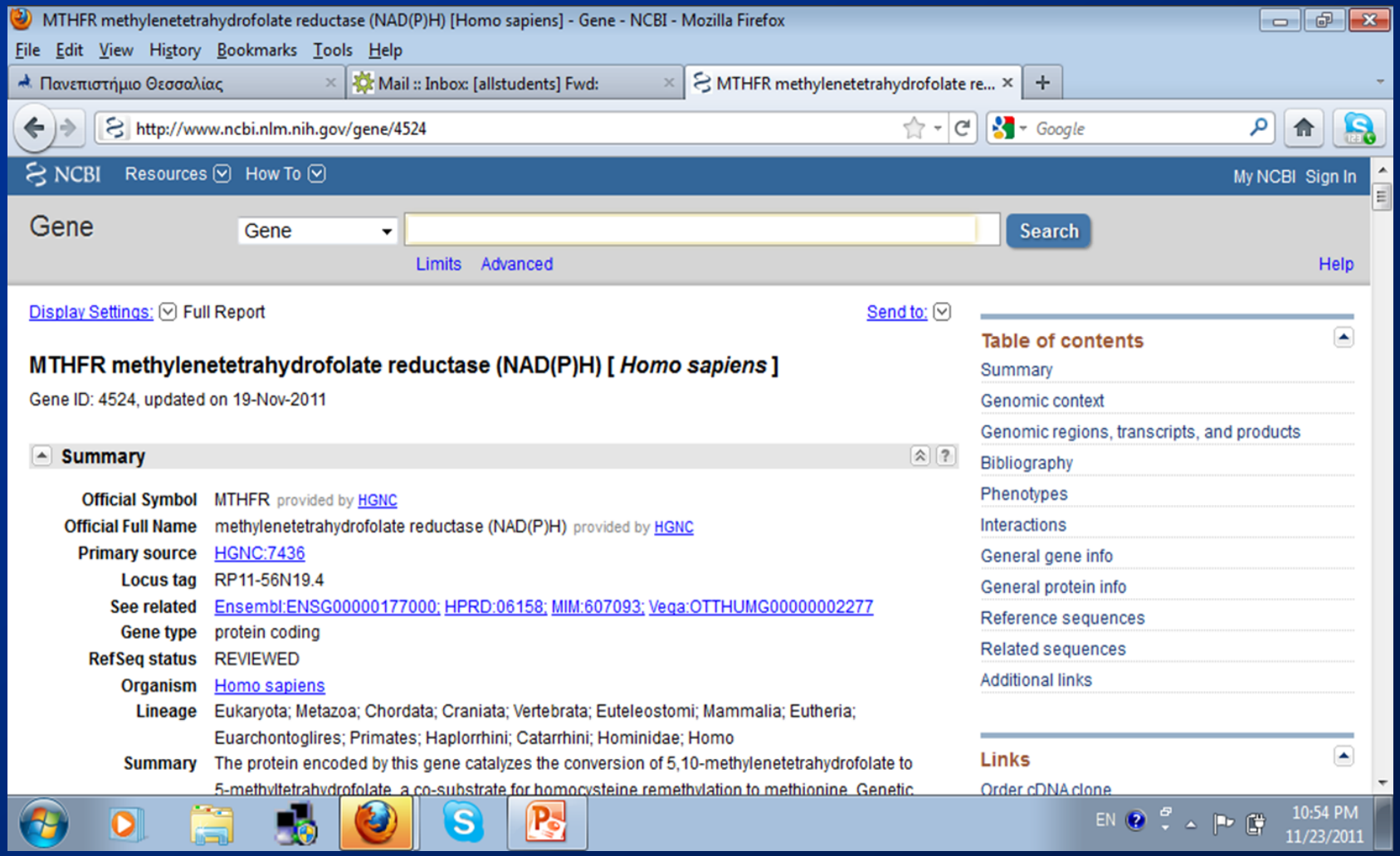
click on the link MIM 607093, hyperlink to OMIM database



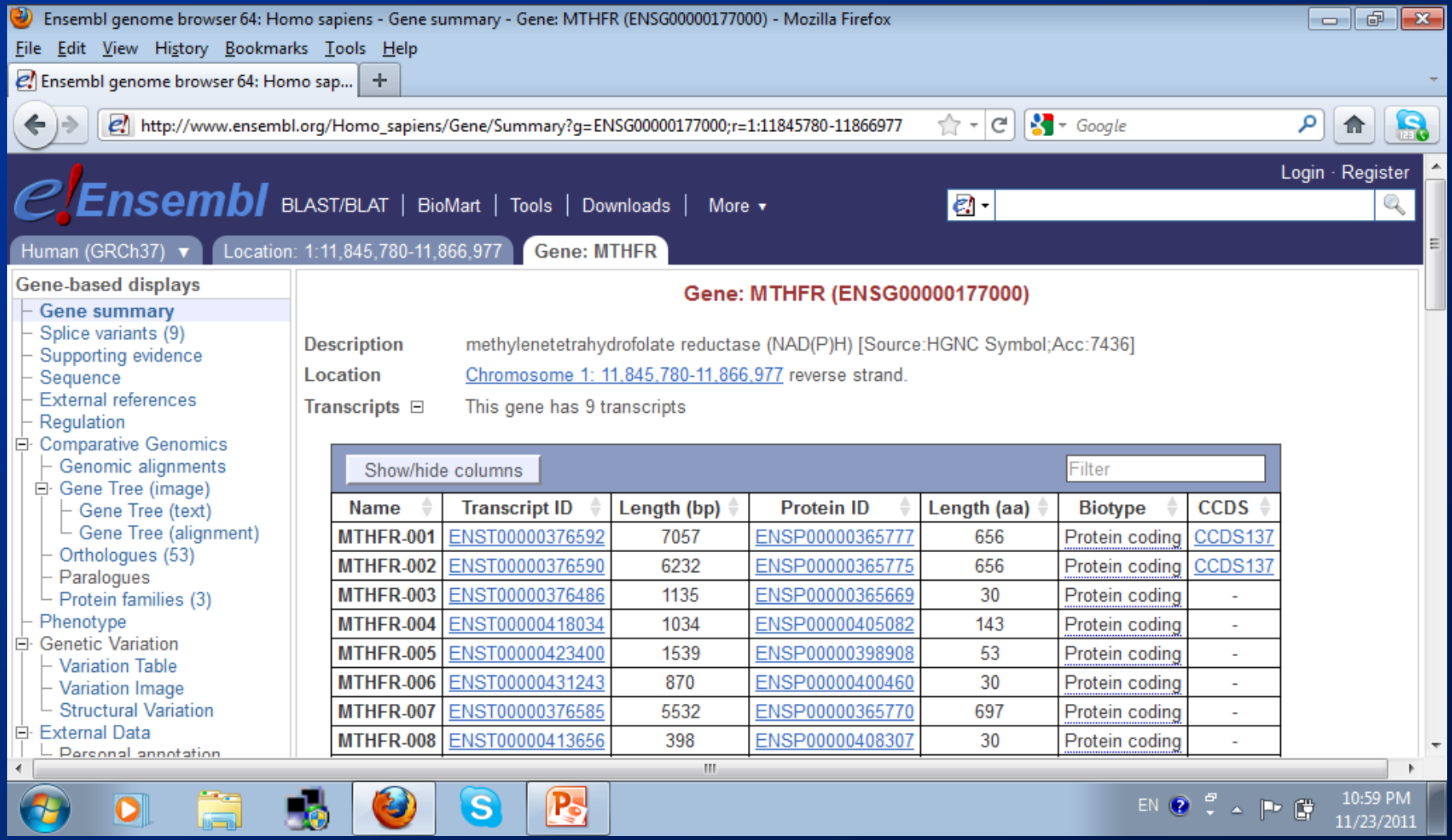
High quality description of the gene in text format

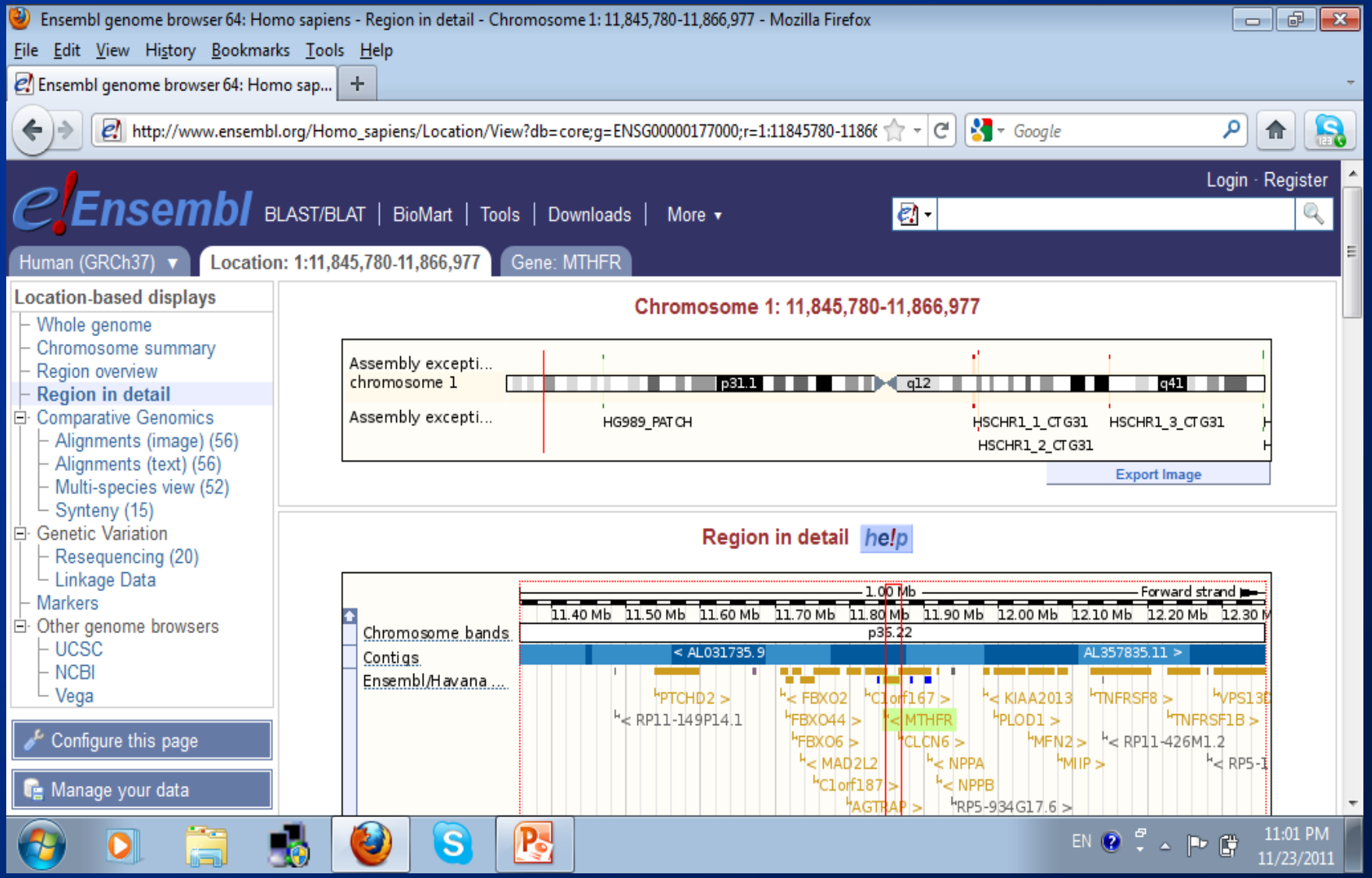


Back to GENE, click on ENSEMBL link



Detailed description of the gene with many bioinformatic tools. Click on the location link to view its location…




Ensembl genome browser 64: Homo sapiens - Region in detail - Chromosome 1: 11,845,780-11,866,977 - Mozilla Firefox
File Edit View History Bookmarks Tools Help
Ensembl genome browser 64: Homo sap...
http://www.ensembl.org/Homo_sapiens/Location/View?db=core;g=ENSG00000177000;r=1:11845780-1186
Google
Login · Register
e!Ensembl
BLAST/BLAT | BioMart | Tools | Downloads | More
Human (GRCh37)
Location: 1:11,845,780-11,866,977
Gene: MTHFR
Location-based displays
Whole genome
Chromosome summary
Region overview
Region in detail
Comparative Genomics
Alignments (image) (56)
Alignments (text) (56)
Multi-species view (52)
Synteny (15)
Genetic Variation
Resequencing (20)
Linkage Data
Markers
Other genome browsers
UCSC
NCBI
Vega
Configure this page
Manage your data
Chromosome 1: 11,845,780-11,866,977
Assembly excepti...
chromosome 1
Assembly excepti...
p31.1
q12
q41
HG989_PATCH
HSCHR1_1_CTG31
HSCHR1_3_CTG31
HSCHR1_2_CTG31
Export Image
Region in detail
help
1.00 Mb
Forward strand
11.40 Mb
11.50 Mb
11.60 Mb
11.70 Mb
11.80 Mb
11.90 Mb
12.00 Mb
12.10 Mb
12.20 Mb
12.30 M
Chromosome bands
p35.22
Contigs
< AL031735.9
AL357835.11 >
Ensembl/Havana ...
PTCHD2 >
< RP11-149P14.1
< FBXO2
C1orf167 >
FBXO44 >
< MTHFR
FBXO6 >
CLCN6 >
< MAD2L2
< NPPA
C1orf187 >
< NPPB
AGTRAP >
RP5-934G17.6 >
< KIAA2013
PLOD1 >
MFN2 >
MIIP >
TNFRSF8 >
TNFRSF1B >
< RP11-426M1.2
EN
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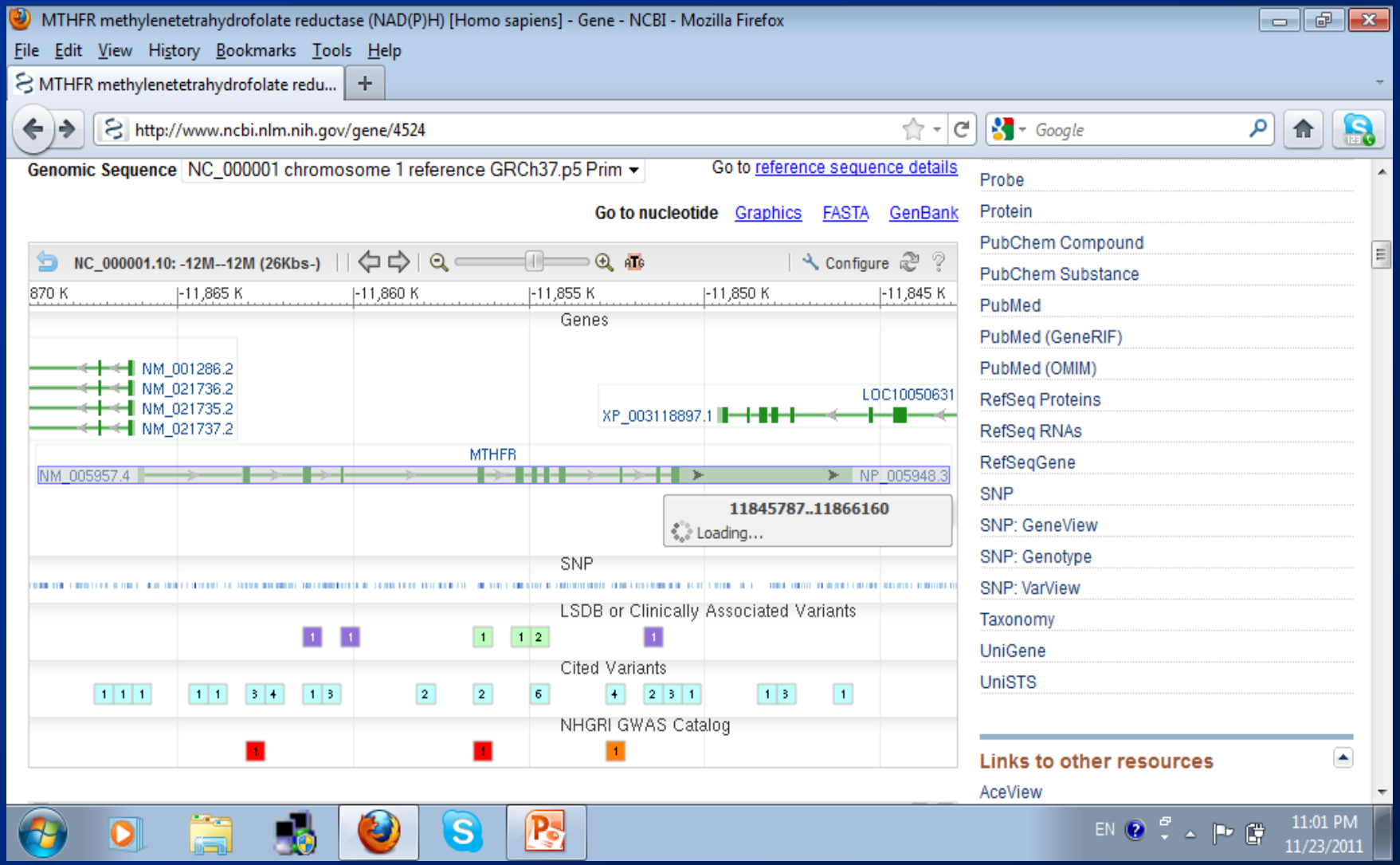
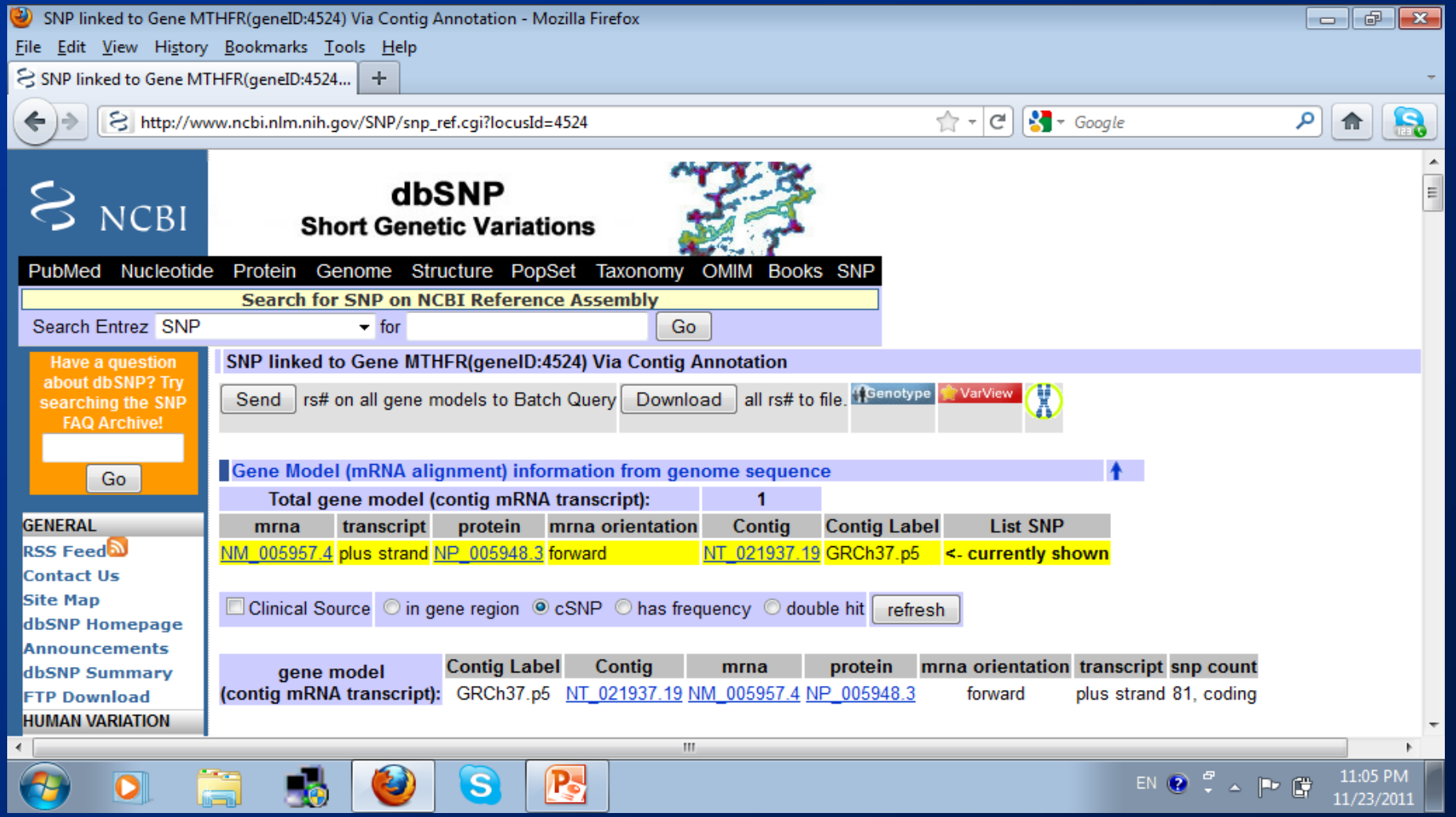
11/23/2011

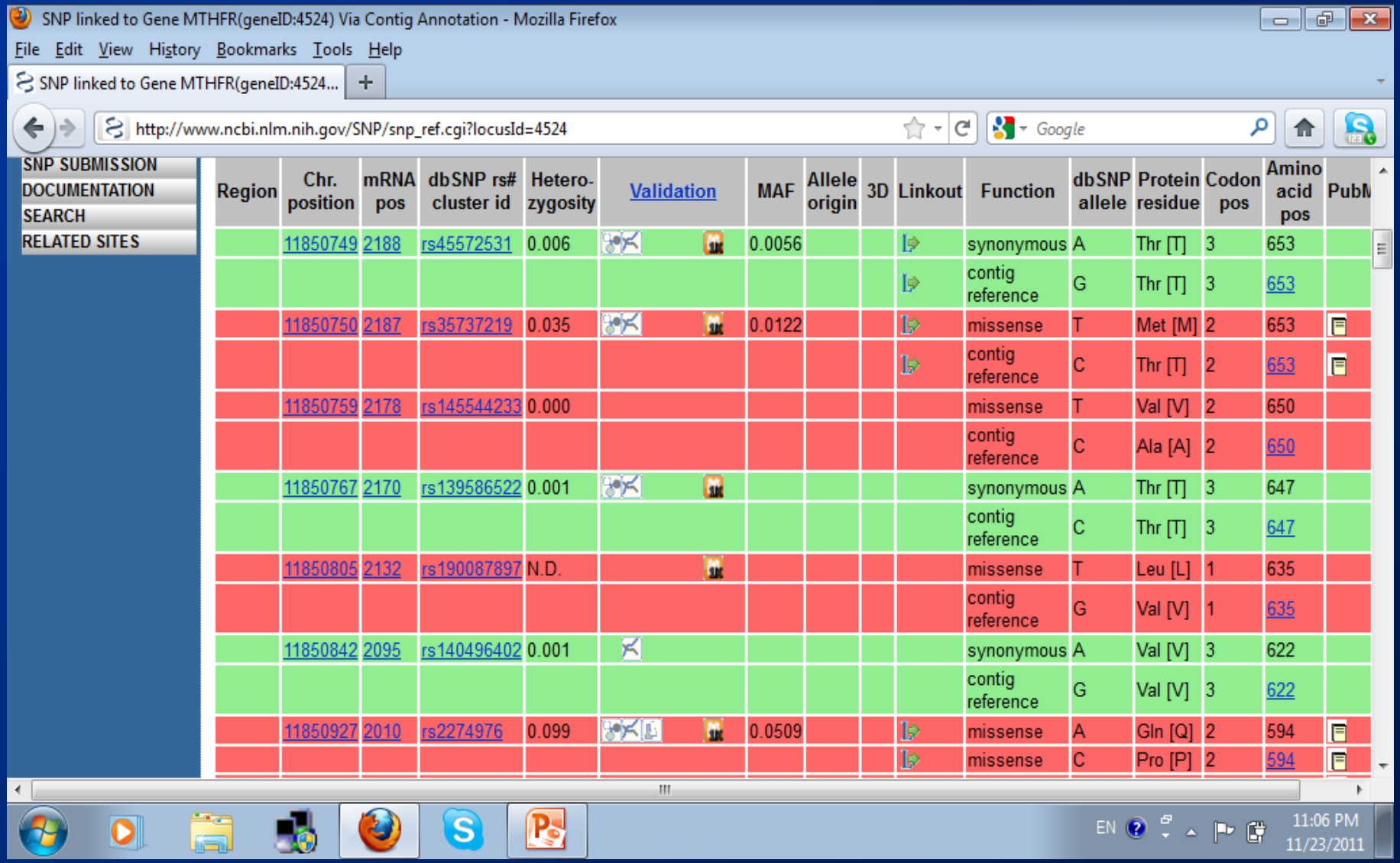
Back to GENE, click on SNP geneview, to search for MTHFR SNPs



dbSNP for MTHFR gene: all coding SNPs are shown (default)

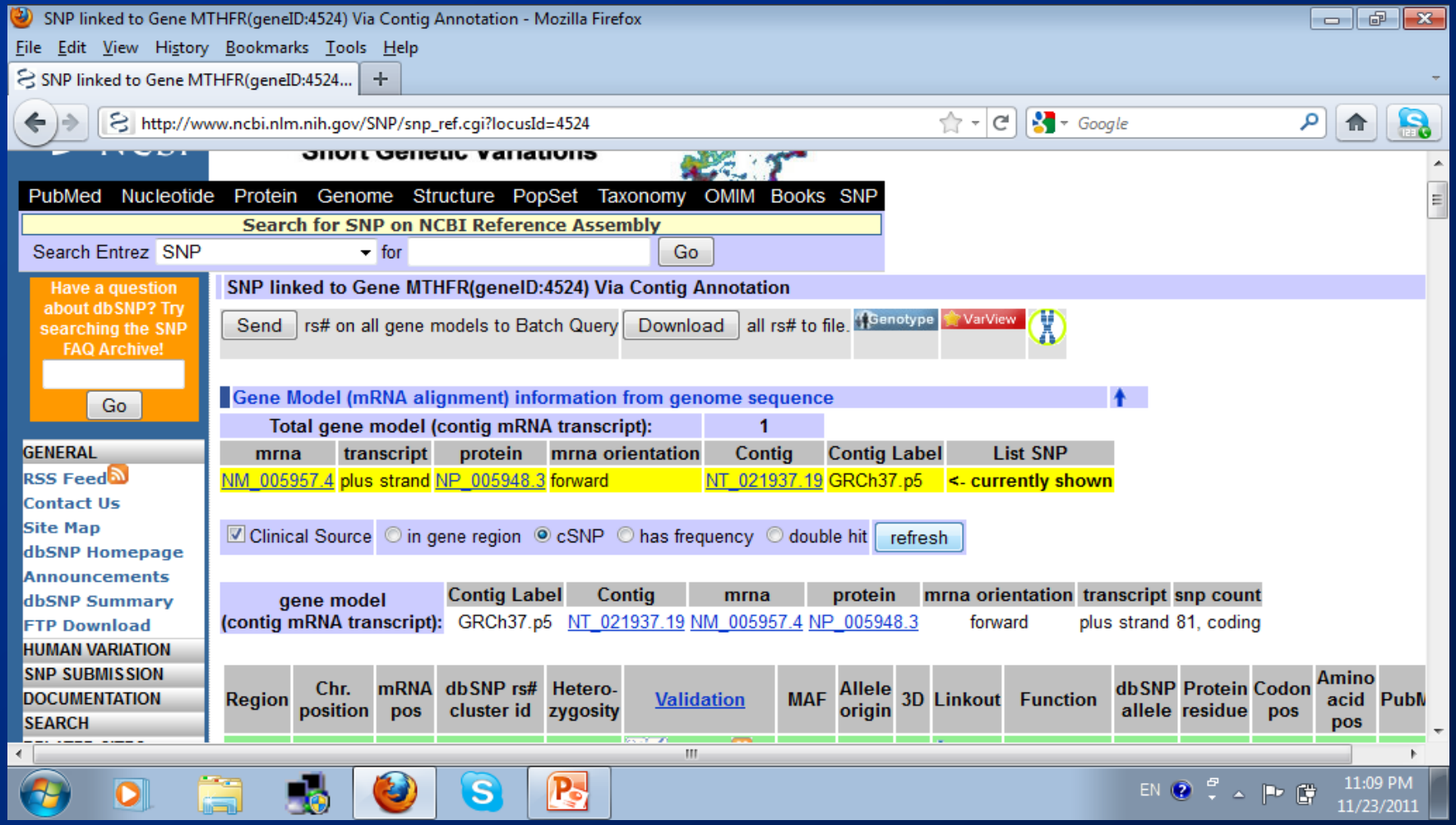


Scroll down…

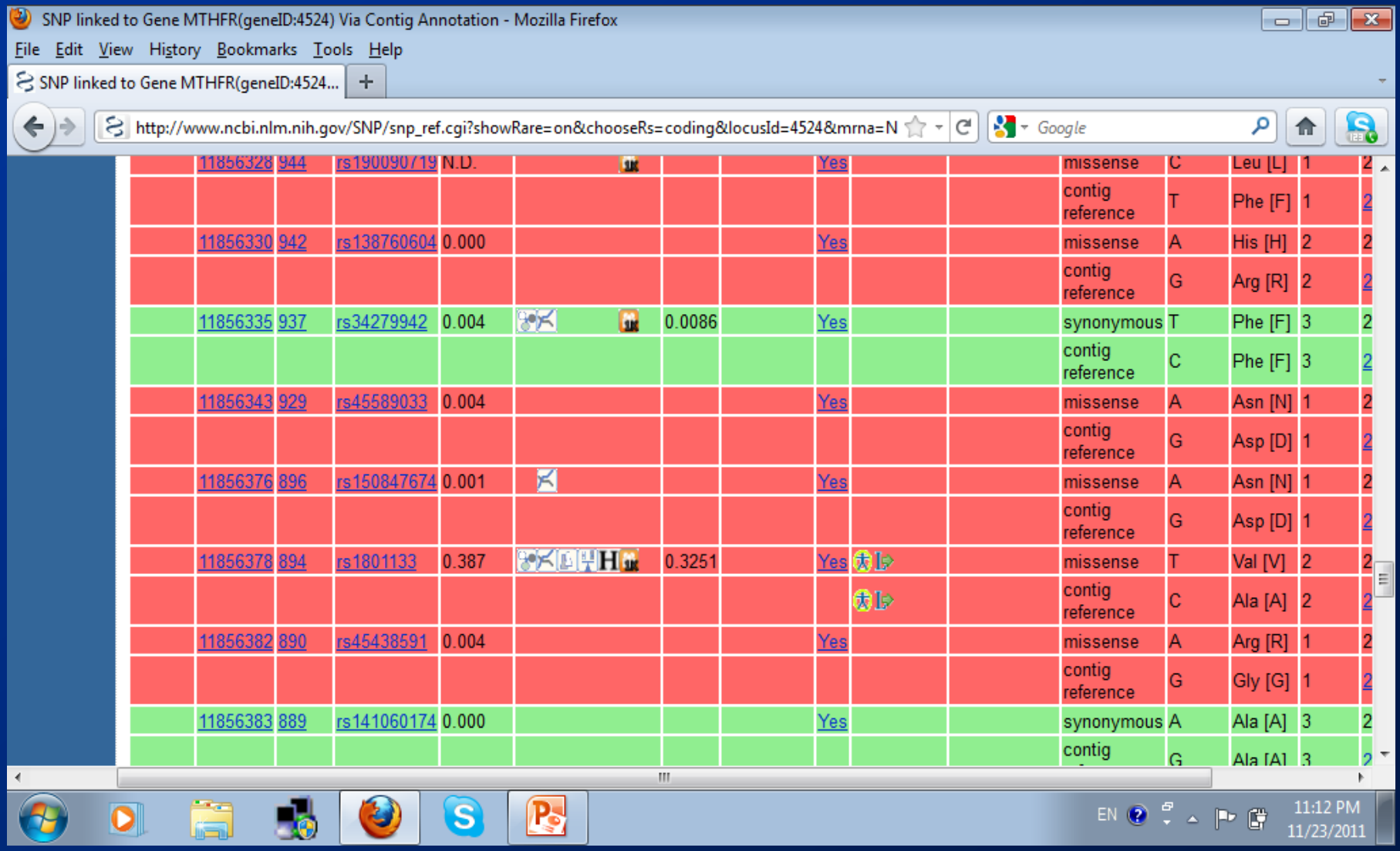


Region	Chr. position	mRNA pos	dbSNP rs# cluster id	Hetero-zygosity	Validation	MAF	Allele origin	3D	Linkout	Function	dbSNP allele	Protein residue	Codon pos	Amino acid pos	PubM
	11850749	2188	rs45572531	0.006		0.0056				synonymous	A	Thr [T]	3	653	
										contig reference	G	Thr [T]	3	653	
	11850750	2187	rs35737219	0.035		0.0122				missense	T	Met [M]	2	653	
										contig reference	C	Thr [T]	2	653	
	11850759	2178	rs145544233	0.000						missense	T	Val [V]	2	650	
										contig reference	C	Ala [A]	2	650	
	11850767	2170	rs139586522	0.001						synonymous	A	Thr [T]	3	647	
										contig reference	C	Thr [T]	3	647	
	11850805	2132	rs190087897	N.D.						missense	T	Leu [L]	1	635	
										contig reference	G	Val [V]	1	635	
	11850842	2095	rs140496402	0.001						synonymous	A	Val [V]	3	622	
										contig reference	G	Val [V]	3	622	
	11850927	2010	rs2274976	0.099		0.0509				missense	A	Gln [Q]	2	594	
										missense	C	Pro [P]	2	594	

From bibliography, we are interested for a SNP with a nucleotide change C677T resulting in aminoacid change Ala222Val. This SNP has been implicated with many disorders and we are interested in identifying its unique rs code. Tick include clinically sources and then click refresh

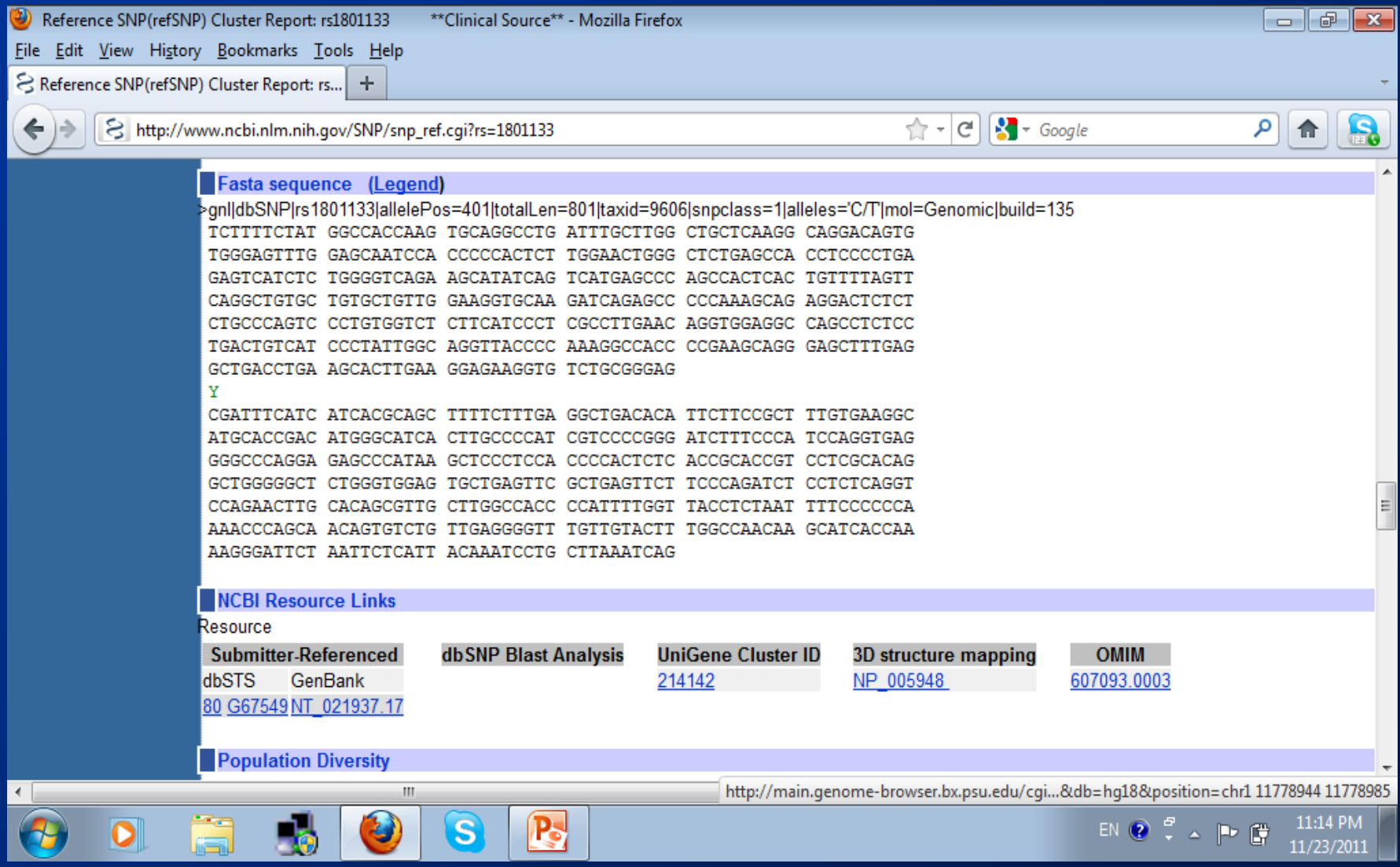


In exon 5, it is rs1801133. Click…

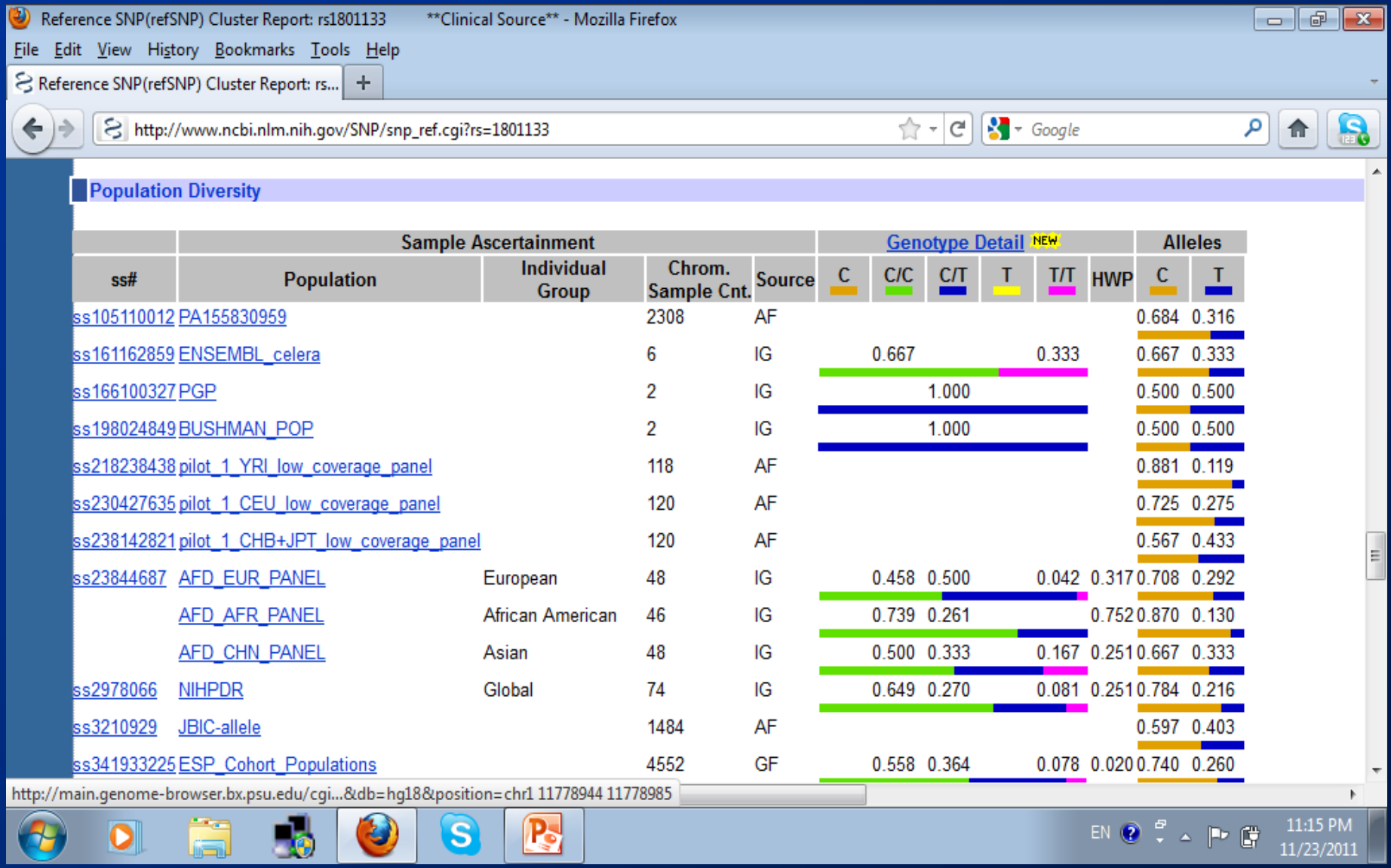


dbSNP for rs1801133

dbSNP for rs1801133



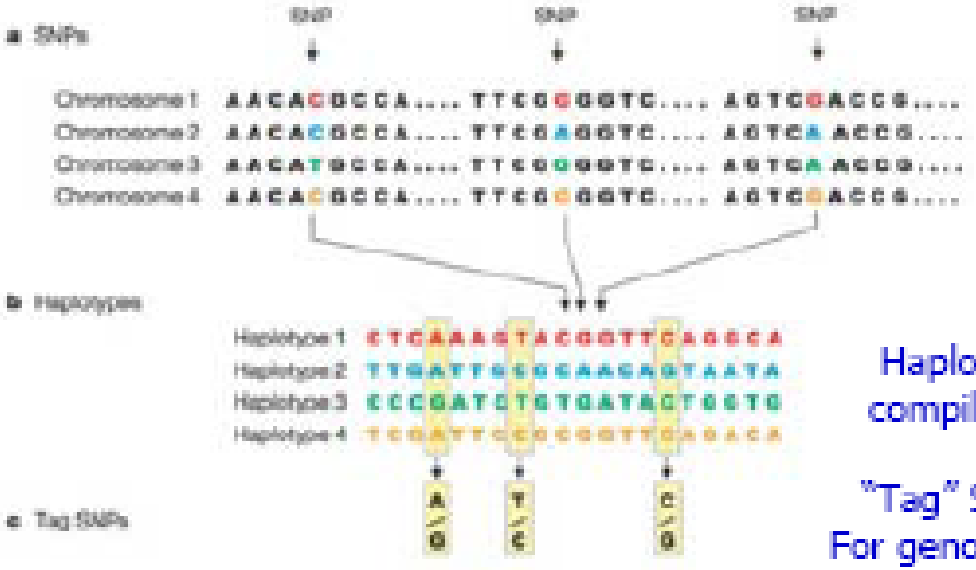
dbSNP for rs1801133



We are now interested to see the haplotype structure of the gene. Is our SNP in LD with other SNPs? Type www.hapmap.org

International HapMap Project

- A catalog of common genetic variants that occur in human beings.
  - what these variants are
  - where they occur in our DNA
  - how they are distributed among people within populations and among populations in different parts of the world

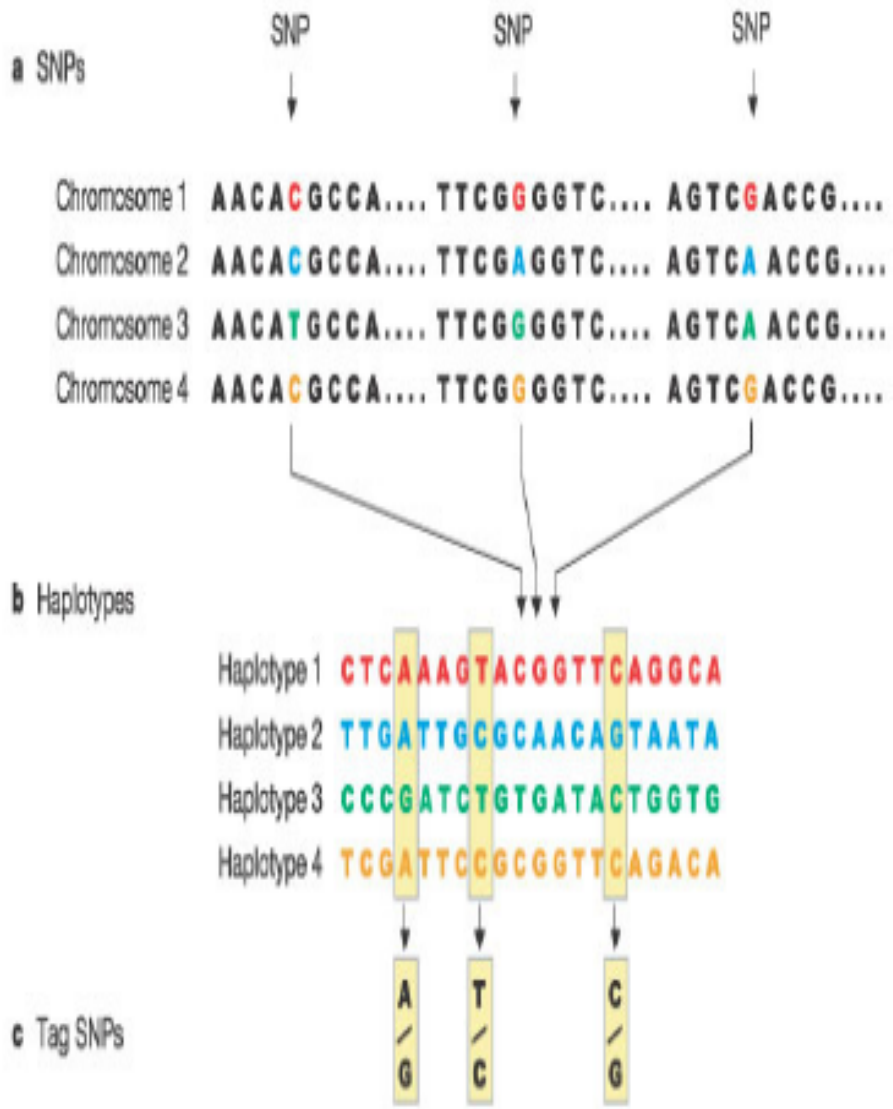


SNPs identification

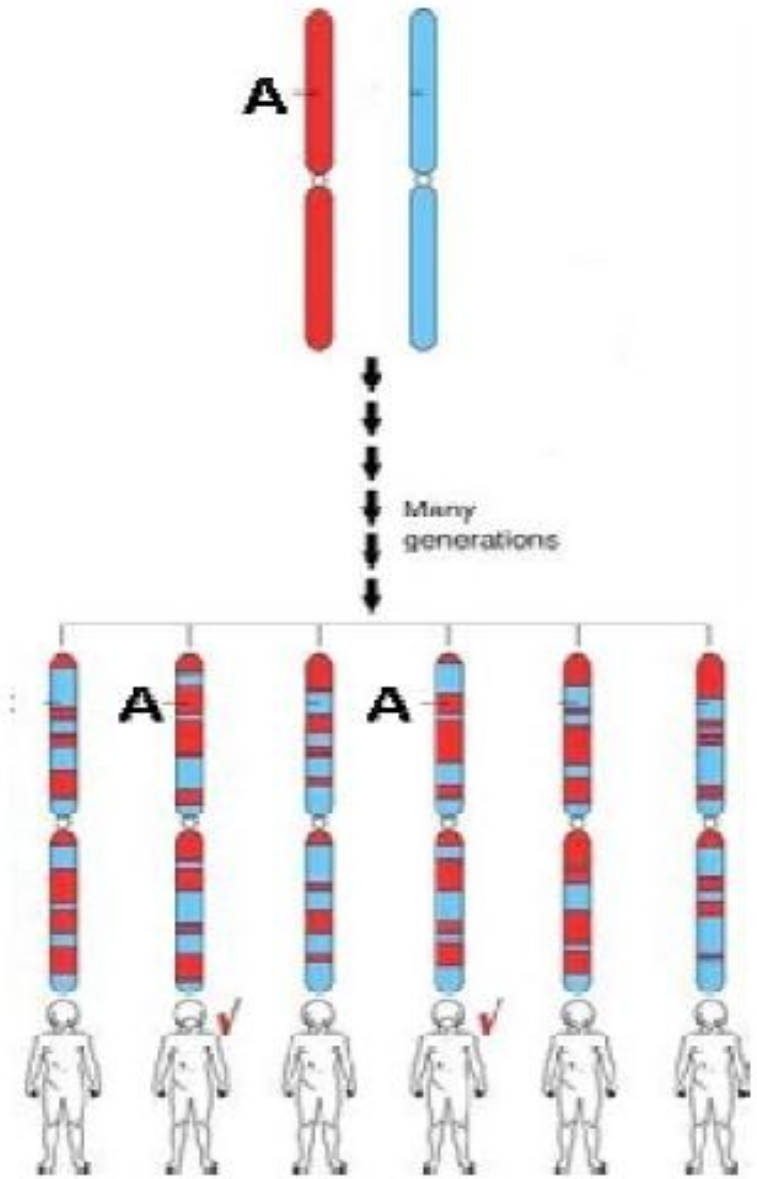
Haplotype compilation

"Tag" SNPs For genotyping

http://www.hapmap.org/originhaplotype

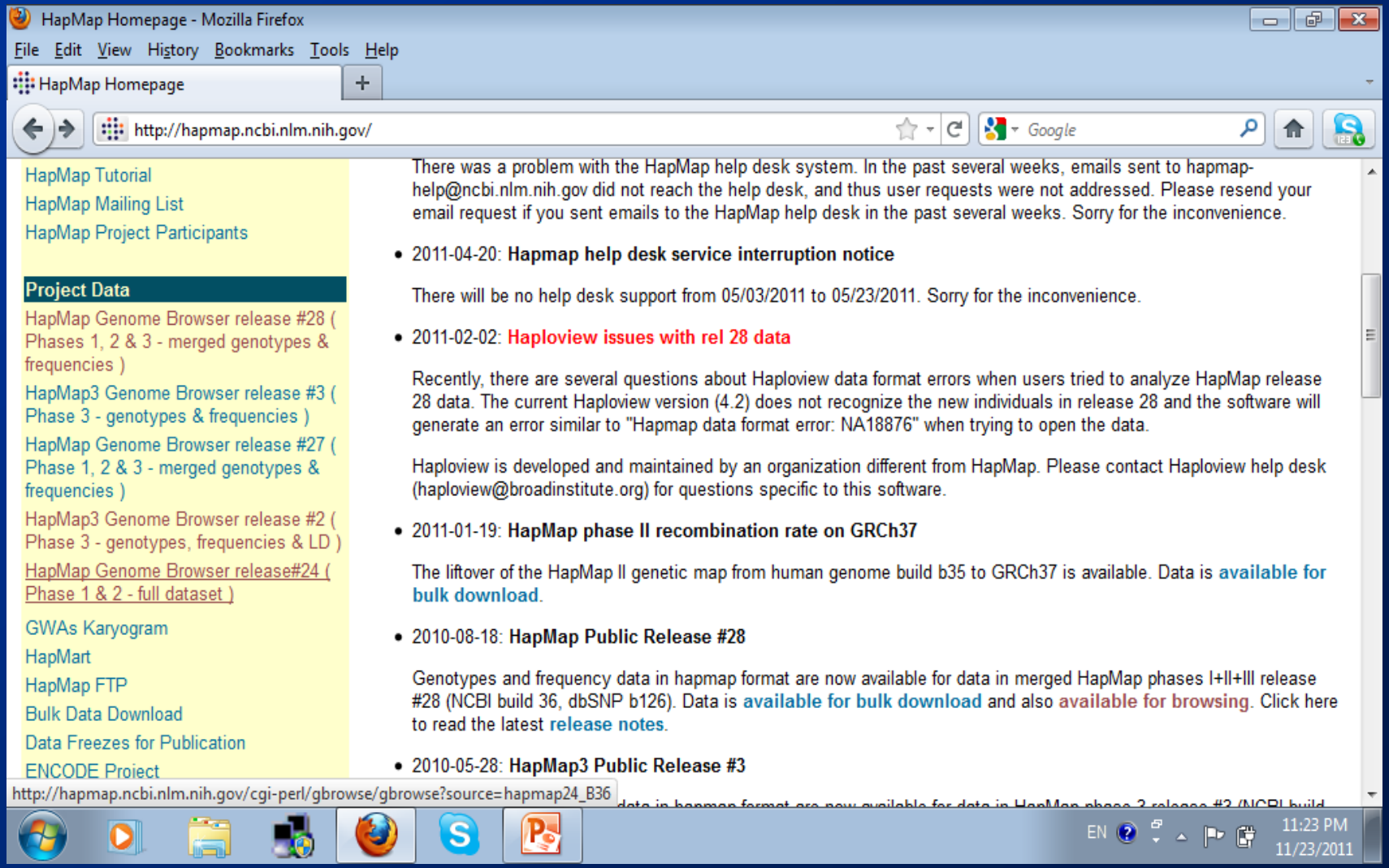


Εικόνα 2: Η κατασκευή του HapMap γίνεται σε 3 στάδια. (a) Προσδιορίζονται SNPs σε δείγματα DNA από πολλά άτομα. (b) Γειτονικοί SNPs που κληρονομούνται μαζί κατατάσσονται σε απλοτύπους (c) Προσδιορίζονται"Tag" SNPs μέσα στους απλοτύπους τα οποία περιγράφουν πλήρως τους απλοτύπους. Με τη γονοτύπωση 3 tag SNPs που φαίνονται στην εικόνα, οι ερευνητές προσδιορίζουν ποιός από τους 4 απλοτύπους είναι παρόν σε κάθε άτομο..

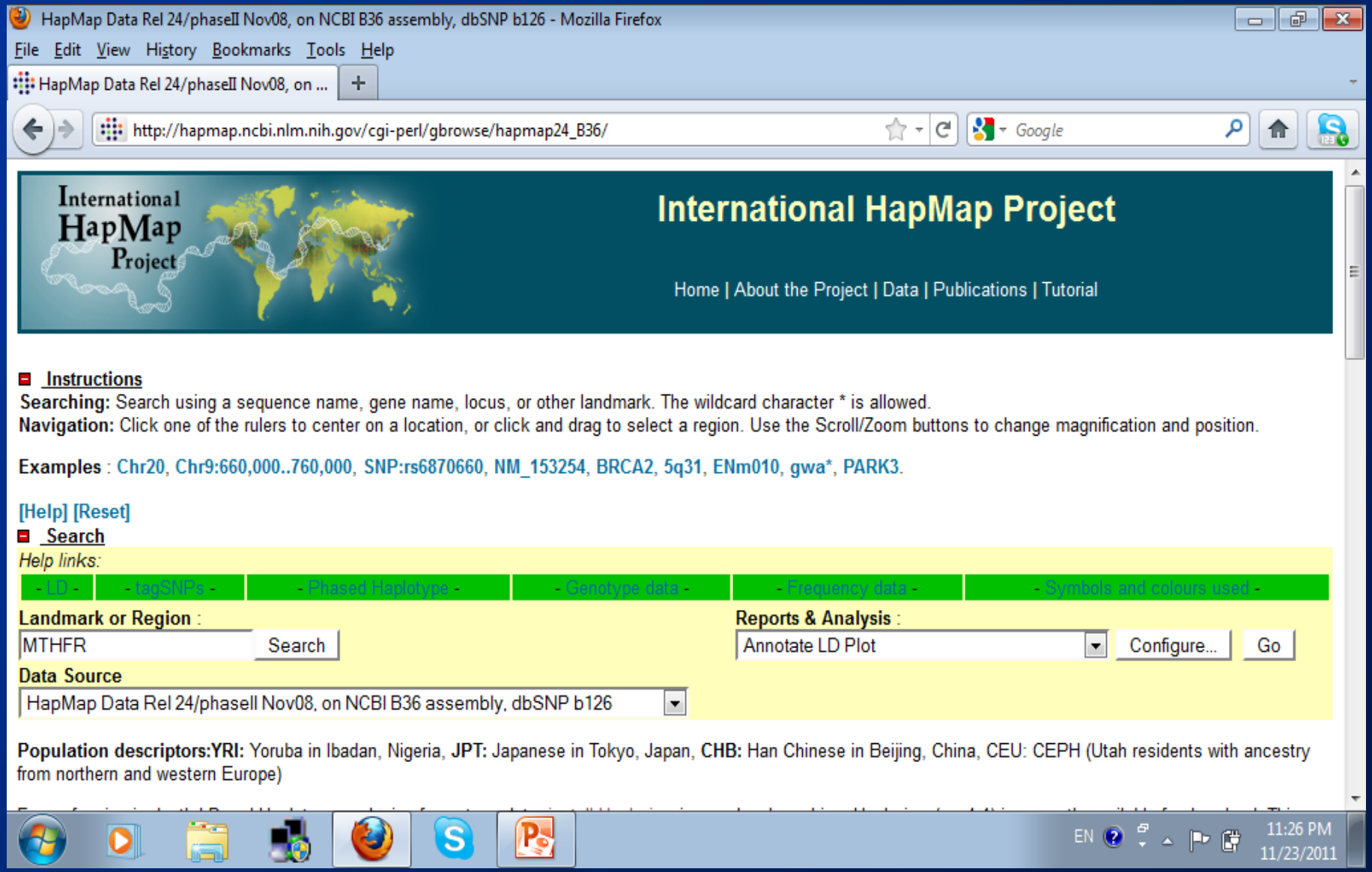


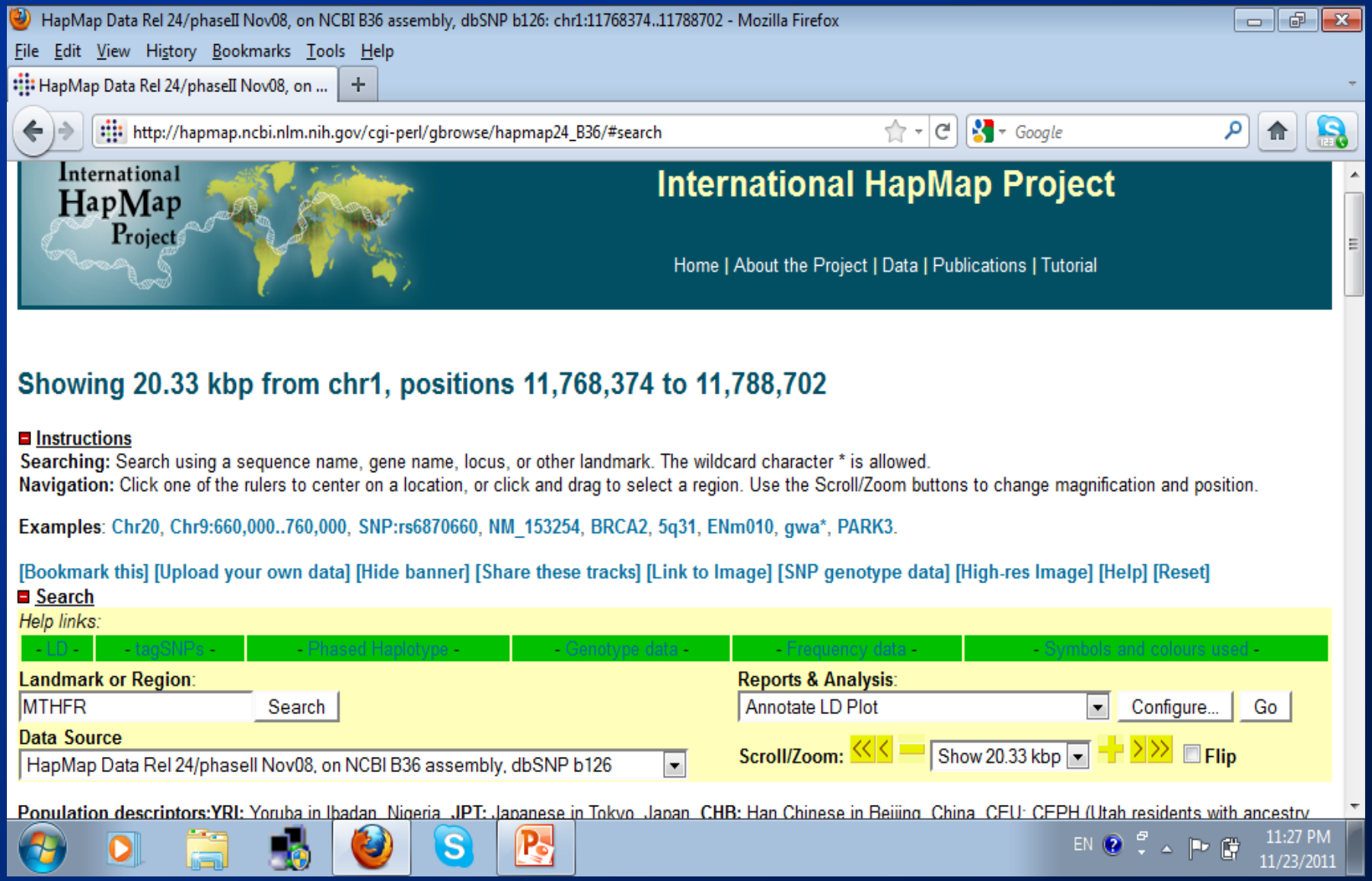
Το διάγραμμα δείχνει 2 προγονικά χρωμοσώματα που αναμιγνύονται μέσω ανασυνδυασμού για πολλές γενιές ώστε να δώσουν διαφορετικά χρωμοσώματα απογόνων. Εάν μια γενετική παραλλαγή που σημειώνεται με το γράμμα Α στο προγονικό χρωμόσωμα αυξάνει τον κίνδυνο για κάποιο νόσημα, οι 2 απόγονοι της σύγχρονης γενιάς που κληρονομούν το συγκεκριμένο τμήμα του χρωμοσώματος, θα έχουν αυξημένο κίνδυνο. Πλησίον της παραλλαγής Α, υπάρχουν πολλοι SNPs που μπορούν να χρησιμοποιηθούν για τον εντοπισμό της Α.

Click HapMap Genome Browser (#24 - full data set)



Search for MTHFR




HapMap Data Rel 24/phaseII Nov08, on NCBI B36 assembly, dbSNP b126: chr1:11768374..11788702 - Mozilla Firefox
File Edit View History Bookmarks Tools Help
HapMap Data Rel 24/phaseII Nov08, on ...
http://hapmap.ncbi.nlm.nih.gov/cgi-perl/gbrowse/hapmap24_B36/#search
Google
International HapMap Project
International HapMap Project
Home | About the Project | Data | Publications | Tutorial
Showing 20.33 kbp from chr1, positions 11,768,374 to 11,788,702
Instructions
Searching: Search using a sequence name, gene name, locus, or other landmark. The wildcard character * is allowed.
Navigation: Click one of the rulers to center on a location, or click and drag to select a region. Use the Scroll/Zoom buttons to change magnification and position.
Examples: Chr20, Chr9:660,000..760,000, SNP:rs6870660, NM_153254, BRCA2, 5q31, ENm010, gwa*, PARK3.
[Bookmark this] [Upload your own data] [Hide banner] [Share these tracks] [Link to Image] [SNP genotype data] [High-res Image] [Help] [Reset]
Search
Help links:
- LD - - tagSNPs - - Phased Haplotype - - Genotype data - - Frequency data - - Symbols and colours used -
Landmark or Region:
MTHFR
Search
Reports & Analysis:
Annotate LD Plot
Configure...
Go
Data Source
HapMap Data Rel 24/phaseII Nov08, on NCBI B36 assembly, dbSNP b126
Scroll/Zoom:
Show 20.33 kbp
Flip
Population descriptors:YRI: Yoruba in Ibadan, Nigeria JPT: Japanese in Tokyo, Japan CHB: Han Chinese in Beijing, China CEU: CEPH (Utah residents with ancestry
EN
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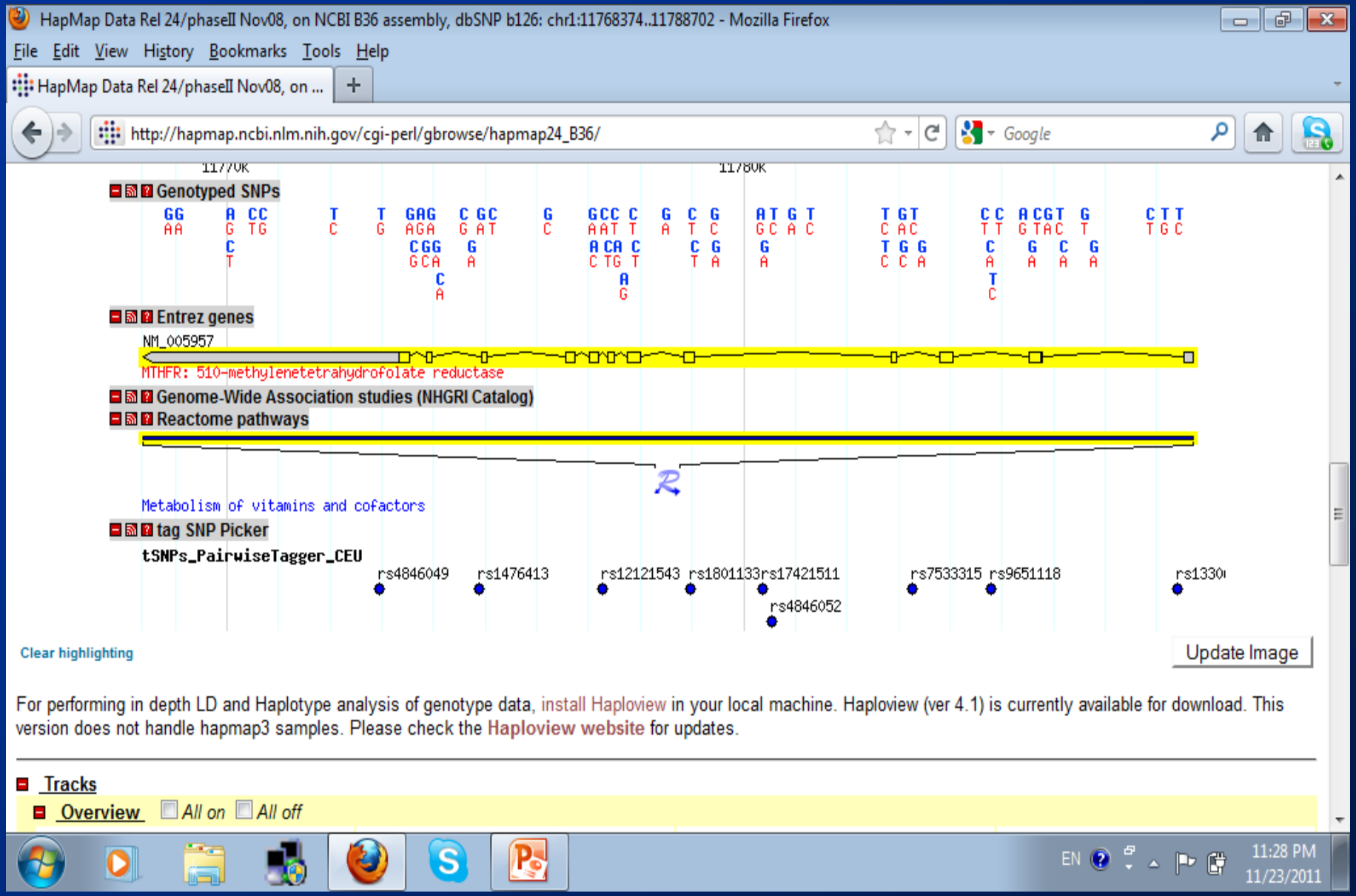
HapMap Data Rel 24/phaseII Nov08, on NCBI B36 assembly, dbSNP b126: chr1:11768374..11788702 - Mozilla Firefox
File Edit View History Bookmarks Tools Help
HapMap Data Rel 24/phaseII Nov08, on ...
http://hapmap.ncbi.nlm.nih.gov/cgi-perl/gbrowse/hapmap24_B36/
Google
11770K
11780K
Genotyped SNPs
Entrez genes
NM_005957
MTHFR: 510-methylenetetrahydrofolate reductase
Genome-Wide Association studies (NHGRI Catalog)
Reactome pathways
Metabolism of vitamins and cofactors
tag SNP Picker
tSNPs_PairwiseTagger_CEU
rs4846049
rs1476413
rs12121543
rs1801133
rs17421511
rs4846052
rs7533315
rs9651118
rs1330
Clear highlighting
Update Image
For performing in depth LD and Haplotype analysis of genotype data, install Haploview in your local machine. Haploview (ver 4.1) is currently available for download. This version does not handle hapmap3 samples. Please check the Haploview website for updates.
Tracks
Overview
All on
All off
EN
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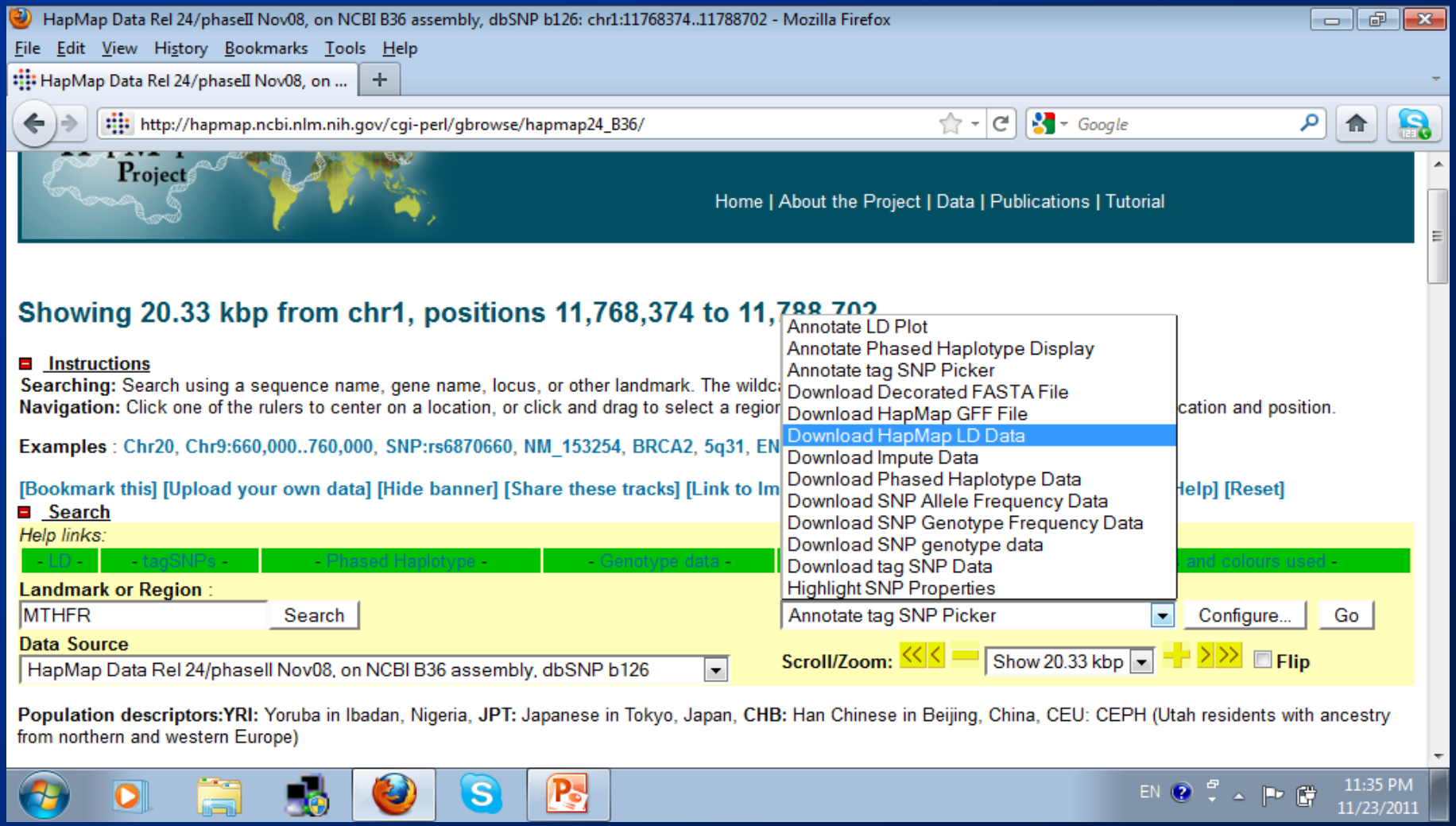
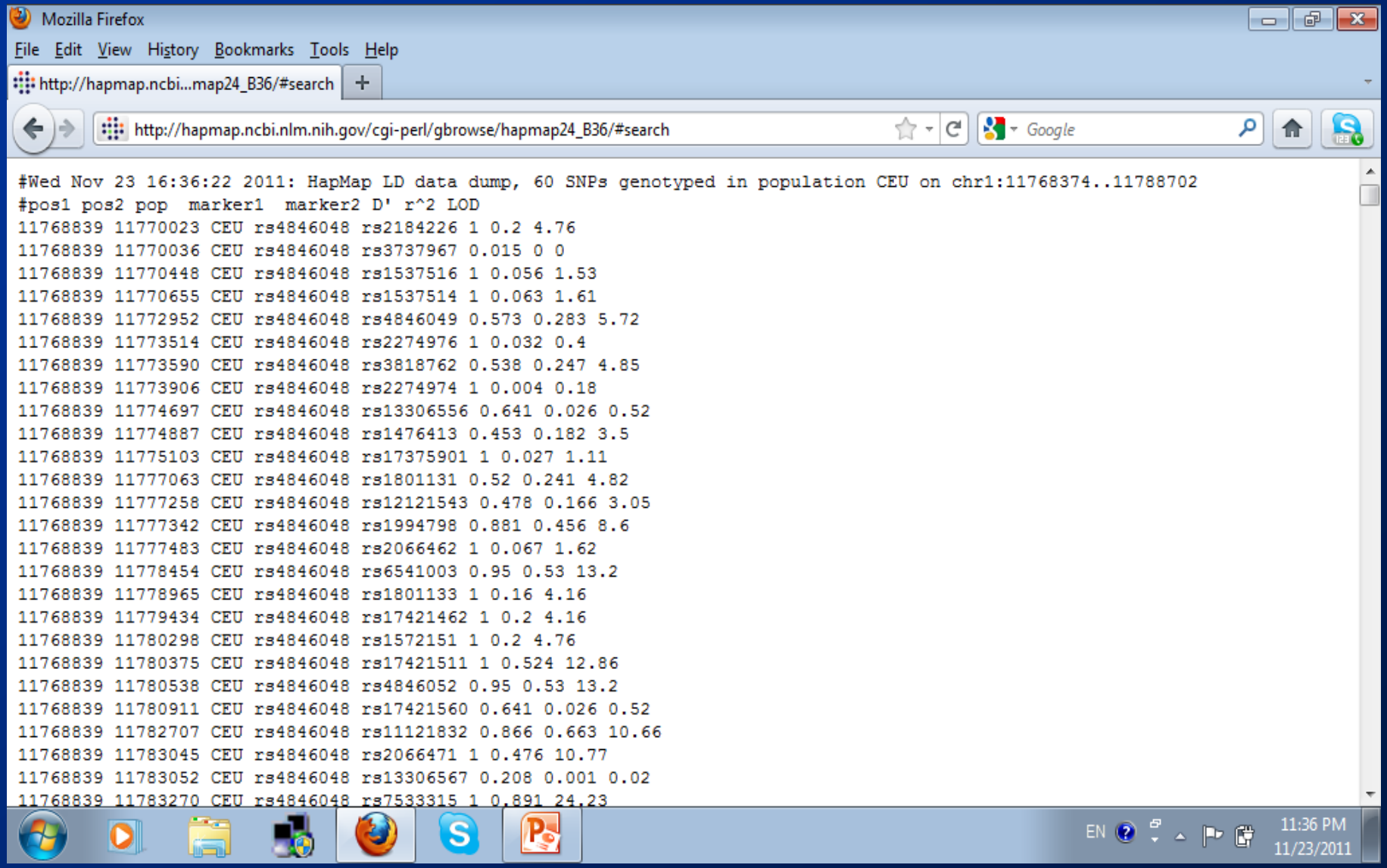
11/23/2011

Click on Download HapMap data to find LD scores for all SNPs, including rs1801133



results


Mozilla Firefox
File Edit View History Bookmarks Tools Help
http://hapmap.ncbi...map24_B36/#search
http://hapmap.ncbi.nlm.nih.gov/cgi-perl/gbrowse/hapmap24_B36/#search
Google
#Wed Nov 23 16:36:22 2011: HapMap LD data dump, 60 SNPs genotyped in population CEU on chr1:11768374..11788702
#pos1 pos2 pop marker1 marker2 D' r^2 LOD
11768839 11770023 CEU rs4846048 rs2184226 1 0.2 4.76
11768839 11770036 CEU rs4846048 rs3737967 0.015 0 0
11768839 11770448 CEU rs4846048 rs1537516 1 0.056 1.53
11768839 11770655 CEU rs4846048 rs1537514 1 0.063 1.61
11768839 11772952 CEU rs4846048 rs4846049 0.573 0.283 5.72
11768839 11773514 CEU rs4846048 rs2274976 1 0.032 0.4
11768839 11773590 CEU rs4846048 rs3818762 0.538 0.247 4.85
11768839 11773906 CEU rs4846048 rs2274974 1 0.004 0.18
11768839 11774697 CEU rs4846048 rs13306556 0.641 0.026 0.52
11768839 11774887 CEU rs4846048 rs1476413 0.453 0.182 3.5
11768839 11775103 CEU rs4846048 rs17375901 1 0.027 1.11
11768839 11777063 CEU rs4846048 rs1801131 0.52 0.241 4.82
11768839 11777258 CEU rs4846048 rs12121543 0.478 0.166 3.05
11768839 11777342 CEU rs4846048 rs1994798 0.881 0.456 8.6
11768839 11777483 CEU rs4846048 rs2066462 1 0.067 1.62
11768839 11778454 CEU rs4846048 rs6541003 0.95 0.53 13.2
11768839 11778965 CEU rs4846048 rs1801133 1 0.16 4.16
11768839 11779434 CEU rs4846048 rs17421462 1 0.2 4.16
11768839 11780298 CEU rs4846048 rs1572151 1 0.2 4.76
11768839 11780375 CEU rs4846048 rs17421511 1 0.524 12.86
11768839 11780538 CEU rs4846048 rs4846052 0.95 0.53 13.2
11768839 11780911 CEU rs4846048 rs17421560 0.641 0.026 0.52
11768839 11782707 CEU rs4846048 rs11121832 0.866 0.663 10.66
11768839 11783045 CEU rs4846048 rs2066471 1 0.476 10.77
11768839 11783052 CEU rs4846048 rs13306567 0.208 0.001 0.02
11768839 11783270 CEU rs4846048 rs7533315 1 0.891 24.23
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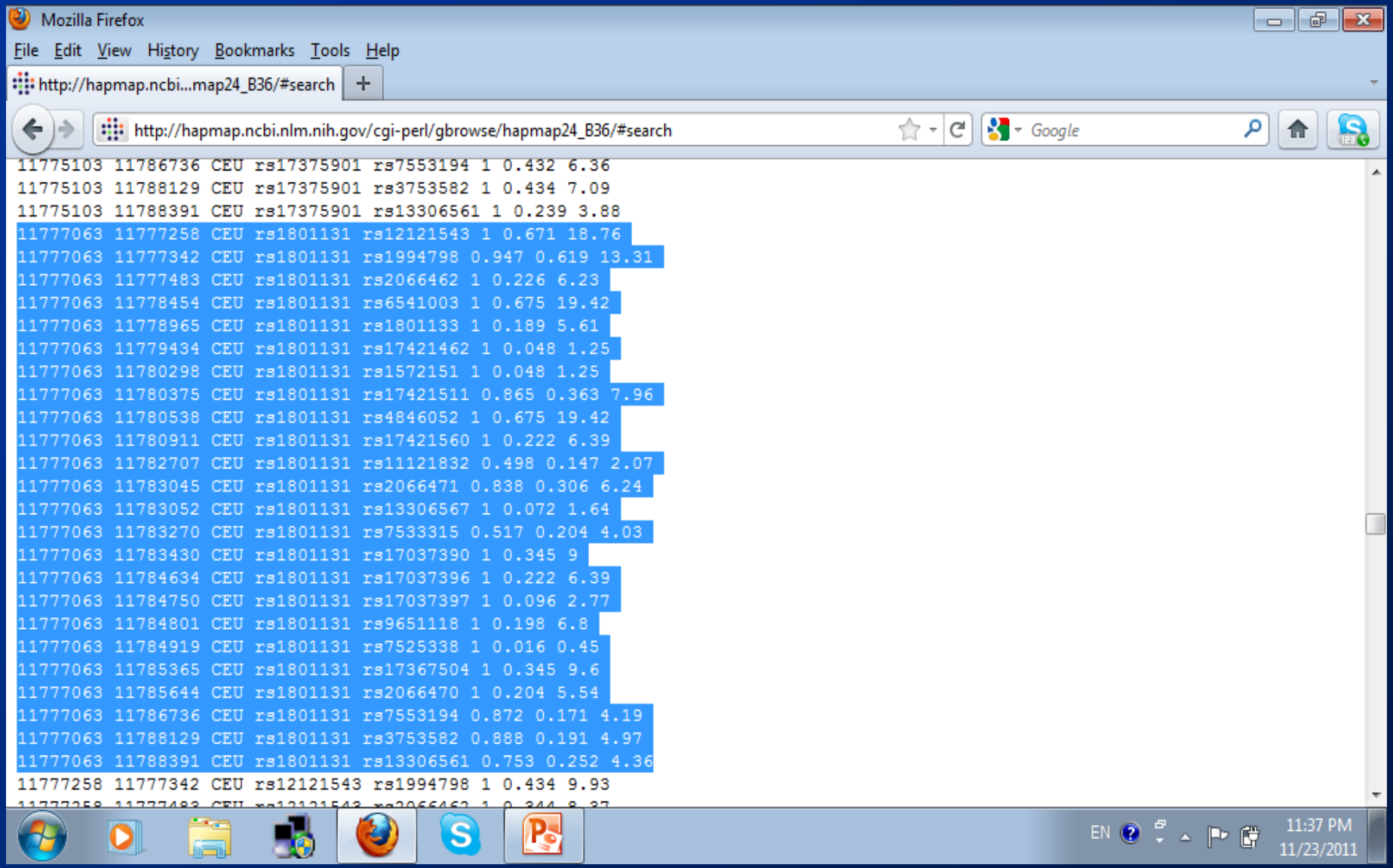
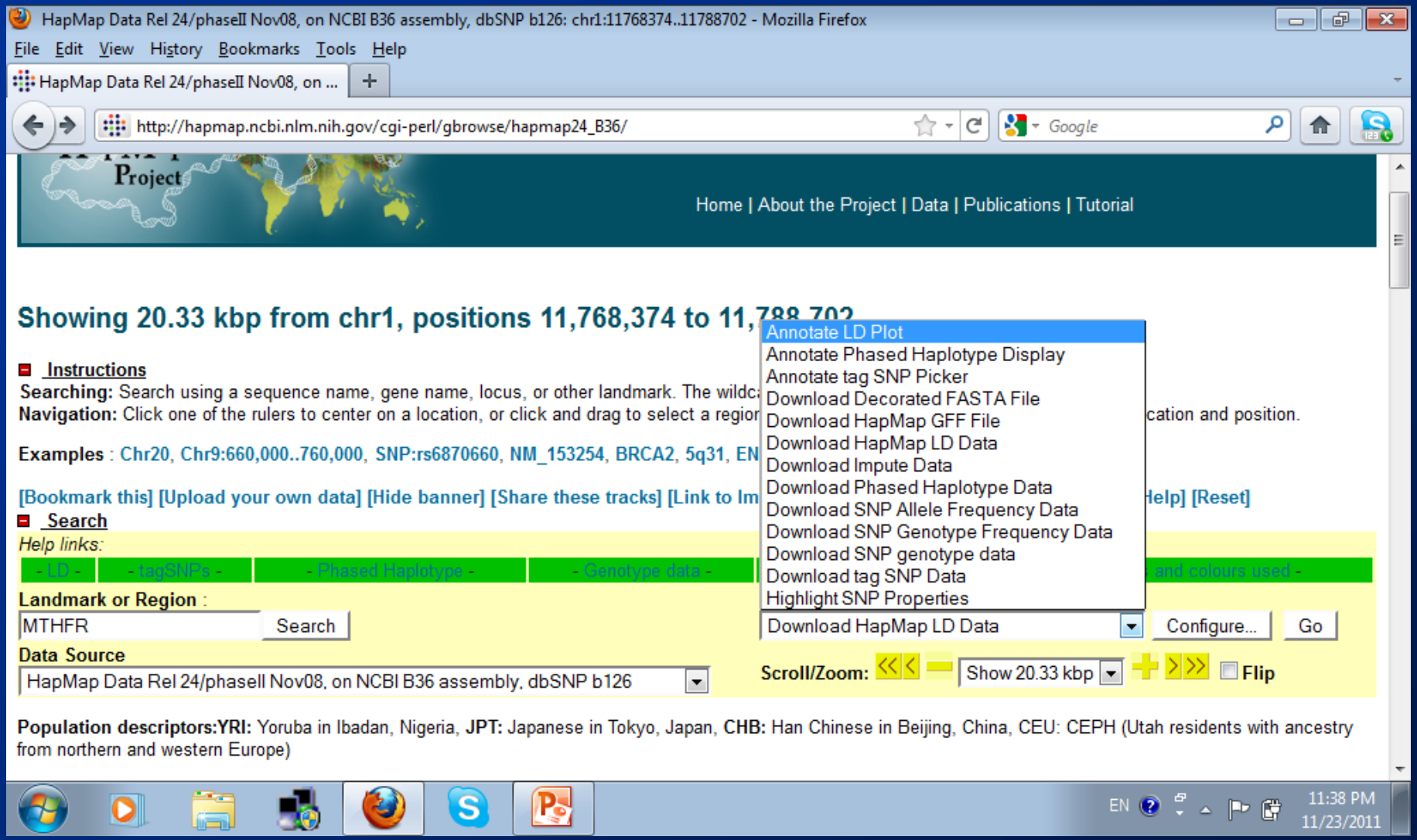
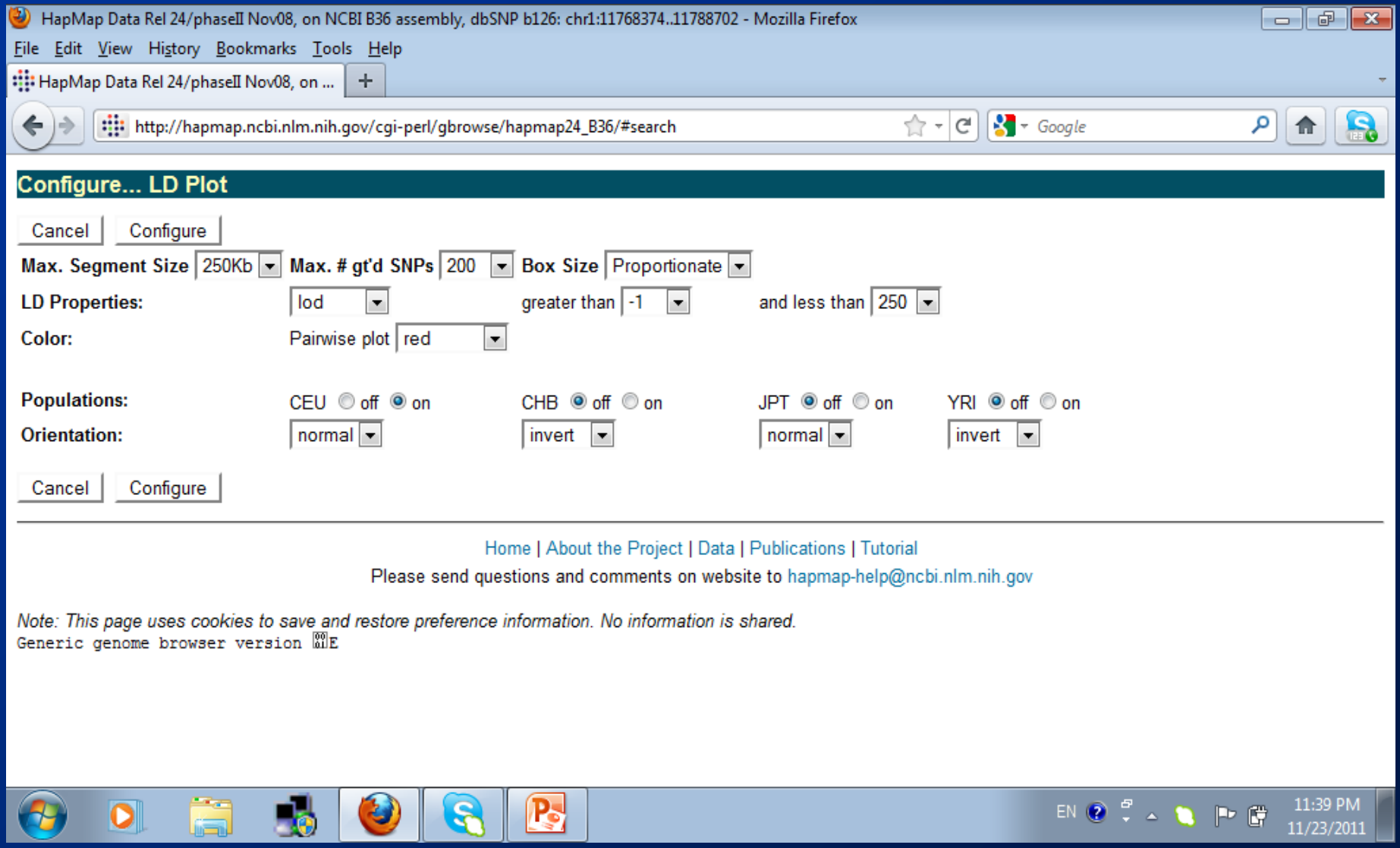
LD results for rs1801133



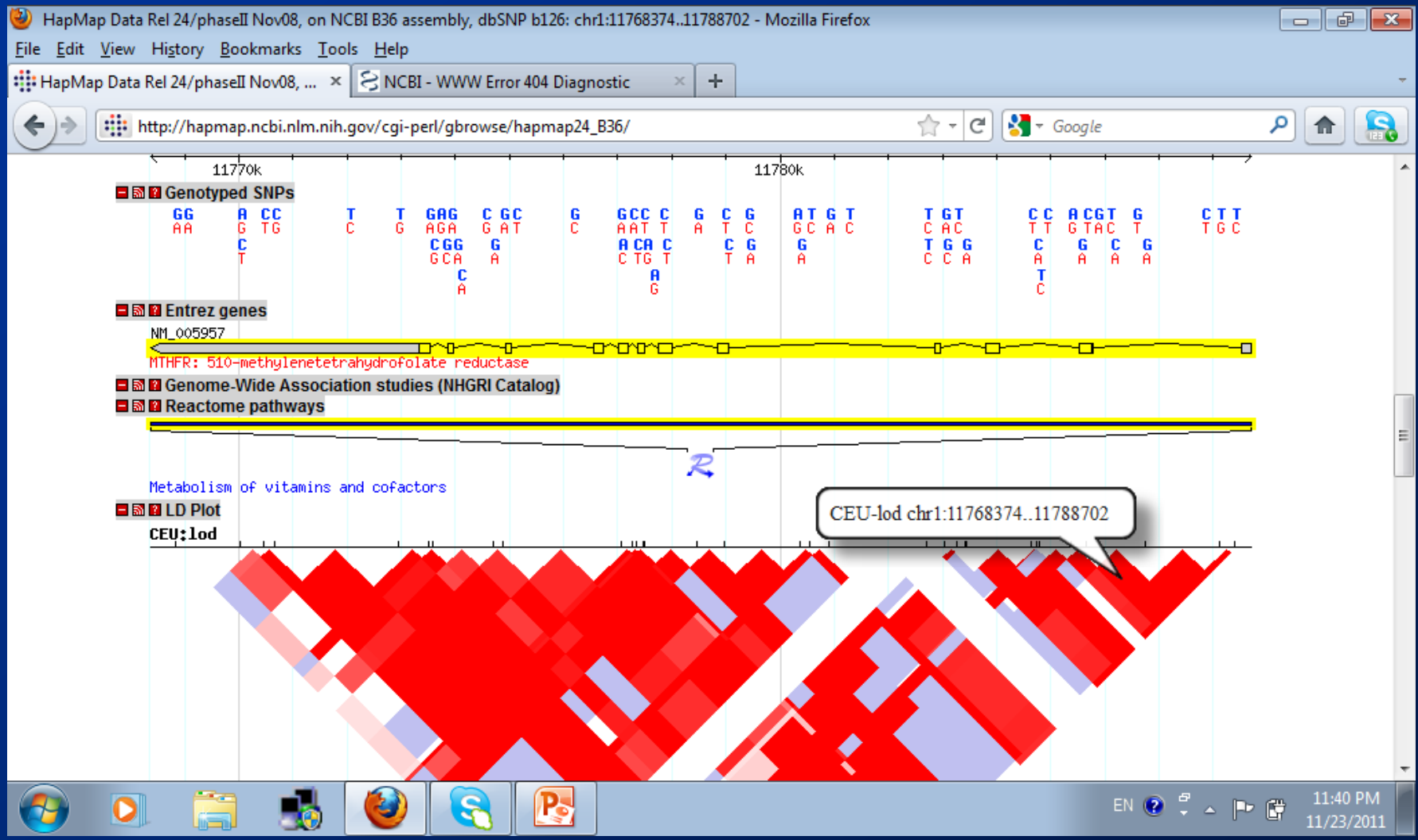
Back to MTHFR page, click Annotate LD plot

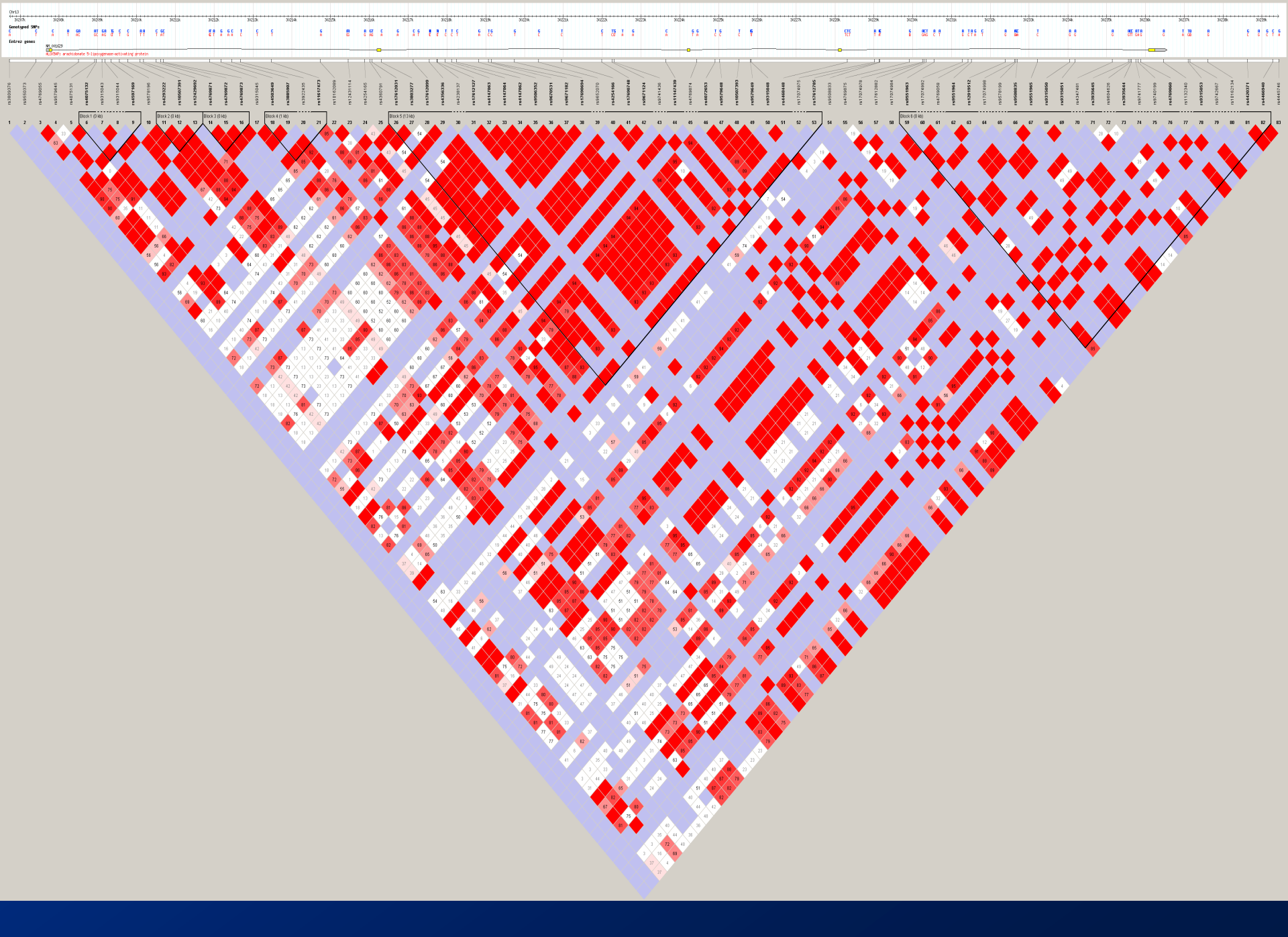


Click configure

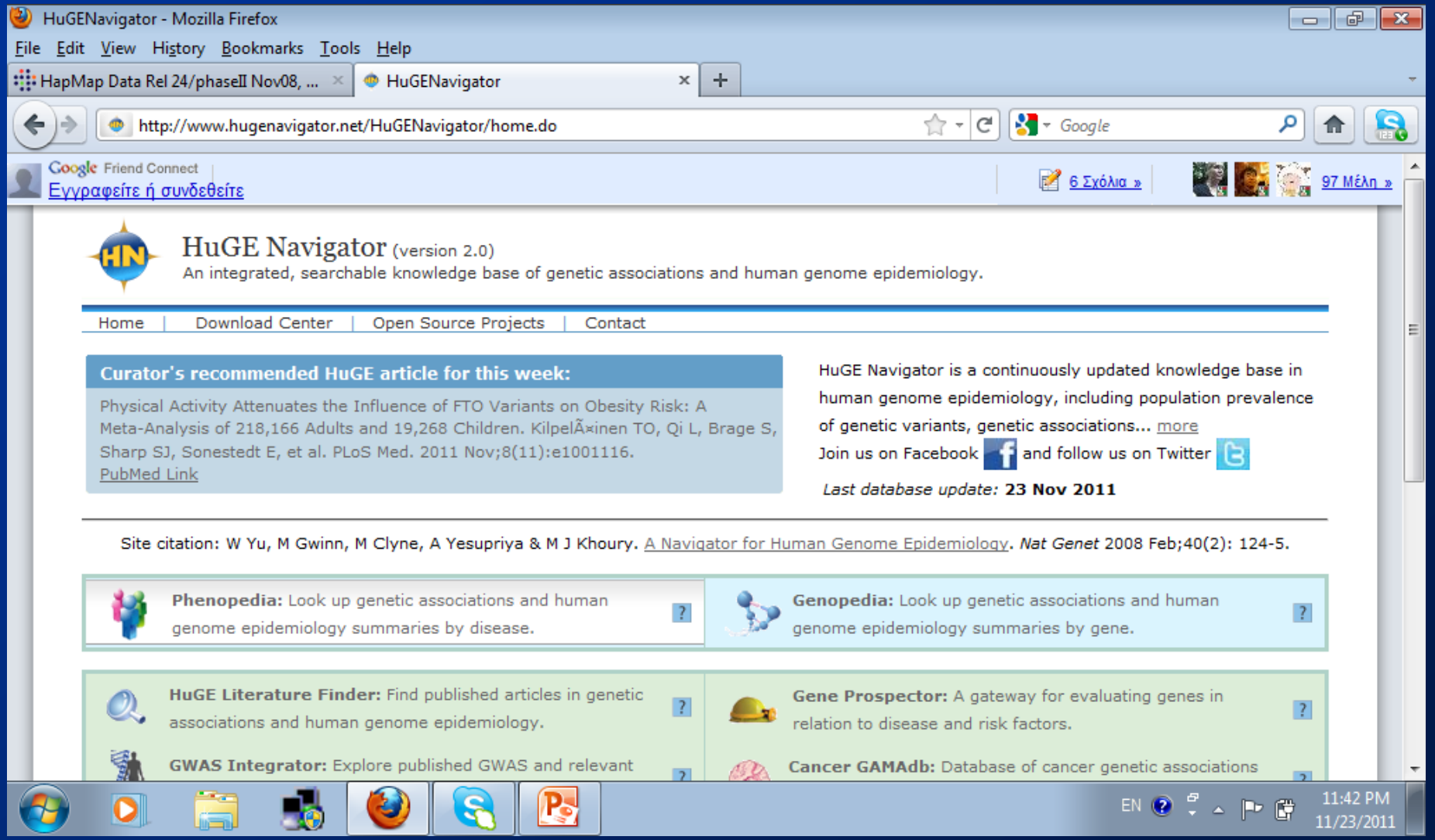


Red color shows regions of High LD

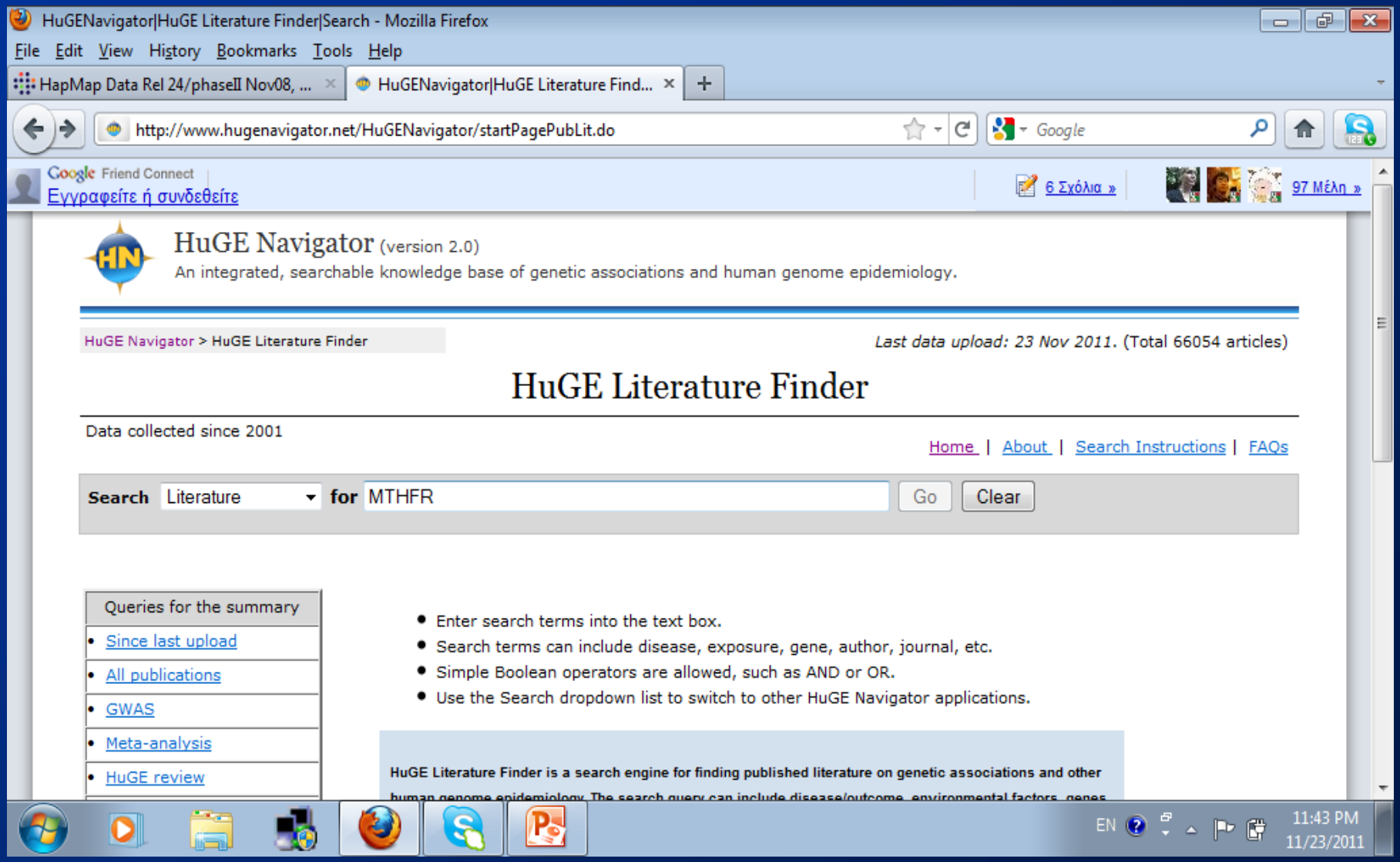



Chr13
Genotyped SNPs
Entrez genes
NM_001629
ENPP1: ectonucleotide 5-(phosphodiesterase-activating protein
Block 1 (0 kb)
Block 2 (0 kb)
Block 3 (0 kb)
Block 4 (1 kb)
Block 5 (13 kb)
Block 6 (0 kb)

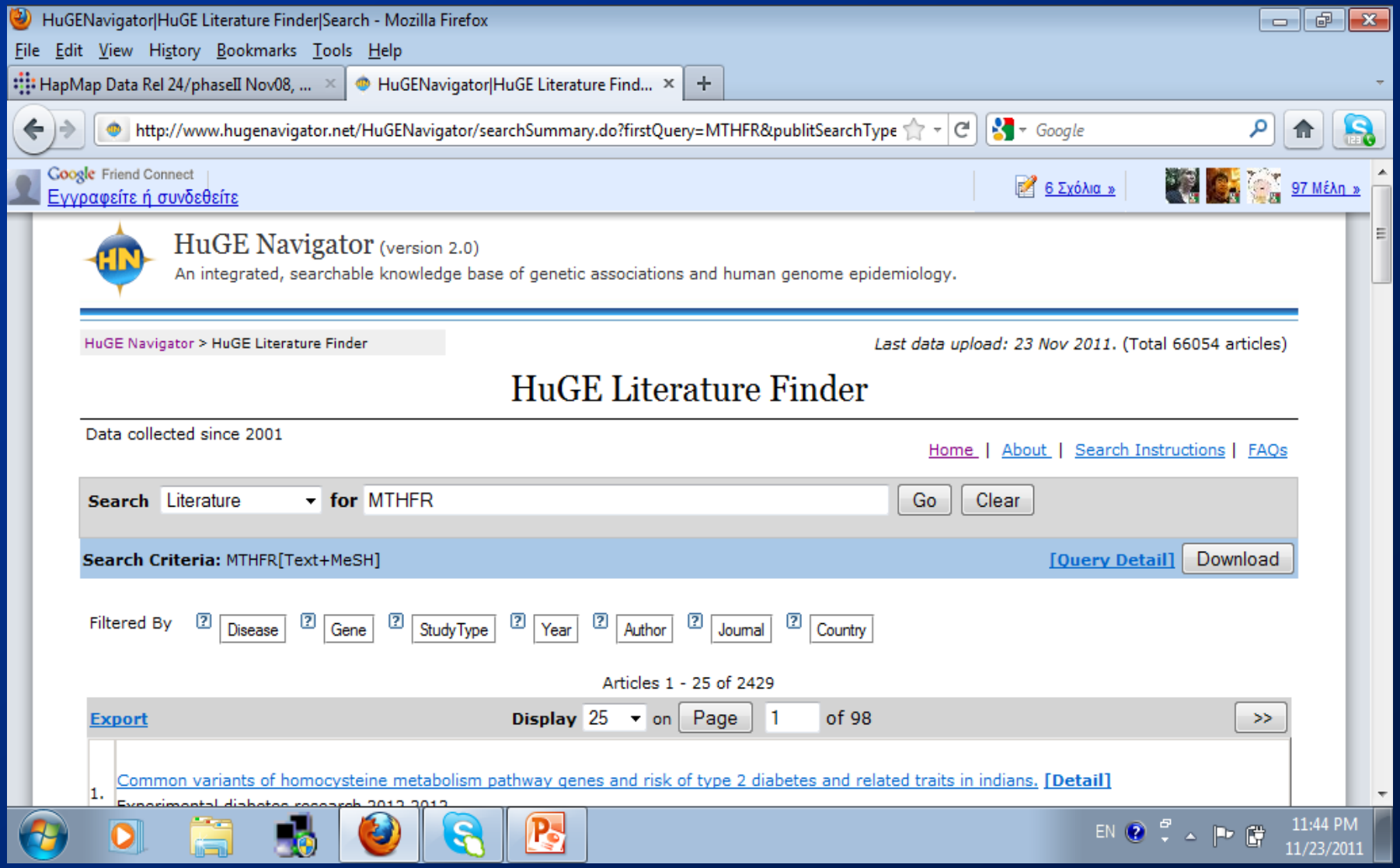
Search for the published literature of MTHFR gene. Go to HuGE Navigator (http://www.hugenavigator.net/), and click on HuGE literature finder



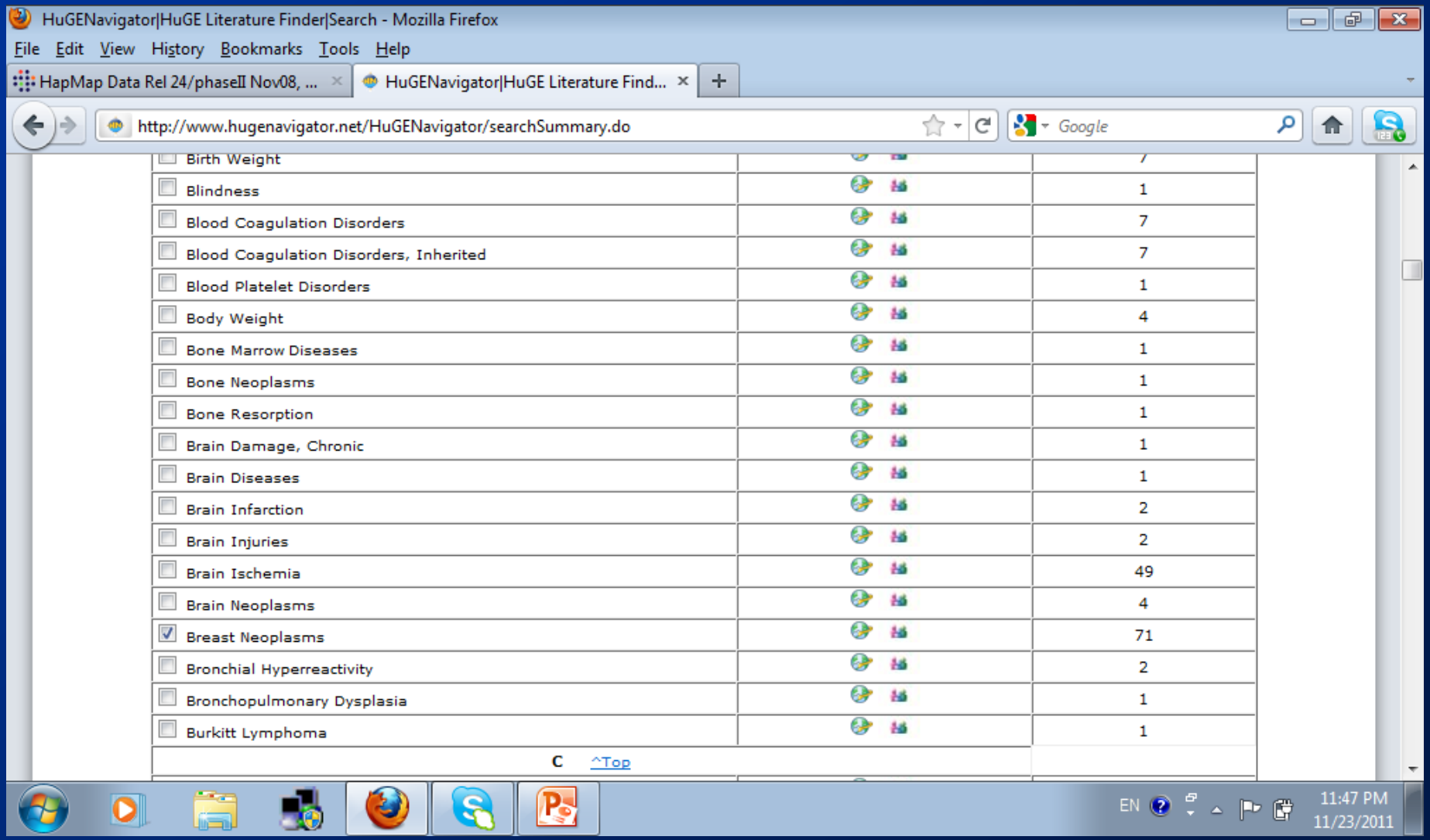
Search literature for MTHFR



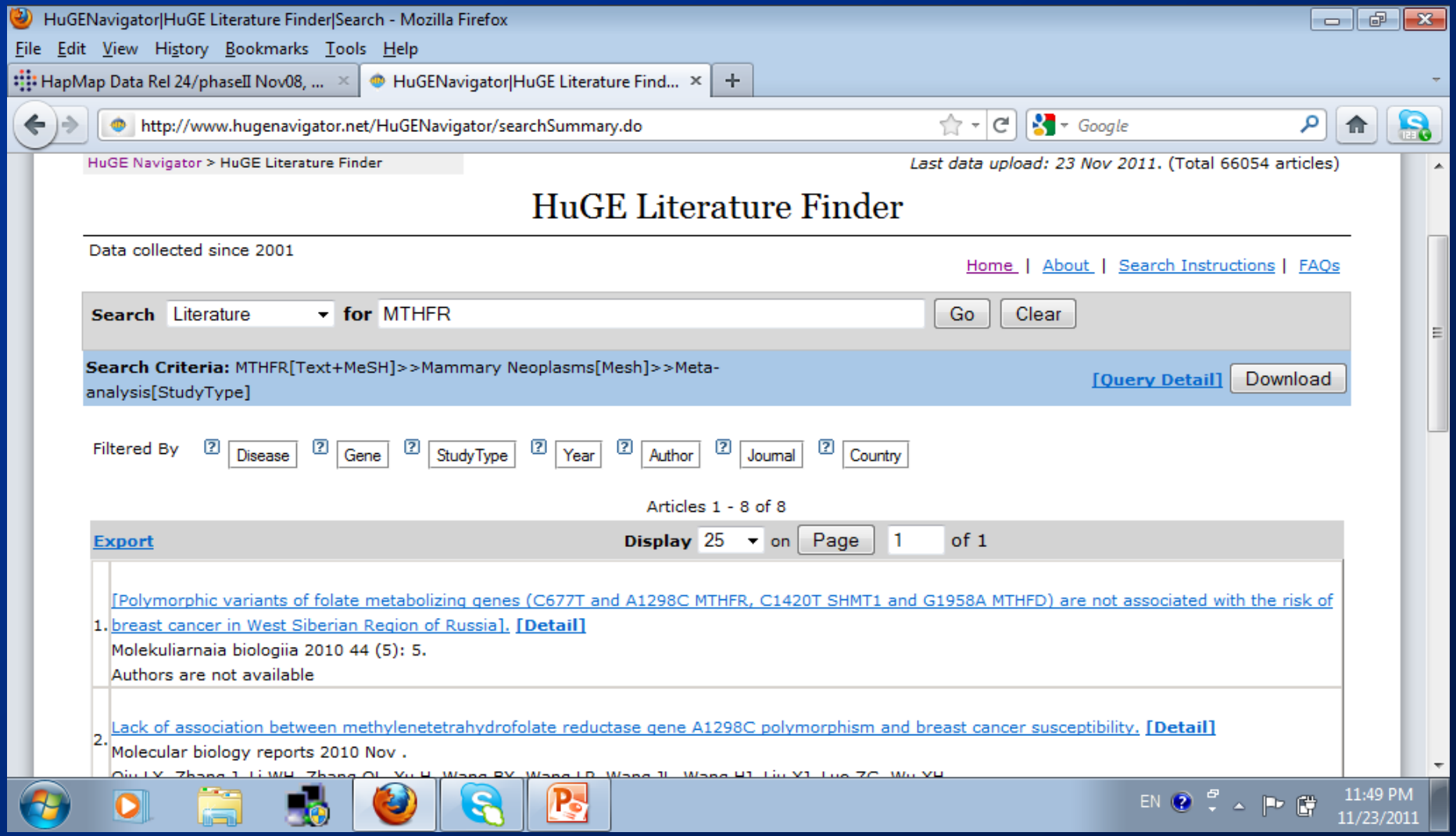
2429 results found!!!



Limit by disease and choose Breast Neoplasms…and click continue

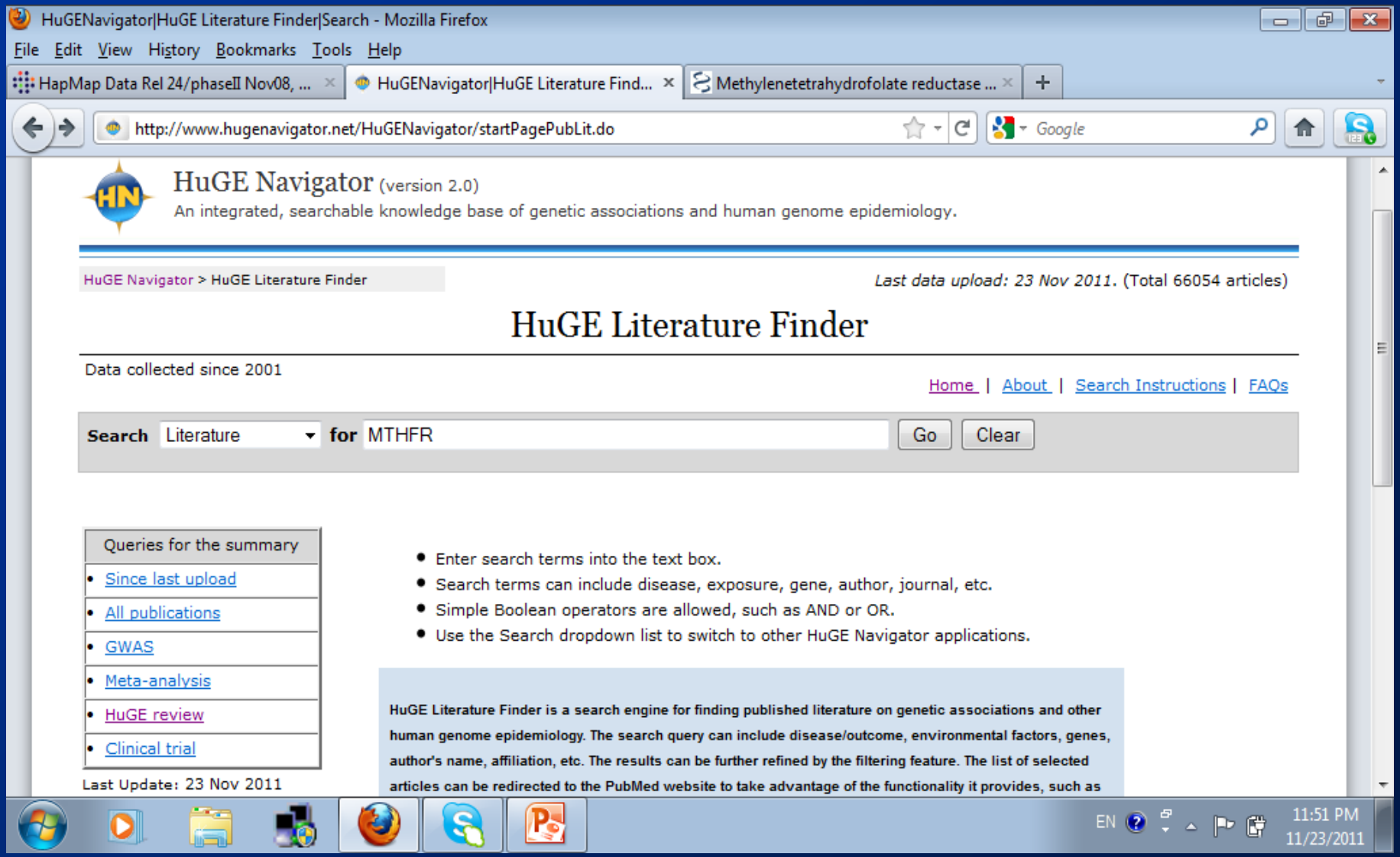


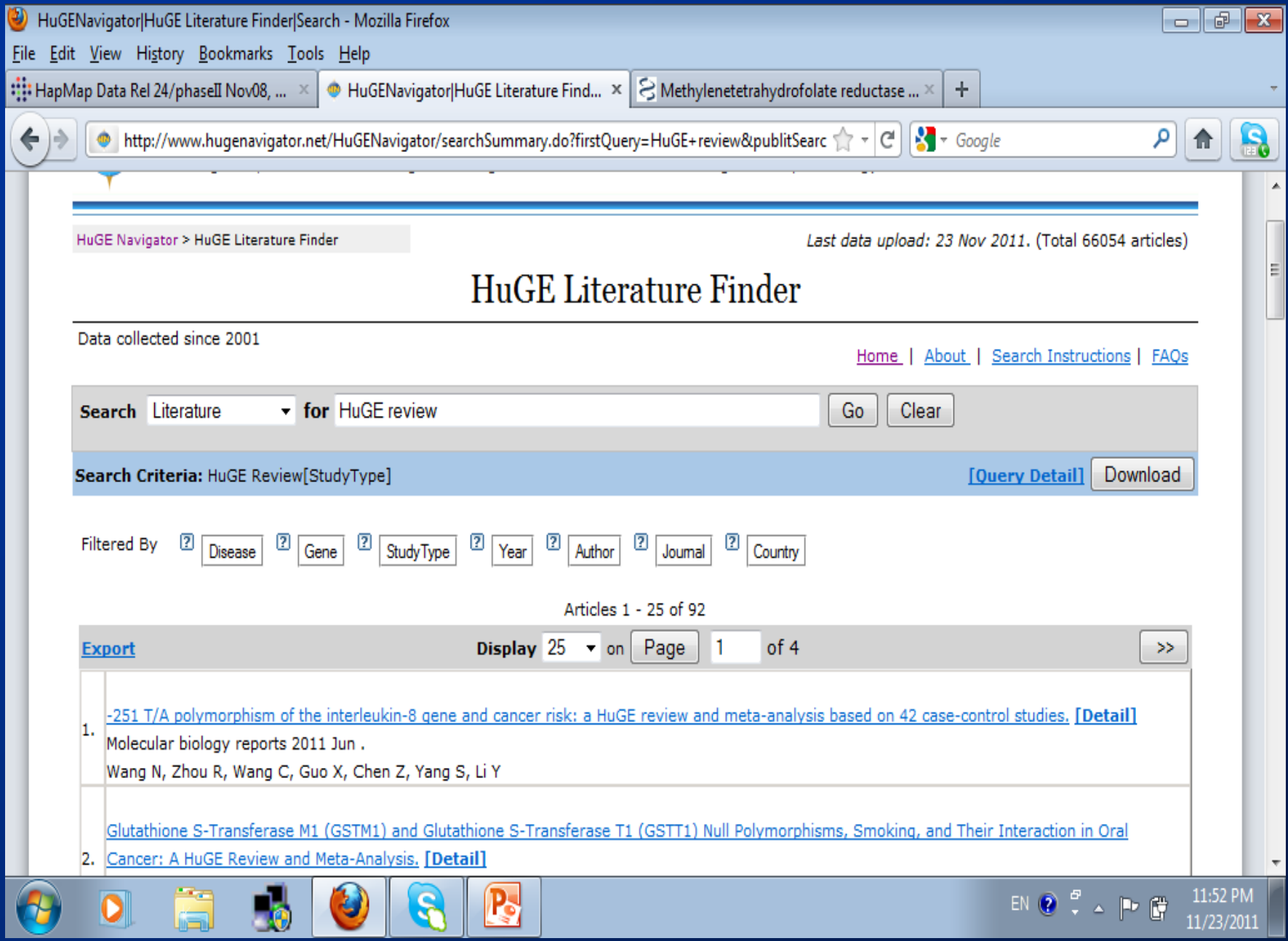
Limit by study type and choose meta-analysis



Click on the title to view the PubMed abstract

Back to HuGE Literature Finder, click on HuGE Reviews, to find state-of-the-art open-access reviews for gene-disease associations




HuGENavigator|HuGE Literature Finder|Search - Mozilla Firefox
File Edit View History Bookmarks Tools Help
HapMap Data Rel 24/phaseII Nov08, ...
HuGENavigator|HuGE Literature Find...
Methylenetetrahydrofolate reductase ...
http://www.hugenavigator.net/HuGENavigator/searchSummary.do?firstQuery=HuGE+review&publitSearc
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Display 25 on Page 1 of 4 >>
1. -251 T/A polymorphism of the interleukin-8 gene and cancer risk: a HuGE review and meta-analysis based on 42 case-control studies. [Detail]
Molecular biology reports 2011 Jun .
Wang N, Zhou R, Wang C, Guo X, Chen Z, Yang S, Li Y
2. Glutathione S-Transferase M1 (GSTM1) and Glutathione S-Transferase T1 (GSTT1) Null Polymorphisms, Smoking, and Their Interaction in Oral Cancer: A HuGE Review and Meta-Analysis. [Detail]
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R. Aber Benoit
Lanilis
Porsal
St. Christ
Plouguerneau
Ploudalmezeau
Le Coq
Pte de Toulinguet
Toulinguet
La Vandree
Parquete
B. du Lis
Les Tas de Pois
Dinant
Camaret
St. Matthews Pt.
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Useful links

- http://www.genecards.org/

GeneCards is an integrated database of human genes that includes automatically-mined genomic, proteomic and transcriptomic information, as well as orthologies, disease relationships, SNPs, gene expression, gene function, and service links for ordering assays and antibodies.


GeneCards V3 - Human Genes | Gene Database | Gene Search - Mozilla Firefox
File Edit View History Bookmarks Tools Help
HapMap Data Rel 24/phaseII Nov08, ...
HuGENavigator|HuGE Literature Find...
GeneCards V3 - Human Genes | Gene ...
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Google
GeneCards®
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View Sample Gene
GeneCards Sections
NTRK1
neurotrophic tyrosine kinase, receptor, type 1
Aliases
Drugs
Genome view
Pathways
Publications
Databases
Expression
Interactions
Paralogs
Summaries
Disorders
External search
IP/Patents
Products
Transcripts
News and Views
Version 3 features
New search engine:
Speedy output
Unlimited hits
Field-specific input
Better minicards
Relational database
What's New
User comments
Xennex PR
Site Map
Version 3.07
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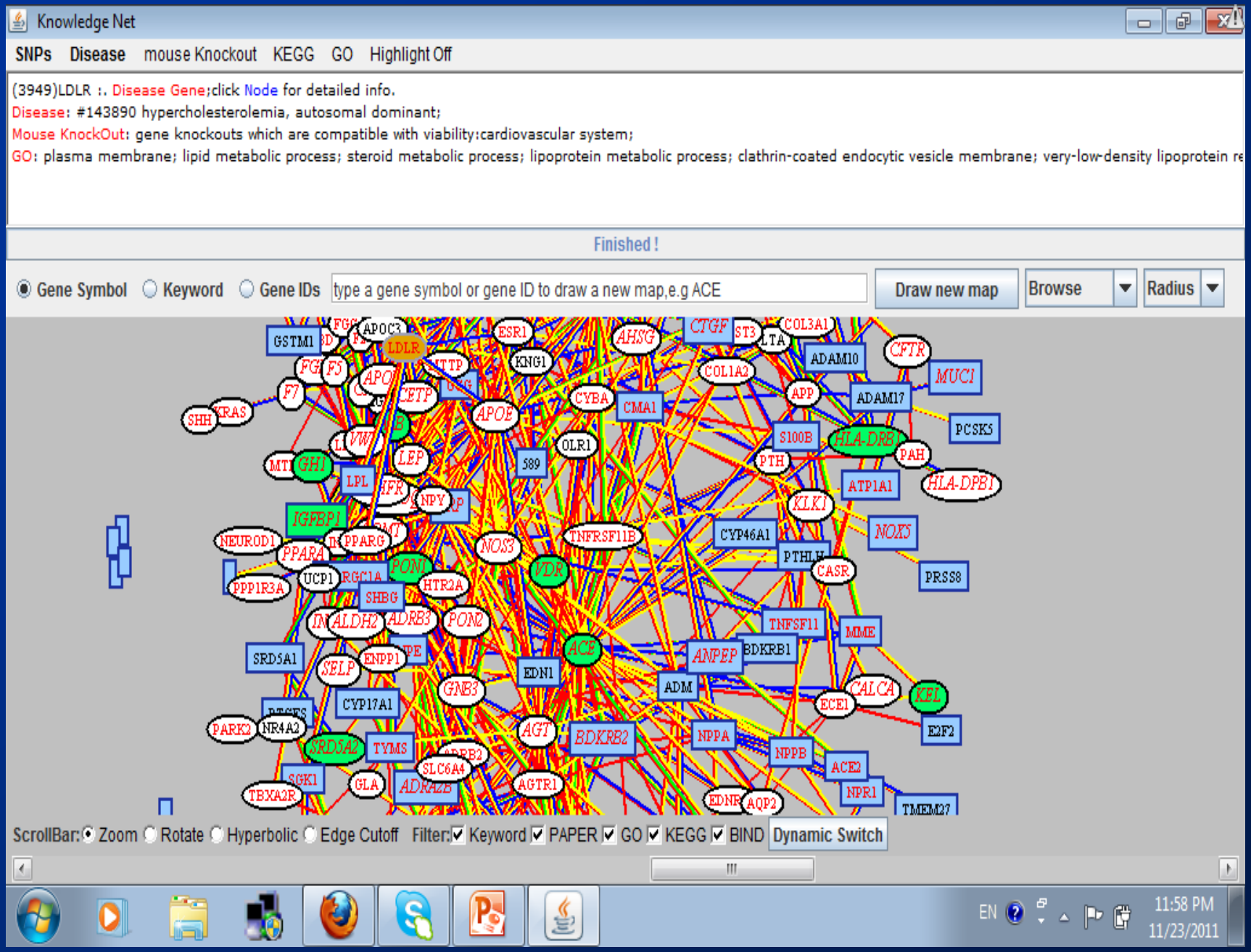
11/23/2011

- http://www.snps3d.org/
- SNPs3D is a website which assigns molecular functional effects of non-synonymous SNPs based on structure and sequence analysis.
- Gene-gene interactions networks


Knowledge Net
SNPs Disease mouse Knockout KEGG GO Highlight Off
(3949)LDLR :. Disease Gene;click Node for detailed info.
Disease: #143890 hypercholesterolemia, autosomal dominant;
Mouse KnockOut: gene knockouts which are compatible with viability:cardiovascular system;
GO: plasma membrane; lipid metabolic process; steroid metabolic process; lipoprotein metabolic process; clathrin-coated endocytic vesicle membrane; very-low-density lipoprotein re
Finished !
Gene Symbol Keyword Gene IDs
type a gene symbol or gene ID to draw a new map,e.g ACE
Draw new map
Browse
Radius
GSTM1
APOC3
LDLR
ESR1
AHSG
CTGF
ST3
LTA
COL3A1
ADAM10
CFTR
MUC1
COL1A2
APP
ADAM17
PCSK5
F7
SHH
KRAS
APOE
CETP
CYBA
CMA1
S100B
HLA-DRB
PAH
OLR1
S89
PTH
MT
GH1
LEP
LPL
NPY
ATP1A1
HLA-DPB1
KLK1
IGFBP1
NEUROD1
PPARA
PPARG
TNFRSF11B
CYP46A1
NOX5
NOS3
PTHLH
CASR
PRSS8
UCP1
PPP1R3A
PON1
VDR
HTR2A
SHBG
ALDH2
ADRB3
PON2
TNFSF11
MME
ACE
ANPEP
BDKRB1
SRD5A1
SELP
ENPP1
EDN1
ADM
CALCA
KEL
ECE1
GNB3
CYP17A1
E2F2
PARK2
NR4A2
AGT
BDKRB2
NPPA
NPPB
ACE2
SRD5A2
TYMS
SLC6A4
SGK1
GLA
AGTR1
NPR1
TBXA2R
EDNRA
AQP2
TMEM27
ScrollBar: Zoom Rotate Hyperbolic Edge Cutoff Filter: Keyword PAPER GO KEGG BIND Dynamic Switch
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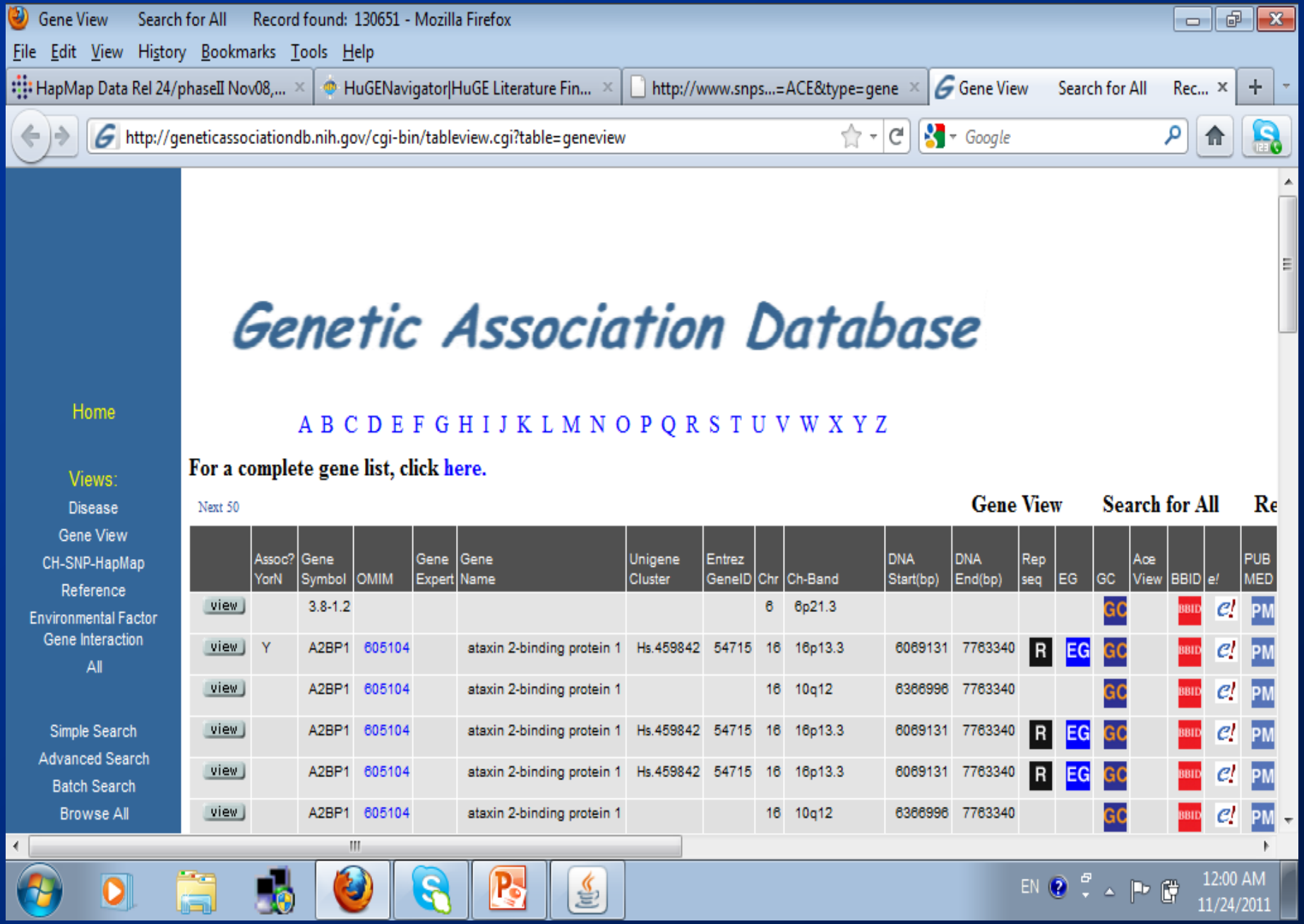
11/23/2011

Genetic Association Database

- archive of human genetic association studies of complex diseases and disorders. The goal of this database is to allow the user to rapidly identify medically relevant polymorphism from the large volume of polymorphism and mutational data, in the context of standardized nomenclature.
- The data is from published scientific papers.
- additional molecular reference numbers and links.
- gene centered.
- http://geneticassociationdb.nih.gov/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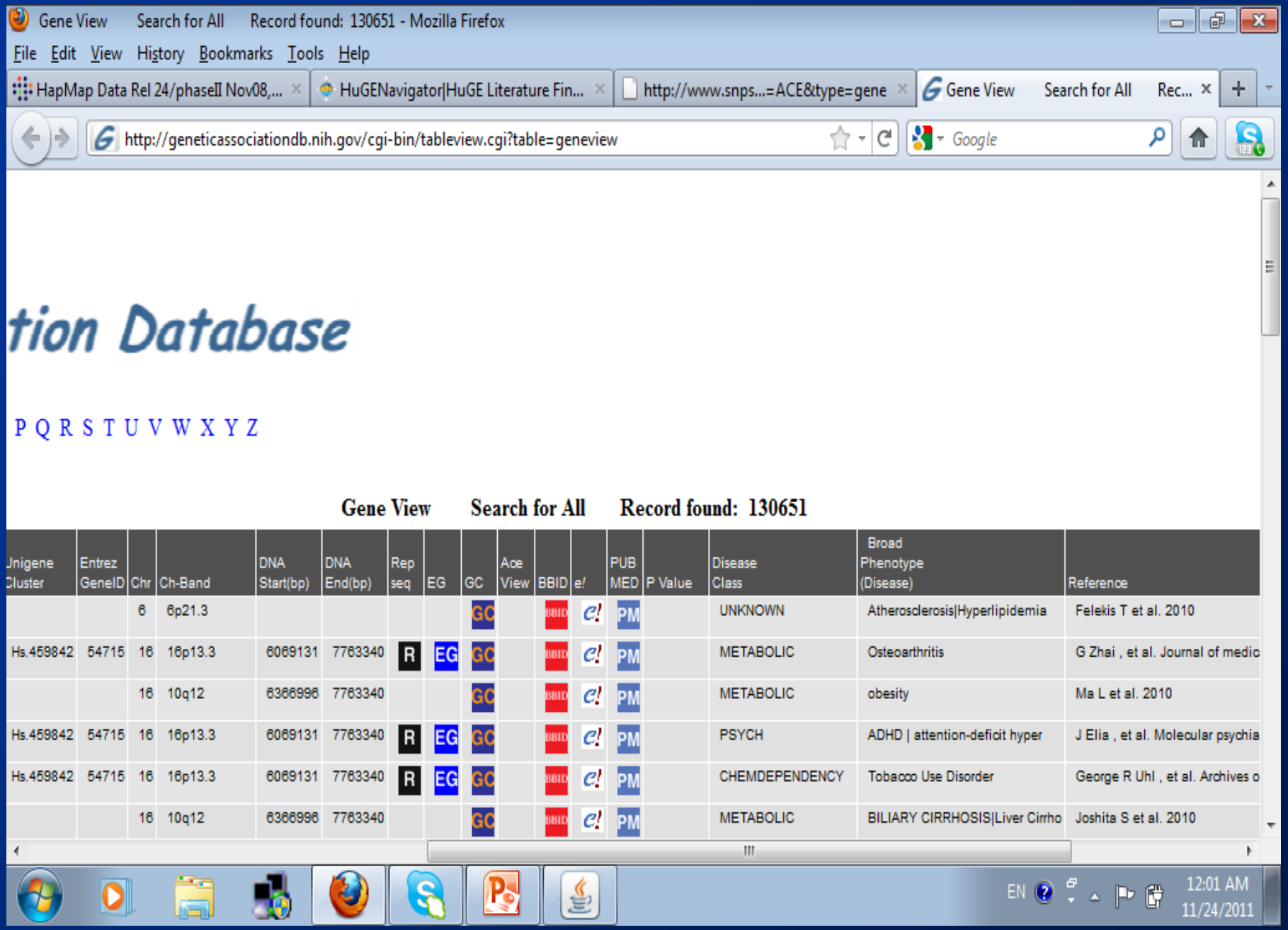
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6 6p21.3 UNKNOWN Atherosclerosis|Hyperlipidemia Felekis T et al. 2010
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16 10q12 6366996 7763340 METABOLIC obesity Ma L et al. 2010
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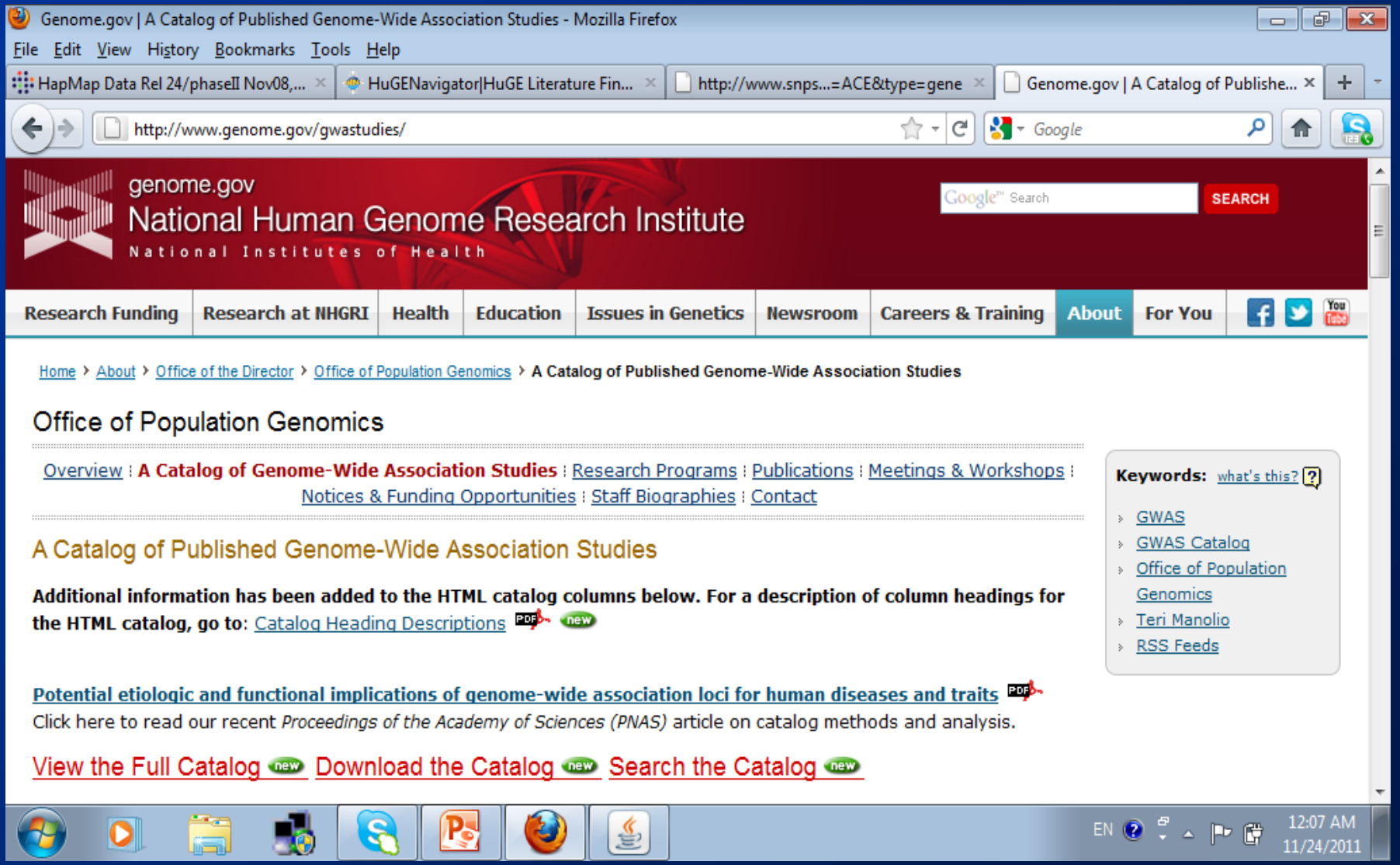

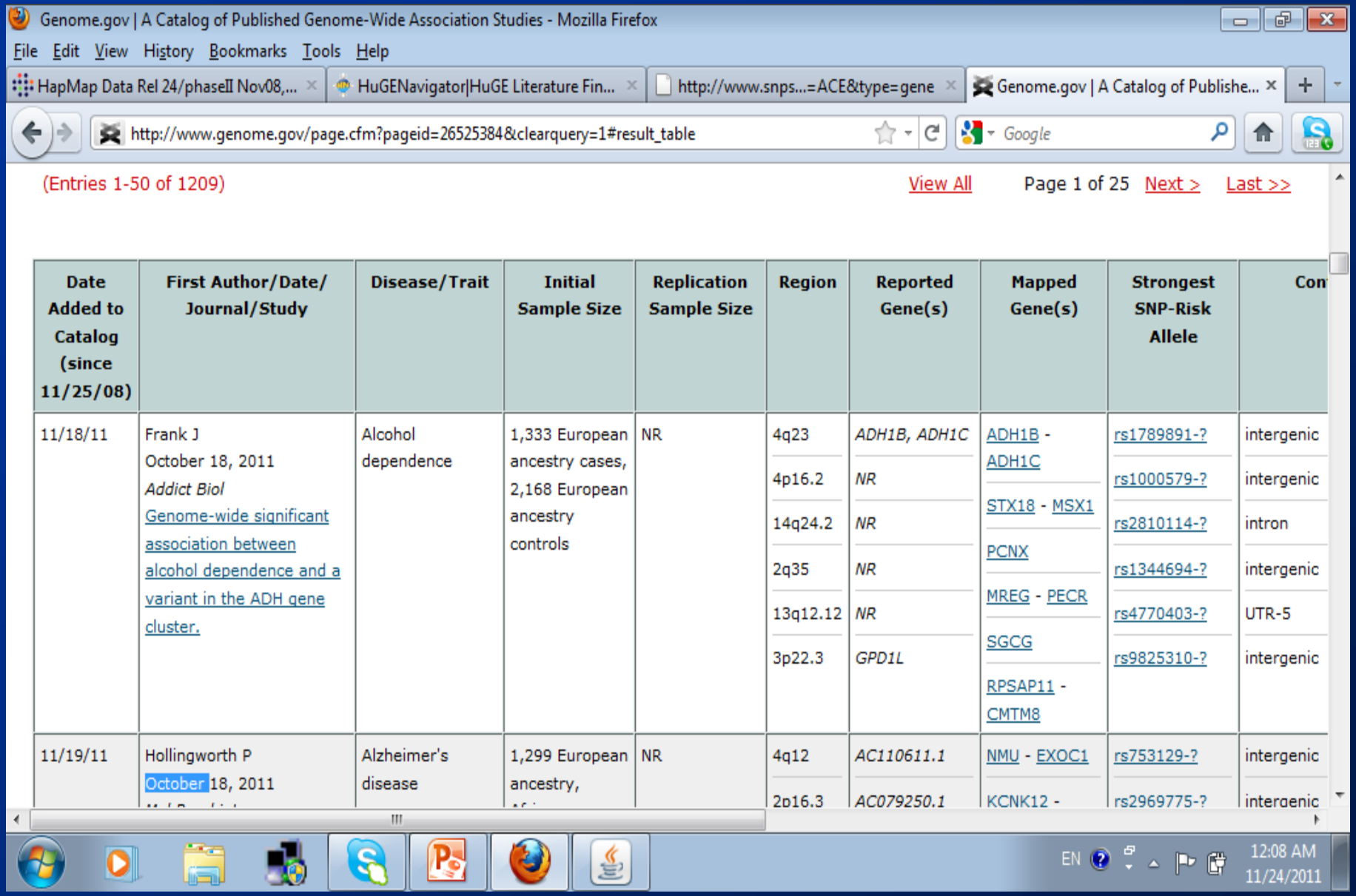

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Date Added to Catalog (since 11/25/08)	First Author/Date/ Journal/Study	Disease/Trait	Initial Sample Size	Replication Sample Size	Region	Reported Gene(s)	Mapped Gene(s)	Strongest SNP-Risk Allele	Con
11/18/11	Frank J October 18, 2011 *Addict Biol* Genome-wide significant association between alcohol dependence and a variant in the ADH gene cluster.	Alcohol dependence	1,333 European ancestry cases, 2,168 European ancestry controls	NR	4q23 4p16.2 14q24.2 2q35 13q12.12 3p22.3	*ADH1B, ADH1C* *NR* *NR* *NR* *NR* *GPD1L*	ADH1B - ADH1C STX18 - MSX1 PCNX MREG - PECR SGCG RPSAP11 - CMTM8	rs1789891-? rs1000579-? rs2810114-? rs1344694-? rs4770403-? rs9825310-?	intergenic intergenic intron intergenic UTR-5 intergenic
11/19/11	Hollingworth P October 18, 2011	Alzheimer's disease	1,299 European ancestry,	NR	4q12 2p16.3	*AC110611.1* *AC079250.1*	NMU - EXOC1 KCNK12 -	rs753129-? rs2969775-?	intergenic intergenic

GENETIC EPIDEMIOLOGY GLOSSARY

M.Tevfik DORAK

Accompanying Genetic Epidemiology Lecture Note & Presentation

ACCE project (analytic validity, clinical validity, clinical utility, ELSI): A CDC sponsored project for evaluating data on emerging genetic tests. It takes its name from the four components of evaluation: analytic validity, clinical validity, clinical utility and associated ethical, legal and social implications (ELSI). For details, see ACCE Project website. See also Grosse & Khoury, 2006 for the clinical utility of genetic testing, Offit, 2008 for issues surrounding genomic disease profiling, and Pharoah, 2008 for the possible utility of genomic profiling in breast cancer risk assessment.

Additive genetic model: In a disease association study, if the risk conferred by an allele is increased r-fold for heterozygotes and 2r-fold for homozygotes, this corresponds to additive model (Lewis, 2002). These data are best analyzed using Armitage trend test for genotype frequencies or by logistic regression in which the genotypes are represented as (-1), 0, (+1). This genotype-based association test does not require the locus to be in **Hardy-Weinberg equilibrium**. In the case of an association with heterozygosity, the additive model test may be statistically non-significant despite the presence of an association. Thus, a non-significant additive model test does not rule out an association. It has been pointed out that "genes do not generally act in a simple additive manner but through complex networks involving gene-gene and gene-environment interactions" (Colhoun, 2003). The effect that cannot be explained by an additive (or heterogeneity / non-interactive) model in complex disease genetics is due to the dominance (epistatic / interactive) model. See also **multiplicative genetic model**. See MODEL-online tool for genetic association analysis for different models.

Additive variance: The component of genetic variance due to the additive effects of alleles segregating in the population. In evolutionary genetics, additive genetic variance is a measure for the potential amount of evolutionary change caused by natural selection. See Genetic Calculation Applets:


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Department of Biomathematics

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ΣΧΟΛΗ ΕΠΙΣΤΗΜΩΝ ΥΓΕΙΑΣ
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The
"PRIZE OF DISTINGUISHED RESEARCHER IN MEDICINE AT UNIVERSITY OF THESSALY"
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Elias Zintzaras

Research Interests

- Mathematical modelling of genetic systems
- Genetic statistics and epidemiology
- Bioinformatics
- Meta-analysis
- Monte-Carlo modelling
- Bioequivalence testing

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