

Ecogenetics and the role of genetics
in personal response differences to
environmental factors

GENES vs ENVIRONMENT

Cystic
fibrosis

Trauma

Cancer

Deafness

Color
blindness

Infection

Diabetes mellitus

Phenylketonuria

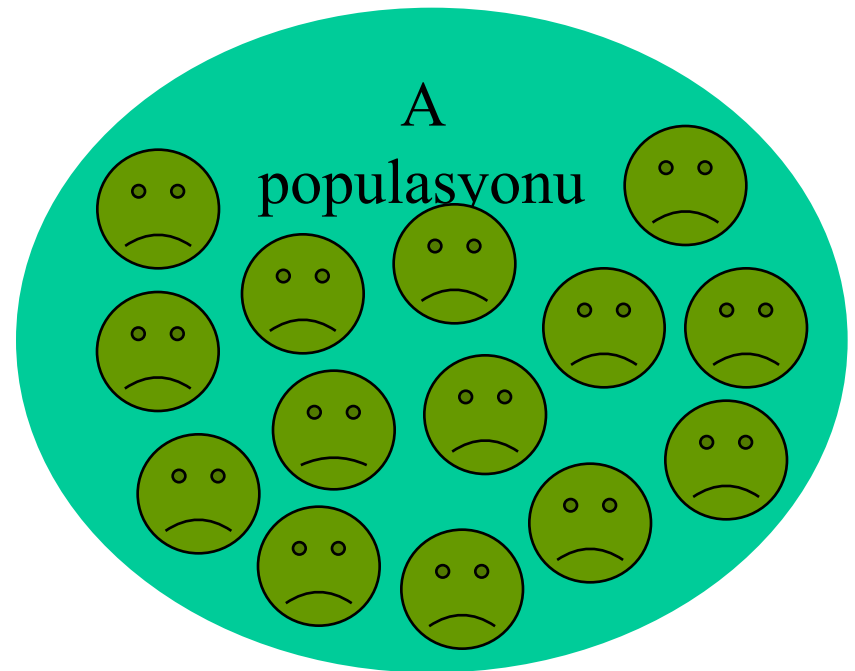
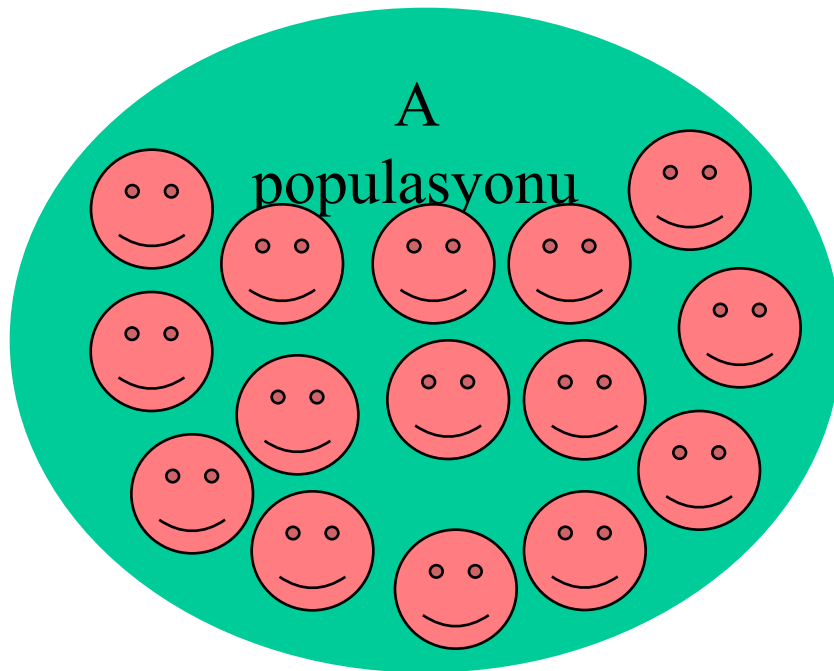
Intoxication

INHERITED

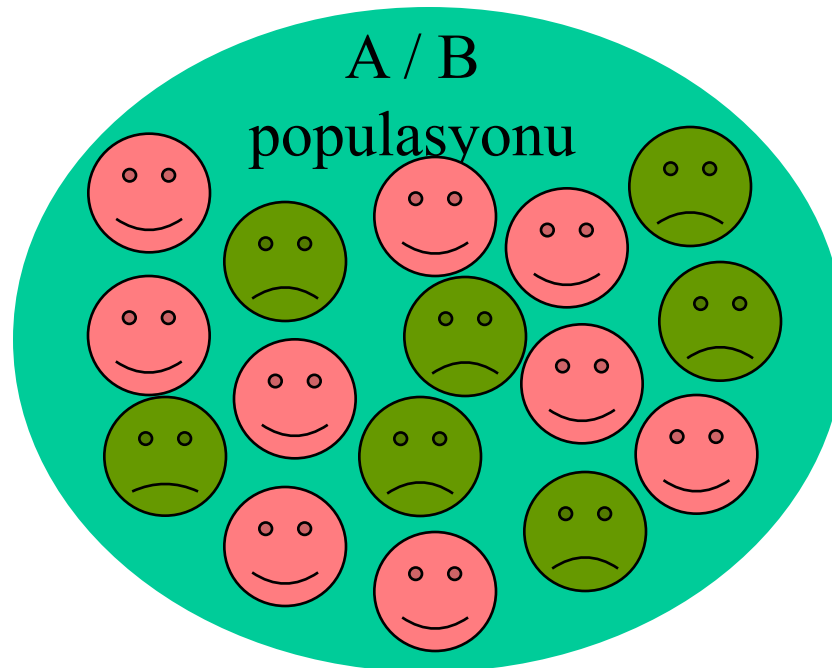
ENVIRONMENTAL

Population vs Environment Differences

- Same genetical background different environments



- Different genetical background same environment



Ecogenetics

It's a branch of genetics that studies genetic traits related to the response to environmental substances. Or, a contraction of ecological genetics, the study of the relationship between a natural population and its genetic structure.

Examples to important polymorphisms that cause different responses to environmental conditions/affects

1. **Alpha 1-antitrypsin (A1AT)** – a protease (peptidase) inhibitor, encoded by *SERPINA1*

A1AT is produced in the liver,

Protects the lungs from neutrophil elastase.

A1AT total deficiency can severely cause inflammation in the respiratory system, pancreas and liver.

Over 75 mutations are detected. Major alleles are M, S and Z

PiMM: 100% (normal)

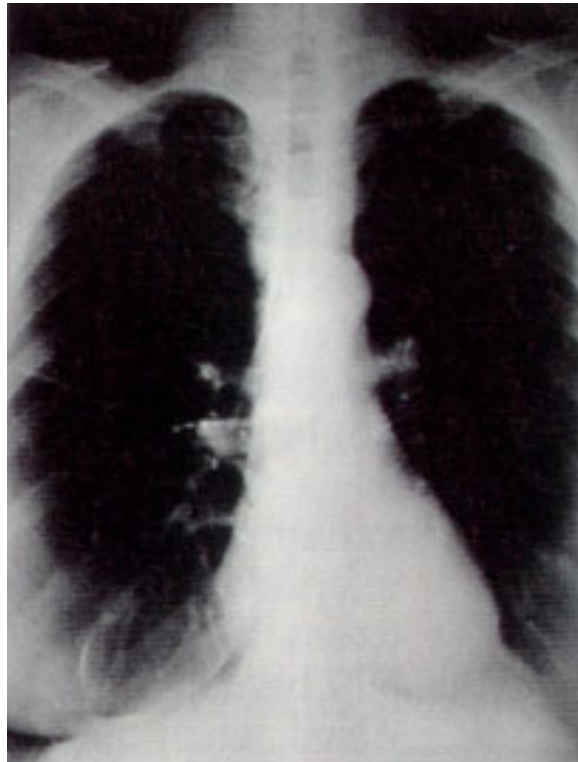
PiMS: 80% of normal serum level of A1AT

PiSS: 60% of normal serum level of A1AT

PiMZ: 60% of normal serum level of A1AT

PiSZ: 40% of normal serum level of A1AT (otherwise normal people may be effected by being exposed to cigarette smoke or air pollution)

PiZZ: 10-15% (severe alpha-1 antitrypsin deficiency - disorder)



Emphysema due to alpha-1
antitrypsin deficiency.

Examples to important polymorphisms that cause different responses to environmental conditions/affects

- Lactase** – an enzyme that digest lactose (diary products – breat milk), encoded by *LCT*
The primary lactase deficiency is caused by the the absence of lactase persistance allele.
MCM6 gene helps control whether the *LCT* gene is turned on or off.

Lactase production usually drops 90% during the first four years of life in humans, though the rate varies widely. This leads to lactose intolerance.

Certain human populations have a mutation (on chromosome 2) which results in persistence of lactase activity (gain of function).

Populations that are lactose intolerant lack this mutation.

Analysis of the DNA of 94 ancient skeletons in Europe and Russia concluded that the mutation for lactose tolerance appeared about 4,300 years ago and spread throughout the European population.

Examples to important polymorphisms that cause different responses to environmental conditions/affects

Primary congenital alactasia, also called congenital lactase deficiency, is an extremely rare, autosomal recessive enzyme defect that prevents lactase expression from birth. People with congenital lactase deficiency cannot digest lactose from birth, so cannot digest breast milk. This genetic defect is characterized by a complete lack of lactase (alactasia).

Persistence of lactase in the intestine permits the “unnatural” continuation of milk ingestion throughout life, enhancing growth and development. One benefit is higher calcium intake, especially in northern climates where sun is insufficient to activate vitamin D.

People without this mutation shut off lactase production and become “lactose malabsorbers”; they may become “lactose intolerant” with symptoms of excess gas (hydrogen) and diarrhea upon eating lactose-containing dairy products.

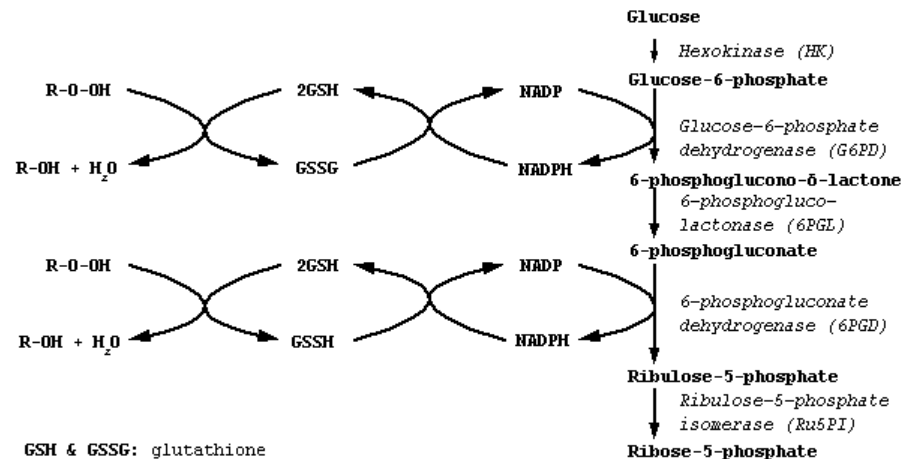
Lactose Intolerance in different populations

Human Groups	Percent Intolerant	Allele Frequency
Swedish	2%	0.14
Europeans in Australia	4%	0.20
Swiss	10%	0.32
American Caucasians	12%	0.35
Finns	18%	0.42
African Tutsi	20%	0.45
African Fulani	23%	0.48
American Blacks	75%	0.87
Australian Aborigines	85%	0.92
African Bantu	89%	0.94
Chinese	93%	0.96
Thais	98%	0.99
American Indians	100%	1.00

Examples to important polymorphisms that cause different responses to environmental conditions/affects

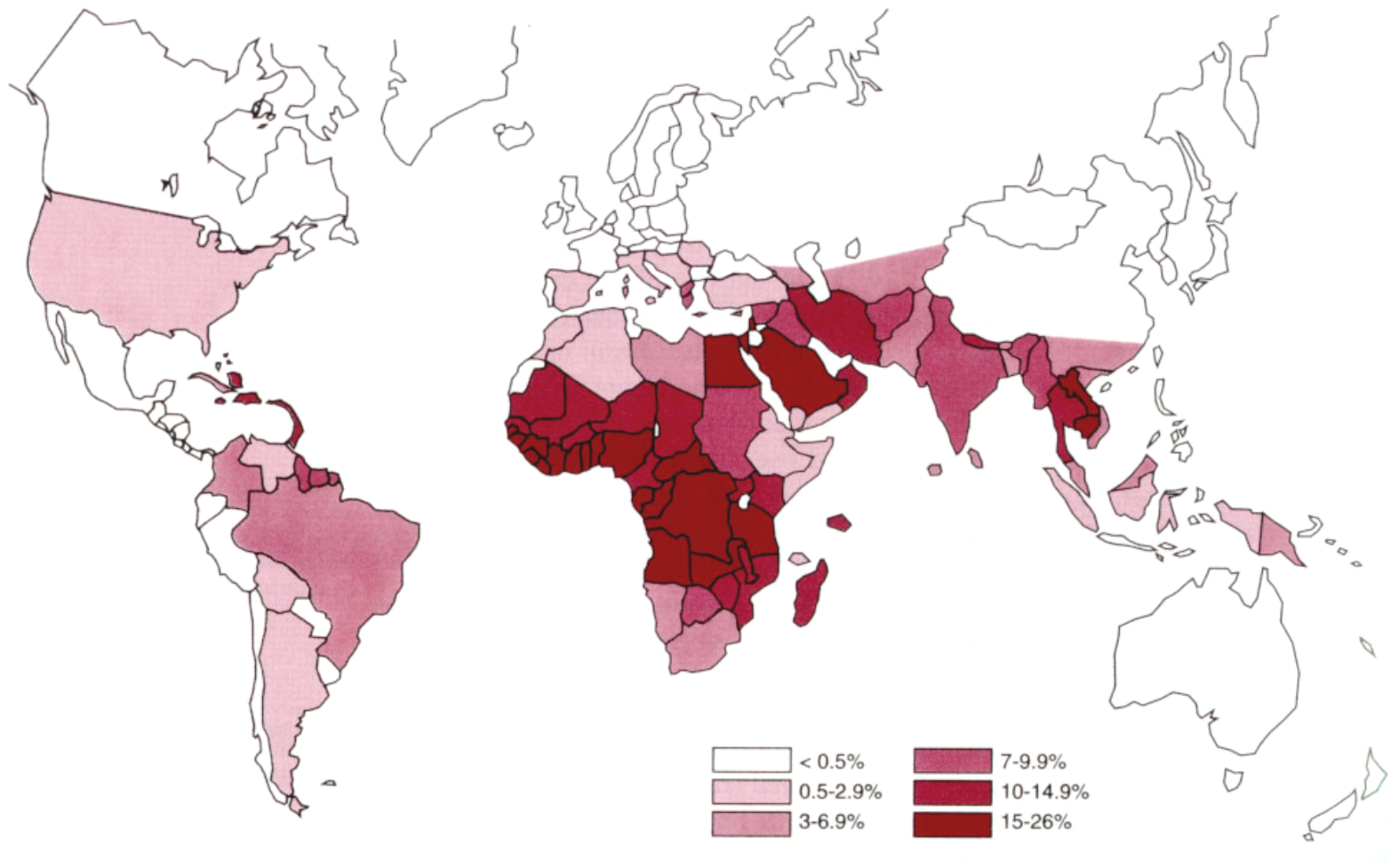
3. **Glucose-6-phosphate dehydrogenase** – an enzyme of pentose phosphate pathway. Functions to supply reducing energy to cells like erythrocytes which are subject to extensive oxidation by maintaining the level of the co-enzyme nicotinamide adenine dinucleotide phosphate. NADPH in return maintains the level of glutathione which protects cells from hemolytic effects of hydrogen peroxide.

The Pentose Phosphate Pathway and Glutathione production



G6PD deficiency is very common worldwide, (400 million globally-30,000 deaths annually). It causes acute hemolytic anemia in the presence of simple infections, ingestion of fava beans, reaction with certain medicines, antibiotics, antipyretics and antimaliarals. Avoiding triggers is important.

Carriers of the G6PD deficiency alleles may be partially protected against malaria.



Distribution of G6PD deficiency worldwide

Examples to important polymorphisms that cause different responses to environmental conditions/affects

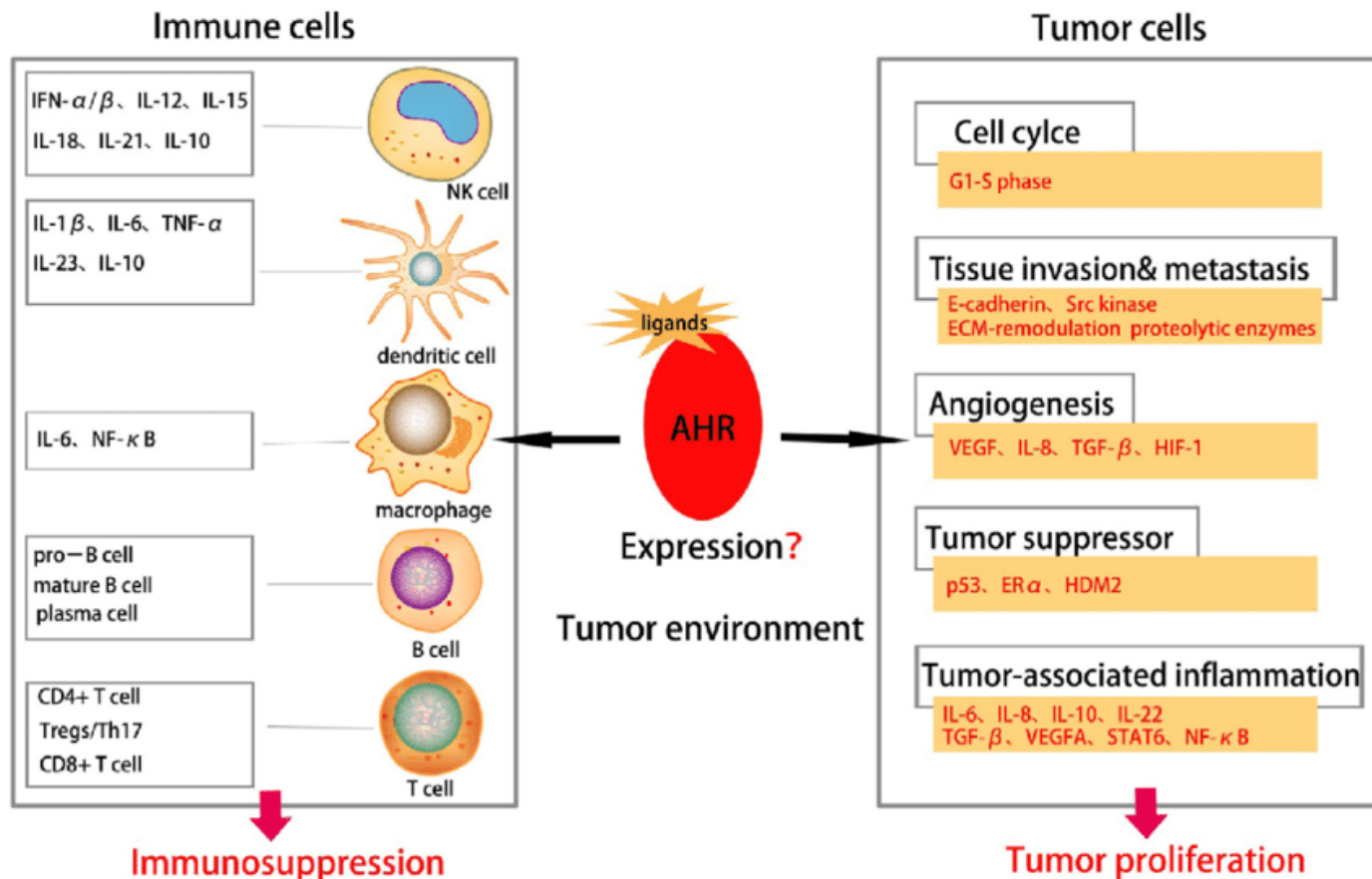
4. **Alcohol dehydrogenases (ADH)** - an effective method for eliminating both endogenous and exogenous formaldehyde was evolutionerly important and this capacity has conserved the ancestral ADH-3 through time.

Alcohol intolerance is due to a genetic polymorphisms various enzymes in the pathway (eg. ALDH) This polymorphism is most often reported in Asian patients.

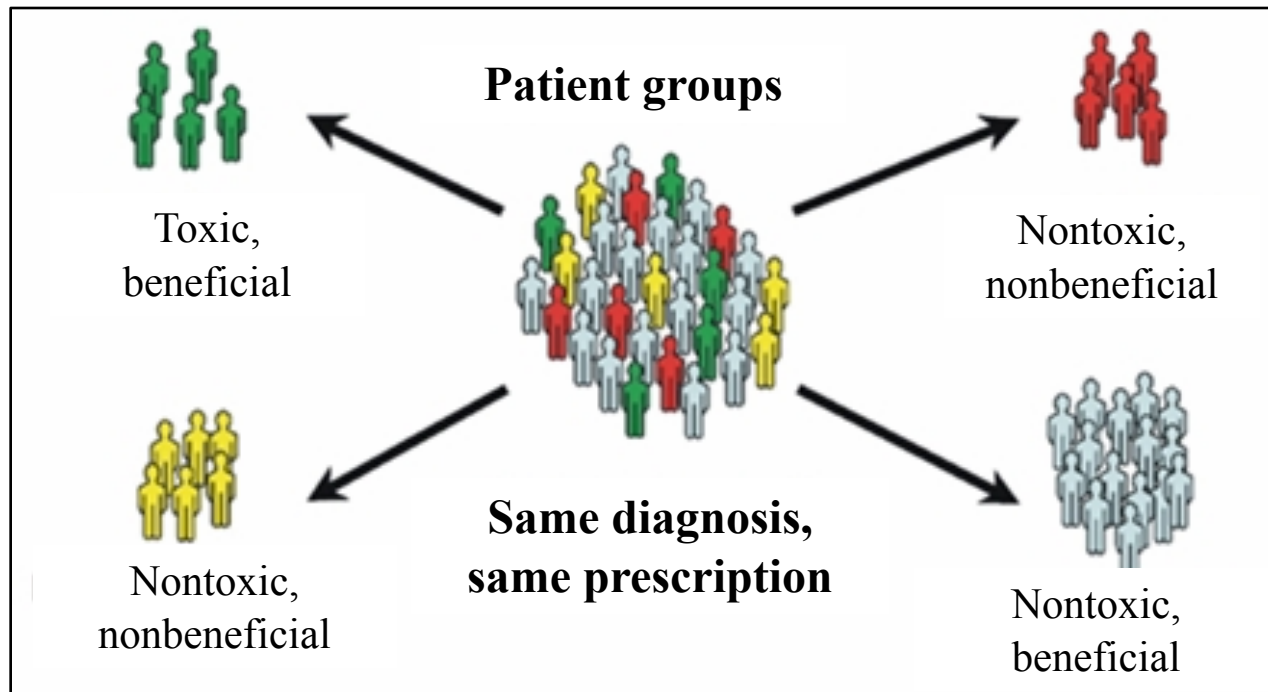
Examples to important polymorphisms that cause different responses to environmental conditions/affects

5. An aromatic hydrocarbon or arene (aryl hydrocarbon)

Arylhydrocarbon hydroxylase (AHH) – converts aromatic hydrocarbons to epoxides. Epoxy compounds. Most of them have carcinogenic effect.



In response to medication



Warfarin

Anticoagulant,
Prevents the thrombosis

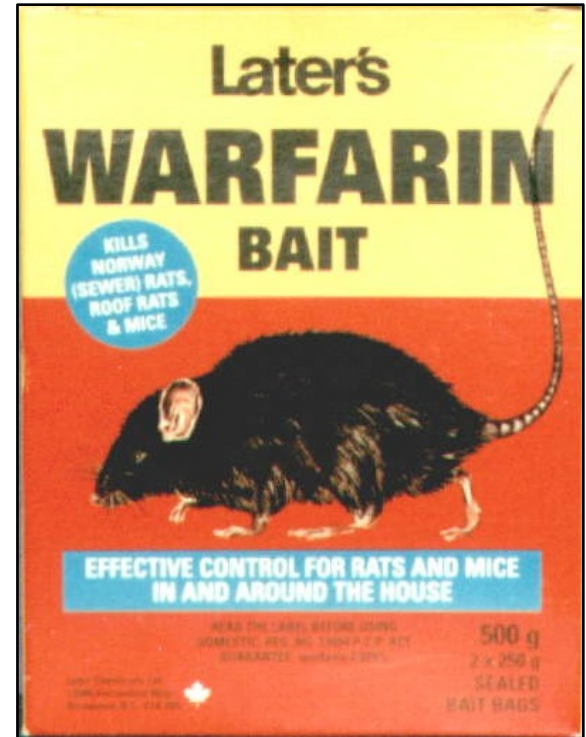


Warfarin
sold under the brand name **Coumadin**
among others

Warfarin mice poison
Inhibits vitamin K
Causes internal bleeding and death.

Optimal Dosing as an anticoagulant varies for people. Due to genetic polymorphism.

Genetic variants (VKORC1, CYP2C9)



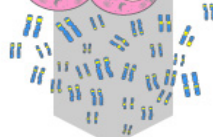
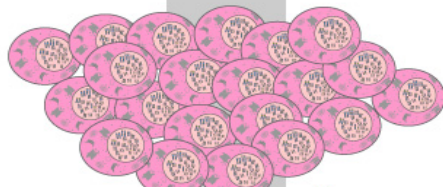
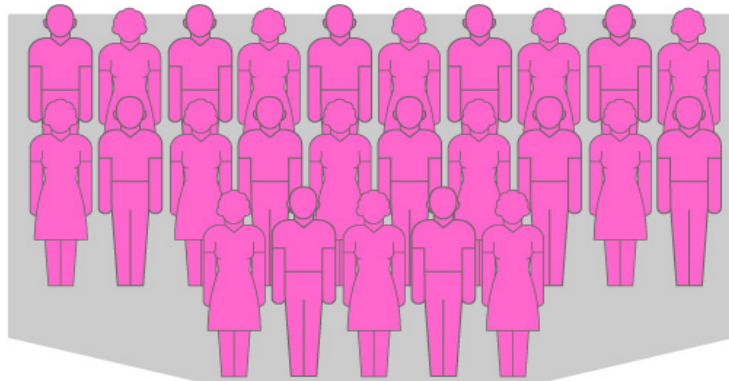
CYP4F2:cytochrome 450, subgroups

1				50				401				450			
QUERY	MSQLSLSWL	LWPVAASPWL	LLLLVGASWL	LAHVLAWTYA	FYDNCRRRLRC			QUERY	HVTQDIVLPD	GRVIPKGIIC	LISVFGTHHN	PAVWPDPEVY	DPFRFDPENI		
CPF2_HUMAN	MSQLSLSWL	LWPVAASPWL	LLLLVGASWL	LAHVLAWTYA	FYDNCRRRLRC			CPF2_HUMAN	HVTQDIVLPD	GRVIPKGIIC	LISVFGTHHN	PAVWPDPEVY	DPFRFDPENI		
O60634	MPQLSLSLGL	LWPMAASPWL	LLLLVGASWL	LARILAWTYT	FYDNCCLRLC			O60634	CCTQDIVLPD	GRVIPKGIIC	LISVFGTHHN	PAVWPDPEVY	DPFRFDPKNI		
CPF3_HUMAN	MPQLSLSLGL	LWPMAASPWL	LLLLVGASWL	LARILAWTYT	FYDNCCLRLC			CPF3_HUMAN	CCTQDIVLPD	GRVIPKGIIC	LISVFGTHHN	PAVWPDPEVY	DPFRFDPKNI		
CPFB_HUMAN	MPQLSLSWL	LCPVAASPWL	LLLLVGGSWL	LARVLAWTYT	FYDNCRRLLC			CPFB_HUMAN	CCTQDFVLPD	GRVIPKGIIC	LINIIIGIHYM	PTVWPDPEVY	DPFRFNQENI		
CPFC_HUMAN	MSLLSLPWL	LFPVAMSPWL	LLLLVVGSWL	LARILAWTYA	FYDNCRRLLC			CPFC_HUMAN	CCTQDIVLPD	GRVIPKGIIC	LIDIIIGVHHN	PTVWPDPEVY	DPFRFDPENS		
Q8VCA4	MPQLDLSWL	LFLAASSPWL	LLLLIGASWL	LARVLTQTYI	FYRTYHHLCD			Q8VCA4	RCTQDIVLPD	GRVIPKGVIC	IINIFATHHN	PTVWPDPEVY	DPFRFDPENI		
CPF4_RAT	MPQLDLSWL	LFLAASSPWL	LLLLIGASWL	LARVLTQTYI	FYRTYHHLCD			CPF4_RAT	RCTQDIVLPD	GRVIPKGVIC	IINIFATHHN	PTVWPDPEVY	DPFRFDPENI		
Q9EP75	MSQLSLSWL	LCPVAFPPWK	TLLLIGASWI	LARILIQIYA	AYRNYRHLHG			Q9EP75	CCTQDILLPD	GRTIPKGIIC	LISIFGIHHN	PSVWPDPEVY	DPFRFDPENI		
Q99N18	MPQLDLSWL	LFLAASSPWL	LLLLIGASWL	LARVLTQTYI	FYRTYHHLCD			Q99N18	RCTQDIVLPD	GRVIPKGVIC	IINIFATHHN	PTVWPDPEVY	DPFRFDPENI		
CPF8_HUMAN	MSLLSLSWL	LFPVAASPWL	LLLLVVGASWL	LARILAWTYA	FYHNGRRRLC			CPF8_HUMAN	GCTQDVVLPD	SRVIPKGNVC	NINIFAIHHN	PSVWPDPEVY	DPFRFDPENA		
CPF1_RAT	MSQLSLSWL	LCPVAFPPWQ	TLLLFGASWI	LAQILTQIYA	AYRNFRRRLG			CPF1_RAT	CCTQDILLPD	GRTIPKGIIC	LISIFGIHHN	PSVWPDPEVY	NPFRFDPENI		
CPF6_RAT	MLQLSLSRLG	MGSLTASPWH	LLLLGGASWI	LARILAWIYT	FYDNCCLRLC			CPF6_RAT	CCSQDIVLPD	GRVIPKGNIC	VISIFGVHHN	PSVWPDPEVY	NPFRFDPENP		
Q99N16	MSQLSLSWMG	LHTAASPWL	LLLLAGASCL	LAYILTQIYG	VFENSLRLRC			Q99N16	CCTQDIVLPD	GRVIPKGVIS	RISIFGTHHN	PAVWPDPEVY	DPFRFDADNV		
Q99N17	MLRLSVSGLD	LGSVVTSSWH	LLLLGVASWI	LARILAWTYS	FYENC SRLSC			Q99N17	RCTRDIVLPD	GRVIPKGNIC	VISIFGIHHN	PSVWPDPEVY	DPFRFDPENP		
Q9D8N4	MSQLSMSWMG	LHTAASPWL	LLLLAGASCL	LAYILTQIYG	VFENSLRLRC			Q9D8N4	CCTQDIVLPD	GRVIPKGVIS	RISIFGTHHN	PAVWPDPEVY	DPFRFDADNV		
Q9GLL1	MLELSVSRGL	FGLVAASPWL	LLLLVVGASWL	LARVLAWTYT	FYDNCRRLLC			Q9GLL1	CCTQDIVLPD	GRVIPKGVIS	IIDIFGTHHN	QSVWPDPEVY	DPFRFDQENI		
CPF5_RAT	MPWLTVSGLD	LGSVVTSTWH	LLLLGAASWI	LARILAWTYS	FCENCSRLRC			CPF5_RAT	RCTQDIVLPD	GRVIPKGNIC	VISIFGIHHN	PSVWPDPEVY	DPFRFDPENR		
Q8N3P5	MPQLSLSWL	LCPVAASPWL	LLLLVGGSWL	LARVLAWTYT	FYDNCRRLLC			Q8N3P5	CCTQDFVLPD	GRVIPK----	-----VY	DPFRFNQENI			
Q9EQ70	MPWLTVSGLD	LGSVVTSTWH	LLLLGAASWI	LARILAWTYS	FCENCSRLRC			Q9EQ70	RCTRHIVLPD	GRVIPKGNIC	VISIFGIHHN	PSVWPDPEVY	DPFRFDPENR		
Q99N19	MLQLCLS WL	MGSLTASPWH	LLLLGGASWI	LARILAWIYA	FYDNC SRLRC			Q99N19	CCTQDVLLPD	GRAIPKGNIC	VISIFGVHHN	PSVWPDPEVY	NPFRFDPENP		
Q99KY6	MLQLCLS WL	MGSLTASPWH	LLLLGGASWI	LARILAWIYA	FYDNC SRLRC			Q99KY6	CCTQDILLPD	GRAIPKGNIC	VISIFGVHHN	PSVWPDPEVY	NPFRFDPENP		
								O60389	CCTQDIVLPD	GRVIPKGIIC	LIDIIIGVHHN	PTVWPDPEVY	DPFRFDPENS		
								Q8N8H4	QCTEDIKLPD	GRIIPKGIIC	LVSIIYTHHN	PTVWPDPEVY	NPYRFDPNP		
								CP46_RABIT	QLSSPVTFPD	GRSLPKGVIV	TLSIYALHHN	PKVWPNPEVY	DPFFAPGS-		
								CP45_RABIT	DLSSPVTFPD	GRSLPKGFTV	TLSIYGLHHN	PKVWPNPEVY	DGGRFTPGS-		



Trp (W) → Gly (G) Val (V) → Gly (G)
 + Warfarin tolerans1 -

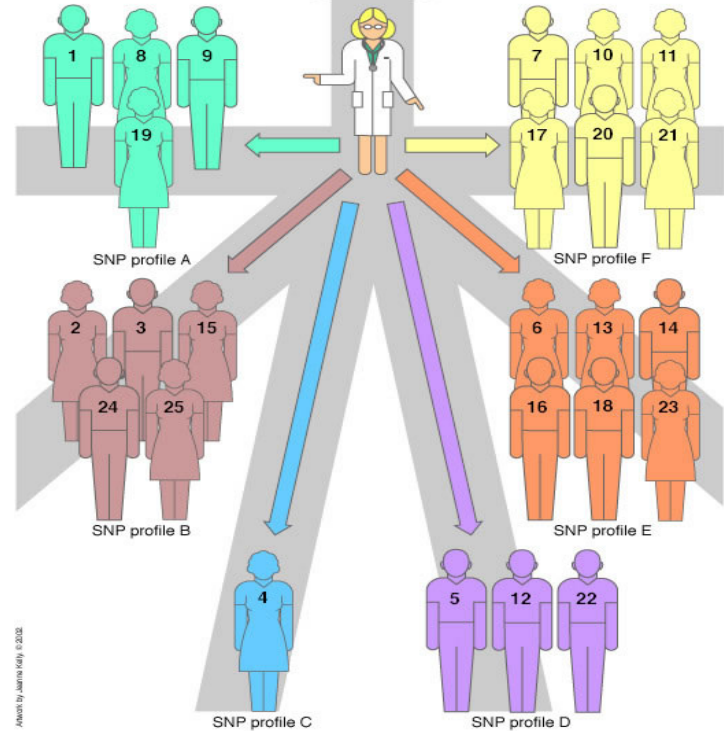
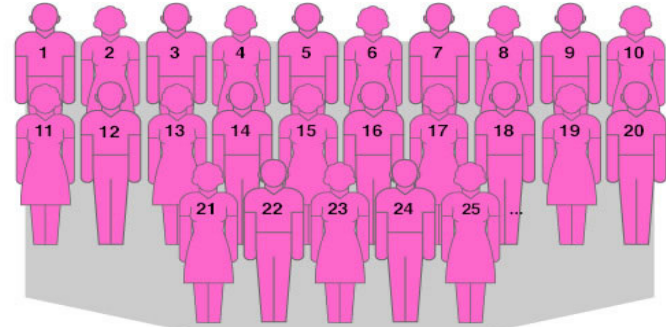
Population differences due to SNPs



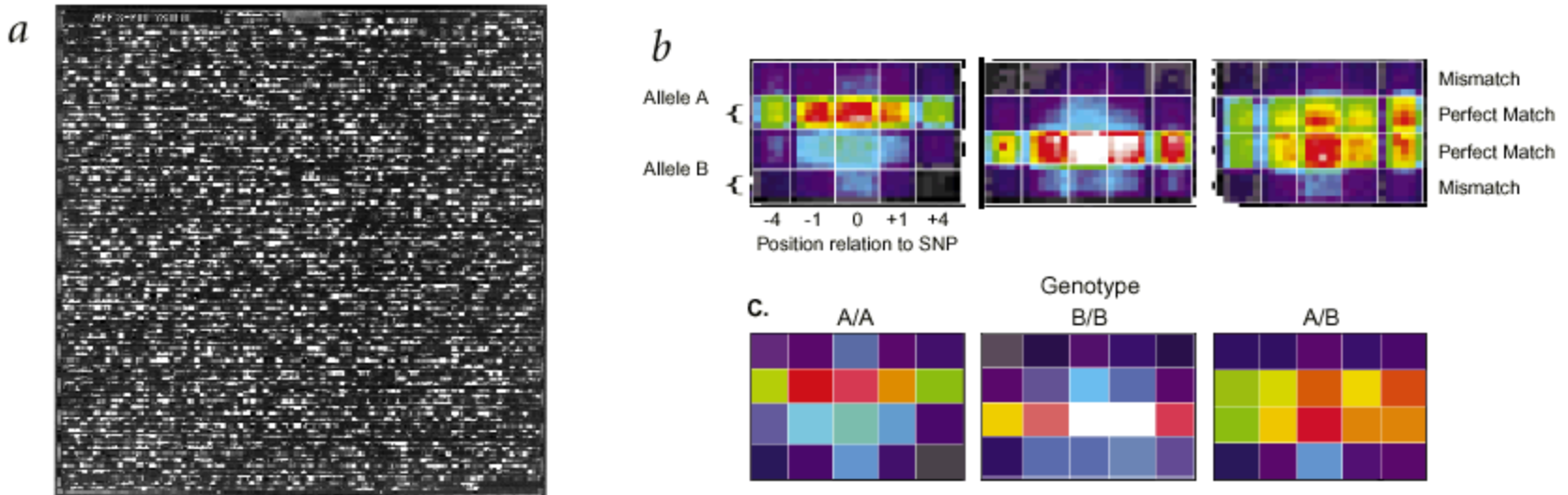
All chromosomes are sequenced
All SNPs are recorded



SNP Data
SNP #1, Chromosome 1, Position 20, G→C
SNP #2, Chromosome 1, Position 25, C→G



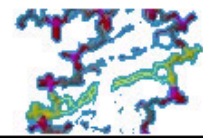
SNP Genotyping



Microarray based high performance SNP studies



Single Nucleotide Polymorphism



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Entrez SNP	ID Numbers	Submission Info	Batch	Locus Info	Free Form	Easy Form	Between Markers
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ANNOUNCEMENT

- NEW!** dbSNP genotype data are now available on the web and on our FTP site ([more info](#)).
- ALERT!** xml brief and submission format reports are dropped from ftp dump starting build 116. Please contact [snp-admin](#) with concerns.

Search by IDs

Note: [rs#](#) and [ss#](#) must be prefixed with "rs" or "ss", respectively (i.e. rs25, ss25)

Reference cluster ID(rs#)

[Advanced ID Search](#)

Submission Information

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