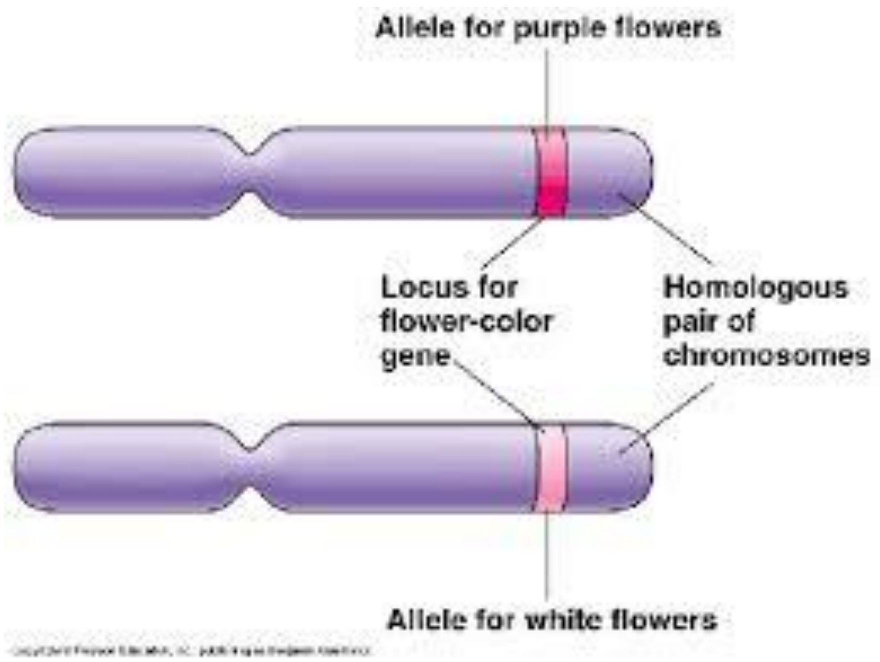
Genetics of Blood Group Systems

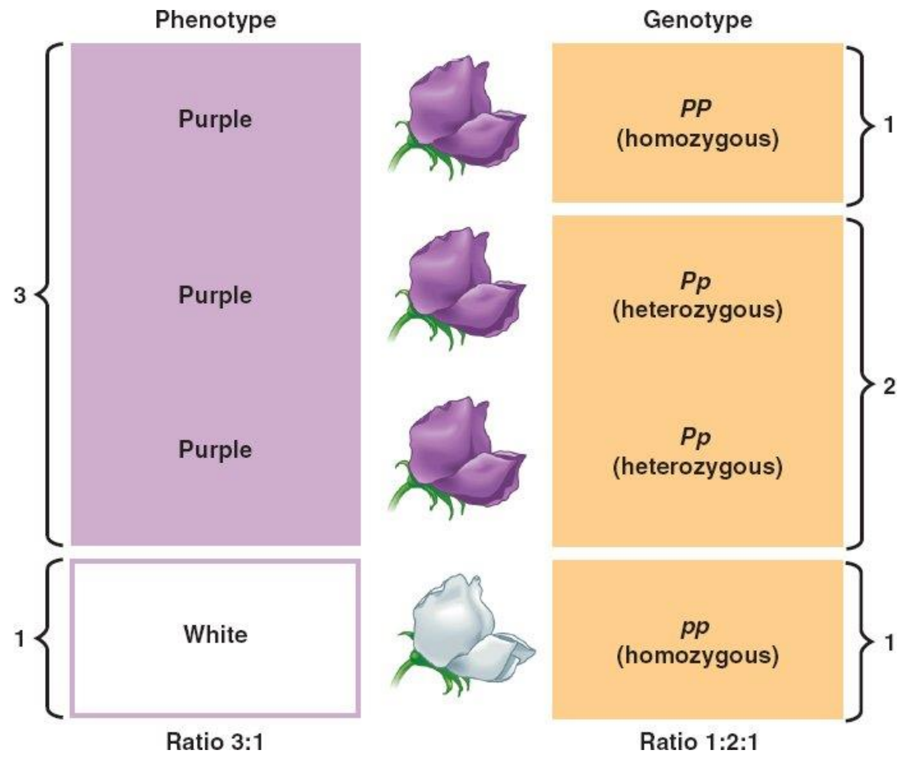
Basic Terminology

- Gene: Section of DNA on chromosome
- Locus: Specific location of gene on chromosome
- Allele: One form of gene at locus
- Antithetical: antigens that represent different forms of a gene product from the same locus
  - Ex. Blood type A and B



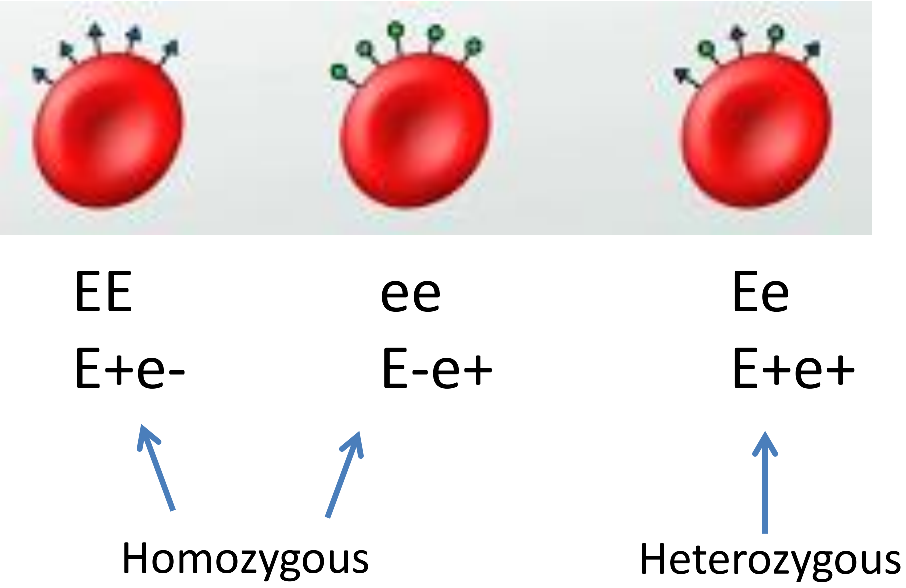
Genotype vs. Phenotype

- Genotype: Sequence of DNA inherited (Pp)
- Phenotype: Anything produced by genotype (enzyme, antigen, eye color, hormone levels, etc.)
  - Rh positive
- Amorph: “silent gene”- does not produce any detectable trait
  - O blood group



Homozygous vs. Heterozygous

- Homozygous: 2 of the same allele
- Heterozygous: 2 different alleles
- Codominant: both alleles are expressed and seen phenotypically
  - Most blood group genes are codominant
- Ex. Heterozygous AB has both A and B antigen on RBCs
- Dosage Effect:
  - Stronger reactions with homozygous expression



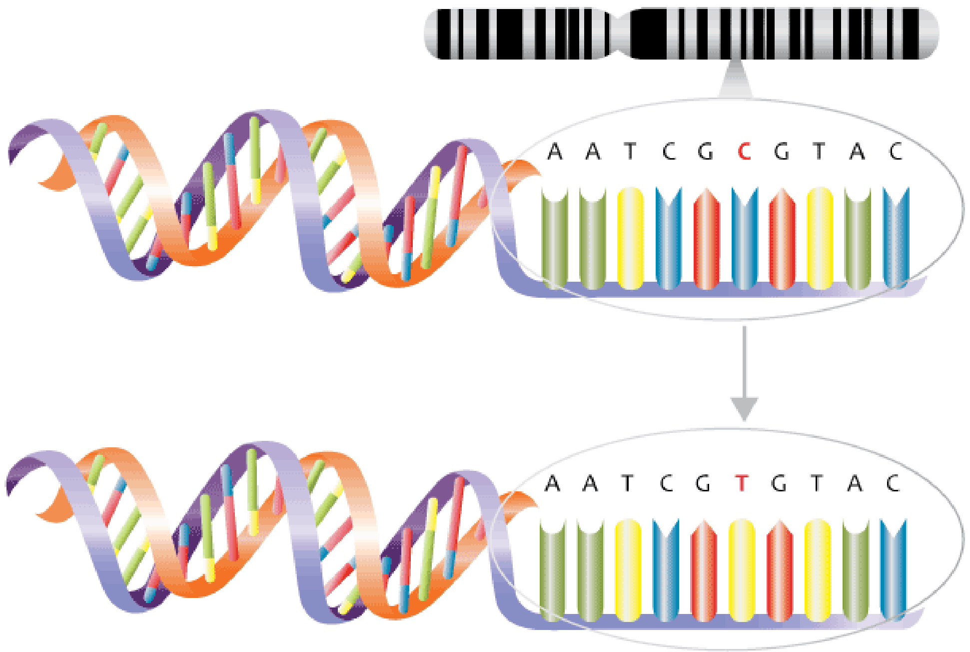
Genetics of Blood Group Systems

- Each blood group system is controlled by a single gene or a few very closely linked homologous genes
- Each of these genes demonstrates 1 or more antigens
- Antigens are mostly glycoproteins with either a carbohydrate epitope or amino acid/protein epitope
- Antigens are usually the result of a single nucleotide polymorphism (SNP)
- Currently 38 blood group systems

System Name	Gene(s)	Number of Antigens
ABO	ABO	4
Rh	RHD, RHCE	55
MNS	GPA, GPB	49
P1PK	A4GALT	3
Kell	KEL	36
Lewis	FUT3	6
Duffy	ACKR1	5
Kidd	SLC14A1	3
Lutheran	BCAM	25
I	GCNT2	1

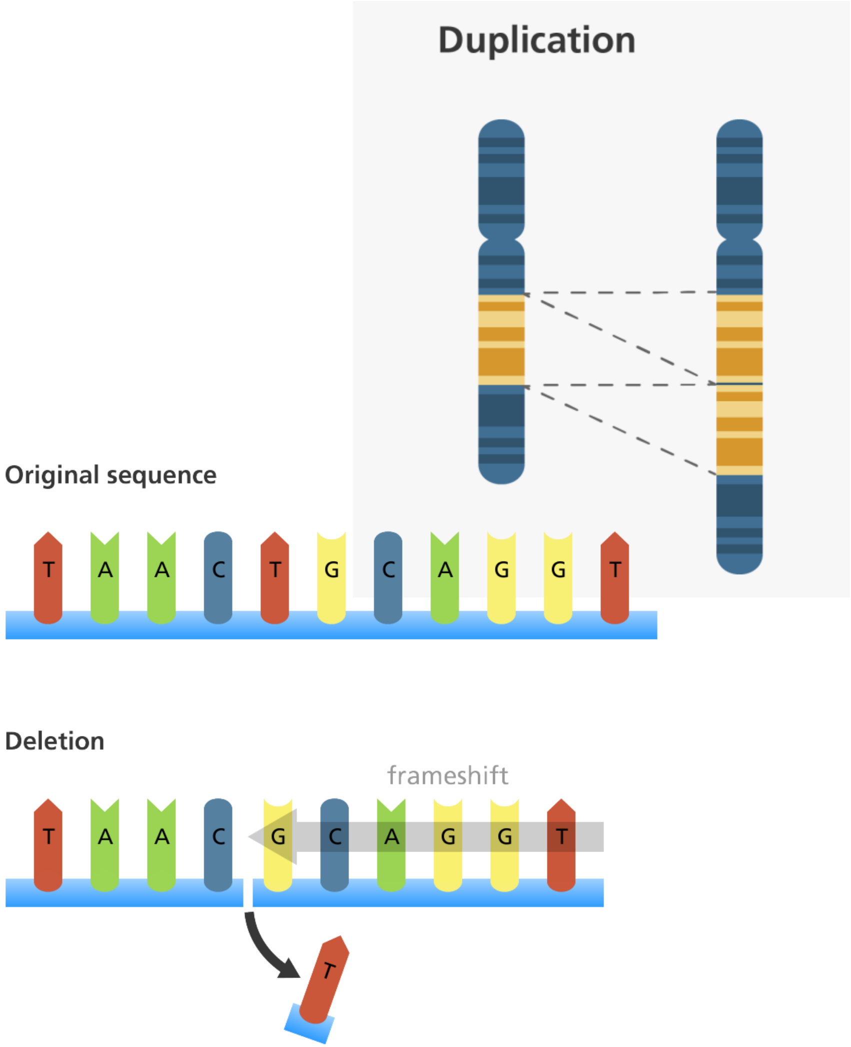
Single Nucleotide Polymorphism (SNP)

- A difference in a single DNA nucleotide – substitution
  - Missense – changes a codon altering amino acid
  - Nonsense – changes a codon to form a stop codon
- Most common type of genetic variation among people
  - Occur almost once in every 1,000 nucleotides
- To qualify as a SNP it must occur in at least 1% of the population
- Usually have no effect on health or development



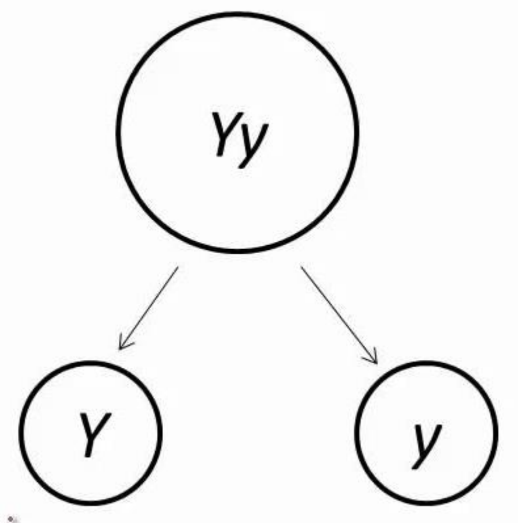
Duplications and Deletions

- Duplication
  - Whole set of DNA duplicated
  - Can cause pseudogenes
  - Ex. Glycophorin A (M and N antigens) duplicated to form glycophorin B
    - Added 2 antigens (S and s) to red cells
- Deletion
  - Delete part of a gene or a single nucleotide
  - Ex. In ABO blood grouping, single nucleotide deletion causes nonfunctional transferase protein
    - Unable to form blood type “A” or “B”
    - Result is blood type “O”

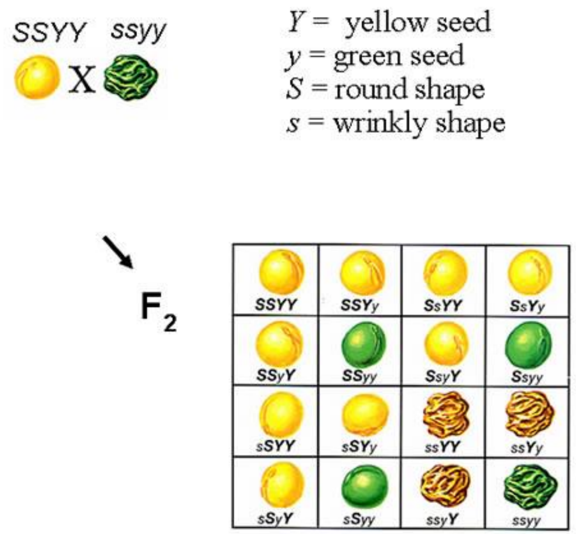


Inheritance

- Inheritance of blood group genes follow the principles of independent segregation and independent assortment
  - Only 1 member of an allelic pair from each parent is passed to the next generation
  - Genes for different blood group systems are inherited separately from each other



Law of independent segregation

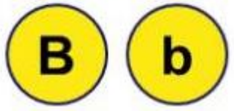


Law of independent assortment

Hardy-Weinberg Equation

- Allows us to calculate the genotype frequency and gene frequency in a population
- Gene (or allele) frequencies tend to remain constant over generations

$$p + q = 1$$



p= gene (allele) frequency of dominant allele (B)
q= gene (allele) frequency of recessive allele (b)

$$p^2 + 2pq + q^2 = 1$$

p^{2}= % of homozygous dominant (BB)
q^{2}= % of homozygous recessive (bb)
2pq= % of heterozygous (Bb)

Different types of Frequencies

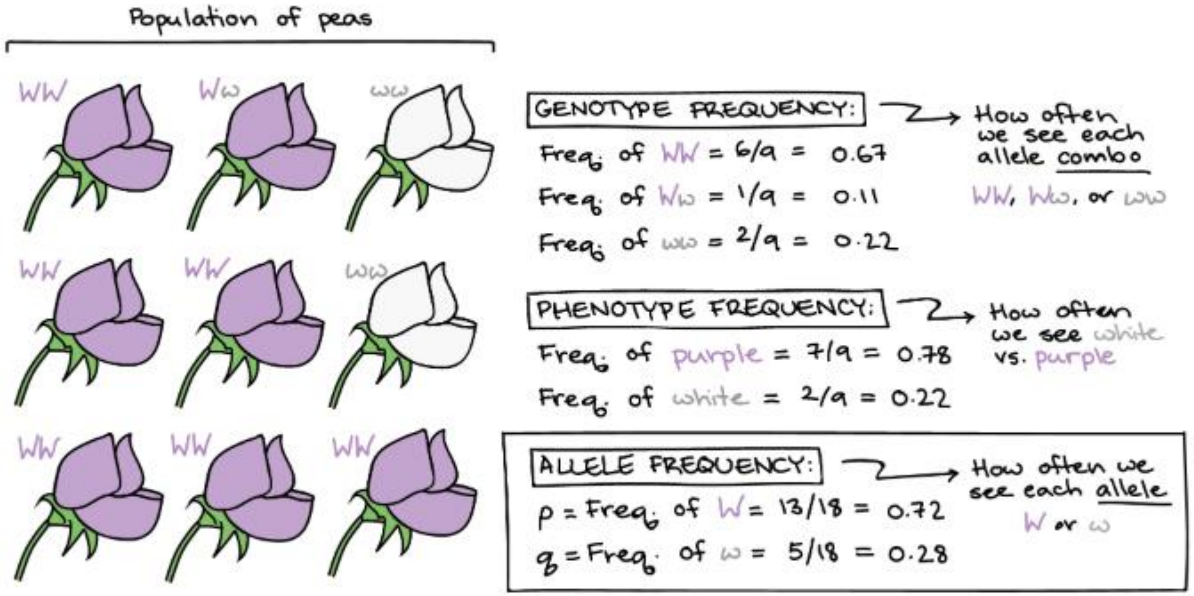
- Gene or Allele frequency
  - how frequently allele appears in population (W or w)
  - Values of p or q
- Genotype frequency
  - How often we see each allele combination in the population (WW, Ww, or ww)
  - Values of p^2, $2pq$, or q^2
- Phenotype frequency
  - How often we see the phenotype in the population (purple or white flowers)
  - Values of $p^2 + 2pq$ = Purple
  - Values of q^2 = White
  - If codominant, then phenotype 1 would be $p^2 + 2pq$ and phenotype 2 $q^2 + 2pq$

W - dominant purple allele

w - recessive white allele

$$p^2 + 2pq + q^2 = 1$$

$$p + q = 1$$



Hardy-Weinberg Example 1

In a population of 1000 people, the frequency of DD and Dd (Rh positive) is 84%. The frequency of dd (Rh negative) is 16%. What is the gene frequency of the D allele?

Always start by figuring out what values you are given and what value you are trying to find.

We are given the following:

- Phenotype frequency of Rh positive (84%) – $p^2 + 2pq$
- Phenotype and genotype frequency of Rh negative (16%) – q^2

We are looking for:

- The gene frequency of the D allele – value of p

Hardy-Weinberg Example 1 Cont

In a population of 1000 people, the frequency of DD and Dd (Rh positive) is 84%. The frequency of dd (Rh negative) is 16%. What is the gene frequency of the D allele?

q^2= dd which is 0.16

$q = \sqrt{0.16} = 0.4$

$p+q=1$

$p=1-q$

$p=1-0.4= 0.6 \times 100 = 60\%$

$$p^2 + 2pq + q^2 = 1$$

$$p + q = 1$$

Hardy-Weinberg Example 2

Determine the gene frequencies of the K and k alleles in a population where the K+ phenotype is observed in 9% of individuals tested. Determine the genotype frequencies of those that are KK, Kk, and kk. Assume these alleles are codominant.

We are given the following:

- Phenotype frequency of K+ = 9% ($p^2 + 2pq$)

We are looking for the following:

- Gene frequency of K (p) and k (q)
- Genotype frequencies of KK (p^2), Kk ($2pq$), and kk (q^2)

Hardy-Weinberg Example 2 continued

- Start by finding the values of K and k (p and q)
- Have the value of $p^2 + 2pq = 9\%$ or 0.09

$p^2 + 2pq + q^2 = 1$	$p + q = 1$
$0.09 + q^2 = 1$	$p = 1\text{-}q$
$q^2 = 1\text{-}\ 0.09 = 0.91$	$p = 1\text{-}.95$
$q = \sqrt{0.91} = 0.95$	$p = 0.05$

- K (or p) = 0.05 or 5%
- k (or q) = .95 or 95%

Hardy-Weinberg Example 2 continued

- Next find the genotype frequencies for KK, Kk, and kk
- We now know K (or p) = 5% and k (or q) = 95%

KK = p^2	Kk = 2pq	kk = q^2
KK = $(0.05)^2$	Kk = 2(0.05)(0.95)	kk = $(0.95)^2$
KK = 0.0025 or 0.25%	Kk =0.0950 or 9.5%	kk = 0.9025 or 90%

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