Current topic 1:
DNA and Human genome project

Lecture 1 – Genetics basics

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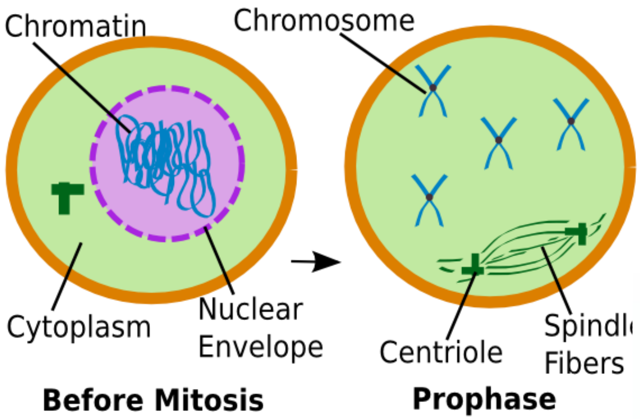
Part A- Human DNA basics

http://study.com/academy/lesson/anaphase-definition-lesson-quiz.html

46 chromosomes

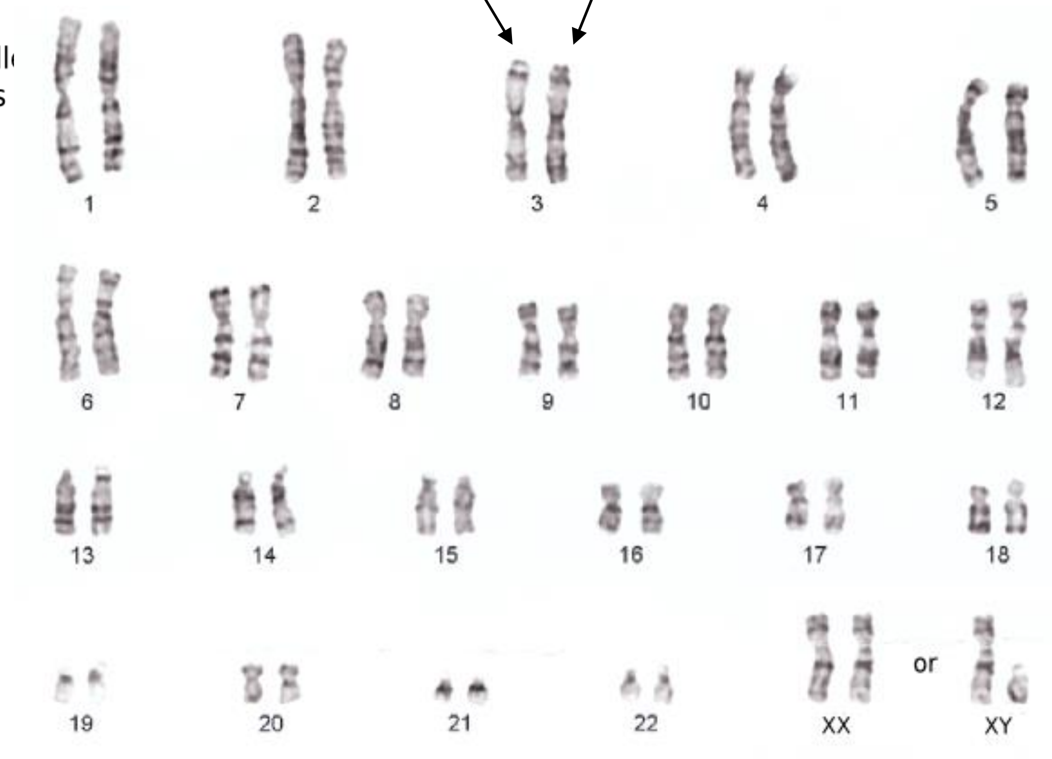
= 46 DNA molecules



www.biologyjunction.com

Comes from mother

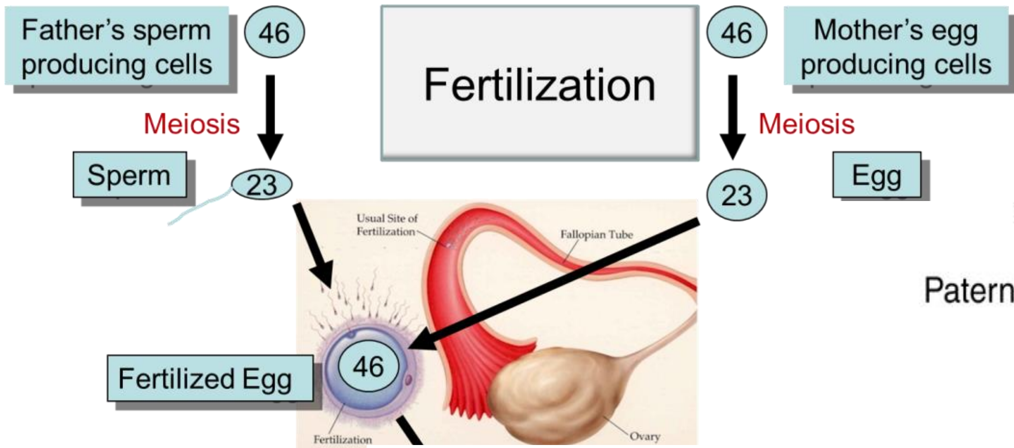
Comes from father



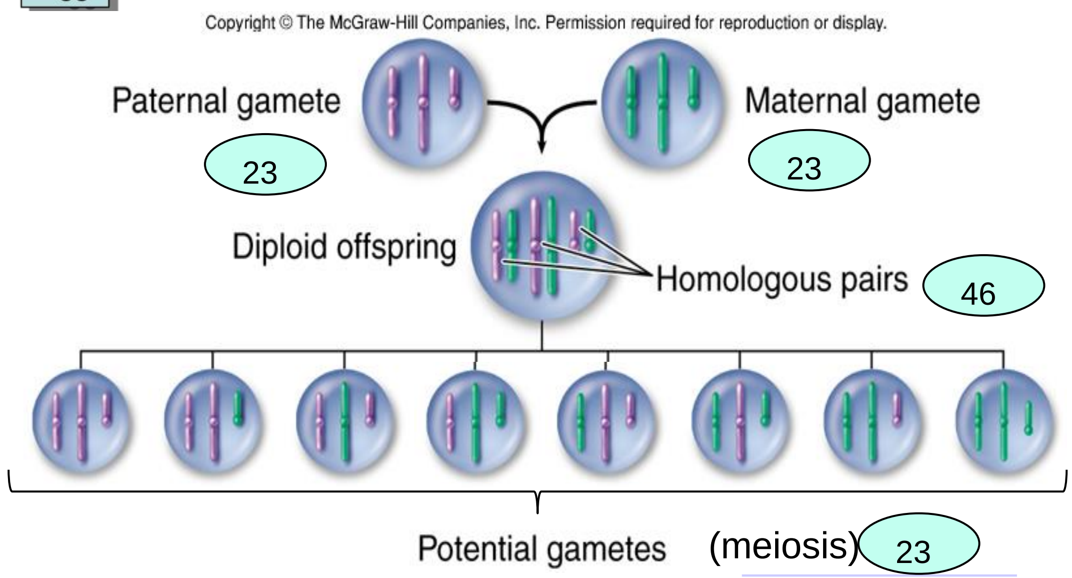
http://study.com/academy/lesson/karyotype-definition-disorders-analysis.html

Karyotype (right): **23 pairs of chromosomes** are seen when the cell starts dividing. 22 pairs of **autosomes** and 1 pair of **sex chromosomes**.

DNA is the hereditary material



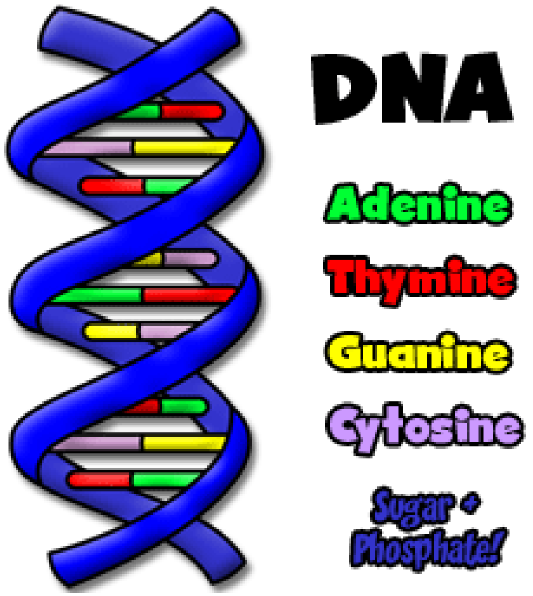
sphweb.bumc.bu.edu



Meiosis (formation of sex cells). In each gamete (sperm or egg), only one chromosome from each pair is present (23 chromosomes)

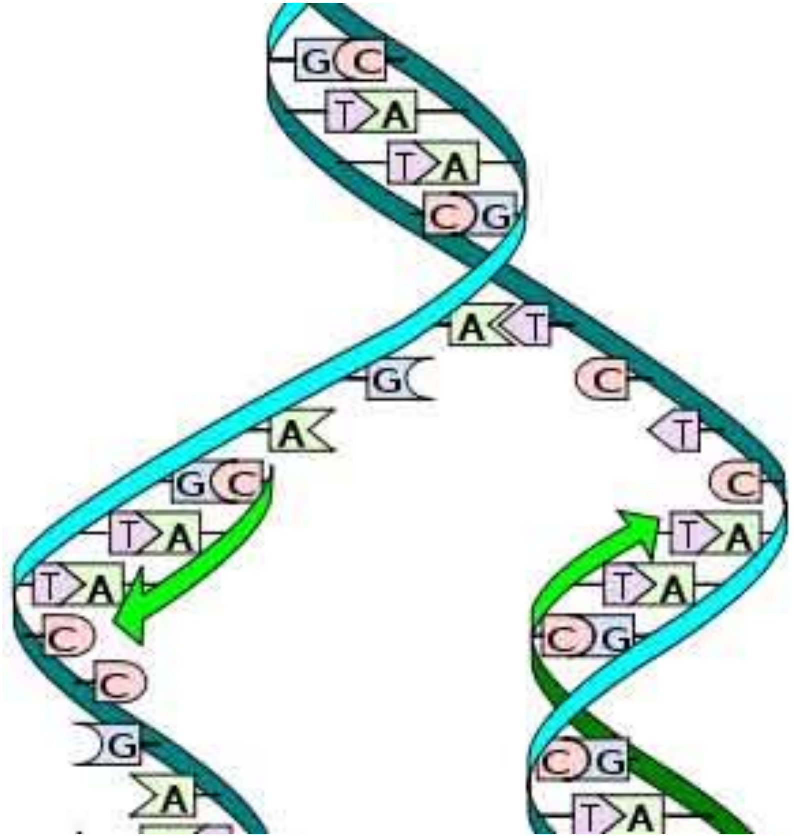
Mitosis (cell duplication). An exact replica of the genome (46 chromosomes) is made and passed on from mother cell to daughter cell.

Mitosis involves semi conservative replication



www.how-to-draw-cartoons-online.com

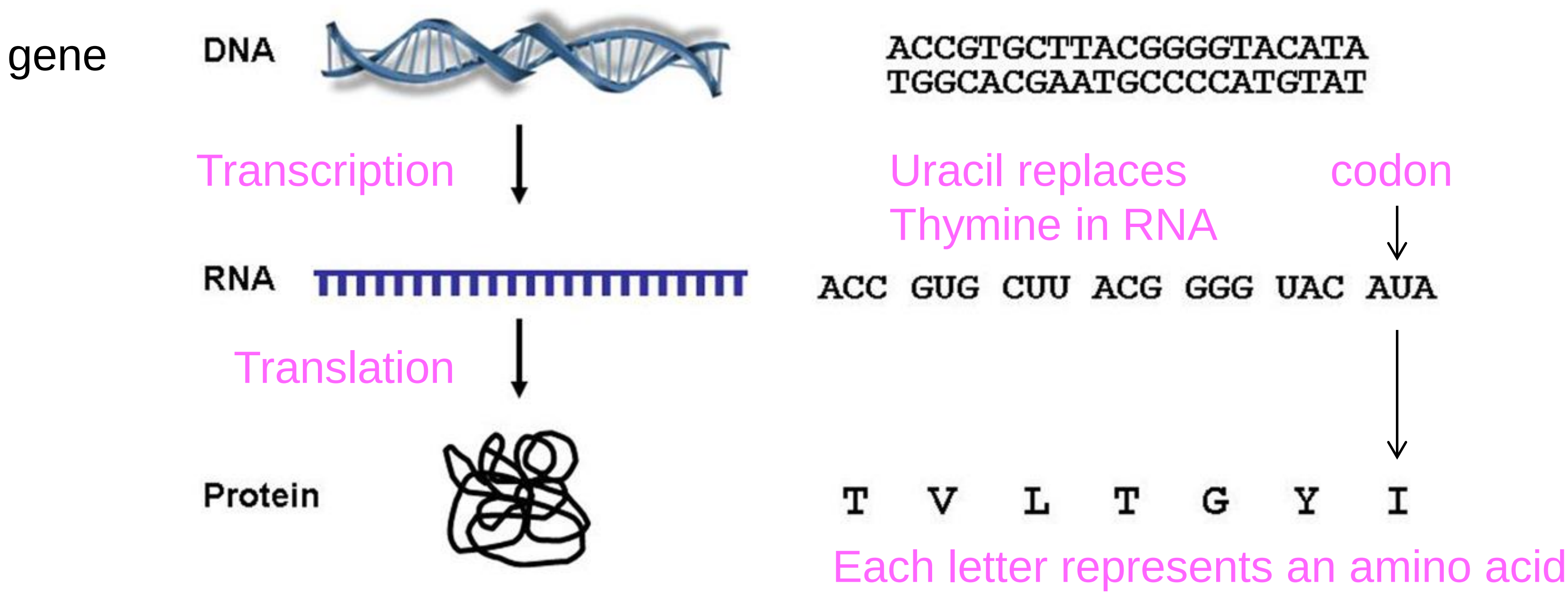
DNA molecule = **double helix with 2 strands** held together by **hydrogen bonds** between **pairs of bases**: **A-T and C-G.**



Before dividing, the cells makes a **duplicate** copy of each DNA molecule using base pair complementarity (semi-conservative replication).

www.scienceprofonline.com

Our genome contains genes which code for proteins.

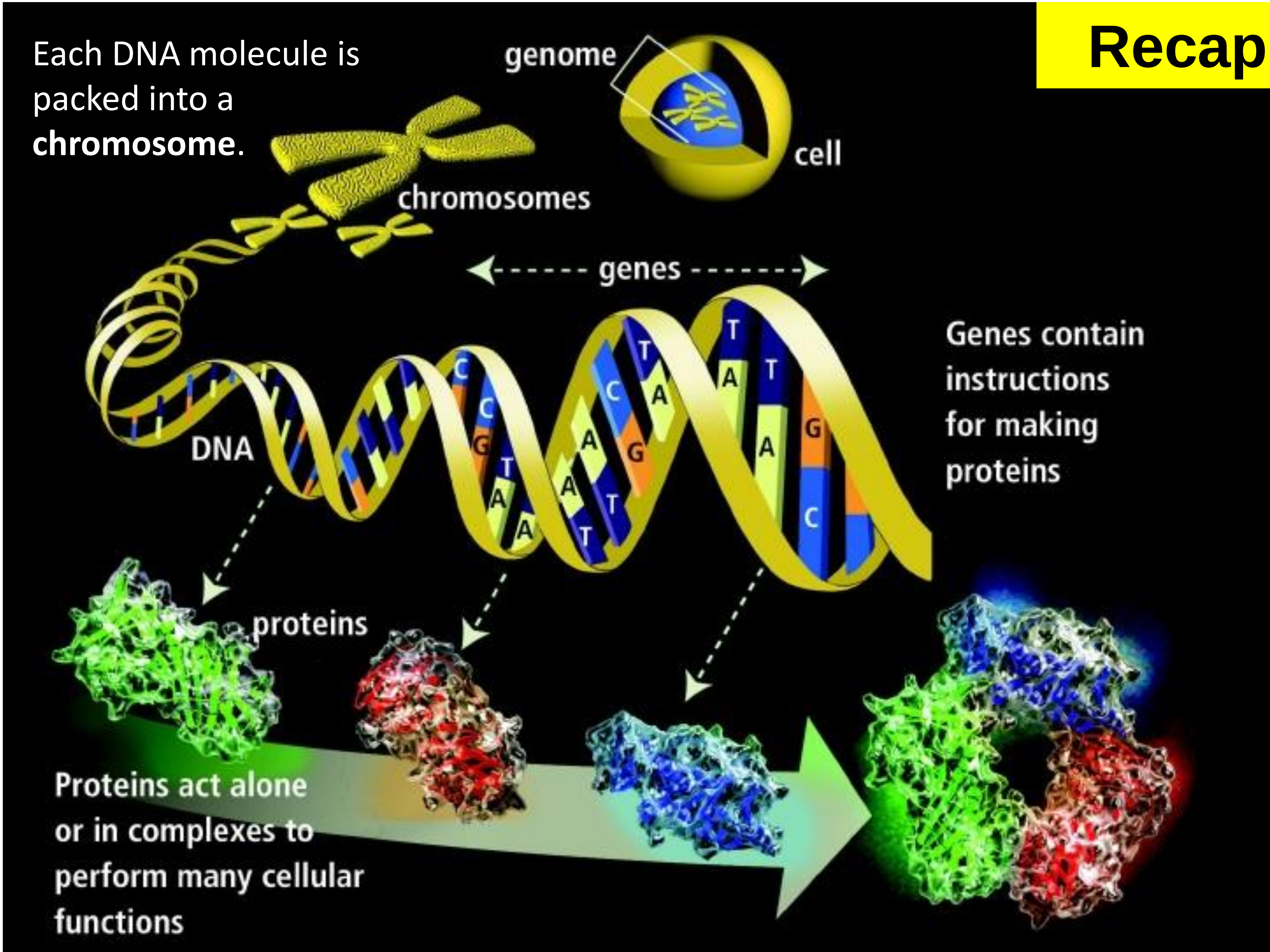


When a gene is **transcribed**, it forms many RNA molecules, which get **translated** into proteins. Proteins often work together to carry out their function.

The restaurant analogy: menu = genome, orders = RNAs, dishes = combination of proteins. The volume of food is controlled by waiters and chefs.

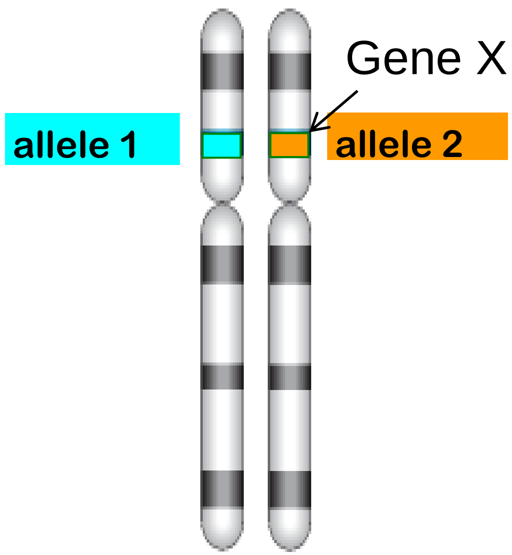
Recap

Each DNA molecule is packed into a **chromosome**.



Alleles and polymorphisms -1

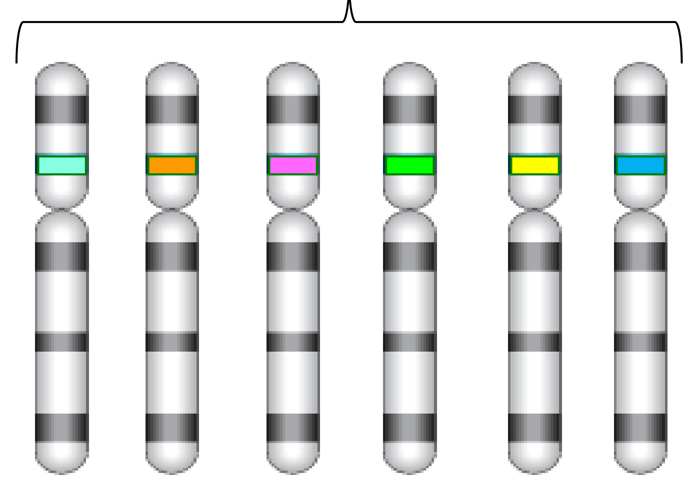
Pair of chromosome



P1 M1

Allele: any of several forms of a gene, usually arising through mutation, that are responsible for hereditary variation.

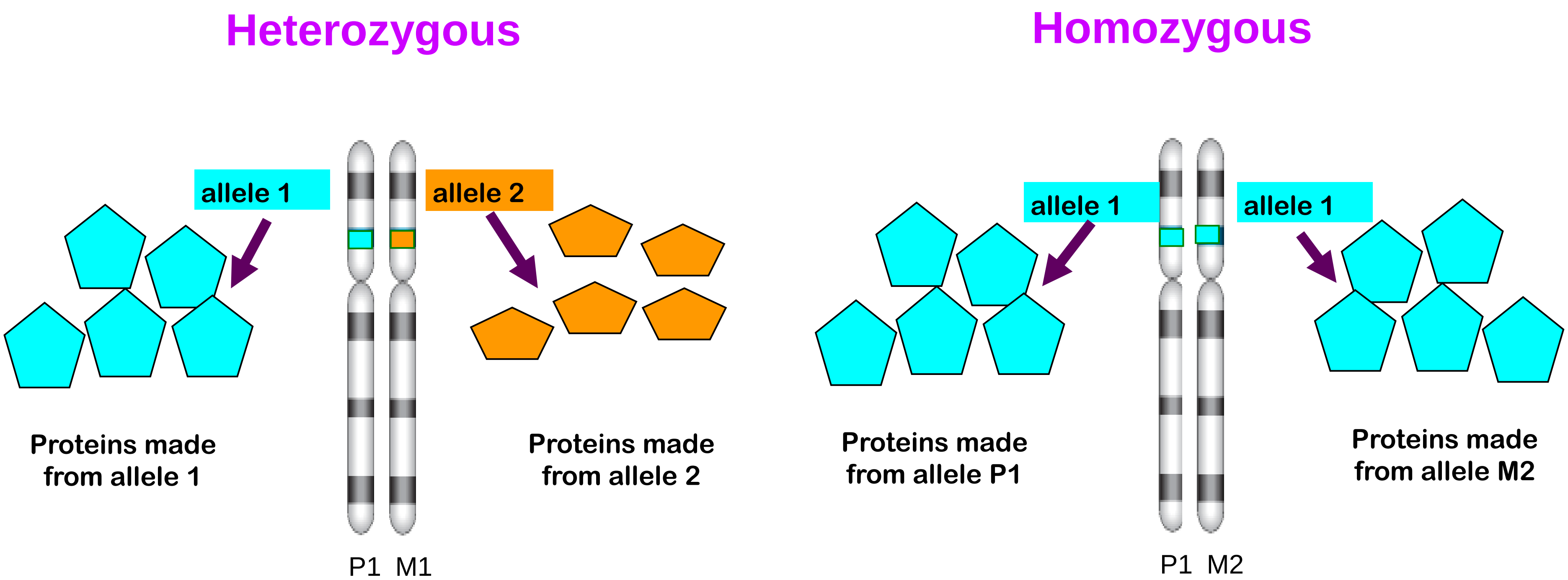
Worldwide, there are 6 different alleles for gene X



Individuals have two alleles per locus. These may be the same or different.

Polymorphism: Existence of several alleles for one **gene locus**. Restaurant analogy: gene = chicken soup, alleles = plain, with corn, with noodles, cajun style, thai style, etc.

Alleles and polymorphisms -2

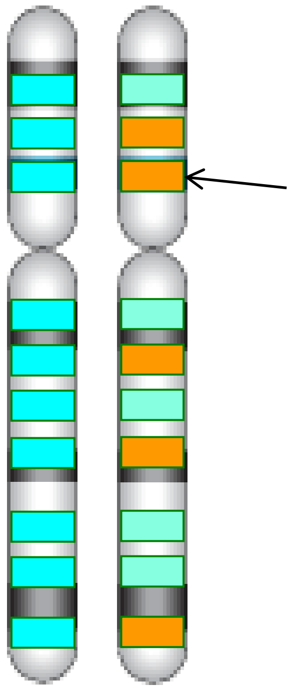


At a locus:

- If a person carries two different alleles, they are **heterozygous**. Inherited different alleles for gene X.
- If a person carries the same allele at a gene locus, they are **homozygous**. Inherited same allele for gene X.

Alleles and polymorphisms -3

Sibling 1 – chromosome 3 (P1+M1)

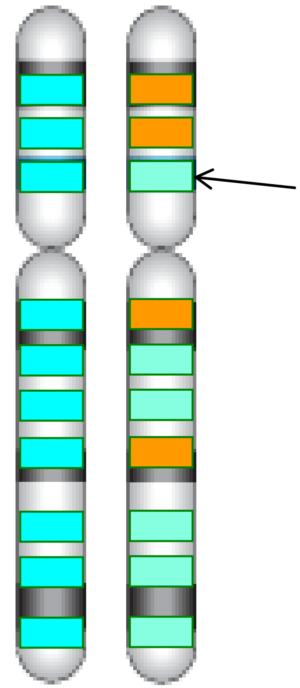


Gene A: homo
Gene B: hetero
Gene X: hetero

P1 M1

P= Paternal, M = maternal

Sibling 2 – chromosome 3 (P1+M2)



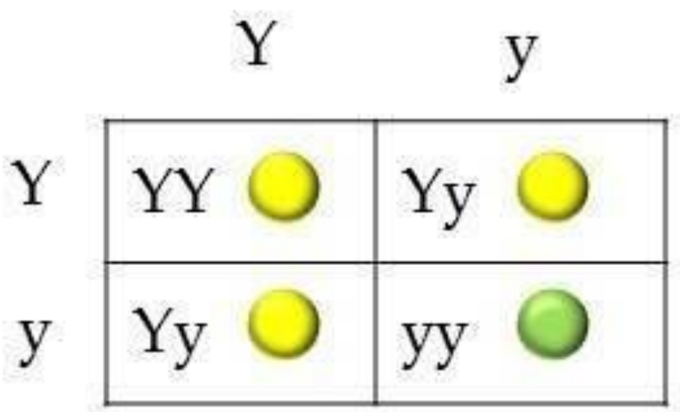
Gene A: hetero
Gene B: hetero
Gene X: homo

P1 M2

At each gene locus, an individual is either homozygous or heterozygous, depending on the chromosomes and alleles inherited from parents. → hereditary variation

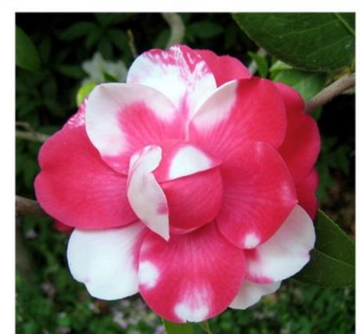
Alleles relationships -1

Which of the mutations below is dominant? Recessive? Co-dominant?



AA

BB



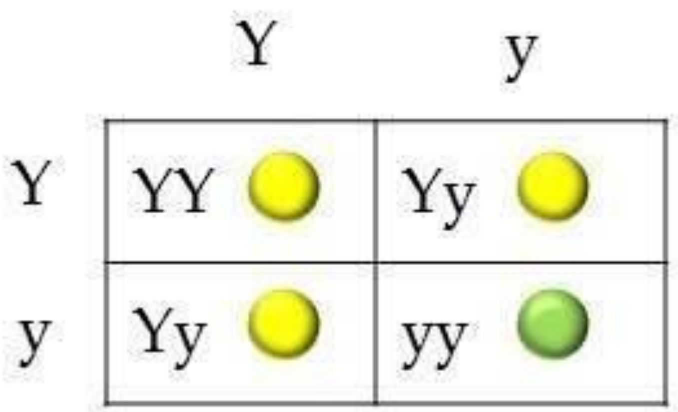
AB

Alleles relationships -2

A **dominant** allele masks the presence of the other alleles. An organism needs only one copy to show the characteristics of its associated trait.

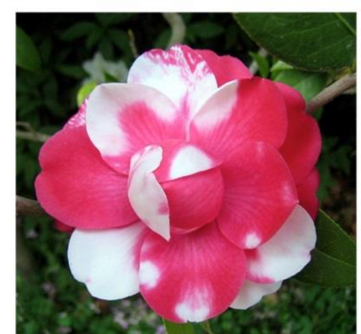
For a **recessive** allele, an organism must have two copies to show the characteristics of its associated trait.

Co-dominant alleles are both expressed in the trait



AA

BB



AB

Alleles relationships -3

Each allele codes for a slightly different version of the protein. Their relationship reflects the relative characteristics or abundance of the <u>proteins</u> they code for.

Below are heterozygous situations.

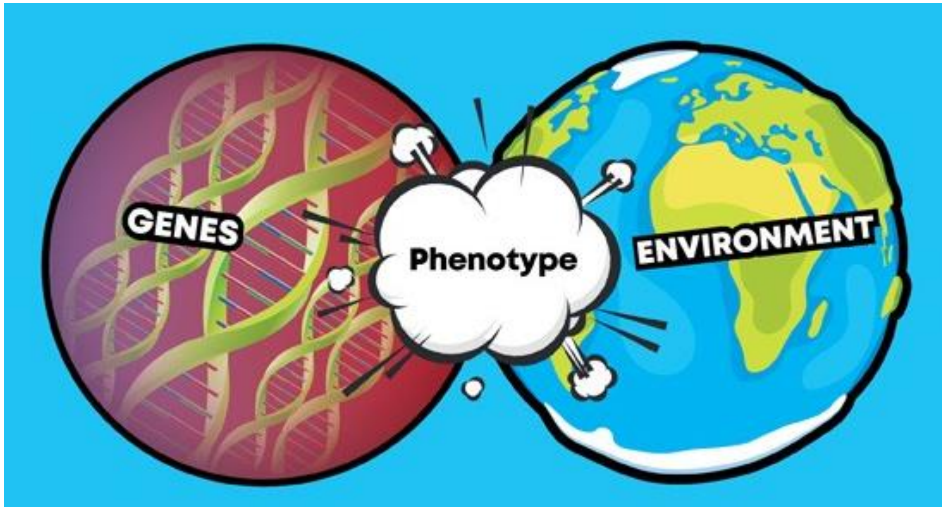
- If an allele codes for a non functioning or less effective protein, it will be **recessive**, because the protein coded by the other allele will take over and be dominant if enough is made
- If an allele makes a more effective protein or one that prevents the other protein to work, it will be **dominant**.
- If an allele is more expressed than the other, more of his protein version will be made and it will be **dominant**.
- If both alleles encode equally functional proteins in the same quantity, we have **co-dominance**.

Part B- From genotype to phenotype

From genotype to phenotype
Nature versus nurture

Genotype:
- Genetic make up of an individual
- Combination of alleles an individual possesses for one or more genes

Phenotype:
- Individual's observable inherited characteristics (one or more traits)
- Morphology, physiology, or behaviour.

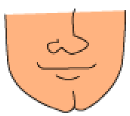
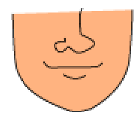
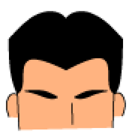
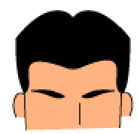
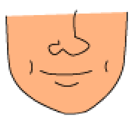
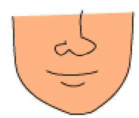
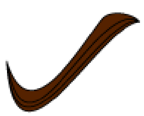
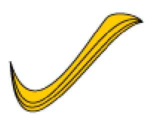
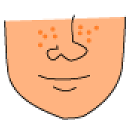
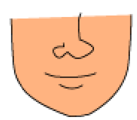


A trait (phenotype) is controlled by one or more proteins (i.e. genotype), and sometimes the environment.

The environment can influence an individual's physiology (e.g. life style), switch genes ON/OFF (e.g. stress, nutrients), and on a grander scale shape natural selection.

Alleles (genes) affect phenotype

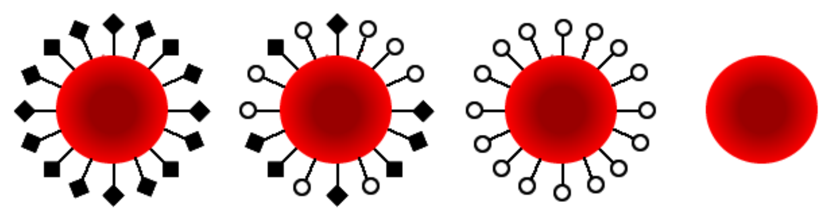
Raise you hand if ….

Dominant allele		Recessive allele	
Cleft Chin		No Cleft	
Widow's Peak		No Widow's Peak	
Dimples		No Dimples	
Brown/Black Hair		Blonde Hair	
Freckles		No Freckles	
Brown Eyes		Gray/Blue Eyes	

Co-dominant and recessive alleles

Blood group

A	AB	B	O



I^AI^A or I^Ai	I^AI^B	I^BI^B or I^Bi	ii

Is **allele frequency** linked to dominance or recessiveness?

Environment affects genotype
Natural Selection

Allele frequency (whether an allele is rare or common in a population) is linked to the genetic fitness it provides its carriers in a given environment.

Genetic fitness = reproductive success: survival to reproductive age + mating success + healthy progeny.

- If an allele provides an advantage, it is likely to be passed on and persist or become more prominent in a given population.
- If the environment changes, the frequency may change again.

Natural Selection – Examples 1

Mutations that allow us to **diversify our diet:**

A mutation that maintains production of lactase during adulthood fitted nicely with our ancestors starting to farm cattle.

A mutation that reduced the function of a tasting receptor for bitter substances allowed us to eat what used to be bitter tasting vegetables (e.g. Brussels sprouts, broccoli…).

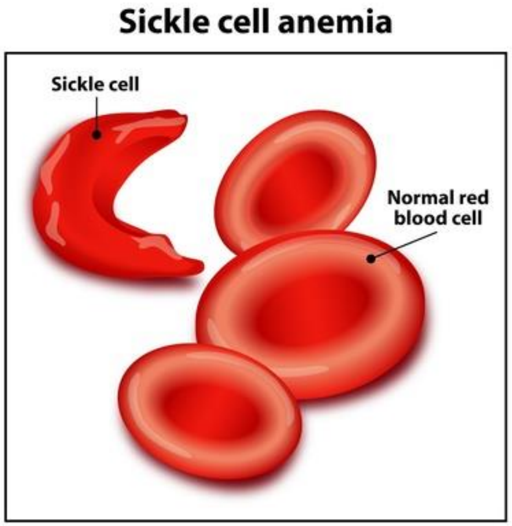
Delicious or bitter? It's in your TAS2R38 gene.

Natural Selection – Examples 2

Mutations that allow us to **combat diseases:**

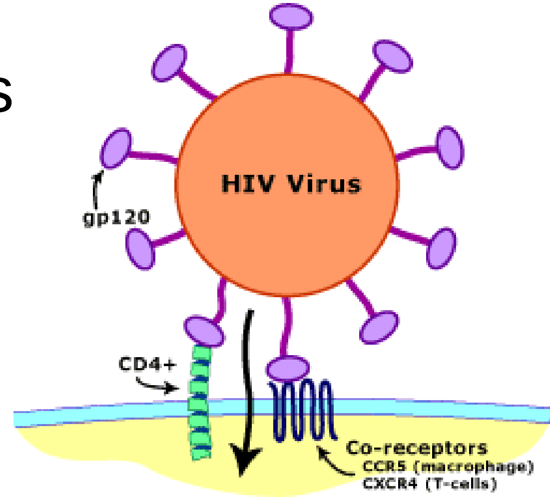
Carriers of the sickle anaemia allele are asymptomatic and get protection from malaria.

People homozygous for the sickle anaemia allele die if left untreated as their haemoglobin is not functioning well.



People homozygous for a mutation affecting a receptor on our immune cells (CCR5) are asymptomatic and immune to HIV. Prominent amongst Europeans as it is thought to have given protection against plague and smallpox epidemics in the past.

The mutated immune cells are less effective against pathogens common in developing countries.



CCR5

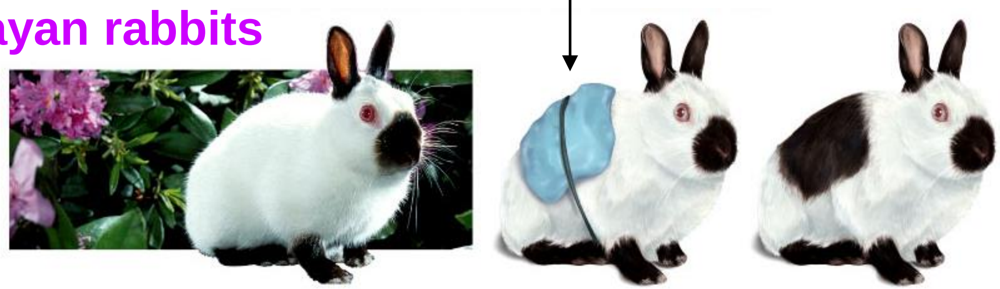
Environment affects individuals phenotype – temperature sensitive alleles

Tyrosinase = enzyme which controls the production of melanin (dark pigment for hair/skin)

Siamese cats only have melanin in their cool extremities because their allele produces a version of tyrosinase unstable when the temperature is a bit higher.

Himalayan rabbits

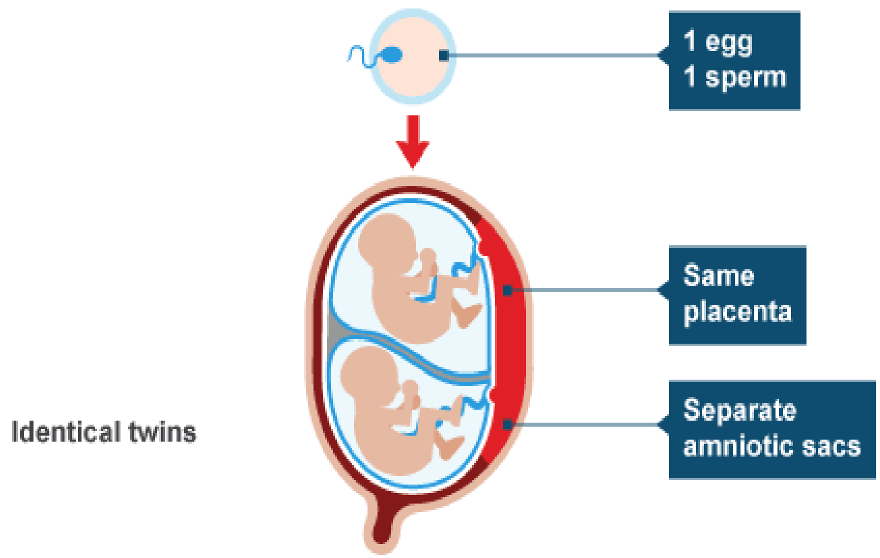
Cool pad



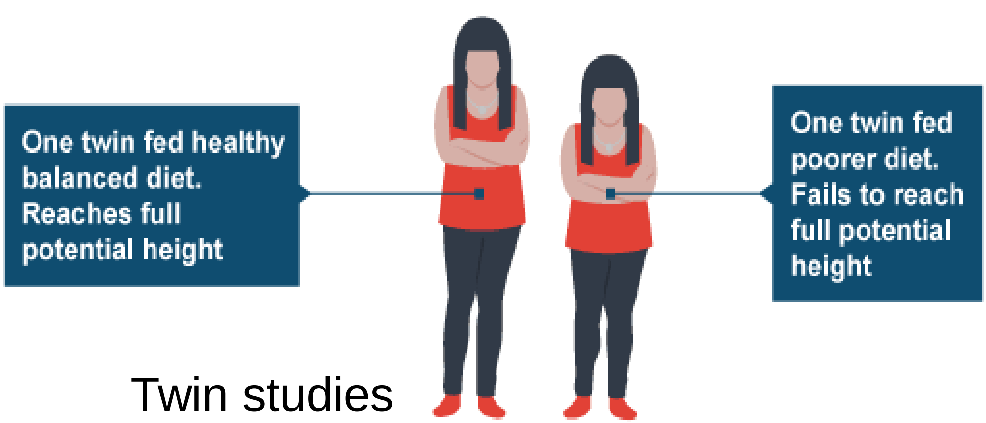
Arctic fox.

Coat colour is also heat sensitive but opposite – different gene

Environment affects individuals phenotype – diet and nutrients



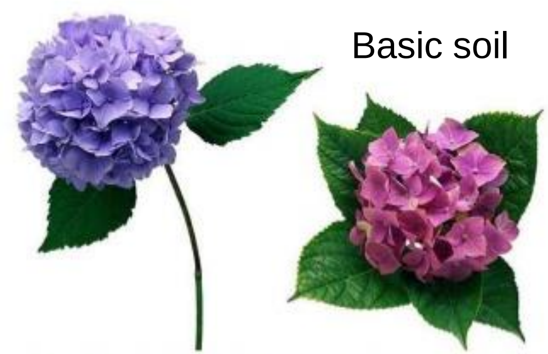
Twins separated at birth



Twin studies

Acidic soil

Basic soil



Color of Hydrangea flowers is influenced by soil pH

Flamingos pink feathers depend on the amount of carotene they get in their food (shrimp).

RECAP so far: what influences phenotype

- Alleles and their associated proteins influence phenotype: dominant, recessive, co-dominant alleles
- Allele frequency is linked to genetic fitness ad reflects the advantage given by a genotype in given environment (natural selection).
- If environment changes, genetic fitness may change (micro-evolution)
- Environment can also affect directly an individual phenotype (e.g. temperature/nutrients/stress may change the way a protein works or whether a gene is switched ON/OFF)

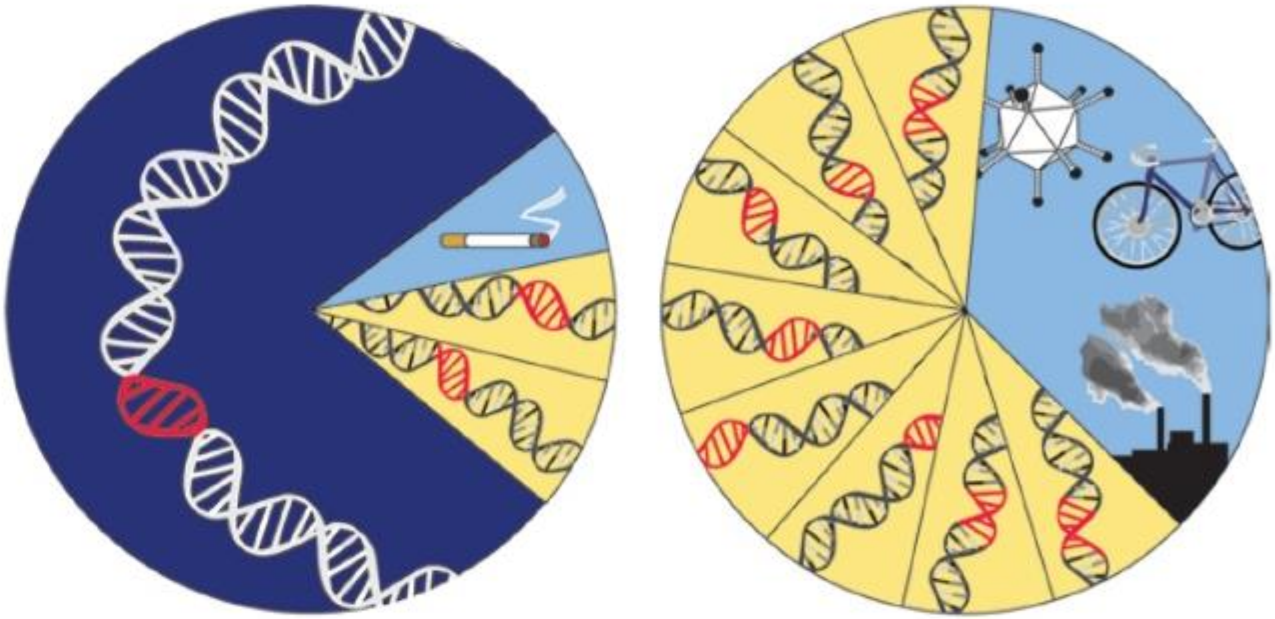
Multifactorial traits - definition

Most phenotypes are due to several genes (i.e. several alleles combinations) + the environment.

Examples: skin colour, height, weight, intelligence, behaviour. These phenotypes are on a continuum

Gene 1	d^1d^1	d^1D^1	d^1D^1	D^1D^1	D^1d^1	D^1d^1	D^1D^1
Gene 2	d^2d^2	d^2d^2	d^2D^2	D^2d^2	D^2d^2	D^2D^2	D^2D^2
Gene 3	d^3d^3	d^3d^3	d^3d^3	d^3d^3	D^3D^3	D^3D^3	D^3D^3
Total number of dark-skin genes	0	1	2	3	4	5	6
	Very light			Medium			Very dark
# of light "d" alleles	6	5	4	3	2	1	0
# of dark "D" alleles	0	1	2	3	4	5	6

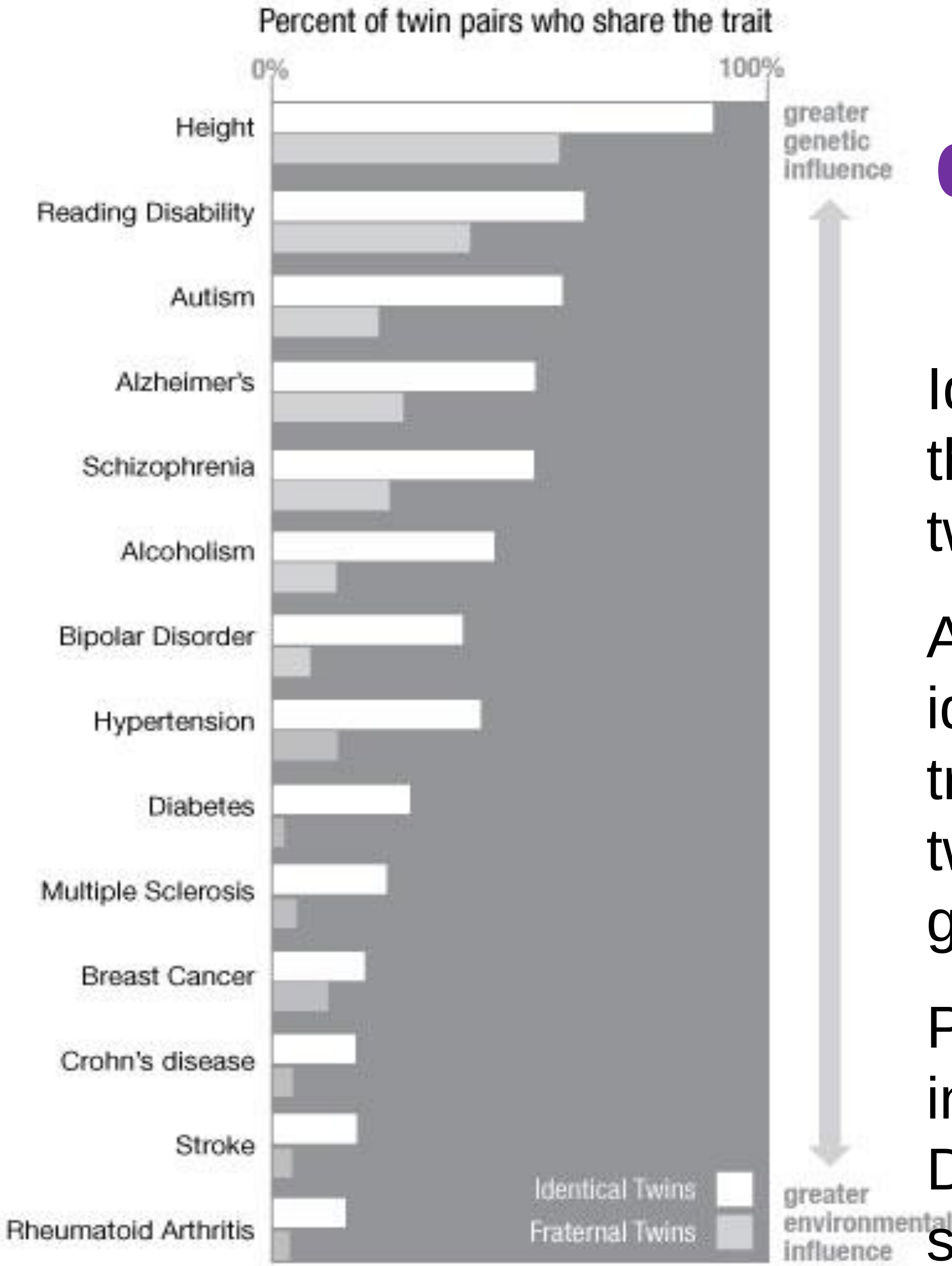
Multifactorial traits - variation



Three genes, but one with stronger effect. Small environment effect

Eight genes, all with small effect and large environment effect

Manolio et al. J. Clin. Invest. 118:1590–1605 (2008).



Multifactorial diseases – twin studies

Identical twins share 100% of their DNA whereas fraternal twins share ~ 50%.

A greater similarity between identical twins for a particular trait compared to fraternal twins provides evidence that genetic factors play a role.

Percentages lower than 100% in identical twins indicates that DNA alone does not determine susceptibility to disease.

Reading that should help with DNA basics

See glossary on Bb

Check this excellent website:

http://learn.genetics.utah.edu/content/inheritance/patterns/

Want to know more – just for fun?

- Genetics of eye colour - it is more complex than what was taught at school - 2 blue eyed parents can have a brown eyed child http://genetics.thetech.org/how-blue-eyed-parents-can-have-brown-eyed-children
- Flamingo pink colour: http://www.allaboutwildlife.com/are-flamingos-pink-because-they-eat-shrimp
- Genetic of the Siamese cat coat colour http://www.cat-world.com.au/siamese-cat-genetics
- Genetics of all the possible cat colours (just to appreciate how complex it is

https://www.stylisticat.com/colour-and-coat-genetics-in-cats.html