3 Genetics

Introduction

- living organism inherits blueprint for life from parents
- chromosomes carry genes in linear sequence
- during meiosis alleles segregate allowing new combinations

3.1 Genes

What is a gene?

- gene: heritable factor consists of length of DNA and influences specific characteristic
- genetics: storage of information in living organisms and how information is passed on
- question about composition of genes: strong evidence it is DNA
- few DNA molecules in cell (46), yet thousands of genes: gene consists of shorter length of DNA than a chromosome and each chromosome carries many genes

Where are genes located?

- genes are linked in groups, each group corresponds to one type of chromosome in a species
- each gene occupies specific position on chromosome it is located: locus of a gene

What are alleles?

- Mendel: differences between varieties of peas he crossed together were due to different heritable factors
- pairs of heritable factors are alternative forms of same gene: alleles
- alleles occupy the same position on one type of chromosome; same locus
- only one allele can occupy the locus of the gene on a chromosome
- most animals have two of each type of chromosome: two alleles (either same or different)

Differences between alleles

- different alleles of gene have slight variations in base sequence; usually one or couple of bases
- positions in gene where more than one base may be present: single nucleotide polymorphisms (SNPs) several snips can be present in gene; even then alleles of gene differ by few bases

Mutation

- new alleles are formed from other alleles by gene mutation; mutations are random changes: no particular mechanism; most significant type is base substitution
- unlikely to be beneficial: mutations are either neutral or harmful, some are lethal
- mutations in body cells are eliminated when individual dies; mutations in gametes can be passed on to offspring causing genetic disease

What is a genome?

- genome: whole of genetic information of an organism
- living organism's genome is entire base sequence of each of its DNA molecules
- humans: 46 chromosomes in nucleus and DNA molecule in mitochondrion
- plant species: genome is DNA and DNA molecules in mitochondrion and chloroplast
- prokaryotes: DNA in circular chromosome and present plasmids

The Human Genome Project

- aim to find base sequence of entire human genome
- project drives rapid improvements in base sequencing techniques
- possible to predict which base sequences that are protein-coding genes
- most of the genome is not transcribed: affect gene expression and highly repetitive sequences
- example of a human genome
- vast majority of base sequences are shared by all humans; many snips contribute to diversity
- comparisons between genomes reveal aspects of evolutionary history

3.2 Chromosomes

Bacterial chromosomes

- prokaryotes have one chromosome consisting of circular DNA containing genes needed for basic life process; it is not associated with proteins, it is naked
- usually only a single copy of each gene (only after replication there are two before cell splits)

Plasmids

- plasmids are small extra DNA molecules, usually in prokaryotes, very unusual in eukaryotes
- contains few genes that may be useful to cell, but not essential e.g. antibiotic resistance
- plasmids are not always replicated at same time as chromosome
- copies can be transferred from one cell to another
- can cross the species barrier: when plasmid is released when prokaryote dies, another takes up
- are used by biologists to transfer genes artificially

Eukaryote chromosomes

- eukaryotic chromosomes are composed of DNA and protein
- long linear DNA molecule associated with histone protein
- adjacent histones separated by short stretches of DNA molecule, not in contact with histone

Differences between chromosomes

- eukaryote chromosomes are too narrow to be visible during interphase in light microscope; during mitosis and meiosis they are fatter and shorter by supercoiling and visible (with stains)
- two chromatids with identical DNA molecules are produced by replication
- chromosomes examined during mitosis show different types
- centromere holding chromatids together can be placed anywhere on chromosome
- every eukaryote has at least two types of chromosomes, most have more (humans: 23)
- every gene in eukaryotes occupies specific position on one type of chromosome: locus
- each chromosome type carries specific sequence of genes
- genes arranged in standard sequence allows parts to be swapped during meiosis

Homologous chromosomes

- carry the same sequences of genes but are not identical because alleles are different
- two eukaryotes of same species will have each chromosome homologous to a chromosome form the other: this allows members of a species to interbreed

Haploid nuclei

- haploid nucleus has one chromosome of each type, one full set of chromosomes
- gametes have haploid nuclei

Diploid nuclei

- diploid nucleus: has two chromosomes of each type, two full sets of chromosomes
- haploid gametes fuse together and produce zygote with diploid nucleus
- many plants/animals consist entirely of diploid cells apart of gametes for sexual reproduction
- two copies of every gene: effects of harmful recessive mutations can be avoided if a dominant allele is present; organisms are often more vigorous

Chromosome numbers

- most fundamental characteristic of species is number of chromosomes: can interbreed
- number of chromosomes can change during evolution of species: decrease of chromosomes fuse or increase if they split; there are some mechanisms doubling the number (rare)

Sex determination

- two sex chromosomes: X (relatively large) and Y (much smaller)
- all other chromosomes are autosomes
- X chromosomes has many genes essential for males and females; all humans have one
- Y chromosome has small number of genes; small part are same as on X chromosome
- remainder of Y chromosome cannot be found on X, not important for female development

- Y causes fetus to develop into male (SRY or TDF); initiates development of male features
- X does not have TDF gene, ovaries develop and female sex hormones are produced
- all offspring inherit a X from their mother; gender is determined at moment of fertilization
- formation of sperm produces half with X and half with Y chromosome

Karyograms
- chromosomes of organism are visible in cells that are in mitosis
- dividing cells stained and placed under microscope slide which bursts the cell
- chromosomes are arranged according to size and structure; distinguished by position of centromere and pattern of banding
- homologous pairs are arranged by size starting with longest, ending with smallest

3.3 Meiosis
Meiosis in outline
- one of the two ways a eukaryotic nucleus divides
- in meiosis the nucleus divides twice: meiosis I and meiosis II
- first division produces two nuclei each of which divides again creating total of four nuclei
- the four nuclei are haploid: meiosis is a reduction division
- halving of chromosome number happens in first division: two nuclei produced by meiosis I have haploid number but each chromosome consist of two chromatids; these separate in meiosis II

Meiosis and sexual life cycles
- cycles of organisms can be sexual or asexual; asexual offspring genetically identical to parent
- sexual life cycle: differences between chromosomes of offspring and parents: genetic diversity
- sexual reproduction involves process of fertilization which is the union of gametes
- fertilization doubles the number of chromosomes
- in animals meiosis happens during process of creating gametes
- evolution of meiosis is a critical step to origin of eukaryotes: sexual life cycle could not occur

Replication of DNA before meiosis
- DNA is replicated during interphase before meiosis, chromosome has two sister chromatids
- two chromatids are genetically identical
- DNA is not replicated between first and second division of meiosis

Bivalents formation and crossing over
- before supercoiling the homologous chromosomes pair up (4 DNA molecules because replication already happened), process is called synapsis
- pair of homologous chromosomes is a bivalent
- after synapsis crossing over takes place: junction is created where one chromatid in each of the homologous chromosomes breaks and rejoins with the other chromatid
- crossing over occurs at random positions; at least one crossover happens in each bivalent
- crossing over is a mutual exchange of genes
- some alleles of exchanged genes are different: chromatids with new combinations are created

Random orientation of bivalents
- after nuclear membrane breaks down, spindle microtubules attach to centromeres
- attachment is different than in mitosis: each chromosome attached to one pole only, two homologous chromosomes in bivalent attached to different poles, orientation (pole to which chromosome is attached to), orientation of bivalents is random, orientation of one bivalent does not affect other bivalents

Halving the chromosome number
- in meiosis the centromere does not divide, whole chromosomes move to poles
- chromosomes in bivalent held together by chiasmata; these slide to end of chromosome and then they separate (disjunction): halves chromosome number of cell
- nuclei formed in first division contain one of each chromosome type: haploid

Meiosis and genetic variation
- a child will inherit unpredictable mixture of characteristics of both parents: unpredictability due to meiosis: every gamete has new combination of alleles: genetic variation
- meiosis can result in gametes with different combinations of genes: two processes for diversity
- random orientation of bivalents: generates genetic variation among genes which are on different chromosome types
- crossing over: without crossing over combinations of alleles on chromosomes would be forever linked: allows that genes are reshuffled, producing new combinations

Fertilization and genetic variation
- fusion of gametes is a significant event
- alleles from two different individuals are combined in one new individual
- combination is unlikely ever to have existed before
- fusion of gametes promotes genetic variation which is essential for evolution

3.4 Inheritance
Mendel and the principles of inheritance
- organisms pass on characteristics when they reproduce
- acquired characteristics cannot be inherited
- early theories: blending inheritance: characters are intermediate of parents
- Mendel creates an alternative theory using pea plants
- Mendel repeated each cross many times and with seven different characteristics
- rediscovering Mendel's work: cross-breedings are done with plants and animals: confirmed

Gametes
- fuse together to form zygote; sex cells
- male and female gametes are different in size and motility: male is smaller and can move, female is larger but moves less or not at all
- gametes contain one chromosome of each type: haploid; nucleus has one allele of each gene
- male and female parents make an equal genetic contribution to their offspring

Zygotes
- gametes fuse and nuclei join together: doubling chromosome number: diploid
- some genes have more than two alleles (ABO blood groups)

Segregation of alleles
- meiosis: diploid nucleus into four haploid nuclei
- if two copies of one allele are present, the gametes receive one copy of it
- if two different alleles are present, 50% of gametes receive one and the other half the other
- segregation: separation of alleles into different nuclei; breaks up existing combinations, creates new combinations

Dominant, recessive and co-dominant alleles
- dominant alleles mask the effects of recessive alleles
- pairs of alleles where both have an effect when they are present together: co-dominant
- usual reason for dominance of one allele is that it codes for a protein that is active and carries out a function while the recessive allele codes for a non-functional protein

Genetic diseases due to recessive alleles
- most genetic diseases are caused by recessive alleles of a gene
- carrier: has one allele for genetic disease, can pass it on
- genetic diseases by recessive alleles appear unexpectedly, parents are unaware that they are carriers; cystic fibrosis as an example

Other causes of genetic diseases
- small proportion of genetic diseases are caused by dominant alleles: not possible to be carrier
- Huntington's disease as an example

- very small proportion of genetic diseases are caused by co-dominant alleles (sickle-cell anemia)
- some genetic diseases show a different pattern of inheritance in males and females: sex linkage
- red-green color-blindness and hemophilia as examples of sex linked genetic diseases

Sex-linked genes
- inheritance pattern where ratios are different in males and females: sex linkage
- geneticists observe that inheritance of genes and of chromosomes show clear parallels and so genes are likely to be located on chromosomes
- Y chromosome might not carry the gene that is present on X chromosome
- in crosses involving sex linkage, alleles should always be shown as superscript letters on X

Genetic diseases in humans
- sickle-cell anemia, cystic fibrosis, hemophilia, Huntington's disease, phenylketonuria (PKU), Tay-Sachs, Marfan's syndrome as examples
- large number of genetic diseases; most are caused by rare recessive alleles
- two alleles must be inherited and the chance is extremely small
- cheaply and quickly sequence of genome: reveals number of rare recessive alleles
- individual can only produce child with genetic disease due to one of the recessive alleles if the other partner has the same rare allele

Causes of mutation
- new alleles are formed from other alleles by gene mutation: random change
- two types of factor can increase mutation rate: radiation (enough energy to cause chemical changes in DNA), chemical substances (chemical changes in DNA)
- no mechanism for mutations; mutation is unlikely to be beneficial, either neutral or harmful
- mutations of genes controlling cell division can cause cell to divide endlessly: tumour: cancer
- mutations are eliminated when individual dies; mutations in gametes can be passed to offspring: origin of genetic diseases

3.5 Genetic modification and biotechnology
Gel electrophoresis
- separation of charged molecules in an electric field according to their size and charge
- gel is immersed in a conducting fluid and an electric field is applied: charged molecules move through the gel: molecules with negative and positive charges move in opposite directions
- proteins may be positively or negatively charged so can be separated according to charge
- eukaryotic DNA molecules must be broken up as they are too long: all DNA molecules are negatively charged and will move in the same direction but not at the same rate
- small DNA fragments move faster than large ones so DNA fragments can be separated by size

DNA amplification by PCR
- polymerase chain reaction is used to make large numbers of copies of DNA
- small samples can be replicated into millions of copies: makes the studying of DNA possible without using up a limited sample
- PCR is used to copy specific DNA sequences: a sequence is selected by using a primer that binds to the beginning of the desired sequence

DNA profiling
- stages: sample of DNA is obtained, sequences that vary considerably between individuals are amplified by PCR, copied DNA is split into fragments using restriction endonucleases (restriction enzymes), fragments are separated using gel electrophoresis, produces a pattern of bands which is the individual's DNA profile, profiles can be compared to see which bands are same and which different

Genetic modification
- molecular biologists developed techniques to transfer genes between species
- the transfer of genes is known as genetic modification
- possible because the genetic code is universal: same polypeptide is produced after translation

- used to treat human diseases, introduce new characteristics in an animal species, producing a variety of crop plants (GM crops)

Clones

- zygote is the first cell of a new organism, produced by the fusion of a male and female gamete
- it is produced by sexual reproduction and will be genetically different
- if an organism reproduces asexually, the offspring is genetically identical
- production of genetically identical organisms is cloning a group of genetically identical organisms is called a clone
- identical twins are the smallest clone that can exist; a better term is monozygotic as not all of their characteristics are identical

Natural method of cloning

- many plants have a natural method of cloning
- natural methods of cloning are less common in animals

Cloning animal embryos

- embryonic cells are pluripotent in their early stages and could theoretically be divided into two different groups of cells which would become two separate individuals
- formation of identical twins could be called cloning, but most animals don't do this naturally
- in livestock, an egg can be fertilized in vitro, cells separated and transplanted into a surrogate mother, this is only possible for a limited number of clones
- this method isn't popular because it can't be seen whether the new individual has desirable characteristics

Cloning adult animals using differentiated cells

- easy to clone an embryo but its characteristics are unknown at that point
- when they're old it is harder to clone them: cells are differentiated
- John Gurdon: nuclei from adult frogs were put into egg cells where the nucleus was removed, the egg cells developed as if they were normal zygotes
- for mammals this is more difficult to achieve, Dolly is the first example
- would have benefits of regrowing human tissue which would not be rejected by the body