3 Genetics

3.1 Genes

Comparing numbers of genes

- we see ourselves as more complex in structure, physiology and behavior so we might expect to have more genes

Sickle cell anemia

- commonest genetic disease: due to mutation of gene coding for alpha-globin polypeptide in hemoglobin (Hb); healthy is Hb^A
- new allele Hb^S forms after base substitution mutation converts sixth codon of gene from GAG to GTG; when transcribed it produces mRNA GUG instead of GAG, changing sixth amino acid in polypeptide from glutamic acid (Glu) to valine (Val)
- change causes hemoglobin molecules stick together in tissues with low oxygen concentration: bundles are rigid enough to distort red blood cells into sickle shape
- sickle cells cause damage to tissue by becoming trapped in blood capillaries
- when they return to lungs they change shape again: over time this damages hemoglobin and plasma membrane reducing lifespan of red blood cell to 4 days
- body cannot replace red blood cells at rapid enough rate: anemia develops
- two copies of allele cause severe anemia; one copy causes mild anemia

3.2 Chromosomes

Measuring the length of DNA molecules

- John Cairns produced images from E. coli: cells grown in culture medium with tritiated thymidine, producing radioactively labelled DNA as it was used during DNA replication; cell walls were digested and cells were gently burst to release DNA onto dialysis membrane; thin film of photogenic emulsion was applied to surface and left in darkness for two months; atoms of tritium decayed and emitted high energy electrons reacting with film; film was developed and examined with microscope; point where a tritium atom decayed, position of DNA was indicated
- images produced by Cairns show chromosome of E. coli is a single circular DNA molecule with length of 1’100 µm, which is remarkably long given that length of cell is only 2 µm
- autoradiography was later used by researchers to produce images of eukaryotic chromosomes
- in contrast to prokaryotic chromosome, fruit fly chromosome was linear rather than circular

Comparing the genome sizes

- genomes of living organisms vary by huge amount
- genome size of eukaryotes depends on size and number of chromosomes; correlated with complexity of organism but not directly proportional: proportion of DNA acting as functional genes is variable and amount of gene duplication varies
- prokaryotes have a smaller genome size

Comparing chromosome numbers

- some eukaryotes have few large chromosomes and other have many small ones
- all eukaryotes have at least two different types of chromosome, so diploid chromosome number is at least four

Karyotypes and Down syndrome

- karyogram: image of chromosomes of organism, in homologous pairs of decreasing length
- karyotype: property of organism, number and type of chromosomes an organism has
- used to deduce whether individual is male (XY) or female (XX)
- used to diagnose Down syndrome and other chromosomal abnormalities; three copies of chromosome 21 in karyogram indicate Down syndrome (trisomy 21)

3.3 Meiosis

Obtaining cells from a fetus

- amniocentesis: passing needle through mother's abdomen wall using ultrasound to guide needle; needle used to withdraw sample of amniotic fluid containing fetal cells
- chronic villus sampling: sampling tool entered through vagina used to obtain cells from chorion (one of membranes from which placenta develops); can be done earlier in pregnancy
- risk of miscarriage: amniocentesis has 1% and chronic villus sampling has 2%

Non-disjunction and Down syndrome

- meiosis is sometimes subject to errors: homologous chromosomes fail to separate (non-disjunction): results in gamete with either extra chromosome or deficient in one: if gamete is fertilized it results in individual with either 45 or 47 chromosomes
- abnormal number of chromosomes often leads to person with syndrome
- Down syndrome (trisomy 21): non-disjunction leading to individual with three chromosomes 21
- most other trisomies in humans are so serious that offspring does not survive
- Klinefelter's syndrome: non-disjunction causing sex chromosomes XXY
- Turner's syndrome: non-disjunction causing only one X chromosome

3.4 Inheritance

ABO blood groups

- example of co-dominance
- before blood transfusions, the patient's blood group must be known to prevent complications due to coagulation of red blood cells
- genotypes I^AI^A and I^BI^B give blood groups A and B respectively while none of them is dominant the genotype I^AI^B gives a new blood group AB
- third allele *i* is recessive so I^Ai and I^Bi give blood groups A and B respectively
- genotype *ii* gives blood group O
- all three alleles cake the production of a glycoprotein in membrane of red blood cells
- I^A alters the glycoprotein by adding acetyl-galactosamine; people without this allele who come in contact with this blood will produce anti-A antibodies
- I^B alters the glycoprotein by adding galactose; people without this allele coming in contact with this blood will produce anti-B antibodies
- genotype I^AI^B alters the glycoprotein by adding both, so no antibodies are produced
- allele *i* does not modify the basic glycoprotein

Cystic fibrosis and Huntington's disease

- cystic fibrosis is the commonest genetic disease in parts of Europe
- due to recessive allele of the CFTR gene (chrom. 7); product of that gene is a chloride ion channel involved in secretion of sweat, mucus, digestive juices
- recessive allele causes sweat to contain excessive amounts of sodium chloride while digestive juices and mucus have insufficient sodium chloride: not enough water moves by osmosis into secretions: sticky mucus builds top in lungs causing infections and pancreatic duct is blocked
- Huntington's disease is due to dominant allele on HTT gene (chrom. 4): gene product is a protein called huntingtin
- dominant allele HTT causes degenerative changes in brain: changes in behavior, thinking and emotions become severe
- person eventually needs full nursing and succumbs to heart failure, pneumonia, or some other infectious disease
- late onset (age 30-50): already has children: can be tested

Red-green color blindness and hemophilia

- sex linkage mostly due to genes located on X chromosome
- red-green color blindness is caused by recessive allele of gene for one of the photoreceptor proteins: these detect specific wavelength ranges of visible light
- males only have one X chromosome: if that chromosome has it, the son has it as well
- daughter must get it from red-green color blind father and recessive from mother

- hemophilia is life threatening genetic disease; most cases are due to inability to make Factor VIII which is involved in blood clotting
- treatment is infusion of Factor VIII purified from blood of donors
- gene for Factor VIII is on X chromosome and is recessive

Consequences of nuclear bombing and accidents at nuclear power stations

- common feature of Hiroshima, Nagasaki, Three Mile Islands, Chernobyl is that radioactive isotopes were released into environment and people were exposed to them
- apart from cancer, other main predicted effects are mutations, leading to stillbirths, malformation or death
- affected children are monitored: no evidence has been found of mutations caused by radiation
- many animals and plants suffered after accident; but there is no clearly demonstrated increase in solid cancers or leukemia due to radiation in the most affected populations

3.5 Genetic modification

Paternity and forensic investigations

- DNA profiling is used in forensic investigations: blood stains, hair or semen
- in each example, DNA is taken from crime scene and compared to suspect or victim
- DNA profiling is used in paternity investigations
- DNA profiles of mother, child, father are needed; if bands in child does not occur in mother nor father, there must be a different father

Techniques for gene transfer to bacteria

- transfer of genes is referred to as genetic engineering
- gene transfer to bacteria usually involves plasmids, restriction enzymes and DNA ligase
- restriction enzymes (endonucleases) are enzymes that cut DNA molecules at specific base sequences; some endonucleases cut the DNA at different points, leaving single-stranded sections (sticky ends) which can be used to link pieces of DNA together
- DNA ligase joins DNA molecules: used to seal the nicks at the sticky ends to create the full sugar-phosphate backbone
- gene has to be transferred: easier to obtain mRNA than actual DNA: reverse transcriptase is an enzyme that makes DNA copies from RNA molecules called cDNA

Risks and benefits of GM crops

- potential benefits and risks can be grouped into environmental, health and agricultural parts
- environmental benefits: pest-resistant, reduces need plow and spray crops, shelf-life improved
- health benefits: nutritional value, crops lacking allergens, produce edible vaccines
- agricultural benefits: resistant to drought, herbicide resistance, resistant to diseases
- health risks: proteins produced could be toxic or cause allergic reactions, antibiotic resistance could spread to bacteria, genes could mutate
- environmental risks: non-target organisms can be affected, genes for herbicide resistance could transfer to wild plants, biodiversity can be reduced
- agricultural risks: unwanted plants with resistance difficult to control, produce resistance to toxin and a new wave of pests, strains adapted to local conditions cannot be developed

Methods used to produce Dolly

- somatic-cell transfer was used; has three stages
- somatic cell is a normal body cell with a diploid nucleus
- adult cells are taken from the udder of a sheep and grown in laboratory, in a medium with low concentrations of nutrients: genes in cell get inactive and lose pattern of differentiation
- unfertilized eggs are taken from ovaries of a different sheep, their nuclei are removed; cultured cells are placed to each egg cell and a small electric pulse causes them to fuse
- embryos are injected into a surrogate mother; one of 29 successfully developed: Dolly