BioMedical Admissions Test (BMAT)

Section 2: Biology

Topics B5 and B6 - DNA and Gene Technologies

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DNA

- In eukaryotic cells DNA is contained within a nucleus in long, thread-like structures called **chromosomes**.
- DNA is a large polymer made of smaller monomers.
- This monomer is a nucleotide, made of three components: a sugar (called ribose), a phosphate and a nitrogenous base.
- There are 4 bases:
    - **Adenine**
    - **Cytosine**
    - **Guanine**
    - **Thymine**
- Nucleotides always pair in a specific way (**complementary base-pairing**): A and T, C and G bond by **hydrogen bonding**
- The joined together nucleotides form a **polynucleotide** chain
- A DNA molecule is made of 2 polynucleotide chains (**strands**) that are twisted around each other to form a **double helix**

Protein synthesis

- A **chromosome** consists of millions of bases of DNA
- A **gene** is a section of a chromosome, which codes for a specific protein
- The cell only uses the **template strand** to make a protein
- The code is read as **triplets**, e.g. ACG CTA, and each triplet codes for a single amino acid.
- There are some triplets that code for the same amino acid
- The sequence of amino acids produces the protein

Gene mutation

- **Mutation:** a change in a DNA sequence.
- Harmful mutations:
    - Mutations can be harmful if it changes a triplet, which will then code for a different amino acid and therefore change the structure of the protein.
    - If the mutation occurs within an enzyme, the **active site** may no longer be complementary to the substrate.
- Most mutations have no effect on phenotype:
    - Because large sections of DNA do not code for proteins
    - Therefore any mutations here are unlikely to affect phenotype
    - These are called **silent mutations**
    - In some cases, this could happen if a change in a triplet occurs but the new triplet still codes for the same amino acid

Genetic Engineering

Genetic engineering is the **modification of an organism's genetic material**. It involves taking a copy of a gene from one organism and inserting that gene into another organism's DNA. This creates a **genetically modified organism** (GMO), which is also called **transgenic**.

Genetically engineering bacterial cells:

1. The **useful gene** is cut from the DNA of an organism using a **restriction enzyme**
    a. This enzyme cuts DNA is a staggered way, which creates **'sticky ends'** (short sections of unpaired DNA)
2. The **bacterial plasmid DNA** is cut open using the **same restriction enzyme**, also creating sticky ends
    a. By using the same restriction enzyme, the unpaired bases on the ends of the plasmid (the sticky ends) are **complementary** to that on the useful genes
3. The useful gene and the plasmid DNA are mixed and the gene is inserted into the plasmid, through **hydrogen bonds** that form between the complementary bases in the sticky ends
4. **DNA ligase** (an enzyme) is used to join the plasmid DNA and the gene together, creating a **recombinant plasmid**
5. This recombinant plasmid is then inserted into a bacterial cell
    a. The plasmid acts as a **vector**, as it carries the gene into the bacterial cell
6. The bacterial cell can be **cultured** through cloning, so multiple **genetically modified** bacteria containing the recombinant plasmid will be made.

Examples of proteins that can be produced through bacteria in this way:

- Hormones, e.g. insulin to treat diabetes
- Enzymes, e.g. rennin for producing cheese
- Blood clotting factors, e.g. factor VIII in order to treat haemophilia
- Antibiotics, e.g. penicillin

Genetically engineering of plants:

- This process is slightly different to the one just discussed, as plant cells do not have plasmids like bacterial cells do
- Instead the bacteria ***Agrobacterium tumefaciens*** is used to make GM plants
    - These have a plasmid called **Ti plasmid** that is able to enter plant cells and the genome when the bacteria infects the plant
- In the previous method, the bacteria cells were cultured through cloning. In a similar way, the plant cells are grown in culture and then develop into new plants that contain the useful gene
- Examples of GM plants:
    - Pest resistance in Bt cotton
    - Disease resistance in bananas

- Adding nutrients to avoid malnutrition in countries, e.g. golden rice infused with □-carotene to prevent vitamin A deficiency

Genetic engineering in medicine:

- **Producing medicine** e.g. insulin, blood clotting factors
  - These can produce larger quantities of medicine
  - Fewer side effects as human proteins
  - However, there are concerns about unknown long-term consequences as relatively recent technology
- **Producing vaccines**, e.g. hepatitis B
  - Can produce more vaccines that are safer and cheaper
- **Producing human-like organs**, e.g. GM pigs
  - Help to reduce shortage of suitable donor organs
  - However, concerns over the spread of disease from pigs to human
  - Ethical objections of using pigs
- **Reducing spread of diseases**, e.g. malaria
  - Modifying *Anopheles* mosquitoes to have a more efficient immune response when infected with parasite so does not survive within them
  - Concerns over the implications of other wild populations of insects

Gene Therapy

- Gene therapy is the use of genes to cure or prevent severe genetic diseases. This is done by introducing a normally-functioning gene into a patient's cells to replace a faulty, mutated gene that causes the disease.
- However, if the therapeutic gene is accidentally inserted too close to a cancer-causing gene then it can cause this gene to be switched on.

Exam Tip - Gene therapy in gametes is a controversial topic. It is a good topic to try to understand, both for the BMAT exam and for medical school interviews!

You may want to look at these videos for more insight into gene therapy.

- Editing Genes Inside the Human Body (7 minutes)
- Genetic Engineering Will Change Everything Forever (16 minutes)

	Body cells	Gametes	Stem cells
Example	**Cystic fibrosis:** can add a gene to lung cells to enable cells to produce a protein to reduce symptoms	Gene therapy on gamete cells is currently **illegal** in the UK	**Sickle cell anaemia:** GM bone marrow cells can be used to create healthy red blood cells for oxygen transport

Pros/ Cons	• Longer lasting treatment
	• Increased quality of life
	• Provides possible cures for genetic conditions, e.g. CF
	• Reduces need for daily medication
	• Less controversial
		• Any therapeutic gene added into a gamete cell will be found in every cell of child formed from gamete, so can prevent offspring developing genetic condition
		• Very **controversial** and currently illegal
		  ○ Could lead to the creation of **"designer babies"**
		  ○ Changes are passed onto offspring so can have unanticipated results on the next generation
			• Provides longer-term cure
			• Can use patient's own stem cells so no need to find a suitable donor and no risk of rejection

Stem Cells

- Stem cells are **undifferentiated** cells, which can renew themselves through mitosis.
- They have the **potential** to become many different types of cells in the body through differentiation.
- Throughout a person's life the ability of stem cells to differentiate changes:
- At fertilisation these stem cells are **totipotent**
  - **Totipotent stem cells**: can differentiate and develop into any of the specialised cells found in an adult
- As mitosis occurs, an embryo has stems cells that are **pluripotent**
  - **Pluripotent stem cells**: can differentiate it to almost every specialised cell, except cells that become the placenta
- Adult stem cells are found in several organs in the body, e.g. liver, brain, heart, and are **multipotent**
  - **Multipotent stem cells**: can only differentiate into a small number of different cells, e.g. in bone marrow they can only differentiate into types of blood cells

Stem cells in medicine:

	Bone marrow stem cells	Embryonic stem cells	Induced pluripotent stem cells (iPSC)
Examples	• Can be used to treat certain **cancers**	• Treat **diabetes** by replacing insulin-secreting cells in the pancreas • Treat **burns** through replacing damaged skin tissue • Replacing **neurons** to treat spinal cord injuries	• Produced in the laboratory using adult body cells (less controversial) so can be used instead of embryonic stem cells • Test effectiveness of **drugs** before used on patient • No rejection as from patient's body
Issues	• Risk of **rejection**	• Risk of **rejection** • **Moral and ethical** objections as they must be taken from human embryos.	

Selective breeding

1. Animals with **desirable characteristics**, e.g. rapid growth, more muscle, are selected
2. These animals are **bred** together
3. The animals with the most desirable characteristics are **selected** from offspring
4. These **offspring** are then bred together
5. Cycle repeated over **several generations** until the desirable trait increases in the population

As well as farm animals like cows or pigs, dogs have also been selectively bred over time. For example, greyhounds have been bred for their intelligence and border collie's for their obedience.

Disadvantages of selective breeding:

- Reduces **genetic variation** within the population so more at risk of disease etc.
- **Inbreeding** increase risk of genetic conditions presenting
- **Ethical** concerns of welfare of animals