The work of Frederick Sanger

Aims
In the task you will:
- discover the important advances that Frederick Sanger made into the sequencing of the genome
- outline the main steps involved in sequencing the genome of an organism
- explain what is meant by ‘Sanger sequencing’
- apply your knowledge to an exam-style question.

Information
Frederick Sanger, a British scientist, died on 19th November 2013, aged 95. He was one of the world’s leading scientists in the study of the genome, achieving two Nobel Prizes for his research. To date, Dr Sanger is the only British scientist to have achieved this honour twice.

Dr Sanger achieved his first Nobel Prize in 1958 for developing techniques to work out the precise sequenced structure of proteins. His work determined the type and order of amino acids that are used to build the hormone insulin.

Building on this work, Dr Sanger then undertook research to determine the order of bases in DNA, known as DNA sequencing. At the time, scientists were aware that DNA was a linear code but no methods existed to read the code. This was true for even simple genomes.

Dr Sanger and his team developed several methods to sequence the nucleic acids DNA and RNA. They produced the first whole-genome sequence, for a bacteriophage virus called phiX174. The virus’s genome contains just over 5000 base pairs. Sanger was awarded his second Nobel Prize in 1980 for developing a technique known as Sanger sequencing (also known as dideoxy sequencing). This method is still used today, and was used extensively in the sequencing of DNA in the human genome.

Task
Your task is to research how to sequence an organism’s genome. You then need to present your research to other students in your group.

You can choose the method by which you present your results; for example, you may wish to produce a factsheet or a presentation.

- Include diagrams where appropriate to help explain the process.
- Make sure that you pitch your findings at A-Level students who have no knowledge of genome sequencing.
- Ensure that all scientific terms are clearly explained.
- Reference any sources you have used.
Sources
You should use a range of sources to help you conduct your research. The Wellcome trust has a range of websites and resources that you may find helpful.

Wellcome trust weblinks:
http://genome.wellcome.ac.uk/doc_WTD021037.html
This website explains simply how the human is sequenced.
http://www.sanger.ac.uk/
This website contains information on the work of Sanger

Extension
Carry out additional research to explain how Sanger sequencing is used to determine the order of bases in the genome.

You should use a range of sources to help you conduct your research.

Wellcome trust weblink:
http://www.yourgenome.org/teachers/sequencing.shtml
This website contains an animation explaining in detail how the process of Sanger sequencing works.
Exam-style question

1 The human-genome project was designed to identify all genes within the human body, to understand more fully how the body functions. It is hoped that, in the future, this research will lead to the prevention and cure of many diseases. The work was a collaboration between many scientists, and was the culmination of biological research begun as far back as the mid-19th century.

1 (a) State what is meant by 'human genome'.

(1 mark)

1 (b) Match the scientist to their contribution to the human-genome project.

<table>
<thead>
<tr>
<th>Scientist</th>
<th>Contribution to human genome project</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sanger</td>
<td>Identification of the helical structure of DNA</td>
</tr>
<tr>
<td>Mendel</td>
<td>Development of technique to sequence DNA bases</td>
</tr>
<tr>
<td>Watson and Crick</td>
<td>Identification of inherited characteristics</td>
</tr>
</tbody>
</table>

(1 mark)

1 (c) Describe the main steps involved in sequencing the genome of an organism.

(6 marks)

1 (d) Gel electrophoresis is an important process used in sequencing DNA bases. The diagram below shows the appearance of parts of the gel produced when comparing three DNA samples.

[Diagram of gel electrophoresis]
1 (d)(i) On the diagram, label the positive and negative electrodes.  

(1 mark)

1 (d)(ii) State and explain which sample contained the largest fragment of DNA.  

(3 marks)

1 (d)(iii) This technique has a number of uses in biology in addition to DNA sequencing.  

State and explain one other use of gel electrophoresis.  

(2 marks)