Bio Factsheet

Number 86

The Human Genome Project (HGP)

The genome is the collective name for all the genes in the basic set of chromosomes of an individual, including the gene positions and sequences on the chromosomes and the base sequences within the genes. The Human Genome Project(HGP) was begun in 1990 and the first analysis of the entire set of human genetic instructions was published in February 2001.

Exam hint *– you will not be expected to know the methods which were used to determine the human genome. Specifications only refer to the uses and implications of knowing and being able to analyse the human genome and exam questions will be restricted to these areas.*

Main aims of the HGP

- to identify all the genes in human DNA.
- to map the positions of the genes on all the human chromosomes.
- to determine the sequences of the chemical base pairs that make up human DNA.
- to develop suitable technological tools for analysis and subsequent use of the genome.
- to store the DNA information in suitable databases for easy retrieval and analysis.
- to make the technological and genome information available to all interested parties, including biotechnologists, industrialists. pharmacists and the medical profession.
- to address the ethical, legal and social issues that may arise from the project.

Findings of the HGP

The human genome has been worked out by using cells from only a few individuals, but both sexes and several different ethnic races were included. The entire genetic code of a human consists of about three billion letters (base pairs) which is 30 times more than in a fruit fly and 250 times more than in yeast. Some of the HGP findings are summarised in Table 1.

Table1. Summary of HGP findings

Chromosome number	Number of base pairs (millions)	Number of genes	Includes genes for regulating or synthesising:
1	280	2968	Rhesus blood groups, Factor V for blood clotting, hereditary prostate cancer, early onset Alzheimer's disease.
2	253	2288	Lactase enzyme, mutant colon cancer genes, mutant Wardenburg syndrome gene.
3	223	2032	Transferrin, histamine receptor, rhodopsin.
4	199	1297	Albumin, alcohol dehydrogenase enzyme, Huntington's chorea.
5	200	1643	Serotonin receptor.
6	189	1963	Major histocompatibility complex, early onset Parkinson's disease, juvenile diabetes.
7	168	1443	Appetite control, cystic fibrosis transport regulator.
8	148	1127	Cell growth and proliferation.
9	142	1299	ABO blood groups, interferon, relaxin.
10	146	1440	Hexokinase, absorption of B_{12} from gut.
11	151	2093	Insulin, beta-globin of haemoglobin.
12	145	1652	Phenylalanine hydroxylase, taste receptors.
13	120	748	Retinoblastoma suppression.
14	111	1098	Early onset Alzheimer's disease.
15	100	1122	Connective tissue fibres, actin of heart muscle.
16	102	1098	Alpha-globin of haemoglobin.
17	88	1576	Gastrin, somatotropin, tumour suppression.
18	88	766	Proteins important in development pathways.
19	70	1454	Cholesterol carriers of blood.
20	70	927	Prion protein associated with CJD.
21	45	303	Eye lens, cataracts, Alzheimer's disease. In Down's syndrome the individual possesses an extra chromosome 21.
22	48	288	Myoglobin.
X	160	1184	Development of femaleness, blood clotting factors VIII and IX, muscular dystrophy.
Y	50	231	Development of maleness

- The actual number of genes located and mapped on the 24 autosomes and 2 sex chromosomes is only 18406, far fewer than expected. There will also be cytoplasmic genes in the genome, but these have not been analysed yet.
- only about 1.1% of the genome consists of genes. The remainder of the DNA appears to be 'repetitive junk' with no apparant genetical or biological function. This redundant, non-coding DNA exists between genes and also, as so called 'introns' within genes. When messenger RNA is made during transcription the introns are 'snipped out' using a special splicing enzyme. The redundant DNA was perhaps important in earlier stages of human evolutionary history but has no apparant 'modern' use.
- many genes are also present as identical genes in organisms distant from humans in the evolutionary hierarchy. For example, about 20% of 'human' genes also occur in yeast and about 50% of 'human' genes also occur in nematode worms and fruitflies. Many genes that occur in bacteria have also been discovered in the human genome and may have been placed there during bacterial infections.
- ethnic and individual differences between people result from very small differences in gene base sequences, totalling not more than 0.01% of the total bases within genes. Most variation appeared to occur in the African gene pool and variations in the gene pools of other races appeared to be 'subsets' of the African gene pool. This perhaps supports the theory that human origins were in Africa.
- many genes have been discovered and located that may cause disease directly, or when mutated may cause disease. Such genes are called **errant genes** . For example, genes relating to asthma, Alzheimer's disease, cystic fibrosis, cancer and haemophilia have been located.

Implications of the Human Genome Project findings for medicine

All diseases have a genetic component, sometimes inherited or sometimes resulting from the body's responses to environmental stresses such as exposure to viruses, toxins, mutagens or radiation. Genetics is beginning to play an increasingly important role in the following medical areas:

- **diagnosis** – an increasing number of gene tests are becoming available commercially which can detect mutant or errant genes in people suspected of having specific diseases or at risk of developing them
- **prediction** – by detecting errant genes in a person's genome it may be possible to predict the onset of disease in later life. The onset of such disease may be a certainty, as with the Huntington's chorea gene (on chromosome 4), or just a probability as with the juvenile diabetes gene (on chromosome 6). The detection of errant genes in a person will also have implications for that person's family because the genes may have been received from parents or passed on to children during the normal course of inheritance.

Remember *– even though a certain gene is present in an individual's genotype it may not be expressed in the phenotype either because it is recessive or because its expression is suppressed Details about gene expression can be found in Factsheet 45, Gene Expression.*

- **treatment** – drug design to date has been a rather 'hit or miss' process, developing and using drugs found to react with about 500 known receptor sites in the body. The HGP has identified many thousands of receptor sites which could now be accurately targetted by drugs. The potential to develop treatment of genetic and acquired disease by **gene therapy** is greatly increased. At present gene therapy is in its infancy, enabling treatment of only a few diseases, such as cystic fibrosis and alpha 1-antitrypsin deficiency.

Remember *- gene therapy involves replacing or supplementing defective genes in an individual with normal genes or adding genes to increase immunity or to inhibit tumour growth. A detailed description of gene therapy can be found in Factsheet 51, Gene Therapy,.*

Ethical, legal and social issues

Knowledge originating from the HGP has huge sociological implications for humans. Some of these are listed below in question and comment form:

- *Who should have access to personal genetic information? How should such information be used?* It is very important that the use of genetic information by, for example, insurers, employers, courts, schools, adoption agencies and the armed forces should be fair to the individual and all involved parties.

- *Who owns and controls genetic information?* It is important that individual privacy and confidentiality is maintained, and that an individual's genetic information is not distributed to other parties without permission.

- *How does personal genetic information affect an individual? Are society's perceptions of an individual altered by such genetic information?* It is important that an individual who suffers from genetic imperfections should not be socially deprived, psychologically traumatised, or stigmatised by society's attitudes towards genetic differences.

- *How reliable and useful is fetal genetic testing at present? Will healthcare personnel counsel parents correctly and sympathetically about the risks and limitations arising from genetic technology?* Before individuals can give consent for procedures to be carried out they must be adequately informed about complex and controversial procedures, about how to assess genetic information for reproductive decisions and about the reproductive rights of parents and children.

- *How will genetic testing be evaluated and regulated for accuracy, reliability and usefulness? Are genetic tests reliable and interpretable by the medical professions?* At present there is little quality control of such procedures. Doctors, other health service personnel and patients must be educated about the new genetic capabilities, their scientific limitations and social risks. Quality control measures and the implementation of standards must be developed properly.

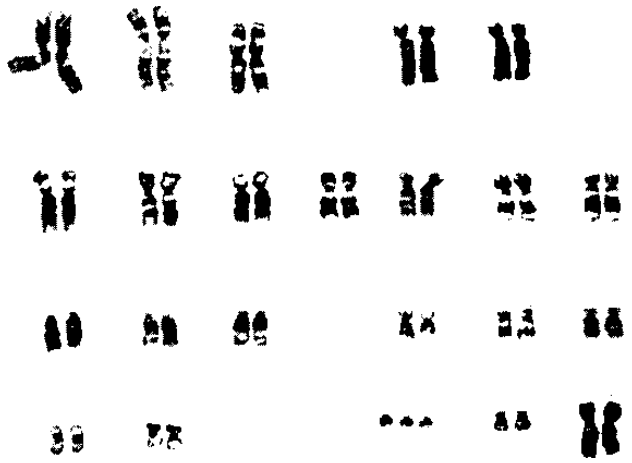
- *Should parents have the right to let their children be tested for adult-onset diseases? Should testing be performed in cases where no treatment is yet available?* Uncertainties exist about gene tests for susceptabilities to disease and for complex conditions such as 'heart disease', especially when the conditions are linked to multiple gene interactions and to gene-environment interactions.

- *Do people's genes make them behave in particular ways or can people always control their behaviour? Are disease-causing genes considered acceptable genetic diversity?* Knowledge of the human genome imposes conceptual and philosophical implications on humans, including human responsibility, free-will versus genetic determination and concepts of health and what is acceptable disease.

- *Who owns genes and the other pieces of DNA?* This has implications for the commercialisation of products, including property rights, patents, copyrights and trade secrets. It also has implications for the accessibility and dissemination of genetic data, materials and methods.

Specimen Question

The picture below shows a karyotype of human chromosomes.



(a) (i) Does the karyotype above represent a full set of human chromosomes? Explain your answer. 2

(ii) A mutation is shown in the above karyotype. Label it on the drawing, name it and suggest how could it have happened. 4

(iii) What was the sex of the individual from which the karyotype was taken? Explain your answer. 2

(b) (i) Name three diseases for which related genes have been located by the Human Genome Project. 3

(ii) Suggest two ways in which the Human Genome Project may improve the medical welfare of disease sufferers. 2

(iii) Suggest two ways in which information gained from Human Genome tests may be misused. 2

Total 15

Answers

(a) (i) yes;
there are 23 pairs which is the diploid number (and one extra chromosome); 2

(ii) label chromosomes 21 (3 chromosome group);
Down's syndrome;
non-disjunction;
unequal segregation/separation of chromosomes during cell division; 4

(iii) female;
if male a large X and small Y would be present but all pairs show equal chromosome sizes; 2

(b) (i) Alzheimer's disease; diabetes (mellitus); Huntington's chorea; (allow other correct examples) 3

(ii) it will allow increased/improved use of gene therapy;
it will enable many more drugs to be developed which will work in much more precise ways than many present day drugs; (allow other valid comments) 2

(iii) it could be used to refuse insurance cover for individuals who contain disadvantageous genes;
it could make it more difficult to find employment if a potential employer is aware of disadvantageous genes within a potential employees genome; (allow other valid points) 2

Total 15

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