ICS 3

Aims

1. Determine the sequences of the 3 billion chemical base pairs that make up human DNA + Genomes of model organisms (e.g. mouse + fruit fly) to provide comparative information necessary for understanding the function of the human genome
2. Identify all the ~20,000-30,000 genes in human DNA → Enable us to understand and eventually treat many more of the 4000 genetic diseases that afflict mankind
3. Store the information in electronic databases available to everyone → Genbank → Facilitate molecular research world wide
4. Improve tools for data analysis of genetic information → Field of bioinformatics developed in parallel with HGP has developed new tools in comparing DNA sequences, translating them into protein data, identifying regions of DNA such as coding and non-coding sequences.
5. Transfer related technologies to the private sector → Develop new technology to facilitate a broad range of biological and biomedical research
6. Address the ethical, legal and social issues that may arise from the project → As advances in genetics have consequences for individuals and society

Implications

- Use info obtained to identify a wide range of disease causing alleles/alleles that give desirable traits
- Human genome contains 3 billion chemical nucleotide bases
- Average gene consists of 3000 bases
- Total number of genes is estimated at around 20,000-30,000
- Chromosome 1 has the most genes and Y chromosome has the fewest
- 99.9% of nucleotide bases are exactly the same in all people
- Functions of over 50% of discovered genes are unknown
- Genes are concentrated in certain regions with vast expanses of non-coding DNA between them
- Less than 2% of the genome codes for proteins
- *Identified about 3 million locations where SNPs occur in humans which act as useful molecular markers
- *Microsatellites (simple sequences) and minisatellites (10-100bp long) also act as molecular markers
- Most genetic mutations occur in males
- All humans today descended from a single man who lived in Africa

Benefits

1. Improved diagnosis of disease in terms of accuracy and speed + Earlier detection of genetic predispositions to disease using SNPs in disease identification
2. Insights gained from comparative genomics (comparing human genome with model

organisms) leads to gene discovery and understanding of disease development
3. Design treatments for genetic diseases by studying the structure and characteristics of molecular alterations/mutations that result in disease + the protein coded for by the gene
4. Cure may one day be possible through gene therapy, switching off the faulty gene with gene knockout techniques or recombination technology to replace abnormal protein
5. Pharmacogenomics → Create drugs based on molecular information that work better and have fewer side effects + Personalise drugs to fit patient's pharmacogenomic profile for greater efficacy
6. DNA identification through SNPs and STRs to identify potential suspects from DNA evidence left at crime scenes + Establish paternity and family relationships + Match organ donors with recipients in transplant programs
7. Study evolution through germline mutations in lineages + Study migration patterns of different population groups → Bioarchaeology, Anthropology, Evolution and Human migration

Ethical, Social, Legal Concerns + 1 example

- Fairness in the use of genetic information
    - e.g. Insurers may raise premiums based on genetic predisposition to disease
    - e.g. Employers may hire and promote based on genetic superiority rather than on merit
    - e.g. Courts may judge a defendant based on a genetic predisposition to violence rather than the severity of the crime itself
- Privacy and confidentiality of genetic information
    - e.g. Risk profiles for diseases may be freely accessible to insurers, employers, schools and used in a discriminatory manner
    - e.g. Genetic information becomes private intellectual property of biotechnology companies as they are able to commercialise the technology derived from the research but no direct benefit for the individuals who contribute their genetic information
- Psychological impact and **stigmatisation** due to an individual's genetic differences
    - e.g. A person's genetic predisposition may affect society's perceptions of the individual in a negative way ⇒ Individual may become an outcast
    - e.g. Negative perceptions of members of minority communities may be strengthened based on genetic predisposition of individuals belonging to a particular race
- Reproductive issues - Adequate informed consent required for complex and potentially controversial procedures, use of genetic information in reproductive decision making and reproductive rights
    - e.g. Foetal genetic testing may not be reliable in some instances involving complex diseases so parents may abort healthy foetuses unknowingly
    - e.g. May aid elements of society that practice eugenics
- Clinical issues - Education of doctors, patients and general public about genetic capabilities, scientific limitations and social risks and implementation of standards and quality control measures in testing procedures

    - e.g. Proper counselling in conjunction with risk profiling where there is no treatment for the diseases
- Uncertainties associated with gene tests for susceptibilities and complex conditions linked to multiple genes + environmental factors
- Conceptual and philosophical implications regarding human responsibility, free will vs genetic determinism and concepts of health and disease
    - e.g. Knowlege of whether genes alone affect behaviour and human physiology are not fully understood + not well studied
- Commercialisation of products including property rights and accessibility of data and materials
    - e.g. Companies may patent DNA sequences and limit their accessibility and development into useful products ⇒ Costly to experiment and share DNA technology

<u>Name 3 ways in which treatment and management of genetic diseases has benefitted from HGP</u>

1. Improved diagnosis
    - Diagnostic tests to screen carriers with faulty genes to inform them of possible risks/make changes in lifestyle to minimise risks
    - Diagnostic tests to screen embryos during prenatal testing to avoid the birth of affected children
2. Allows for design of treatments for genetic disorders where mutation of gene is identified
    - Via gene therapy, replacing abnormal protein with recombinant proteins, drugs to block action of enzymes/proteins coded for by faulty genes, switching off faulty genes via gene knockout techniques such as antisense RNA technology
3. Pharmacogenomics
    - Knowing about the genes which affect a person's response to a drug allows the tailoring of drugs prescribed to fit the patient's pharmacogenomic profile for greater efficacy/avoid dangerous side effects