GENETIC ENGINEERING IN DRUG PRODUCTION

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Genetic engineering started as a science in 1861 when a monk Gregor Mendel discovered a concept which 120 years after his death would have revolutionised biology.

His basic concept was this: the external characteristics of all organisms are governed by relatively simple laws which may be directly related to the existence of chemical factors in the organism itself.

Discoveries slowly followed which led to the great discoveries of the 1970s after which genetic engineering exploded into different branches of nearly all the biological sciences.

Nowadays genetic engineering or molecular biology as it has also been called has a bearing which is considerable in the fields of drug production.

One of the important steps which lead to genetic engineering as we know it today was the discovery of the restriction endonucleases which are enzymes having the property of restricting DNA at specified sites determined by the sequence of the amino acids. This together with the discovery and employment of the ligase and polymerase enzymes lead to the first proper genetic engineering experiment three years later which involved the insertion of a DNA molecule into a bacterium in such a way that the recombinant (as it is called) molecule is passed on to the offspring of the bacterium. Other discoveries followed and served to increase the utility and importance of the new science. Microorganisms were employed as vectors (holders for foreign DNA). This led to an array of tools including endonucleases, ligases, polymerase vectors, plasmids etc. with which the first drugs could be produced. Oncogenes were discovered in 1979. These oncogenes are genes which normally determine the rate and amount of growth in a mammalian cells and they have been discovered to be greatly implicated in cancerous growths. This discovery opened the path for genetic engineering to find a cure for at least some cancers.

Today, a large amount of research is being conducted in the field so as to increase our understanding of the genome primarily of Homo sapiens and secondarily of other species. Bacteria are being utilised to house a predetermined section of genetic code. For example, if one needs to synthesize a determined protein of pharmacological interest which is not synthesized easily in vivo from the organism in which it is found naturally, the genetic code determining the structure of that protein is

isolated and inserted into a plasmid (a piece of circular DNA which has determined properties interesting to the scientist which assist in the future expression of the selected gene). This plasmid is inserted into a vector which at first normally consisted of a bacterium (Escherichia coli). Nowadays however genetic engineering of plants has advanced greatly and plants are being used both as vectors and as the source of the genetic code. In fact this could lead to great gains in pharmacological production since plants have always been a major source of drugs. Genetic engineering has the potential to greatly increase the output of drugs from plants as well as giving scientists the possibility of modifying micro organisms of modifying basic compounds to render them with greater activity and/or fewer side effects.

Genetic engineering is therefore nowadays used to a great extent in drug production. There are various ways in which this technique may be used to manufacture drugs giving rise to a large (and ever increasing) amount of drugs and related compounds used in medicine. Some of the drugs and medicinal compounds produced by the industry can be seen below:

Table 1

Compound Name	Initial Develop-	Date Released	Trade Name	Use of the Drug
Human Insulin	1977	1982	Humulin	Diabetes
Human Growth Hormone	1979	1985	Protropin	Growth disorders
Hepatitis B vaccine	1981	1986	Recombivax HB	Hepatitis B
IFN-alpha	1977	1986	Roferon-A	Various
t-PA (Activase)	1982	1987	Tissue Plasminogen Activator	Myocardial Infarction

Table 1 cont.

Compound Name	Initial Develop-	Date Released	Trade Name	Use of the Drug
EPO (erythro-poietin	1984	1988	Epogen	Anaemia
IL-2 Interleukin -2	1982	1989	Proleukin	AIDS, Cancer, renal cell carcinoma viral infections, rheumatoid arth-rytis, lymphokine activated killer cell therapy
IFN-gamma	1979	1989	Immuneron	renalcell carcinoma Kaposi's sarcoma AIDS, skin cancer, rheumatoid arth-ritis, bacterial infections
Antihemo-philic factor	1983	1991	Factor VIII	haemophilia
G-CSF Granulocyte colony sti-mulating factor	1983	1991	Neupogen	Chronic neutrope-nia, cancer, burns, leukemia, AIDS, septicemia, bone marrow transplant actions in combi-nation with chemo-therapy

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The rate of drugs produced by different companies all over the world produced either directly by using genetic engineering or with the help of biotechnological techniques is always increasing . Some of the latest

products include a new revolutionary test for the HIV virus which sensitive and can detect infection with the virus after only 24 hours as compared with previous tests which could detect infection only after a period measured in months.

Table 2: Impact of Genetic Engineering on Medicine

Phase	Impact on	Substance	Applications
Pilot Phase 1980-1985	Moderate Long term	Human Insulin Monoclonal Antibodies	Diabetes, Improved Diagnostics
Biotech Phase as of 1984	Increasing Influence	Interferons	Viral infections
		Interleukins CSF	Blood cancers and some tumours
		Viral components CD4	Some tumours. Immunodeficiency. Adjuncts to cancer therapy. New vaccines AIDS
Pharmacological phase as of 1990	Major Progress in all areas	Agnosists and antagonists of proteins genetically modified proteins and antibodies	Cancer autoimmune diseases, immunodeficiency organ transplants CNS diseases
Gene Therapy phase as of 1995	Innovative Therapies	Genetic Diagnosis Somatic Cell gene therapy. Pharmacological effect on genetic activity	Diagnosis of inherited diseases. Innovative disease prevention. Some Tumours, cure for inherited disease

The table above gives a concise summary of the progress (actual and planned) of the science of genetic engineering when applied to drug production.

As can be seen from the table new and important advances are planned and expected for genetic engineering . In the future one can expect to perform a genetic diagnosis and to cure inherited diseases of genetic origin directly by gene therapy. This type of cure has already been performed on a young patient with ADA. ADA is a rare genetic deficiency in which patients have an enzyme missing the enzyme adenosine deaminase which prevents the development of an immune system. Thus patients suffering from this disease have to live in a plastic bubble. Scientists are removing defective cells from a patient and inserted into an intact ADA gene into these cells and then reinfused these cells into the patient. One hopes that these cells, which are now healthy, will multiply and replace the defective ones. The complete results of this experiments are still not known, however expectations are very optimistic.

Other studies were carried out. The use of genetically engineered drugs in Malta were investigated as was the possibility of producing some drugs biotechnologically in Malta. Foreign companies were also asked to submit information as to what was the extent of their use of genetic engineering in their manufacturing processes. At the time of writing results for these experiments were not available. However the centres of biotechnology research and development seem to be centred in Switzerland and the United States.