WHAT IS GENETIC ENGINEERING?

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Genetic engineering, more accurately called recombinant DNA gene technology, is an extremely modern science arising from fundamental research in the early 1970s. Before that time, biochemists had no possible way of studying individual genes in detail simply because there were no methods available for making pure preparations of a gene. Genetic engineering has changed all that. We can now use a combination of enzymic and biological procedures to isolate any gene from any source in pure form. The principles involved in this are relatively simple, but the consequences are enormous. It is likely that the next few years will see a detailed understanding of how genes are regulated, of what happens (in cancer and other diseases) when gene regulation is upset, and of how individual genes can be used to benefit agriculture, medicine, and commerce. In this brief paper, some background of molecular biology is given as a basis for understanding what genes do in living cells and how recombinant DNA technology allows the isolation of individual genes. Later discussions will then concentrate on practical possibilities for using these genes.

GENES SPECIFY PROTEIN PRODUCTS

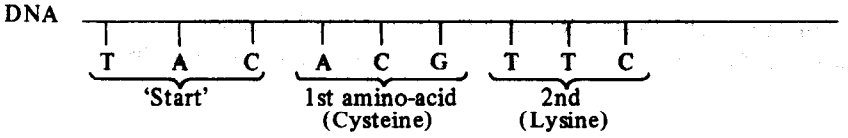
Genes are not hypothetical particles invented by Mendel to confuse students of genetics. A gene is a specific segment of DNA contained in a chromosome, and the chromosome may have thousands of genes side-by-side. The biological role of a gene is to carry the blueprint to direct the synthesis of a particular protein. The globin gene specifies globin protein for haemoglobin, the insulin gene for insulin, the keratin genes for wool (or hair) proteins, and so on. All living systems depend upon a collection of proteins to carry out all the functions of development, energy conversion, movement, growth, reproduction. Name any function required to support a life form: the job is done by a protein. A rabbit is a rabbit because its genes specify rabbit proteins; the same applies to yeast, bacteria, plants – any living organism. The chromosomes of each organism carry a set of genes which is peculiar to that organism and which specifies the synthesis of particular proteins. Of course, proteins from different species that have been selected for the same job (such as haemoglobin) will be very similar in their make-up. So it is no surprise that haemoglobins from mice or men are almost identical – they have evolved as oxygen-carrying molecules. The genes for these proteins are also closely related. The closer species are on an evolutionary scale, the more alike are their genes.

WHY PROTEINS ARE ABLE TO DO ANY BIOLOGICAL JOB

Each protein consists of twenty different kinds of molecules joined to each other – twenty amino-acids. An average protein might be some 300 amino-acids long and the key point is that each of the amino-acids has different properties. Furthermore, the order of the amino-acids in the chain completely dictates the property of the protein. Thus, there is an alphabet of twenty letters (amino-acids) which can make up words (proteins). Clearly a vast array of 'words' can be constructed, especially if each one is some 300 'letters' long. The theoretical number of proteins is twenty to the three-hundredth power (20^{300}) – a huge number of combinations, giving rise to enormous diversity of protein structure and function.

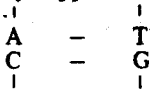
HOW GENES SPECIFY PARTICULAR PROTEINS

Chemically speaking, one gene is virtually identical to any other gene. The DNA consists of a 'backbone' of sugar molecules (deoxyribose) joined by a phosphate bridge. The third component consists of bases: A (adenosine), C (cytosine), G (guanine), and T (thymine). The crucial point is this: *the only way in which one gene differs from another is the ORDER OF THE FOUR BASES.* It is the order of bases in the DNA which specifies the order of amino-acids in a protein. The way in which this is done is illustrated below. The bases are 'read' in groups of three – that is, each set of three bases codes for one amino-acid.

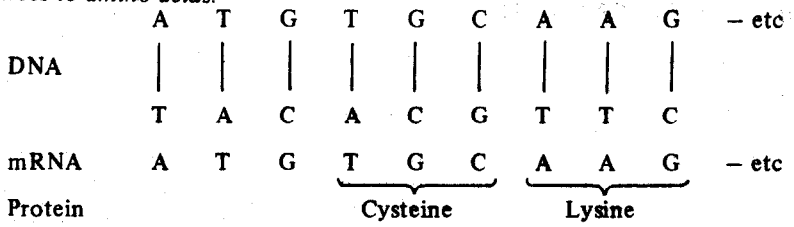


THE CONCEPT OF COMPLEMENTARY BASE-PAIRING

The above diagram is over-simplified. DNA consists of two strands – and there is an invariant rule. That is, wherever there is an A in one strand it lines up opposite a T in the complementary strand. Similarly, C is always opposite G.



This has very important consequences for genetic engineering and for identifying genes because *one* strand of a gene can always find its *complementary partner* even in a complex mixture of DNA. *In protein synthesis, ONE of the DNA strands is copied into a complementary base sequence called messenger RNA (mRNA) and this long polymer is decoded in threes to amino-acids.*



GENETIC ENGINEERING: ISOLATING SPECIFIC GENES

The smallest viruses have only about five genes and so they are 'molecular parasites'. They depend upon many of the proteins coded by host genes in the tissues they infect. Even with this simple structure, the job of isolating a single gene in pure form from a small virus is not done simply by physical or chemical means. As noted before, the chemical structure of one gene is precisely the same as that of another. Imagine the problem then, in trying to isolate a single gene from the very much more complicated chromosome system of (say) humans. Instead of five genes, there may be a million genes. How can we possibly isolate a single one of these in pure form?

That is precisely what genetic engineering can do. There are four steps required:

1. The ability to chop chromosomal DNA down into gene-sized pieces. This can be done with great accuracy by special enzymes called *restriction enzymes.* They recognise a particular sequence of bases in DNA and cut the molecule there.
2. Joining each individual 'gene piece' to an individual replicating piece of DNA called a *vector.* These vectors are found in bacteria as 'mini-chromosomes' and are well known in medicine and agriculture because they carry genes for antibiotic resistance.
3. Arranging conditions such that each 'gene piece' combined with its 'vector' (the gene has recombined with the vector, hence the term 'recombinant DNA'), is taken up by an

individual bacterial cell. Thus all the separate genes, each attached to a vector, are now distributed in separate bacterial (*E. coli*) cells. These cells can be distributed on an agar plate by normal microbiological procedures, such that *single* cells, held in agar, group into *single colonies*. As the colony grows, so the gene plus vector replicates in each cell of the colony.

4. Selecting the colony which contains the gene you want. This is the most difficult part – but we can utilise the fact that all living organisms decode their genes in the same way. A bacterial colony containing a human growth-hormone gene (attached to its vector) will make growth hormone. This can be detected by a specific antibody or by biological testing of colony extracts for growth-hormone activity.

THE FUTURE

The staggering fact is that methods are available to isolate any gene from any source in pure form. That means that we can call upon the whole of biology for genes and use them for specific purposes. We are not limited to breeding programs among compatible species for introducing new genes into plants or farm animals. In addition, we can introduce *single* genes to benefit production characteristics without introducing unwanted genes (as so often occurs by conventional breeding).

There is a great deal more to be learnt about genes – especially the way in which they are controlled. We are committed to this kind of basic research in the Department of Biochemistry. But there is already sufficient knowledge and know-how to make a start on the practical applications of the 'new genetics' made possible by recombinant DNA technology. We are also committed to that – for detection of pathogens in plants, to improve growth efficiency in farm animals, and to improve wool production. It is an extraordinarily exciting time since there are almost limitless opportunities for the applications of genes in agriculture, medicine, and commerce.