

What's what in Biotechnology?

- *What is ...?*
- *What's the difference between ...?*
- *What's the answer to ...?*

Biotechnology is highly multi-disciplinary, dependent not only upon scientists in biology and chemistry, and engineers, but also upon financial, legal, and managerial experts. Each specialist group tends to lapse into shorthand when describing concepts and materials in its own field. This practice complicates communication both within and outside the biotechnology field.

The aim of this briefing paper is to explain concepts and jargon frequently used in biotechnology. The central role of the molecule that lies at the heart of biotechnology – DNA – will be described, as well as the techniques and tools biotechnologists use to alter the characteristics of living organisms. The briefing paper aims to answer frequently asked questions about the developments in biotechnology and to clarify terms which are used interchangeably.

DNA-makes-RNA-makes-protein

Biotechnology is founded upon an ever-increasing understanding of the mechanisms that maintain living organisms and allow them to reproduce from generation to generation. At the heart of life is deoxyribonucleic acid, **DNA**, the long, double helix molecule that carries the hereditary genetic instructions necessary to produce organisms. The genetic composition of an organism – its **genotype** – in conjunction with environmental influences determine its appearance and physical characteristics – its **phenotype**. One only has to remember how a human being changes in size, shape and behaviour during a 70-80 year lifetime to know that the correlation is not simple.

The genetic instructions for a human being – its **genome** – are contained on DNA that is around 1.6 metres long but only one fifth of a millionth of a centimetre wide. Every cell of our bodies contains a copy of this DNA divided into 46 parts of discrete length – the **chromosomes**. These are so highly condensed that they can fit into the cell's nucleus which measures 3-4 millionths of a metre in diameter. Between them, human chromosomes carry some three thousand million units of chemical coding. The units are known as **bases** and come in four types – adenine, thymine, cytosine and guanine, or A, T, C, and G. It is the sequence of these bases in the DNA molecules which determines the biochemistry of cells and physiology of organisms.

While DNA is a good carrier of information, it is relatively inert. Most of the cell's activities are carried out not by DNA but by **proteins**, very large molecules that consist of chains of units called amino acids. Biochemists encapsulate the relationship between DNA and protein in what they call the "Central Dogma" – "DNA-makes-RNA-makes-protein". **RNA** (ribonucleic acid) is similar in structure to DNA except that the base uracil (U) replaces thymine and that it is usually found as single-stranded molecules, whereas DNA is found as double-stranded molecules.

The reading of the code in DNA to produce a protein begins in the nucleus with a process called **transcription**. In this process, an RNA copy of a **gene** – a particular section of DNA that carries the instructions to make one protein – is produced. After a certain amount of

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biochemical processing the RNA copy – called **messenger RNA** (mRNA) – is decoded by a small piece of biochemical machinery called a **ribosome**. This decoding process is called **translation**. In essence what the ribosome does is to read three bases of mRNA – a **codon** – at a time. Each codon specifies that a particular amino acid is joined to a growing chain of protein. Certain codons also specify the start and end of a protein. A single piece of mRNA may be translated in turn by many ribosomes. Thus a single gene on a chromosome may give rise to many copies of a protein.

Traditional and modern biotechnology

Much of the excitement in the modern biotechnology of the past 20 years or so has been associated with scientists' increasing ability to control these basic processes of biology. In traditional biotechnologies, such as brewing, silage making, dairy production, and agriculture, mankind has always harnessed and adapted living organisms. Crops and domestic animals have been selected by farmers for particular traits – high yields, hardiness, resistance to disease, for example. The microbes used in the manufacture of antibiotics today have been developed through mutation and selection from earlier, much lower-yielding strains. But increased understanding of basic biology has now enabled researchers to control more precisely the introduction of novel traits.

By altering its DNA using the techniques of recombinant DNA, an organism can be persuaded to produce more of a particular protein or to produce an altered form of a protein. Significantly, researchers can put small pieces of DNA from one organism into the genome of another, unrelated organism, thereby crossing natural boundaries between species. Thus human genes can be inserted into bacteria or into yeast, enabling human proteins of medical value to be produced in controlled cultures. Similar techniques of genetic engineering are also being used in animal and plant breeding, and in most of the areas of traditional biotechnologies.

What is ...?

Antisense molecule

A molecule which binds specifically to a (sense) strand of RNA or to a DNA helix and stops it being used to code for a protein. Antisense molecules are usually chemical derivatives of DNA or RNA.

Bioremediation

Cleaning up the environment using living organisms. Microorganisms and plants degrade or absorb toxic pollutants or heavy metals on polluted land, in water or in the air.

Combinatorial chemistry

A technique in which millions of molecules are produced by randomly combining their components. Combinatorial chemistry combined with the high-throughput screening techniques of biotechnology offers important new opportunities for drug design.

DNA bases or base-pairs

The bases of DNA are composed of carbon, hydrogen, nitrogen and oxygen and come in four types: adenine, thymine, guanine, or cytosine (A,T,G,C). It is the order of the bases which provides the coding in genetic information. The base or base-pair is thus similar to the bit of computing jargon. Researchers use the terms “bases” and “base-pairs” virtually interchangeably.

DNA probe

A small piece of labelled DNA that can bind to a particular DNA sequence, e.g. (part of a) gene. It is used to demonstrate the presence of that particular DNA sequence.

Downstream processing

The group of techniques such as centrifugation, filtration and chromatography used to recover and purify the products of an enzymatic conversion or a microbial production process.

Enzyme

A protein that facilitates a biochemical reaction.

Expression (of a gene)

The production of a protein, coded for by a gene, by cellular machinery.

Gene therapy

A method being developed to tackle diseases by administering DNA or RNA as drugs. The principle is that DNA or RNA, coding for one or more genes, is injected, ingested, or inhaled to be integrated into the genome of cells in the body with the help of weakened viruses or artificial particles. Once integrated, the normal cell machinery decodes it and produces proteins that remedy the defects that cause the disease. A possible important method for the future is the introduction of encapsulated cells into the

body in which the genes have been modified. (See Page 4 for the difference between germline and somatic cell gene therapy.)

HUGO

The Human Genome Organisation, an international body which has been involved in coordinating the Human Genome Project, the project to obtain the entire human genetic sequence.

Immobilisation

A technique whereby biological molecules, enzymes, organisms, or cells are attached to surfaces or trapped in matrices. Immobilisation protects fragile biological material and enables it to be recycled.

Monoclonal antibodies

Antibodies are components of the immune response which bind to foreign matter – **antigens** – in the body. The natural immune response towards a single antigen triggers the production of a mixture of antibodies. However, by using a specially constructed hybrid cell – a **hybridoma** – researchers can produce a clone of identical antibodies, “monoclonal antibodies”. These are used extensively in research and in medical diagnosis.

Open reading frame (ORF)

A region of DNA which could be a gene but which has not yet been shown to code for a protein.

Orphan Drug

Orphan Drug legislation in the United States and elsewhere (but not yet in Europe) encourages drug companies to develop treatments for rare diseases. It does this by guaranteeing the first company to develop a drug the exclusive rights to sell products for several years (seven in the USA). Human growth hormone and erythropoietin produced using recombinant DNA techniques were both developed as orphan drugs by US biotechnology companies.

PCR

Polymerase Chain Reaction, a method for repeatedly duplicating trace amounts of DNA in order to provide detectable quantities for analysis. PCR is frequently used for DNA fingerprinting (DNA profiling) in forensic science.

Phage display

A laboratory technique for evolving molecules that bind specifically to other

molecules. Phages (short for bacteriophages) are parasites of bacteria that consist of a length of DNA, or less commonly RNA, surrounded by a protein coat. Researchers can produce billions upon billions of subtly varying phages with slightly different coat proteins in a single experiment. They then find which of those will bind to a surface coated with the target molecule. The phages that bind can be grown and the DNA that codes for the binding protein isolated.

Plasmid

A small circular piece of DNA from bacteria which encodes specialist functions such as antibiotic resistance and which can be passed from one organism to another. A much used part of the plant genetic engineers toolkit is Ti plasmid. This plasmid is derived from the bacterium *Agrobacterium tumefaciens*, which causes crown gall disease in plants, and provides a means for transferring new genes into plants.

Secondary metabolite

Substances produced under certain circumstances, for example suboptimal living conditions, which are not necessary for the metabolism of the organism.

Somatotropin

Human growth hormone produced through genetic engineering that is used to treat growth hormone deficiency in children (hypopituitary dwarfism).

TPA

Tissue plasminogen activator, a protein used as a treatment to dissolve the blood clots that cause heart attacks and strokes.

Transposon

A small segment of DNA that can move, via excision and subsequent insertion, from one location to another on the DNA. A gene which is carried by a transposon is often referred to as a “**jumping gene**”. Transposons carrying genes that confer antibiotic resistance are the major source of antibiotic resistance in bacteria.

What's the difference between ...?

Microbes, bacteria, fungi, yeast, virus?

Microbe is a loose term encompassing a range of microscopically small organisms. Bacteria like *Escherichia coli* are usually single cells, while fungi

frequently grow as long, multicelled filaments. Those filaments can aggregate to form larger masses visible to the naked eye as mushrooms or toadstools. Yeast is a fungus that does not form filaments. Algae are microbes too. So are viruses, although they must inhabit living cells in order to exist.

Bt, BST and BSE?

Bt is short for *Bacillus thuringiensis*, a soil bacterium which produces a protein that is toxic to a variety of insects, but not to animals and humans. The protein is used as insecticide for more than 25 years. Plant genetic engineers now also transfer the gene coding for the Bt-protein into plants to make them resistant to insects. Bovine somatotropin (BST) is a growth hormone of cattle used to increase the yield of milk in dairy cows and to produce leaner meat in beef herds. BSE is bovine spongiform encephalopathy, a brain degenerative disease caused by infectious protein particles known as prions. There is increasing evidence that it can pass to humans through the diet and cause a related neurological syndrome, Creutzfeldt-Jacob Disease.

Chimaeric and transgenic organisms?

A chimaera is any organism made of cells of differing genetic composition. A chimaera may originate from an embryo into which cells have been introduced from another embryo of either the same or a different species. Transgenic organisms have an additional piece of DNA originating from a different species in all their cells. For example, the geep – an animal form obtained by mixing embryonic cells of sheep and goats – is a chimaera but is not transgenic.

Conjugation, transduction and transformation?

These are three natural processes for genetic transfer in bacteria which researchers have adapted as tools in genetic engineering. Conjugation is a process where small pieces of DNA called plasmids pass from a donor cell to a recipient through a tube, grown for this purpose. In transduction, the DNA is carried into cells by a virus. Transformation is a more passive process whereby DNA enters a cell through pores or a damaged region of the cell wall.

DNA and RNA?

DNA – deoxyribonucleic acid – is the genetic material in most organisms; RNA

– ribonucleic acid – is the genetic material in some viruses, and performs other functions within the cell, too (see introduction).

EPO and IPO?

EPO stands for European Patent Office. Patenting through the EPO affords protection in all EU countries and Switzerland. EPO also stands for erythropoietin, a protein that stimulates the production of red blood cells. IPO stands for Initial Public Offering, a money-raising activity (also known as flotation) for a biotechnology company by which privately-held shares in the company are offered for general sale through stock exchanges like NASDAQ in New York or the London Stock Exchange. After going public, a company is said to be listed or quoted.

Fermentor and Bioreactor?

Although the two terms are used more or less interchangeably to describe vessels in which controlled biological processes occur, fermentor is usually reserved for vessels in which living cells grow freely. In bioreactors, the active principles could also be purified enzymes, cell extracts, or whole cells growing on surfaces.

Germline and somatic cell gene therapy?

Researchers have been careful to distinguish these two broad classes of gene therapy. Somatic cell gene therapy involves adding or replacing genes in cells which are not involved in reproduction. Thus cancer cells might be made more susceptible to drug treatments by adding genes which cause the immune response to be activated. The genetic changes made would not be passed on to the next generation. In germline gene therapy, on the other hand, the changes would be made in reproductive cells or in very early embryonic cells. These changes would be passed on to succeeding generations. Although it could represent a one-time cure for a genetic defect, germline gene therapy is generally not considered ethically acceptable and forbidden by law in many countries.

Genetic modification, genetic engineering, genetic manipulation and recombinant DNA techniques?

These are all essentially synonymous terms used as shorthand to describe the process by which genes can be transferred by researchers from one organism to another. The process has two main phases. The first, which takes place in the test tube, is the extraction of DNA from

the cells of a donor organism and the construction of a carrier molecule – a **vector** – which contains the particular gene of interest. The second phase involves implanting the vector into the recipient organism, which is usually a single cell. If the implant takes, the engineered cell will have acquired a novel characteristic.

In vitro and in vivo?

Terms used to describe experiments which take place in the test-tube (*in vitro*) or in living organisms (*in vivo*). With the increasing use of computer simulations and information technology in biology, researchers now also conduct experiments *in silico*.

Mapping and sequencing?

Although they run concurrently, gene mapping and genome sequencing can be regarded as the two stages of the human (or other) genome projects. Mapping determines the positions of genes relative to each other on chromosomes. Sequencing is the determination of the order of individual bases or base-pairs within genes and other pieces of DNA.

mRNA, rRNA, tRNA, rDNA, cDNA, mtDNA, dsDNA and ssDNA?

The small letters preceding RNA designate different types of natural RNA which serve different functions in the cell. Thus, mRNA is messenger RNA, rRNA is ribosomal RNA, and tRNA is transfer RNA. Confusingly, rDNA is shorthand for recombinant DNA and cDNA is shorthand for copy DNA (DNA which has been copied from mRNA). You may also come across mtDNA (mitochondrial), dsDNA or ssDNA (double- and single-stranded).

Peptide, polypeptide, protein?

All three are molecules composed of strings of amino acid building blocks. The term peptides is used for short chains of amino acids containing between two and thirty amino acids. Longer chains are polypeptides. Proteins are principally polypeptides, but they may contain more than one polypeptide chain or may have some additional chemical groups (fats, carbohydrates, metals). Moreover, the term protein has connotations of function as well as composition.

Primary, secondary, tertiary, quaternary structure?

Large biological molecules like DNA, polysaccharides, or proteins are

composed of chains of smaller subunits (nucleotides, sugars, and amino acids, respectively). The sequence of the subunits is their primary structure. The three-dimensional arrangement of the whole molecule is its tertiary structure. Recognisable bits of that three-dimensional conformation – loops, helices, twists, turns – are the secondary structure. Quaternary structure is the spatial arrangement caused by the interaction between two or more large molecules in a complex.

Ribosome and ribozyme?

A ribosome is the piece of molecular machinery composed of RNA and protein that translates the genetic coding on mRNA into proteins – and there are thousands of ribosomes in each cell. A ribozyme is a piece of RNA which, like an enzyme, catalyses a chemical reaction.

What's the answer to ...?

Are all clones artificial?

No. Clones are identical offspring, and cloning is the process of producing them. Identical twins are clones, as are plants grown from cuttings. Cloning a gene is part of genetic engineering, the use of microorganisms (usually) to make identical copies of a gene for research or practical purposes.

How many genes are there in a genome?

The genome is the total genetic content of an organism and the number of genes varies between organisms. Bacteria have around 5,000, the bakers' yeast *Saccharomyces cerevisiae*, has 7,573 (European researchers have counted them), while humans have around 80,000. In humans, genes only account for about 4% of the genome; the rest is sequences of DNA which perform functions other than coding for protein, although in most cases, researchers do not yet understand what.

Is biotechnology 100% safe?

No. Nothing is 100% safe and biotechnology is no exception. But biotechnology's track record is good. Government rules controlling genetic engineering research and its products have been in place since 1975 in the USA, and in most of the European countries soon afterwards. Regulations have been relaxed considerably in recent years when none of the anticipated potential risks materialised.

Who formulates the rules that govern biotechnology research and biotechnology products?

In Europe, national governments have established regulations covering safety, novel foods, environmental products, and patenting in biotechnology. Generally, these have to operate within parameters set by the European Union.

Why do biotechnology companies make the news so often?

They have to. Start up biotechnology companies may not sell products for between five and ten years. Instead, they sell bits of the company itself. Generating news about financial and business issues, and about research results is, therefore – like advertising any product – a vital part of getting attention and the right price.

Why was herbicide resistance one of the first traits that plant genetic engineers conferred upon crop plants?

When plant genetic engineering began in 1983, genes for herbicide resistance were available (they came from bacteria) whereas genes for disease resistance or drought-resistance were not. Furthermore, plants that acquired such genes could be readily identified, since herbicides did not kill them. Finally, there was a market for herbicide-tolerant seed, especially for plants with tolerance to more environmentally friendly herbicides.

FURTHER SOURCES OF INFORMATION

A Multilingual Glossary of Biotechnological Terms by H.G.W. Leuenberger, B. Nagel and H. Kölbl, VCH Weinheim, Weinheim (D), 1995, ISBN 3-906390-13-6

Biotechnology from A to Z by W. Bains, Oxford University Press, Oxford (GB), 1993, ISBN 0-19-963334-7

Biotechnology Glossary GB, F, D, IT, NL, DK, ES, PO, GR by EC Commission Translation Services, Elsevier Science Publishers Ltd., London (GB), 1990, ISBN 1-85166-569-2

Genetics for Beginners by S. Jones and B. Van Loon, Icon Books, Cambridge (GB), 1993, ISBN 1-874166-12-9

Glossary of Biotechnology Terms by M. Fleschar and K. Nill, Technomic Publishing Corporation Inc., Lancaster Pennsylvania (USA), 1993, ISBN 0-87762-991-9