Bio Factsheet

Number 45

Gene Expression

It is through gene expression that the phenotypes of organisms are assembled. This Factsheet will summarise the nature of gene expression and will explain some of the mechanisms by which gene expression is regulated. Before reading this Factsheet you will need to be familiar with basic genetics such as monohybrid and dihybrid inheritance and have an outline knowledge of epistasis.

A summary of the nature of gene expression

Gene expression is the way in which characters under the control of a specific gene appear in the phenotypes. The simplest situation involves a gene with one pair of alleles which code for contrasting phenotype characteristics. One allele is dominant and one allele is recessive and in a heterozygote, the dominant condition is always expressed and thus appears in the phenotype. The expression of the recessive allele is suppressed in the presence of the dominant allele. The recessive allele can only be expressed when the dominant allele is absent i.e. when the individual is homozygous recessive.

Many genes have a more complicated relationship with the phenotype, for example, where more than one pair of alleles may regulate a character and have to be controlled together, or where the expression of one gene is dependent on the presence or absence of another gene. Although alleles are always present in the genotype, they may or may not be expressed in the phenotype.

Gene expression may also be influenced by mutation. Gene (point) mutation alters the chemical nature of an allele, which may have a direct effect on how it is expressed in the phenotype and so a new characteristic may be shown. Chromosome mutation may alter the position of the gene or its alleles on the available chromosomes. This may alter the pattern of interaction with other genes.

In order for an allele to express itself as a phenotypic character, it must first be activated. Once it is activated, it exerts its effect by influencing protein synthesis (Fig 1). The three-dimensional structure of the protein governs its nature and properties and is dependent on the specific amino acid sequences in the polypeptide units. This in turn was dependent on the codon sequence in the gene that was responsible for the specific protein manufacture. The proteins produced may be structural, influencing phenotypic appearance, or enzymes, influencing biochemical processes, hormone manufacture and behaviour.

> ***Exam Hint:*** *Gene expression is not an easy topic! Make sure you know the basics...*
> 1. *What a gene is*
> 2. *How the information in genes is used to produce an enzyme or hormone*
> 3. *How an enzyme can influence what we look like - i.e. influence our phenotype*

The need for gene expression to be regulated

The zygote receives a full set of chromosomes and genes from each gamete and thus has a full genetic blueprint for the life of the organism. However, during growth and differentiation many different types of cell appear and each obviously uses different parts of the genetic blueprint.

All cells will use the genes or alleles for initiating the synthesis of the enzymes for glycolysis and the Kreb's cycle, since all cells carry out these basic processes. However, an **adipose** cell will use the genes or alleles that confer the ability to store or mobilise fat, whereas a **beta cell in the islets of Langerhans** will use the gene or allele for manufacturing insulin. Such a beta cell would not store fat and the genes that confer the ability to store fat must be switched off or suppressed. In the same way, recessive alleles are switched off in the presence of their dominant alleles. Some genes may operate only at certain periods during life. For instance, during foetal development, certain sequences of events occur related to sequences of gene 'switch on' and 'switch off'. Even the process of death may be switched on or genetically controlled, by the presence of oncogenes, which cause cancer. These may be activated when a certain age is reached, or may be prematurely activated by carcinogenic chemicals or by radiation in the environment.

A mechanism must exist, therefore, that keeps most genes switched off but allows some genes to function, either continuously or periodically, according to the requirements of the cell or organism.

An insight into a mechanism for controlling gene expression was shown by the work of the French scientists, François Jacob and Jacques Monod, in 1965, when they were awarded a Nobel prize for their discoveries. Their research investigated enzyme synthesis in the bacterium Escherichia coli, but the model they proposed is also applicable to higher animals and plants.

The Jacob-Monod model of gene control

Much of what is know about gene control comes from studies of prokaryotic organisms. This is because, compared to eukaryotes, they have simpler structures and they are also quicker and easier to culture.

One of the best-understood examples of gene regulation is that concerning the use of lactose by the bacterium Escherichia coli. E. coli uses three enzymes during its metabolism of lactose (see overleaf).

Fig 1. How DNA controls phenotype

Codon on gene → Matches anticodons on tRNA → tRNA carries a specific amino acid → Specific order of amino acids determines protein → Protein may have carbohydrate or lipid added by golgi body → Protein with complex tertiary or quarterary shape e.g. enzyme → Structural protein affects phenotype

These are:

1. **Beta-galactosidase permease**
   This is involved with the transport of lactose into the bacterial cell. It is coded for by a gene designated **y**.

2. **Beta-galactosidase**
   This hydrolyses lactose into its component monosaccharides, glucose and galactose. It is coded for by a gene designated **z**.

3. **Acetylase enzyme**
   This catalyses an intermediate stage of lactose metabolism. It is coded for by a gene designated **a**.

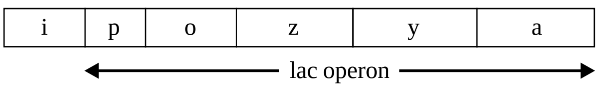
Jacob and Monod found that these enzymes were **inducible**, meaning that they are only synthesised in the cell when their substrate, lactose, is present in the growth medium. If the cells were transferred to a medium lacking lactose, then the enzyme synthesis by the genes ceased within three minutes and only traces of the enzymes could then be found. The three genes (called **structural genes**) which code for the enzymes must thus be regulated in some way so that they respond to the presence or absence of lactose and only make the enzymes when they are needed.

By using mutations which affected the activity of the three enzymes, Jacob and Monod found that the genes z, y and a were in sequence, side by side on the bacterial chromosome (see Fig 2).

In addition to the z, y and a genes there are two other genetic components involved in lactose use, but they do not code for enzymes. There is a **regulatory gene**, designated **i**, and an **operator site**, designated **o**. These control the action of the three structural genes. The arrangement of these components is shown in Fig 2. The operator site is located next to the z gene in the chromosome. The regulator gene i is separated from o by a **promotor region**, designated **p**, which is the site where the enzyme **RNA polymerase** attaches during transcription of the DNA to mRNA.

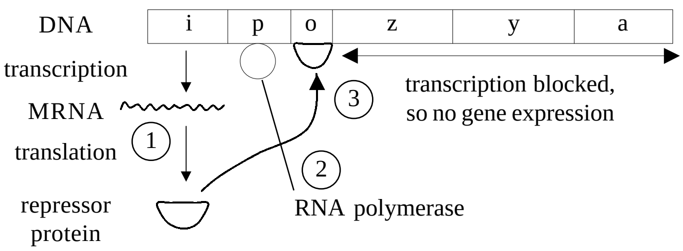
The DNA section containing p, o, z, y and a is termed the **lac operon** (Fig 2).

Fig 2. The structure of the lac operon



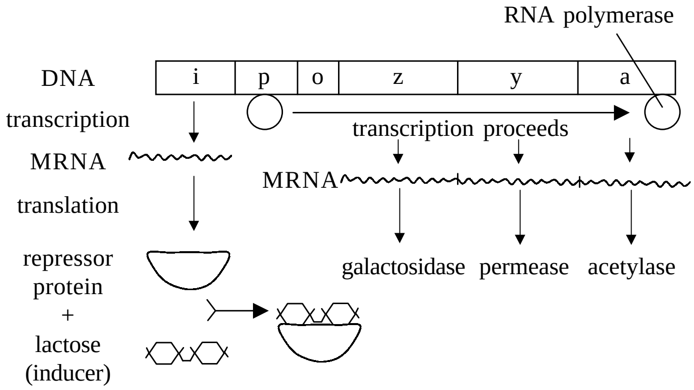
1. When lactose is absent, a **repressor protein** is made by gene i.
2. This repressor protein binds to the operator site.
3. This blocks the process of transcription. Since mRNA cannot then be made, the genes z, y and a are effectively 'switched off' or repressed. This can be seen in Fig 3.

Fig 3. The lac operon in the repressed state



When lactose (the inducer) is present, it binds to the repressor protein and alters its shape or chemical nature (Fig 4). This prevents the repressor from blocking the operator site and so transcription can proceed. The genes are thus 'switched on' and copied onto mRNA and can then be translated into enzymes at the ribosomes. The lactose can then be metabolised.

Fig 4. The lac operon in the induced state



Gene regulation in eukaryotic cells

Although mechanisms of gene regulation in eukaryotes probably incorporate the features of the prokaryotic operon control, they are far more complicated and are not well understood. Genes with related functions are known to be generally grouped into **gene clusters**, but the regulatory control may include several such clusters together, some of which are on different chromosomes. The genome of eukaryotes is far larger than that of prokaryotes and is also more complex. Thus within a eukaryotic gene there is the **exon DNA** which is actually the coding part and also the **intron DNA**, which is non-coding, and splits the gene into two or more sections. The intron functions are unknown but may be involved in gene control. During transcription to mRNA, the intron sections of DNA, or transcribed RNA, are cut out using enzymes and the coding sections then spliced together before translation can occur. The eukaryotic DNA is also bound up with **histone** proteins to form **chromatin**. It is thought that the histones may also influence gene expression.

It has been discovered by experiments in the fruit fly, Drosophila, that all the genes within a gene cluster contain a length of DNA with the same base sequence in each gene, although the remaining bases in the gene differ widely from gene to gene. This length of DNA is known as the **homeobox** and may be involved in the control of gene expression. In Drosophila it is known that gene mutations involving the homeobox sequence influence all the characters regulated by that gene cluster, but that a mutation in the non-homeobox section of a gene only influences the character controlled by that gene.

Some examples of gene inducers are known in eukaryotic cells and probably act by inactivating the relevant repressor substance. They may operate on the DNA or on the mRNA, influencing either transcription or translation respectively. Examples are:

1. **Light**, which regulates the operation of genes concerned with pigmentation development and photosynthetic enzyme synthesis in green plants. The nature of the bonding in the repressor molecules may be altered by light so that the repressors are inactivated.

2. Most of **foetal development** is regulated by inducers. For instance, the primitive streak produces a chemical that causes the development of the notochord. This in turn produces another chemical which causes the development of the brain and spinal cord. This also explains why these structures are formed alongside each other.

3. Carcinogenic chemicals (and radiation) may prematurely induce **oncogenes** (cancer-forming genes) into operation. Examples of such carcinogens are mustard gas, benzidine and ortho-tolidine. There is a school of thought that oncogenes are present in an organism to switch on the death process at a certain time in life, when the biological usefulness of an individual to the species is finished.

> ***Exam Hint:*** *Examination questions on this topic are almost invariably in the form of an essay, since the subject matter does not lend itself easily to structured questions. An essay on gene expression should contain an introduction about the nature of gene expression and the need for its control. There should then be a section dealing with the lac operon in detail. This should then be followed by a section on eukaryotic gene control, summarising the present state of knowledge. The essay could conclude with a short section about oncogenes.*

Practice Question

(a) Describe, referring to an appropriate example in each case, the following methods of gene expression.

(i) Codominance (3 marks)

(ii) Multiple alleles (3 marks)

(iii) Epistasis (3 marks)

(b) With reference to the lac operon, explain the nature of gene repression and gene induction. (10 marks)

Answers

(a) (i) When both alleles are present in the genotype/heterozygous;
they are both expressed/both contribute to the phenotype/cause an intermediate phenotype;
e.g. no white patches, small white patches, large white patches in coats of cats/red, white and pink snapdragon or carnation flowers;

(ii) When the gene controlling a character has more than two alleles;
may be a polygene with hundreds of alleles;
e.g. ABO blood group system with three alleles/height in humans with hundreds of alleles;

(iii) When the expression of one gene in either dominant or recessive state;
is allowed or inhibited by the expression of another gene called the epistatic gene;
e.g. coat colour in rabbits/rats/mice/flower colour in sweet peas;

(b) Three structural genes lie adjacent on the bacterial chromosome;
code for the synthesis of three enzymes involved in lactose metabolism;
the genes only produce these enzymes when lactose is present in the bacterial growth medium;
in the absence of lactose, the repressor protein blocks the operator site on the DNA;
thus RNA polymerase cannot operate to enable transcription;
the repressor protein was produced by a repressor gene;
if lactose is present it acts as the inducer;
binds to the repressor protein, so that this does not block the operator site;
thus the RNA polymerase can now catalyse transcription of the three structural genes into mRNA;
suitable diagram to show this;

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