Glossary

Common terms in molecular biology – part 2 (g–p)

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G protein – A GTP-binding protein involved in transmitting a signal from a cell surface receptor to an intracellular effector.

Gel electrophoresis – A technique for separating molecules of DNA, RNA or protein according to their relative size and charge by passing them through a porous gel matrix under the influence of an electrical field.

Gel shift or 'retardation' analysis – Technique used to detect the specific binding of a protein to a particular sequence of DNA. The DNA/protein complex migrates more slowly in gel electrophoresis than 'unbound' DNA, ie, it is retarded.

Gene – A region of genomic DNA specifying the coding and controlling sequences for the expression of a protein.

Genetic engineering – The processes by which genes can be isolated from cells and manipulated (eg, mutated) *in vitro* before re-introduction into the same or a different species.

Genome – The genetic complement of a cell organelle, species, etc (eg, nuclear genome, mitochondrial genome, *Drosophila* genome).

Genotype – The hereditary information encoded in nucleic acid.

Germline mutation – Mutation inherited from one or other parent and present in every cell of the body.

Growth factor – Protein (first messenger) that binds to specific cell surface receptors and modifies cell growth.

Growth factor receptor – Protein that spans the plasma membrane with an extracellular growth factor binding domain and an intracellular signalling domain which is activated by growth factor binding.

Hairpin – Double helical region formed by base pairing between adjacent (inverted) complementary sequences in a single strand of RNA or DNA.

Haploid – Chromosomes containing one copy of each autosome and one sex chromosome. This is characteristic of gametes of diploid organisms.

Heterochromatin – Regions of highly condensed chromatin in the interphase nucleus visible with a light microscope.

Histones – A class of nuclear proteins involved in maintaining the higher order structure (folding) and function of genomic DNA.

hnRNA – Heterogeneous nuclear RNA, the immediate product of transcription, ie, before the splicing out of introns to produce mRNA.

Homeobox genes – A highly conserved 180 bp sequence coding for the 'homeobox' DNA binding domain.

Homeodomains or Homeobox domain – A highly conserved domain of 60 amino acids preserved from yeast to man and playing a role in development.

Homozygous genes – Both copies of a given gene are identical in a diploid organism.

Homozygous deletion – Deletion of both alleles at a locus.

Hotspot – Site at which frequency of mutation or recombination is very much increased.

Housekeeping (constitutive) genes – Genes that are expressed in most cell types.

Hybridisation (also known as annealing) – Two single-stranded DNA or RNA molecules that are homologous or complementary to each other and form DNA–DNA, RNA–RNA, and DNA–RNA hybrids.

Initiation codon – The ribonucleotides 'AUG' that translate into the amino acid methionine is usually the first amino acid codon of every mRNA.

In-situ hybridization – The use of labelled single-strand RNA or DNA probes to detect the presence of complementary denatured DNA sequences in tissue sections or chromosome spreads.

Integration – Incorporation of foreign DNA (eg, viral) into host cell DNA.

Introns – Transcribed sequences spliced out of mature mRNAs. They may have a regulatory or structural function.

Karyotype – A complete set of metaphase chromosomes from individual cells.

Kb – kilobases, 1000 bp for DNA and RNA.

Kinase – An enzyme which catalyses the addition of a phosphate group into a specific residue of a protein or nucleic acid. The protein kinases most commonly studied phosphorylate the hydroxylamino acids, tyrosine, serine and threonine.

Leader – Non-translated sequence at the 5' end of mRNA that precedes initiation codon.

Ligand – A molecule (eg, growth factor) which specifically binds to a receptor or other protein.

Lineage – The developmental ancestry of a particular cell type.

Linkage – Co-segregation of two genetic loci on the same chromosome, at frequencies greater than would be expected at random.

Locus – Position on a chromosome at which a particular gene resides.

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Long terminal repeat—A repetitive element of the integrated provirus that is generated during viral DNA synthesis and contains a transcription control element that regulates virus expression.

Loss of heterozygosity—Loss of one allele at a locus followed by duplication of information from the remaining locus leading to homozygosity. Suppressor genes were discovered through this observation.

mtDNA—Mitochondrial DNA.

Methylation—Modification of a base by addition of a methyl group. Conversion of cytosine to 5-methylcytosine is thought to be associated with reduced transcriptional activity of a gene.

Microsatellites—(see also Repeated sequences) - Single tandemly repeated sequences form microsatellite sequences consisting of dinucleotides or trinucleotide repeats. Insertions or deletions of sequences leads to genetic instability and tumours.

Molecular cloning—The insertion of a foreign DNA segment of a finite length into a vector that replicates in a specific 'host'.

mRNA—Messenger RNA, the product of DNA transcription and hnRNA splicing which serves as a template for protein translation.

Mutations—A stable heritable alteration in the DNA, which can be passed from cell to progeny. Some mutations are deleterious and lethal while others can be passed on. Gene mutations may involve:

- *gross alterations*, ie, millions of base pairs, which result in chromosomal changes, such as duplication, deletions and translocations.
- *mutations involving entire genomes*, such as triploidy.
- *point mutations*.
 - (a) Synonymous mutations (about one quarter of the random-based mutations): base replacement does not lead to a change in amino acid, but the codon is different. For example, a change in the codon from UUU to UUC, both of which code for phenylalanine, will not alter the structure of the protein.
 - (b) Missense mutations (about 70%): base replacement changes the codon and the amino acid, eg, phenylalanine to leucine by changing from UUU to UUA.
 - (c) Nonsense mutations (about 5%): in which base replacement changes the codon to one of the three termination codons, ie, protein synthesis is stopped. For example, UUU to UAA.
 - (d) Frame shift mutation: deletions or insertions that are not multiples of three bp; mutation leads to change in frame of triplets as they are translated into proteins.

Nested primer—A primer used to increase specificity of sequencing or re-amplification of a polymerase chain reaction product.

Noncoding DNA—The 99%+ of the cell's DNA which does not code for amino acid sequences, or structural RNAs.

Northern blot—Standard technique for identifying specific RNA molecules. Transfer of RNA from an agarose gel to nitrocellulose filter on which it can be hybridised to a complementary DNA.

Nuclear matrix—Scaffold postulated as structural support for chromatin loops and many nuclear enzymes, eg, topoisomerases.

Nucleoid—Histone-free DNA prepared from a cell lysed in nonionic detergent and high salt (2M NaCl). Nuclear matrix attachments are preserved.

Nucleosomes—Histone complexes (octamers) around which the DNA helix is wound as the first level of DNA packing.

Oligonucleotide—A short sequence of several nucleotides.

Oncogenes—Genes whose product can transform eukaryotic cells to become malignant. Over 70 oncogenes are now known. These oncogenes have been grouped into several families:

- integral membrane tyrosine kinase, eg, V-erb in breast cancer.
- membrane-associated tyrosine kinase, eg, V-Abelson in chronic myeloid leukaemia.
- serine tyrosine kinase, eg, V-MOS in sarcoma.
- growth factor families, eg, V-SIS in glioma.
- Ras family.
- nuclear protein family, eg, myc in small cell lung cancer.
- miscellaneous - Rel in leukaemia.

Open reading frame—A sequence of translatable codons not interrupted by stop codons.

p,q—The short arm (p) and the long arm (q) of a chromosome.

Packing—The process by which 50 cm of chromosomal DNA is folded and compressed into a specific higher order structure in order to fit into the volume of a cell nucleus.

Paracrine—A mechanism of growth stimulation involving the secretion of a growth factor which interacts with a specific plasma membrane receptor on a neighbouring cell.

Phage—Bacteriophage, a bacterial virus.

Phenotype—The biological expression of a cell's or organism's genotype.

Physical map (of genome)—A map based on actual distances in base pairs between loci, as opposed to a genetic map which allocates distances between loci on the basis of recombination frequency, or genetic linkage data.

Plasmid—Extrachromosomal circular DNA in bacteria; useful for DNA cloning.

Ploidy—Number of copies of chromosome set present in a cell.

Polymerase chain reaction—An *in vitro* method which exponentially amplifies specific DNA sequences. Primers, enzymes (Taq) and bases are added to the reaction.

Polymerase—Enzyme which catalyzes the addition of deoxyribonucleotides (G, C, A or T in DNA) or ribonucleotides (G, C, A or U in RNA) to the 3' end of a nucleotide chain as part of DNA replication or RNA transcription.

Polymorphism – Multiple alternative forms of a gene or protein. Occurs naturally in population.

Polysome – An mRNA associated with a series of ribosomes involved in translation.

Primer – Short oligonucleotide which binds to specific single-stranded target nucleic acid sequence enabling polymerase to initiate strand synthesis.

Probe – A short, specific DNA sequence labelled with ³²P or biotin which can be used to detect complementary sequences on blots, etc.

Promoter – A DNA sequence that binds with RNA polymerase to initiate transcription.

Promoter/enhancer sequence – DNA sequence that is a control point for gene transcription. Promoter sequences are usually

in the vicinity of the 1st exon; enhancer sequences may be many Kb upstream or downstream of the gene.

Proofreading ability – The ability of a polymerase enzyme to detect and correct mistakes that have been made in DNA synthesis.

Protein kinase – Family of enzymes catalyzing the transfer of a high energy phosphate from ATP to specific residues on proteins (often tyrosine, but also serine/threonine); one of the major mechanisms for regulation of protein function.

Proto-oncogene – A cellular gene whose alteration has been shown to be involved in malignant transformation.

Pro-virus – A viral genome integrated into a host cell genome.

Adverse drug reaction of the month

Hepatitis B vaccine and neurotoxicity

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The availability of an effective vaccine against hepatitis B in recent years represents a major breakthrough in the prevention of a serious and occasionally fatal infection. In the UK, immunisation against hepatitis B is recommended for high-risk groups including healthcare workers. However, in certain cases, vaccination can lead to serious and unexpected adverse reactions. We describe the case of a male patient who developed cranial nerve palsies following hepatitis B vaccination.

Within 24 h of admission, the patient’s vestibular symptoms began improving, and had completely resolved by five days. The facial nerve palsy took two months to resolve completely. A repeat MRI scan performed three months after the initial presentation failed to show any evidence of a structural abnormality within the brain.

Discussion

The two main diagnoses considered in the patient were a first episode of multiple sclerosis

Adverse drug reaction report

A 35-year-old previously fit and healthy male healthcare worker was admitted with a two-day history of progressively worsening vertigo, and a one-day history of nausea and inability to close his left eye. He also complained of tinnitus but not of deafness. All these symptoms had been preceded by an upper respiratory tract viral infection for five days. The patient was not on medication; however, four days before admission, he had received a booster dose of recombinant hepatitis B vaccine (Engerix B[®]). On examination, the patient had a left lower motor neuron facial nerve palsy and second degree nystagmus with the fast phase towards the right side, both of which suggested a left pontine lesion. There were no cerebellar signs or any other abnormal neurological signs. The erythrocyte sedimentation rate was normal. Magnetic resonance imaging (MRI) of the brain on admission did not show evidence of demyelination. The lumbar puncture was normal, and in particular, there was no oligoclonal IgG. Visual evoked responses were also normal. All viral titres were non-significant.

Suspected adverse drug reactions reported with hepatitis B vaccination
Neurological <ul style="list-style-type: none">● relapse of multiple sclerosis● Guillain-Barre syndrome● polyneuropathy● transverse myelitis● facial nerve palsy● cerebellar ataxia● visual loss● uveitis
Cutaneous <ul style="list-style-type: none">● angioedema● erythema nodosum● erythema multiforme● urticaria● lichen planus● systemic lupus erythematosus
Miscellaneous <ul style="list-style-type: none">● acute glomerulonephritis● polyarthrititis

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