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Glossary

An asterisk indicates a related entry.

Active genes. Genes transcribed in the cell type in question. Some genes are active in all cells (housekeeping genes) whilst others are specific to one cell type (e.g. haemoglobin gene in erythrocytes). Associated conformational features include looser duplex winding around nucleosomes*, less histone* H1 binding and situation in euchromatin.

Adduct. (see drug adduct).

Alkylation. Process of covalent binding of reactive alkyl group of drug (e.g. CH_2Cl) to biological molecules (DNA bases or proteins) which have an excess of electrons.

Alleles. Alternative DNA sequences at a locus, can be coding or non-coding.

Amplification. Increase in copy number of a chromosomal region, typically by tandem* duplication.

Anchorage dependence. The dependence of normal cells on an appropriate surface/substrate on which to grow in culture.

Annealing. Complementary base pairing of homologous single strands of nucleic acids, e.g. attachment of primers* to denatured target DNA in PCR.

Antisense. A nucleotide sequence (RNA or DNA) complementary* to the coding (sense*) sequence.

Apoptosis. An active mechanism of cell death in which DNA degradation and nuclear destruction precede loss of plasma membrane integrity and cell necrosis.

Autocrine. A mechanism of growth stimulation involving the binding of a growth factor* secreted by a cell to its own plasma membrane receptors, cf. paracrine*.

Bacterial transformation. The uptake of foreign DNA by a bacterium which may result in, e.g. antibiotic resistance or some other phenotype.

BSO. Buthionine sulphoximine, an inhibitor of γ-glutamyl cysteine synthetase, leads to depletion of GSH*.

Carcinogen. A physical or chemical agent which has a causal role in the development of cancer (these are often, but not always mutagens*).

CDC. Cell division cycle proteins involved directly in the control of the cell cycle, e.g. CDC 2 (p34) is a kinase* enzyme.

cDNA library. A collection of DNAs produced by reverse transcription* from the mRNA* of a cell population of interest and inserted into a suitable vector*.

cDNA. DNA complementary* to RNA and synthesised from it by reverse transcription*.

Cell line. A cell culture composed of a single immortalised* stem cell population.

Cell strain. A cell culture composed of a mixture of clonal populations.

Cellular oncogene. proto-oncogene* altered, e.g. by mutation* which leads it to acquire an altered cellular function that contributes to carcinogenesis.

Centimorgan. Unit representing a recombination* frequency of 1% or approx. 1 million base pairs (Morgan 'coined' the term).

Centromere. Specific DNA sequences that attach the chromosome to the mitotic spindle during M phase.

Chromatin. Chromosomal DNA together with a variety of associated proteins, the most abundant of which are histones*.

Cleavable complex. DNA-drug adduct* or intercalation which stabilises topoisomerase II* binding to DNA and which, on deproteination, reveals strand-breakage.

Cloning. the generation of multiple identical copies of a DNA sequence by replication* in a suitable vector*, e.g. phage* or plasmid*.

Codon. A triplet of nucleotides coding for one amino acid.

Commitment. (see Determination).

Complementary bases. Bases which are hydrogen bonded specifically in DNA duplex or in DNA/RNA heteroduplex.

Complementation. Is said to occur when a cell deficient in a particular function, e.g. repair of ultraviolet DNA damage, is restored to normal function by addition of foreign DNA, by a technique such as cell fusion. This process has been used to show that a number of different gene defects can be involved in single human DNA repair disorders, e.g. xeroderma pigmentosum.

Constitutional deletion. Deletion inherited in the germline* from one or other parent and present in every cell of the body (usually examined in lymphocytes), cf. somatic*.

Contact inhibition. Inhibition of cell division in cell culture by cell–cell contact.

Copy number. The number of copies of a gene present in genomic* DNA.

CpG islands. Sequences relatively rich in the dinucleotide CpG; often associated with genes and possibly involved in transcriptional regulation.

Cyclic AMP. A ubiquitous intracellular messenger* synthesised from ATP by plasma membrane bound adenylate cyclase* (activated by a G protein*).

Cytokines. Proteins which act as intercellular signals to coordinate the immune response.

Deletion. Loss of a segment of a chromosome (see constitutional deletion and somatic deletion).

Denaturation. (a) Of DNA; melting (separation) of the complementary* strands caused by high temperature or chemical conditions, usually reversible. (b) Of protein; loss of higher order structures caused by high temperature or chemical conditions, usually irreversible.

Determination. A commitment* to follow a given developmental lineage (pathway).

Differentiation. An increase in specialisation towards a specific function.

DNA chromatin. Structural packing of DNA double helix into nucleus. Hierarchy of helix coiled around histones (to form a nucleosome*); twisting of these into a 30 nm wide fibre; coiling of this fibre into loops attached to the nuclear matrix and coiling of loops/matrix into chromosome bands.

DNA cloning. A technique involving the integration* of a specific DNA sequence into a self-replicating element (plasmid* or virus) that reproduces itself in bacteria to generate huge numbers of identical copies.

DNA library. Collection of different cDNAs* or fragments of genomic* DNA propagated in a cloning vector* (phage* or plasmid*) from which specific sequences can be isolated (cloned*).

Dosage effect. The effect on a cell's morphology/behaviour from having more or less than the usual diploid number of normal genes.

Double minutes. Extra pairs of chromosomal fragments visualised on metaphase spreads, associated with amplification*, e.g. multidrug resistance (MDR), *myc* oncogene.

Down-regulation. Process by which a cell loses its sensitivity to growth factor* stimulation (often by endocytosis of growth factor receptors*).

Downstream. Beyond the 3′ end of a gene sequence, cf. upstream*.

Drug adducts. DNA modified by covalently bound drug or reactive sidegroup of drug.

Eco*RI*. A restriction endonuclease originally isolated from a strain of *E. coli*.

Endocrine. A mechanism of growth stimulation involving the secretion of a growth factor* which binds to a specific cell receptor* after diffusing through the circulation.

Epitope. Antigenic determinant (there may be several per molecule).

Eucaryotic cell. Cells which have a nucleus (yeast, mammalian cells), cf. procaryotic* cells (bacteria).

Euchromatin. The decondensed form of chromatin* typical of the interphase nucleus.

Exons. Transcribed sequence not spliced out of mature RNAs (cf. introns).

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 relative size and charge by passing them through a porous gel matrix under the influence of an electric field.

Gel shift or "retardation" analysis. Technique used to detect specific binding of a protein to a particular sequence of DNA. The resulting DNA protein complex migrates more slowly in gel electrophoresis than "unbound" DNA, i.e. it is retarded.

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

Genetic engineering. The processes by which genes can be isolated from cells and manipulated (e.g., mutated*) *in vitro* before reintroduction into the same or a different species.

Genome. The genetic complement of a cell organelle, species etc, e.g., nuclear genome, mitochondrial genome, *Drosophila* genome.

Genotype. The hereditary information encoded in nucleic acid cf. phenotype*.

Germline deletion. (see constitutonal deletion).

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

Glutathione S-transferases. Family of enzymes which are responsible for conjugation reactions involving GSH*.

Growth factor receptor. Proteins that span the plasma membrane with an extra-cellular growth factor* binding domain* and an intracellular signalling domain which is activated by growth factor binding.

Growth factor. Proteins (first messengers*) that bind to specific cell surface growth factor receptors* and modify cell growth, e.g. EGF, PDGF.

GSH. Reduced glutathione; conjugation to GSH* may be an important step in detoxification for a number of drugs.

Heterochromatin. Regions of highly condensed chromatin* in the interphase nucleus visible with a light microscope, cf. euchromatin*.

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*, i.e. before the splicing* out of introns* to produce messenger RNA* (mRNA).

Homeobox genes. A family of transcription factors which all possess a highly conserved 180bp sequence coding for the "homeobox" DNA binding domain.

Homogenously staining regions. Regions of chromosome visualised on metaphase spreads corresponding to hugely amplified* gene sequences (see also double minutes).

Homozygous deletion. Deletion of both alleles at a locus.

Housekeeping genes. Genes that are expressed in most cell types, cf. tissue-specific genes which are expressed only in selected cell types.

Hybridisation. The base-pairing of complementary* single strands of nucleic acid that leads to the double-stranded molecule.

Hydrogen bonding. (see weak forces).

Immortalised cells. Cells not restricted by a specific number of cell divisions.

Immunotherapy. Therapies designed to enhance the immune response to infective disease or tumours by vaccination, cytokine administration, adoptive transfer of immune cells or antibody administration.

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

Initial induced damage. Ionising radiation-induced damage after chemical modification (indirect ionisation and radical scavenging by thiols or DNA proteins) but before enyzmatic repair (i.e. within microseconds of a photon/nucleus interaction).

Integration. Incorporation of foreign DNA (e.g. viral) into host cell DNA.

Interleukin 2. A protein secreted by activated T lymphocytes which stimulates proliferation of lymphocytes, and activates cytotoxic functions of macrophages and lymphocytes.

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

Jumping. A modification of the walking* technique. Clones* with large interstitial deletions* are used so that areas of the genome some distance apart can be covered.

Karyotype. The chromosomal composition of a cell.

Kb. Kilobases.

Kinase. An enzyme which catalyses the addition of a phosphate group onto a specific residue of a protein or nucleic acid.

Ligand. A molecule (e.g. growth factor*) which specifically binds to a receptor.

Lineage. The developmental ancestry of a particular cell type.

Linkage. (Genetic or locus linkage), co-segregation of two genetic loci*, e.g. coding or non-coding* on the same chromosome, at frequencies greater than would be expected at random.

Locus. Position on a chromosome.

Loss of heterozygosity. Loss of one allele* at a locus followed by duplication of information from the remaining locus leading to homozygosity.

Matrix. (see nuclear matrix).

Messengers. The term applied to molecules (generally small) that can transmit signals between and within cells.

Methylation. Modification of a base by addition of a methyl group. Conversion of cytosine to 5-methylcytosine is thought to be associated with transcriptional inactivity of a gene in or near which it occurs.

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

Multipotent. A cell with the capacity to differentiate along one of several cell lineage pathways (cf. *unipotent*—a cell with the capacity to differentiate along only one pathway).

Mutagen. A physical or chemical agent which introduces a nonlethal change in the cell's DNA sequence.

Mutation. Any alteration in DNA sequence, as a result of point mutation*, deletion*, translocation*, etc.

N-CAM. Neural cell adhesion molecule, a plasma membrane glycoprotein expressed on the surface of nerve and glial cells involved in cell-cell adhesion (a member of the immunoglobulin family).

Nested primer. A primer used to increase specificity of sequencing or reamplification of a PCR product, located between the two original primers.

Non-coding 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 (see Southern blot, named after the man who first invented this method for DNA analysis).

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

Nucleoid. Histone*-free DNA prepared from a cell lysed in non-ionic 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*.

O^6-alkyguanine-DNA alkyltranferase. An enzyme which removes alkyl groups from the O^6 position on guanine following alkylation. It is inactivated by this transfer, i.e. acts as a suicide inhibitor.

Oligonucleotide. A sequence of several nucleotides.

Open Reading Frame (ORF). A sequence of translatable codons* not interrupted by stop* codons, which could therefore code for a polypeptide.

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

P-glycoprotein. Membrane glycoprotein coded by mdr which functions as an active drug efflux pump.

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, cf. endocrine*.

Phage. Bacteriophage, a bacterial virus.

Phenotype. The biological expression of a cell or organism's genotype*, e.g. cell morphology, surface receptors expressed.

Phosphorylation/dephosphorylation. The addition/removal of a high energy phosphate group to/from a specific residue in a protein, resulting in the modulation of some specialised function, e.g. signal pathways*.

Physical map. 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 equivalently, genetic linkage* data.

Plasmid. A double-stranded circle of DNA capable of being automonously replicated in bacteria; useful for DNA cloning*.

Point mutation. Substitution of one base by another.

Polyglutamation. Metabolism of folates or antifolates involving the addition of glutamic acid residues. Leads to retention in the cell and may alter enzyme kinetics.

Polymerase chain reaction (PCR). An *in vitro* method which uses enzyme synthesis to exponentially amplify specific DNA sequences.

Polymerases. Enzymes which catalyse the addition of deoxyribonucleotides (G, C, A or T in DNA) or ribonucleotides (G, C, A or U in RNA) the 3′ end of a nucleotide chain as part of DNA replication* or RNA transcription*.

Polymorphism. Multiple alternative forms of a protein e.g. G6PD polymorphism, an RNA or a DNA sequence occurring naturally in a population. Used in linkage analysis*.

Post-mitotic. Describing a mature cell that can no longer undergo cell division, e.g. neuron.

Primers. 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 ^{32}P or biotin which can be used to detect complementary* sequences on blots, etc.

Procaryotic cells. Cells lacking a cell nucleus (e.g. bacteria).

Promoter/enhancer sequences. DNA sequences that are control points for gene transcription*. Promoter sequences are usually in the vicinity of the 1st exon*; enhancer sequences may be many Kbp* upstream or downstream* of the gene.

Proofreading ability. The ability of a polymerase enzyme to detect and correct mistakes that it has made in DNA synthesis.

Protein kinase. Family of enzymes catalysing the transfer of a high energy phosphate from ATP to specific residues on proteins (often tyrosine); 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.

Provirus. A viral genome integrated into a host cell genome.

Ras. A GTP-binding regulatory protein involved in growth factor* stimulation (see G protein). Capable of oncogenic activation.

Receptor. Cell surface protein which binds a specific molecule (ligand) and transmits a signal.

Recombination. "Crossing over", a mechanism of exchange of genetic material between a pair of homologous chromosomes.

Renaturation of DNA. The ability of denatured* DNA to resume its normal double-strand conformation (see denaturation*).

Repetitive sequences. Approximately 30% of genomic* DNA consists of repeated, non-coding* nucleotide sequences such as tandem repeats* or satellite* DNA, with no known functions.

Replication. Duplication of genomic* DNA during S phase.

Restriction endonuclease. A group of endonucleases each of which cleaves double-stranded DNA at a specific 'recognition site' ('restriction site') determined by the exact DNA sequence. Names indicate the bacterium of origin, e.g. the endonuclease *Eco*RI originates from *E. coli.*

Restriction fragment-length polymorphism (RFLP). A polymorphism* in the size of restriction fragments due to a sequence difference between alleles*, usually in noncoding* regions.

Restriction fragments. The products of digesting DNA with restriction endonucleases*.

Restriction map. Schema showing the positions of cutting sites of specific restriction enzymes* in DNA: often used as a way of characterising specific genomic* sequences, many Kb* in length.

Retroviral transduction. Incorporation of part of a host genome*, e.g. a proto-oncogene*, into the genome of a newly formed retroviral particle; the presumed origin of the retroviral oncogenes.

Retroviruses. RNA viruses which reverse transcribe* their RNA into DNA using reverse transcriptase* as part of their intracellular life cycle.

Reverse transcriptase. An important enzyme used by retroviruses*. The purified enzyme is useful in synthesis of cDNA* *in vitro.*

RNA. Ribonucleic acid.

Second messenger. Cytoplasmic molecules that transmit chemical signals within the cell following growth factor* (first messenger) binding/activation to a cell surface receptor*.

Senescence. Programmed cell ageing.

Sense strand. A sequence of nucleotides coding for a sequence of amino acids, cf. antisense*.

Signal pathway. Sequence of chemical interactions that selectively amplify and transmit messages (e.g., growth stimulus) across the cell.

Somatic mutation. Mutation* arising *de novo* in a somatic* cell cf. germ cell* mutation.

Southern blot. Standard technique for identifying specific DNA sequences; typically chromosomal DNA is digested with a restriction enzyme* and the DNA fragments separated by gel electrophoresis*. The separated fragments are denatured (converted to single stranded form) and transferred (blotted) onto special membrane (nitrocellulose filter). A radioactively labelled probe* will hybridise* to a complementary* sequence on the filter which is detected by autoradiography. In northern blotting, RNA molecules are separated by electrophoresis without prior digestion.

Splicing. The process whereby introns* are removed from freshly transcribed RNA (heterogeneous nuclear or hnRNA*) to produce messenger RNA* (mRNA).

Start/stop codons. The AUG sequence in mRNA* coding for the amino acid methionine marks the starting point of translation*. UAA, UAG and UGA are stop* codons in mRNA which signal the end of the protein.

Stem cell. A cell which undergoes unequal division to produce dissimilar daughters—also used to mean any cell capable of indefinite multiplication.

Superfamily. Structurally related genes arising by duplication and divergence of ancestral genes.

Supercoiling. Increase or decrease in the number of turns of one strand of DNA about the other in the double helix due to twisting of the DNA about its own axis. DNA packed on a nucleosome is supercoiled, and the degree of supercoiling is altered *in vivo* by topoisomerases.

Tandem duplication. Process generating tandem repeats.

Tandem repeat. DNA sequences repeated head to tail in genomic DNA. Responsible for homogeneously staining regions (HSR's)

Taq polymerase. The heat stable enzyme used in PCR*, isolated from algae that live in hot springs (see polymerase).

Telomere. Specific DNA sequences located at both ends of a chromosome.

Topoisomerase. Enzymes that relax DNA supercoiling* and open up the helix during replication and transcription*. type 1: DNA enzyme which uses a reversible single strand break to catalyse relaxation of negative supercoiling. type II: this enzyme uses the energy from ATP to produce negative supercoiling via a reversible double stranded break.

Transcription factors: Specific regulatory proteins that control gene expression (transcription*) by recognising and binding to specific DNA promoter/enhancer* sequences nearby.

Transcription. Copying of genomic* DNA sequences into complementary* RNA.

Transduction. The transfer of a chemical signal e.g., conversion of a growth factor* (first messenger) signal outside the cell into a cytoplasmic signal carried by second messenger molecules.

Transfection. Uptake of foreign DNA by a cell (*in vitro*).

Transfer. (see Southern blot).

Translation. Protein synthesis based on an mRNA* template.

Translocation. Exchange of chromatin* between non-homologous chromosomes.

Tumour suppressor gene. A class of genes for which inactivation contributes to oncogenesis.

Tyrosine kinase. (see protein kinase).

Upstream. Beyond the 5′ end of a gene sequence, i.e. preceding the start of coding sequence, cf. downstream*.

Vector. A independently replicated DNA molecule (e.g. a phage or plasmid*) into which a specific DNA sequence can be integrated* and replicated* (e.g. in a bacterial host).

Viral oncogene. Gene in a virus* responsible from its oncogenic effects in an animal host.

Walking. A technique of mapping segments of DNA (up to several hundred kb*) through the identification of overlapping DNA fragments in a genomic DNA library (see DNA library).

Weak bonds. Noncovalent interactions (ionic bonds, hydrogen bonds and van der Waals attractions) which are responsible for the three dimensional shape of protein molecules and for protein–protein interactions, e.g. antigen–antibody binding.

Western blot. A technique for identifying specific protein species, analogous to Southern and northern blotting.

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