A

A (1) Adenine (as a base, or the corresponding nucleoside or nucleotide).
(2) L-Alanine (alternative to Ala).

Å Ångström unit, 10^{-10} m; a unit of length used e.g. to indicate intermolecular distances.

A_{260} See the entry ULTRAVIOLET ABSORBANCE.

A box The adenine riboswitch aptamer (see RIBOSWITCH).

A-DNA One of the conformations adopted by dsDNA: a right-handed helix with ~11 base-pairs per turn.

(Note that aDNA – with lower-case 'A' and no hyphen – is used to refer to ANCIENT DNA.)

(cf. B-DNA and Z-DNA.)

A-EJ Alternative end-joining – a process of DNA repair found in some prokaryotes: see NON-HOMOLOGOUS DNA END-JOINING.

A family (of DNA polymerases) A group of DNA-DEPENDENT DNA POLYMERASES that include prokaryotic, eukaryotic and viral enzymes. Members of the A family include some phage polymerases (although not those from phages φ29 or T4) and the *Escherichia coli* pol I (involved e.g. in the maturation of Okazaki fragments and in BASE EXCISION REPAIR).

Also included in this family is POLQ (= pol θ; pol theta), an enzyme found in human and other eukaryotic cells. POLQ is able to carry out translesion synthesis of DNA, and it may participate in base excision repair, a suggestion supported by the *in vitro* demonstration of 5′-deoxyribose phosphate lyase activity – a role apparently involved in single-nucleotide base excision repair [Nucleic Acids Res (2009) 37(6):1868–1877].

(See also B FAMILY, X FAMILY and Y FAMILY.)

A site (of a ribosome) The aminoacyl ('acceptor') site at which tRNA molecules carrying the second and subsequent amino acids bind during translation. (cf. P SITE.)

A-to-I editing (RNA editing) See RNA EDITING.

A-tract In genomic DNA: a nucleotide motif that is reported to be associated with regions of the most pronounced curvature of the molecule; an A-tract is a poly(A) (i.e. poly-adenosine) sequence. In the genome of *Escherichia coli*, A-tracts were reported to be distributed 'quasi-regularly' in both coding and non-coding sequences; the A-tracts occur in clusters ~100 bp long, with consecutive A-tracts exhibiting a periodicity of 10 to 12 bp. It was suggested that the clusters of A-tracts may constitute a form of 'structural code' for DNA compaction in the NUCLEOID [Nucleic Acids Res (2005) 33:3907–3918].

Studies on the mechanics and dynamics of DNA suggested a rationale – incorporating A-tracts – for the stable bending of DNA [Nucleic Acids Res (2008) 36(7):2268–2283].

Studies on *eukaryotic* genomes have reported that A-tracts are absent specifically in those coding sequences (exons) that correspond to the locations of nucleosomes. It was concluded that the pattern of absence/presence of A-tracts in the genome constitutes a code for the presence/absence – respectively – of nucleosome locations. [The coexistence of the nucleosome positioning code and genetic code on (eukaryotic) genomes: Nucleic Acids Res (2009) doi: 10.1093/nar/gkp689.]

Studies on *ad hoc* synthetic DNA, to investigate the nature of nucleosome-associated sequences, reported that a number of motifs thought to influence nucleosome formation did not show such influence [Nucleic Acids Res (2010) doi: 10.1093/nar.gkq279].

A-tract sequences have been used to study DNA looping in the *lac* operon; it was thought that the lower energy needed to bend these sequences may have contributed to some cases of loop formation [Nucleic Acids Res (2012) doi: 10.1093/nar/gks019].

(See also CLASS A FLEXIBLE PATTERNS.)

***A1AT* gene** See α_1-ANTITRYPSIN (under 'alpha').

AAA ATPases 'ATPases associated with diverse cellular activities': ATPases which are found in various locations, such as proteasomes and peroxisomes. They are categorized as AAA+ PROTEINS.

The AAA ATPases have a role in the loading of the SLIDING CLAMP onto DNA during DNA REPLICATION [BMC Struct Biol (2010) 10:3, doi: 10.1186/1472-6807-10-3].

AAA+ proteins A family of NTPases whose members include proteins with diverse functions; AAA ATPASES are examples of this group.

[AAA+ proteins (review): Genome Biol (2008) 9(4):216.]

AAAVs Avian adeno-associated viruses (see the entry AAVS).

AAS Aminoalkylsilane (3-aminopropyltriethoxysilane; APES): a reagent used e.g. to bind tissue sections to glass (for *in situ* hybridization etc.).

[Uses (e.g.): Am J Pathol (2006) 169(1):258–267; Nucleic Acids Res (2008) 36(16):5335–5349; J Clin Microbiol (2011) 49(3):808–813; Curr Mol Med (2012) 12(2):113–125.]

***aat* gene** In *Escherichia coli*: a gene encoding the enzyme that catalyzes addition of a leucine or phenylalanine residue to the N-terminal of proteins that are synthesized with either an N-terminal arginine residue or an N-terminal lysine residue; the addition of a Leu or Phe residue facilitates degradation of the protein. This activity is predicted by the N-END RULE (q.v.).

AatII A RESTRICTION ENDONUCLEASE from *Acetobacter aceti*; its recognition sequence/cutting site is GACGT↓C.

AAUAAA In a pre-mRNA: a polyadenylation signal upstream of the site at which the molecule is cut and polyadenylated; the polyadenylation sequence is similar in various organisms, although there are variations.

Other *cis*-acting elements may have roles in regulating the

Dictionary of DNA and Genome Technology, Third Edition. Paul Singleton.

polyadenylation of human mRNAs – including upstream U-rich sequences similar to those which have been identified in yeast and plants.

As well as acting as a polyadenylation signal, this sequence was reported to affect the *rate* of transcription [RNA (2006) 12(8):1534–1544].

AAV Adeno-associated virus: see the entry AAVS.

AAV Helper-free system A commercial gene-delivery system (Stratagene, La Jolla CA) in which the genes in two plasmids provide functions necessary for production of infective AAV virions (see AAVS) without the need for a helper virus; these virions are used to deliver genes to target cells within which viral DNA – containing the gene of interest – integrates in the host cell's DNA.

The gene/fragment is cloned in a replication-deficient AAV vector: a plasmid in which the insert is bracketed by a pair of inverted terminal repeats (= ITRs); these ITRs are necessary for subsequent viral packaging. This plasmid is then used to transfect PACKAGING CELLS – which are *co-transfected* with two other plasmids: (i) a plasmid containing the genes that encode viral capsid and replication functions, (ii) a plasmid containing genes that encode the lytic phase of AAV. The resulting infective (*but still replication-deficient*) virions that are produced in the packaging cells can then be used to infect the required target cells (in which the gene of interest can be expressed).

This GENE-DELIVERY SYSTEM has been used e.g. to express siRNAs [Mitochondrion (2007) 7(4):253–259]; to deliver an anti-angiogenic gene (for investigating age-related macular degeneration) [Mol Vision (2008) 14:471–480]; and to study some features of food/energy metabolism [J Neurosci (2009) 29(1):179–190].

The system was used in studies on gene therapy for solid tumors [Genet Vaccines Ther (2010) 8:8], and studies on the inhibition of hepatitis C virus replication [Antimicrob Agents Chemother (2010) 54(12):5048–5056].

(See also the entries VIRAPORT RETROVIRAL GENE EXPRESSION SYSTEM and VIRAPOWER LENTIVIRAL EXPRESSION SYSTEM.)

AAVs Adeno-associated viruses (also known as: adeno-satellite viruses): defective viruses that are able to replicate only when certain functions are provided by a co-infecting *helper virus* (an adenovirus or herpesvirus) or, in certain *in vitro* systems, when the functions are provided by plasmid-borne genes (as e.g. in the AAV HELPER-FREE SYSTEM).

The AAVs are parvoviruses in which the genome is linear ssDNA. Positive and negative strands of the viral DNA are encapsidated in separate virions.

Functions provided by adenovirus type 5 (for AAV type 5) include both positive and negative effects. For example, the E4Orf6 function (involved in replication of AAV5 genomic DNA) – together with E1b – degrades AAV5 capsid proteins and Rep52 [J Virol (2007) 81(5):2205–2212].

The functions provided by herpes simplex virus type 1 (for the early stages of AAV replication) were reported to involve nine proteins from the helper virus [PLoS Pathog (2009) 5 (3):e1000340].

The AAVs infect a wide range of vertebrates. Initial stages of infection, including internalization of DNA, occur without a helper virus. [Cloning an *avian* AAV (an AAAV) and the generation of recombinant AAAVs: J Virol (2003) 77:6799–6810.]

AAVs are used, for example, in GENE THERAPY. Efforts are being made to increase the efficacy of AAV vectors in gene therapy by designing the CAPSID on the basis of e.g. information obtained from studies on the naturally occurring capsid variants of AAVs in mammals [see: Gene Therapy (2009) 16: 311–319]. (See also KU70.)

An inducible and highly efficient system was reported for the production of recombinant AAV vectors in insect (Sf9) cells [Proc Natl Acad Sci USA (2009) 106(13):5059–5064].

AAV vectors, encoding genes of the α and the β subunits of hexosaminidase, were inoculated, *intracranially*, into mice in order to assess the potential of gene therapy for treatment of the human GM2 gangliosidoses such as Tay–Sachs disease and Sandhoff disease [Proc Natl Acad Sci USA (2006) 103 (27):10373–10378]. A simpler method for delivering genes to the brain cells was reported later. Thus, AAV9 was used, in mice, for gene delivery to cells of the central nervous system (the brain and spinal cord) by *intravenous injection*. It was thought that this approach may allow the development of gene therapy for e.g. some human neurodegenerative diseases [Nature Biotechnol (2008) 27:59–65].

AAV vectors were also used for the genetic manipulation of cultured neurons [Brain Res (2008) 1190:15–22].

It was reported earlier that, in human cells, AAV DNA (in the absence of helper virus) integrates in the genome with an apparent preference for CPG ISLANDS. More recently, AAVs have been reported to integrate, site-specifically, into a locus on chromosome 19, and the occurrence of such integration is apparently influenced by the TRP-185 protein [J Virol (2007) 81(4):1990–2001]. Palindromes of length greater than about 40 bp are reported to be significant targets for the integration of recombinant AAV vectors [J Virol (2007) 81(20):11290–11303].

The site of insertion of AAVs within chromosome 19 was reported to contain a (347 bp) sequence capable of enhancing the promoter and transcriptional functions of AAV vectors in liver cells; it was believed that inclusion of this fragment in AAV vectors may thus facilitate their use for the expression of transgenes [Gene Therapy (2009) 16:43–51].

AAVS1 (AAVS1; *p84*, *PPP1R12C*) In the (human) genome: the normal site of insertion of an adeno-associated virus (AAV); *AAVS1* is located in the gene encoding protein phosphatase 1 on chromosome 19.

AAVS1 is used as a 'safe harbor' locus for targeted insertion of transgenes; in this locus, transgenes have been reported to be expressed consistently and to maintain function over many cell generations without apparent disturbance to normal cell function.

[Uses of *AAVS1* as a safe harbor locus: Genome Res (2010)

20(8):1133–1142; Nucleic Acids Res (2010) doi: 10.1093/nar/gkr409; PLoS ONE (2011) 6(5):e20514.]

AB1380 A strain of the yeast *Saccharomyces cerevisiae* – see the entry SACCHAROMYCES for some details.

(See also YEAST ARTIFICIAL CHROMOSOME.)

abacavir A NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITOR used e.g in antiretroviral therapy; CSF–plasma ratios indicate that it may reach therapeutic levels in cerebrospinal fluid (CSF).

A trial that compared abacavir with nevirapine (as part of a combined therapy) reported that abacavir tended to produce a lower rate of serious adverse effects, suggesting a wider use of this drug in resource-limited settings [Trop Med Int Health (2008) 13(1):6–16].

Abacavir sometimes causes a (potentially life-threatening) hypersensitivity reaction which has been associated with the allele HLA-B*5701; screening for HLA-B*5701 can help to identify patients at risk of the reaction [PLoS Currents (2010) doi: 10.1371/currents.RRN1203].

AbaSDFI A restriction enzyme which is a homolog of PVURTS11 (q.v.).

abasic site *Syn.* AP SITE.

abasic-site mimic See the entry RPA.

ABC excinuclease See the entry UVRABC-MEDIATED REPAIR.

Abelson murine leukemia virus See the entry ABL.

aberrant RNA (aRNA) See the entry ARNA (sense 2).

abl (*ABL*) An ONCOGENE first identified in the *Abelson murine leukemia virus*.

The v-*abl* product has TYROSINE KINASE activity.

The human homolog of v-*abl* (c-*abl*) is usually present on chromosome 9; in most patients with CHRONIC MYELOGENOUS LEUKEMIA it has been translocated to chromosome 22, forming a chimeric gene, *bcr-abl*, that encodes a (tumor-specific) tyrosine kinase (P210). (See also IMATINIB.) Chromosome 22 containing *bcr-abl* is referred to as the Philadelphia chromosome (also called Ph^1).

Subcellular localization of c-Abl protein at an early stage in myogenic differentiation was reported to be influenced by its acetylation [EMBO Rep (2006) 7(7):727–733].

abortive transduction TRANSDUCTION in which the transduced DNA persists in a recipient cell as a stable and extrachromosomal (but non-replicating) molecule; when the recipient divides only one daughter cell receives the DNA fragment.

absorbance (ultraviolet) See ULTRAVIOLET ABSORBANCE.

abzyme *Syn.* CATALYTIC ANTIBODY.

Abzyme® A reagent kit (Abbott Laboratories) used for detecting antibodies in the context of hepatitis B.

acceptor splice site (acceptor splice junction) In a pre-mRNA: the splice site (consensus AG) at the 3′ end of an intron.

(cf. DONOR SPLICE SITE.)

accession number A number that refers to a (unique) database entry for a given sequence or gene. Examples: (i) GenBank® accession number X17012 (data on the gene for rat insulin-like growth factor II); (ii) GenBank® AY024353 (referring to data on the *ftsZ* gene of the bacterium *Sodalis glossinidius*); (iii) GenBank® AM160602 (referring to data on the mRNA of the gene for cinnamyl alcohol dehydrogenase in a species of oak (*Quercus ilex*)).

(See also ANNOTATION.)

AccuPrime™ GC-rich DNA polymerase A DNA polymerase (Invitrogen, Carlsbad CA) optimized for DNA synthesis on 'difficult-to-amplify' templates, including those with a GC content >65%. Targets up to 5 kb may be amplified with this polymerase.

[Uses of AccuPrime™ (e.g.): J Bacteriol (2008) 190(24): 8096–8105; J Exp Clin Cancer Res (2008) 27:54; FEMS Microbiol Lett (2009) 294(1):32–36; BMC Biotechnol (2011) doi: 10.1186/1472-6750-11-1.]

AccuProbe® A family of PROBES (Gen-Probe, San Diego CA) used for identifying certain medically important bacteria by detecting specific sequences of nucleotides from lysed cells. The method involves a *hybridization protection assay*. In this assay, an added reagent cleaves the acridinium ester label on all the *unbound* probes. Labels on the *bound* probes (which are protected from cleavage by virtue of their position in the probe–target duplex) react with a second reagent – producing a chemiluminescent (light) signal. The light produced by this reaction is measured in RLUs (i.e. relative light units). The threshold value (in RLUs) for a positive result must be carefully examined [see for example: J Clin Microbiol (2005) 43: 3474–3478].

[Use for *Staphylococcus aureus*: J Clin Microbiol (2008) 46(6):1989–1995. Use for *Streptococcus pneumoniae* (as a reference): J Clin Microbiol (2008) 46:2184–2188. Use for *Mycobacterium avium*: J Clin Microbiol (2008) 46(8):2790–2793. For identifying *Mycobacterium* species: Emerg Infect Dis (2009) 15(1):53–55, Emerg Infect Dis (2009) 15(2): 242–249, J Clin Microbiol (2012) 49(8):3054–3057.]

(See also PACE 2C and TMA.)

acetosyringone A phenolic substance which promotes activity of the *vir* operon in species of the plant-pathogenic bacterium *Agrobacterium* (see CROWN GALL).

(See also AGROINFILTRATION.)

Acetosyringone has been used e.g. for studies on terpenoid metabolism in the tomato plant [Plant Physiol (2009) 149(1): 499–514], and studies on the transformation of wheat [Plant Cell Rep (2009) 28(6):903–913].

Agrobacterium can also transfer the T-DNA to other types of cell, including e.g. human and fungal cells; acetosyringone was used to promote transfer of T-DNA from *Agrobacterium* to the fungus *Aspergillus fumigatus* for (random) insertional mutagenesis [PLoS ONE (2009) 4(1):e4224].

***N*-acetyl-L-cysteine** See the entry MUCOLYTIC AGENT.

acetylation (of histones) HISTONE acetylation is regulated e.g. by the opposing effects of histone acetyltransferases (HATs) and histone deacetylases (see entry HDAC); the (de)acetylation of histones can affect the *structure* of CHROMATIN – and this may alter accessibility of DNA for processes such as transcription and repair. Dysregulation of the acetylation status of histones (due e.g. to aberrant activity of HDACs) can lead to e.g. the development of cancer (if a tumor-suppressor gene is

inactivated).

The acetylation of histones can be studied/manipulated e.g. by using HDAC *inhibitors* – for some examples of inhibitors see the entry HDAC.

[Genome-wide analysis of histone acetylation and its effect on gene expression in (the protozoan) *Entamoeba histolytica*: BMC Genomics (2007) 8:216.]

A general perception is that transcription of genes requires – as a pre-condition – an 'open' form of CHROMATIN (the so-called *euchromatin*) in the vicinity of the given genes; acetylation of vicinal histone(s) is usually regarded as an important factor associated with the presence of euchromatin. (In some types of chemotherapy, i.e. EPIGENETIC THERAPY, an inhibitor of HDACs is sometimes included in order to promote 'open' chromatin in the vicinity of specific gene(s) with the object of contributing to de-repression of the genes.) However, histone acetylation is only one factor that regulates gene expression; thus for example, it was reported that drug-induced formation of 'open' chromatin, involving the hyperacetylation of vicinal histone(s), was not, on its own, sufficient to de-repress lytic-cycle genes in an Epstein–Barr virus [J Virol (2008) 82(10): 4706–4719]. Nevertheless, the complexity of this issue may be indicated by a study in which histone acetylation, but not DNA demethylation, *was* found to be sufficient to break the latency of gammaherpesvirus 68 in a mouse cell line [PLoS ONE (2009) 4(2):e4556]. (See also the breaking of latency in HIV-1 in the entry AIDS (in the section: *Quiescent HIV-1*).) A further influence on transcription is the effect of a number of proteins encoded by the POLYCOMB-GROUP GENES (q.v.).

In a genomewide study of HDACs in *Schizosaccharomyces pombe* – a fission yeast – the patterns of histone acetylation, HDAC binding, and nucleosome density were compared with gene expression profiles; it was found that different HDACs may have different roles in repression and activation of genes [EMBO J (2005) 24(16):2906–2918]. Following *damage* to DNA in *S. pombe*, the restoration of chromatin structure was reported to involve deacetylation of histone H3 by Hst4 (a putative HDAC) [Eukaryotic Cell (2008) 7:800–813], while recovery from DNA damage was reported to involve Mst1 (a histone acetyltransferase) [Genetics (2008) 179(2):757–771].

In (human) nucleosomes, the acetylation of certain lysine residues depends primarily on HATs, but the effect of these enzymes appears to be promoted by binding protein HMGN1 [EMBO J (2005) 24(17):3038–3048].

Acetylation of the histone *chaperone* NUCLEOPHOSMIN, as well as histone acetylation, apparently promotes transcription [Mol Cell Biol (2005) 25(17):7534–7545], while chaperone-stimulated, histone-acetylation-independent transcription has also been reported [Nucleic Acids Res (2007) 35:705–715].

The c-Abl protein (see ABL) was reported to be a substrate for the p300 and other histone acetyltransferases.

It was suggested that a high level of acetylation of histones might advance the *timing* of replication of particular genomic regions [Nucleic Acids Res (2012) doi: 10.1093/nar/gkr723].

(See also entries METHYLATION (of histones) and DEMETHYLATION (of histones)

***N*-acetylmuramidase** See the entry LYSOZYME.

***N*-acetylneuraminic acid** (NANA) See NEURAMINIDASE.

ACF APOBEC-1 complementation factor: see RNA EDITING.

aCGH Array-based COMPARATIVE GENOMIC HYBRIDIZATION (also called microarray-based CGH): a development of the original CGH method in which – instead of using metaphase chromosomes as the hybridization target – the hybridization target is an array of clones of specific genomic sequences which may be in the form of e.g. cosmids, cDNAs, or large-insert BACs (BACTERIAL ARTIFICIAL CHROMOSOMES).

As in the original CGH method, differentially fluorophore-labeled fragments of whole-genome preparations – from both the experimental and reference sources – are applied to the array. After allowing time for hybridization, the relative copy number of a given sequence in the experimental preparation is indicated by the comparative level of fluorescence from the experimental and reference fluorophores with respect to that particular sequence in the array. As each of the clones in the array represents a known region of the genome, a change in copy number recorded at a particular clone will identify the specific gene(s) whose copy number has changed.

aCGH has a much better level of resolution compared with the original CGH protocol; that is, CGH is quite insensitive to closely-spaced aberrations in a chromosome because it has a limit of resolution reported to be, at best, about 10 Mb. By contrast, the level of resolution in aCGH is adjustable as it depends on how the clones are spaced along the genome.

[aCGH study on chromosome 17 centromere copy number: J Pathol (2009) 219(1):16–24.]

[aCGH study on genes of *Aedes aegypti*: PLoS ONE (2010) 5(12):e15578, doi: 10.1371/journal.pone.0015578.]

[aCGH designed for pre-natal diagnosis: BMC Med Genet (2010) 11:102.]

[aCGH study on the eye: Mol Vis (2011) 17:448–455.]

[aCGH detection of somatic abnormalities: Mol Cytogenet (2011) 4:3, doi: 10.1186/1755-8166-4-3.]

[aCGH in studies on myelodysplastic syndrome: Leukemia (2011) doi: 10.1038/leu.2010.293].

Some genomic rearrangements which remain unresolved by aCGH may be clarified by the HAPPY MAPPING approach.

Achilles' heel technique A technique in which a RESTRICTION ENDONUCLEASE is targeted to one *particular* recognition site when multiple copies of that site are freely available. In one method, a triplex-forming oligonucleotide (see TRIPLEX DNA) is used to mask the required cleavage site. While this site is masked, the remaining sites are methylated in order to inhibit subsequent cleavage; the triplex is then removed and specific cleavage can be carried out.

(See also PROGRAMABLE ENDONUCLEASE.)

aciclovir Alternative spelling for ACYCLOVIR. [Use of spelling acyclovir (e.g.): J Virol (2011) 85:4618–4622; Antimicrobial Agents Chemother (2012) 56:875–882, doi: 10.1128/AAC.05662-11.]

acid-fast bacilli Those bacilli (i.e. rod-shaped bacteria) which,

when stained with the Ziehl–Neelsen (or similar) stain, resist decolorization with mineral acid or an acid–alcohol mixture. This kind of staining method is used for screening respiratory specimens, e.g. samples of sputum, and for examining other types of specimen, for *Mycobacterium tuberculosis* (an acid-fast species).

Ac*M*NPV *Autographa californica* NPV: see the entry NUCLEAR POLYHEDROSIS VIRUSES.

AcNPV *Syn*. Ac*M*NPV – see the entry NUCLEAR POLYHEDROSIS VIRUSES.

acquired immunity (to viruses etc. in archaeans, bacteria) See the entry CRISPRS.

acquired uniparental disomy See LOSS-OF-HETEROZYGOSITY.

acquired UPD See LOSS-OF-HETEROZYGOSITY.

acridines Heterocyclic, fluorescent agents that bind to dsDNA (primarily as an INTERCALATING AGENT) and to single-stranded nucleic acids (and to the backbone chains of double-stranded nucleic acids). Acridines have antimicrobial activity and they are mutagenic; they are used e.g. as stains for nucleic acids, and can also be used for CURING plasmids.

acridinium ester label (on probes) See ACCUPROBE.

acrocentric Refers to a CHROMOSOME in which the CENTROMERE is located close to one end.

acrydite hybridization assay An assay in which molecules of labeled ssDNA or ssRNA, passing through a polyacrylamide gel by electrophoresis, are captured (bound) by complementary oligonucleotides immobilized in a central 'capture zone' within the gel; all the molecules of nucleic acid that are *not* complementary to the capture oligos pass through the central capture zone – and continue migration to the end of the gel strip. The complementary oligos are prepared with a 5′-end acrydite group that binds them to the polyacrylamide matrix so that they are immobilized in the gel. (Note that the central region of the gel strip is prepared separately.)

acrylamide A toxic, water-soluble agent (CH_2=CH–$CONH_2$) which can be polymerized to POLYACRYLAMIDE by catalysts such as *N*,*N*′-methylene-*bis*-acrylamide ('Bis') that promote cross-linking.

actinomycin C_1 *Syn*. ACTINOMYCIN D.

actinomycin D An antibiotic (a substituted phenoxazone linked to two pentapeptide lactone rings) produced by some species of *Streptomyces*; it is also active against tumor cells.

This agent has been regarded as an INTERCALATING AGENT that inhibits transcription by DNA-dependent RNA polymerase. A study on DNA binding by actinomycin D has suggested support for a model in which biologically significant binding involves *pre-melted* DNA (found *in vivo* in transcription bubbles); in cancer cells this could be linked to enhanced activity of DNA-unwinding enzymes, the drug remaining bound after dissociation of the enzymes [Nucleic Acids Res (2012) doi: 10.1093/nar/gks069].

The drug was reported to have a relatively low affinity for AT-rich promoter regions, so that *initiation* of transcription from such promoters may be little affected.

activation domain (AD) See YEAST TWO-HYBRID SYSTEM.

activation-induced cytidine deaminase (AID) An enzyme in germinal center B lymphocytes (B cells) which is an absolute requirement for affinity maturation and class switching in the normal development of antibodies; AID deaminates cytidine to uridine.

Note. The reagent BISULFITE also deaminates (unmethylated) cytidine to uridine.

(See also CYTIDINE DEAMINASE and RNA EDITING.)

The autosomal recessive form of HYPER-IGM SYNDROME has been linked to a deficiency of AID (see the table in the entry GENETIC DISEASE).

The ssDNA substrates of AID have been reported to occur uniquely in actively transcribed genes – transcription-induced negative supercoiling apparently enhancing formation of the single-stranded targets for this enzyme [PLoS Genet (2012) 8(2):e1002518].

AID was also reported to inhibit retrotransposition of L1 – suggesting that it has function(s) in addition to creating antibody diversity [Nucleic Acids Res (2009) 37(6):1854–1867].

activation/regulation of genes (*DNA technol*.) See e.g. entry CONDITIONAL GENE ACTIVATION/REGULATION.

activin A protein, present in gonadal tissues, which is used e.g. in culture media for the maintenance of (human) embryonic stem cells.

(See also STEM CELL.)

activity-based probe A type of probe used for the real-time study of APOPTOSIS (q.v.).

acute myeloid leukemia (AML) The term that includes any of a highly heterogeneous group of diseases which, collectively, comprise the commonest form of acute leukemia. AML has been associated with a range of different mutations, including mutations in epigenetic modifiers. [Mutations in epigenetic modifiers in myeloid malignancies: Adv Hematol (2011) doi: 10.1155/2012/469592. DNA methylation signatures identify biologically distinct subtypes in AML: Cancer Cell (2009) doi: 10.1016/j.ccr.2009.11.020.]

Fewer than ~10% of cases involve the t(8;21) translocation [J Biomed Biotechnol (2011) doi: 10.1155/2011/104631].

Leukemic cells usually carry the CD33 antigen – which has been a target for antibody-based therapy: see e.g. MYLOTARG.

[Recent advances in treating AML: F1000 Med Rep (2010) doi: 10.3410/M2-55.]

(cf. CHRONIC MYELOGENOUS LEUKEMIA.)

acyclonucleotide Any analog of a deoxyribonucleotide (or a ribonucleotide) in which a non-cyclic moiety carries the base. One example is a monomer of glycerol nucleic acid (see the entry GNA). Polymerization of certain acyclonucleotides on a DNA template was achieved with THERMINATOR DNA POLYMERASE.

acyclovir (alternative spelling: aciclovir) 9-(2-hydroxyethoxymethyl)guanine: an antiviral agent active against a number of herpesviruses, including herpes simplex. In cells, acyclovir is phosphorylated to the monophosphate by the viral thymidine kinase; it is then converted to the active triphosphate form via host-encoded enzymes. The active form of the drug inhibits

viral DNA polymerase; the DNA polymerase of the host cell is much less sensitive.

In cells which are not virally infected, acyclovir appears not to be significantly phosphorylated.

Acyclovir has been used topically and systemically.

In $CD4^+$ T cells not detectably infected with herpesviruses, acyclovir was reported to show consistent inhibition of HIV-1 replication [J Virol (2011) 85(9):4618–4622].

***N*-acyl-homocysteine thiolactone** See QUORUM SENSING.

***N*-acyl-L-homoserine lactone** (AHL) See QUORUM SENSING.

acylneuraminyl hydrolase *Syn*. NEURAMINIDASE.

AD primer (arbitrary degenerate primer) See TAIL-PCR.

Ada protein (in *Escherichia coli*) See the entry DNA REPAIR.

adaptamer See the entry ORFMER SETS.

adaptive response (to alkylating agents) See DNA REPAIR.

adaptor A short, synthetic, double-stranded fragment of DNA which is similar in principle to a LINKER – but which generally offers more flexibility. Thus, for example, the two ends of an adaptor may consist of dissimilar STICKY ENDS – one end able to bind to a (complementary) sticky end on a DNA fragment and the other able to bind to a different sticky end on a vector molecule, facilitating the integration of fragments and vectors made by different restriction enzymes. An adaptor may also include restriction site(s) and/or primer-binding sites (to make alternative sticky ends and/or for transcription).

[Ligation of adaptors to *RNA*: Nucleic Acids Res (2012) 40 (7):e54.]

(See also NOTI.)

ADAR1 A dsRNA ADENOSINE DEAMINASE involved e.g. in RNA EDITING.

(See also Zα in the entry Z-DNA.)

add The adenine RIBOSWITCH (q.v.).

ADD domain (in DNA methyltransferases) See METHYLATION (of DNA) in the section: *Coupling of DNA methylation with histone methylation*.

AdEasy™ XL adenoviral vector system A commercial GENE-DELIVERY SYSTEM (Stratagene, La Jolla CA, USA) which uses ADENOVIRUS-based vectors. It facilitates the preparation of a recombinant adenoviral vector containing the gene/fragment of interest.

Initially the gene/insert is cloned in a small SHUTTLE VECTOR (~7 kb) which includes: (i) the left and right ITRs (inverted terminal repeats) of the adenovirus genome; (ii) two regions homologous to two sequences in another plasmid, pAdEasy-1 (see later), (iii) a gene encoding resistance to kanamycin; and (iv) a recognition site for the restriction endonuclease PmeI. After cloning, the shuttle vector is linearized – by cleavage with PmeI; linearization leaves the two homologous regions (see above) in terminal positions.

The linearized shuttle vector is inserted, by transformation, into a strain of *Escherichia coli*, BJ5183-AD-1, that already contains the (circular) plasmid vector pAdEasy-1. pAdEasy-1 (~33 kb) includes modified genomic DNA of human adenovirus serotype 5 with deletions in both the E1 and E3 regions. Recombination takes place (in *E. coli*) between the linearized shuttle vector and (homologous) regions in pAdEasy-1. Cells containing recombinant plasmids are selected on media that contain kanamycin.

The recombinant plasmids are isolated, and the next stage is conducted *in vitro*.

Recombinant plasmids are cleaved by a restriction enzyme, PacI, at selected sites, yielding a linear construct with adenoviral terminal sequences (i.e. ITRs). This construct is used to transfect specialized, competent AD-293 cells – within which infective adenovirus virions (containing the gene/fragment of interest) are produced; the virions are released for subsequent use in gene-expression studies in mammalian cells.

The principle of the AdEasy™ system was exploited in the production of oncolytic adenovirus [BMC Biotechnol (2006) 6:36].

The AdEasy™ XL vector system has been used in a range of studies [see e.g. Nucleic Acids Res (2006) 34(12):3577–3584; Vaccine (2007) 25(52):8687–8701; Mol Ther (2008) 16(5):886–892; J Clin Invest (2009) 119:976–985; Cell Cycle (2009) 8(2):257–267; Biochim Biophys Acta (2009) 1793(8): 1379–1386; J Exp Clin Cancer Res (2009) 28(1):75; BMC Immunol (2009) 10:14; Mol Neurodegener (2011) 6:13; Mol Biol Cell (2012) 23:781–791; PLoS ONE (2012) 7:e36712.]

adefovir A NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITOR.

adenine See the entry BASE. (See also BAT-26.)

adenine phosphoribosyltransferase An enzyme (EC 2.4.2.7) which forms adenosine monophosphate (AMP) from adenine and 5-phosphoribosyl-1-diphosphate.

In humans, a deficiency of adenine phosphoribosyltransferase (an autosomal recessive disorder) can cause excretion of adenine (in the urine) and the formation of a highly insoluble product, 2,8-dihydroxyadenine, which can give rise to kidney stones and renal failure.

adeno-associated viruses See the entry AAVS.

adeno-satellite viruses See the entry AAVS.

adenosine A ribonucleoside (see the entry NUCLEOSIDE).

adenosine deaminase An enzyme (EC 3.5.4.4) which catalyzes the conversion of adenosine to inosine.

(See also ADAR1.)

adenosine deaminase deficiency The congenital deficiency of adenosine deaminase activity that is characterized by defective purine metabolism and a lack of normal development of T cells (with a consequent marked immunodeficiency in which the patient is susceptible to infection by various opportunist pathogens). Adenosine deaminase deficiency has been treated successfully by GENE THERAPY.

(See also GENETIC DISEASE (table).)

adenosine-to-inosine editing (RNA editing) See RNA EDITING.

***S*-adenosyl-L-methionine** A methyl group (CH_3–) donor that is used in various reactions.

Adenovirus A genus of icosahedral, non-enveloped viruses of the family *Adenoviridae*; the genome is linear dsDNA. These viruses infect mammals and birds; each type of adenovirus is usually specific for one, or a limited range, of closely related host species.

Adenovirus pathogenesis (in humans) commonly involves respiratory-tract infections, while some adenoviruses are able to induce tumors in rodents (rats). The *oncogenic* potential of adenoviruses has been investigated by using Ad5 adenovirus *dl520* to infect human U2OS cells, and monitoring levels of the Myc protein (see MYC); it was reported that the (virus-encoded) E1A protein interacts with the cell's p400, resulting in the stabilization of Myc and induction of Myc target genes [Proc Natl Acad Sci USA (2008) 105:6103–6108]. (See also HEPATOCELLULAR CARCINOMA SUPPRESSOR 1.)

The adenovirus virion is ~70–90 nm in diameter; the capsid encloses a core containing genomic DNA (which is closely associated with an arginine-rich polypeptide). The 5′ end of each strand of the DNA is covalently linked to a hydrophobic 'terminal protein' (TP).

Both ends of the genomic DNA are characterized by an inverted terminal repeat (ITR) – which varies in length in the different types of adenovirus; the 5′ end residue is commonly dCMP.

During infection, the core enters the nucleus, releasing viral DNA. Replication of viral DNA involves TP and also a virus-encoded DNA polymerase, as well as other virus- and host-encoded proteins. TP, synthesized in precursor form, binds covalently to DNA during replication and is later cleaved to the mature (DNA-bound) TP. A TP-mediated form of DNA replication also occurs in PHAGE φ29 (q.v. for details).

Expression of late viral genes, encoding structural proteins, is accompanied by the cessation of cellular protein synthesis.

Some 10^5 virions may be formed within a single host cell.

Adenoviruses as vectors

Adenoviruses are employed as VECTORS in a variety of types of investigation, including gene therapy. (See e.g. ADEASY XL ADENOVIRAL VECTOR SYSTEM.) The re-targeting of adenovirus type 5 vectors to cell-surface $\alpha_v\beta_6$ integrin molecules resulted in reduced hepatotoxicity and a better uptake by tumor cells following systemic delivery [J Virol (2009) 83(13):6416–6428].

Titers of recombinant adenoviruses in packaging cells may be optimized in various ways: see e.g. PACKAGING CELL.

Variable genome size in replication-deficient vectors may affect viral stability [J Virol (2009) 83(4):2025–2028].

[Adenoviruses (vaccine vectors): Mol Therapy (2009) 178: 1333–1339.]

Adenovirus dodecahedron base

A construct, which consists of twelve copies of a pentameric adenoviral capsid protein (involved in penetration of cells) has been used as a vehicle for increasing the uptake, by cells, of the antitumor agent bleomycin (which was tethered to the construct) [PLoS ONE (2009) 4(5):e5569].

adenovirus dodecahedron base See the entry ADENOVIRUS.

adenoviruses Viruses of (i) the genus ADENOVIRUS – *or* (ii) the family *Adenoviridae*.

adenylate cyclase An enzyme (EC 4.6.1.1) which catalyzes the conversion of ATP to CYCLIC AMP.

In *Escherichia coli*, the activity of this enzyme (*cya* gene product) is regulated e.g. in association with the CATABOLITE REPRESSION system.

(See also BACTERIAL TWO-HYBRID SYSTEM.)

In mammals, the enzyme forms part of a plasma membrane complex and is regulated e.g. via certain G PROTEINS; it is activated by some bacterial exotoxins (e.g. PERTUSSIS TOXIN).

Anthrax toxin (EF component) and *cyclolysin* (a virulence factor synthesized by the Gram-negative bacterial pathogen *Bordetella pertussis*) both exhibit adenylate cyclase activity, which is stimulated by CALMODULIN.

adenylate kinase An enzyme (EC 2.7.4.3) which catalyzes the (reversible) conversion: 2ADP↔ATP + AMP.

adenylic acid See the table in the entry NUCLEOSIDE.

aDNA *Ancient* DNA – see the entry ANCIENT DNA.

ADO See the entry ALLELE DROP-OUT.

AdoMet Abbreviation for *S*-adenosyl-L-methionine.

ADP-ribosylation The transfer, to a protein, of an ADP-ribosyl group from NAD^+, mediated by ADP-ribosyltransferase (EC 2.4.2.30).

In eukaryotes ADP-ribosylation can (for example) regulate the properties of HISTONES.

In *Escherichia coli*, RNA polymerase is ADP-ribosylated (with change in activity) following infection with bacteriophage T4.

ADP-ribosylation is an intracellular effect of some bacterial exotoxins (e.g. cholera toxin and PERTUSSIS TOXIN).

Polymerized ADP-ribosyl subunits (up to 50) may be found on certain eukaryotic proteins.

adult stem cell See the entry STEM CELL.

Aedes aegypti A species of mosquito which can act as a vector in the transmission of e.g. DENGUE and yellow fever.

[Genome: Science (2007) 316(5832):1718–1723.]

(See also ARBOVIRUSES.)

It was reported that NUMTS are prevalent in the genome of *A. aegypti*, suggesting that future phylogenetic or population genetic studies should be carried out with nuclear, rather than mitochondrial, DNA markers [BMC Genet (2009) 10:11].

A. aegypti has been targeted in a method for the control of dengue fever: see the entry GMMS (in the section: *Gene drive systems*).

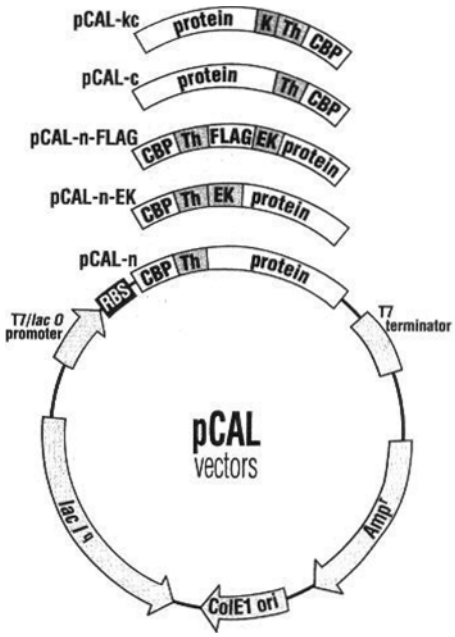
aerobic anoxygenic photosynthetic bacteria See the footnote in the entry CYANOBACTERIA.

affinity capture electrophoresis Electrophoresis in a medium containing immobilized capture probes; it is used e.g. for the sequence-specific isolation of a fragment of ssDNA – or a fragment of triplex-forming dsDNA.

(See also ACRYDITE HYBRIDIZATION ASSAY.)

affinity chromatography Chromatography in which particular molecules are isolated (adsorbed) owing to their affinity for an immobilized ligand – any non-specific unbound molecules being removed from the immobilized matrix. This procedure may be used e.g. for isolating/purifing a given type of molecule (see e.g. GENE FUSION (uses)).

Affinity® protein expression and purification A product of Stratagene (La Jolla CA) designed to facilitate the expression



Affinity® protein expression and purification. The range of pCAL vectors (see entry for details of the method). CBP (in each vector) refers to calmodulin-binding peptide. EK = enterokinase; K = Kemptide sequence; Th = thrombin proteinase. (See also entry for FLAG.)

Courtesy of Stratagene, La Jolla CA, USA.

and purification of proteins expressed in prokaryotic systems; the product includes various pCAL plasmid vectors shown in the diagram (on this page) – each encoding a CALMODULIN-binding affinity tag.

Protein expression is maximized by a vector that includes a T7/LacO promoter system. In suitable strains of *Escherichia coli* (e.g. BL21(DE3)), T7 RNA polymerase is expressed in the presence of the inducer IPTG and drives expression from the T7/LacO promoter system on the plasmid. Tight control of expression is achieved with a plasmid-borne copy of *lacI*^{q}. Efficient translation of the protein of interest is promoted by using the strong ribosome-binding site (RBS) of T7 gene 10.

pCAL vectors contain a ColE1 origin of replication and an ampicillin-resistance gene.

All pCAL vectors encode a CALMODULIN-binding peptide (CBP) tag which forms a fusion product with the expressed protein and permits high-level purification following a single passage through CALMODULIN-AFFINITY RESIN. The (small) size of the CBP tag (approx. 4 kDa) may be expected to have a smaller effect on the protein of interest compared with larger tags – such as the (26-kDa) glutathione *S*-transferase (GST) affinity tag.

One pCAL vector includes a KEMPTIDE SEQUENCE that can be used e.g. for *in vitro* labeling of the expressed protein with protein kinase A (PKA) and ^{32}P.

All of the pCAL vectors include a cleavage site (for enterokinase or thrombin proteinase) for removal of the CBP tag.

One of the pCAL vectors includes a FLAG® sequence.

Affinity® vectors were used e.g. in studies on a fluorescent reporter protein [Proc Natl Acad Sci USA (2008) 105:20038–20043]; a light-activated DNA-binding protein [Proc Natl Acad Sci USA (2008) 105(31):10709–10714; and HMG box proteins [Mol Endocrinol (2008) 22(5):1141–1153].

affinity resin See e.g. NICKEL-CHARGED AFFINITY RESIN.

affinity tag *Syn.* AFFINITY TAIL.

affinity tail (affinity tag) Part of a FUSION PRODUCT which can facilitate detection/isolation of a recombinant protein e.g. by AFFINITY CHROMATOGRAPHY or by the use of an affinity resin (such as a NICKEL-CHARGED AFFINITY RESIN).

Some affinity tails are small peptides. One advantage of a *small* affinity tail is that it is less likely to interfere with the function of the fusion protein – so that its removal may not be necessary.

(See also FLAG®, PESC VECTORS and SIX-HISTIDINE TAG.)

Large (protein) tails, for example glutathione *S*-transferase, may improve the solubility of the fusion protein but they may need subsequent removal in order to avoid interference with the function of the recombinant target protein.

(See also CHAMPION PET SUMO VECTOR.)

A highly temperature-stable affinity tail, a lectin, stable up to 80°C, may be useful for proteins originating from thermophilic organisms; the fusion proteins bind specifically to an agarose matrix that contains D-mannose, and the affinity tail can by cleaved by an enterokinase [BioTechniques (2006) 41 (3):327–332].

[Affinity as a tool in life science (a review): BioTechniques (2008) 44(5):649–654.]

(See also AFFINITY PROTEIN EXPRESSION AND PURIFICATION.)

aflatoxins Heat-stable toxins produced by certain fungi (strains of *Aspergillus flavus* and *A. parasiticus*); the molecule of an aflatoxin contains a bifuran moiety fused with a (substituted) coumarin.

[Genes for aflatoxin biosynthesis: Appl Environ Microbiol (2005) 71:3192–3198.]

Aflatoxins damage DNA (producing e.g. mutations, strand breakage) and they inhibit repair.

Aflatoxins are highly carcinogenic in mammals. They have been associated e.g. with cases of hepatocellular carcinoma.

These toxins may affect different species in different ways.

In mouse hepatocytes, it was found that α-mannan protects against DNA damage from aflatoxin B_1 [Int J Mol Sci (2009) 10(2):395–406].

AFLP Either of *two distinct* PCR-based approaches for TYPING

bacteria.

One approach ('amplified fragment length polymorphism'), includes a number of variant forms of arbitrarily primed PCR (AP-PCR), including e.g. RAPD analysis.

The other approach, outlined here, involves initial digestion of genomic DNA with two types of RESTRICTION ENDONUCLEASE; it is sometimes called 'amplified restriction fragment length polymorphism', but this was not recommended by the original authors [see comments in: Nucleic Acids Res (1995) 23:4407–4414].

In the digested genome each fragment is flanked by STICKY ENDS produced by one or other of the two types of restriction enzyme. Two types of adaptor molecule (A, B) are added; the A molecules have *one* sticky end which binds to sites cleaved by one of the restriction enzymes, and B molecules have *one* sticky end that binds to sites cleaved by the other enzyme. A site cleaved by EcoRI (left) and a matching adaptor (right) is shown below:

```
5′-----NNG          AATTGNNNNN-3′
  -----NNCTTAA          CNNNNN
```

Fragment–adaptor binding is followed by ligation – but the cleavage site of EcoRI is *not* regenerated, avoiding repeated restriction. Fragments (with their adaptors) are amplified by PCR. Each primer is complementary to a sequence that covers part of an adaptor and the (contiguous) restriction site of the fragment. Each primer's 3′ end extends beyond the restriction site for one (or several) nucleotides; thus, a given primer will be extended only if the primer's 3′ terminal selective nucleotide(s) align with *complementary* base(s) in the fragment. In the example given above, one template strand is:

```
5′-----NNGAATTGNNNNN-3′
```

and a primer with a deoxycytidine (C) selective 3′ nucleotide will bind as follows:

```
5′-----NNGAATTGNNNNN-3′
      CCTTAACNNNNN-5′      ← primer
```

The same principle holds for each primer-binding site: only some of the primers will be extended owing to their selective 3′ end.

The PCR products undergo gel electrophoresis, and bands of products (made visible e.g. by the use of labeled primers) form the *fingerprint*.

AFLP discriminated easily between *Clostridium botulinum* types A, B, E and F, but only limited intraspecies differences were reported in isolates of *Brucella*.

AFM ATOMIC FORCE MICROSCOPY.

agar A complex mixture of galactans obtained from certain red algae (e.g. *Gelidium*); these compounds form part of the cell wall and/or intercellular matrix.

Agar comprises two main components: AGAROSE and agaropectin. Agaropectin is a mixture of sulfated galactans, some of which contain glucuronic acid and/or other constituents.

An agar *gel* is used as a matrix in many types of solid and semi-solid microbiological medium; this translucent jelly-like material is prepared by heating a mixture of agar – e.g. 1.5% w/v – and water to >100°C and cooling to room temperature; gelling begins at about 40–45°C.

Agar can be an inhibitory factor in PCR (cf. GELLAN GUM).

One report indicated that agar promotes TRANSFORMATION in *Escherichia coli* [J Bacteriol (2009) 191(3):713–719].

agarose The major constituent of AGAR: a (non-sulfated) linear polymer consisting of alternating residues of D-galactose and 3,6-anhydro-L-galactose. Agarose is used e.g. as a medium in GEL ELECTROPHORESIS for the separation of large (and small) fragments of nucleic acid.

(See also QIAQUICK GEL EXTRACTION KIT.)

(cf. POLYACRYLAMIDE.)

age-related macular degeneration See the entry AMD.

agnoprotein A regulatory protein, encoded by JC VIRUS, which plays a major role in the infective cycle; it may be involved in facilitating the transport of virions from the nucleus (where virus assembly occurs) to the cytoplasm.

Mutant, phosphorylated forms of agnoprotein are unable to sustain the infective cycle [J Virol (2006) 80(8):3893–3903].

Expression of a transfected agnoprotein-encoding gene was reported to give rise to inhibition of the low-fidelity pathway of DSB (double-strand break) repair, involving protein KU70.

Ago protein See ARGONAUTE.

Agrobacterium A genus of motile, Gram-negative bacteria that are found primarily in the rhizosphere (i.e. root environment of plants).

GC% of the genomic DNA: 57–63.

Optimal temperature for growth: 25–28°C. Various mono- and disaccharides can be metabolized; glucose is metabolized e.g. via the Entner–Doudoroff pathway and the hexose monophosphate pathway.

Colonies which develop on media containing carbohydrates are generally mucilaginous, copious slime being formed.

Most species are pathogenic to plants – *A. tumefaciens* and *A. vitis* are causal agents of CROWN GALL.

(Some relevant entries: AGROINFECTION, BINARY VECTOR SYSTEM, FLORAL DIP METHOD and TRIFOLITOXIN.)

Agrobacterium was used for random insertional mutagenesis in the fungus *Aspergillus fumigatus* (by the insertion of T-DNA: see CROWN GALL) [PLoS ONE (2009) 4(1):e4224].

Taxonomic note

One paper classified all *Agrobacterium* species in the genus *Rhizobium* [Int J Syst Evol Microbiol (2001) 51:89–103], *A. tumefaciens* being renamed *Rhizobium radiobacter*, and *A. vitis* renamed *R. vitis*. The name *Agrobacterium tumefaciens* has been, and continues to be, widely used in publications.

agroinfection A method for introducing viral DNA (or cDNA) into plant cells.

In the original procedure, viral DNA is inserted into the T-DNA region of the Ti plasmid of bacterium *Agrobacterium*

tumefaciens (see the entry CROWN GALL for details of the Ti plasmid); thus, when infecting a plant, *A. tumefaciens* injects viral DNA (within the T-DNA) into plant cells.

Currently, the commonly used procedure involves the use of a *binary vector* system. In this approach the gene/sequence of interest is inserted into a small (binary) vector in which it is flanked, on each side, by the left border and right border of T-DNA. The binary vector, containing the gene, is inserted into an engineered strain of *Agrobacterium tumefaciens* that contains the *vir* (virulence) region of the Ti plasmid, which is concerned with transfer of DNA into plant cells. This strain is then used to infect a plant. When the *vir* genes are activated, DNA from the *binary vector* (specifically, the DNA from the section bracketed by the left and right borders of T-DNA) is transferred into the plant cells – such transfer being mediated by factors encoded by the *vir* region acting in *trans*.

For developing transgenic plants it is desirable to minimize the content of extraneous DNA which is transferred to plant cells through the vector system, particularly when such plants are to be made available in a general agricultural setting; the content of extraneous DNA is covered by certain laws which relate to transgenic plants. To this end, a number of minimal T-DNA vectors have been suggested [BioTechniques (2006) 41(6):708–710].

[High-efficiency expression of proteins in plants from agroinfection-compatible TMV (tobacco mosaic virus) expression vectors: BMC Biotechnol (2007) 7:52.]

Agroinfection was used e.g. to study resistance to disease in the potato and avirulence genes in *Phytophthora infestans* (the late blight pathogen) [PLoS ONE (2008) 3(8):e2875].

[The efficient production of human acidic fibroblast growth factor in pea (*Pisum sativum* L.) by agroinfection of germinated seeds: BMC Biotechnol (2011) doi: 10.1186/1472-6750-11-45.]

(See also FLORAL DIP METHOD; cf. AGROINFILTRATION.)

agroinfiltration A procedure, used for inserting a vector into plant cells, in which cells of the plant-pathogenic bacterium *Agrobacterium tumefaciens* (containing the vector, and in the presence of ACETOSYRINGONE) are injected with a syringe via leaf stomata.

[Uses (e.g.): Plant Physiol (2007) 145(1):5–16 and (2009) 149(2):1005–1016.]

Agroinfiltration has been used in a study on the insertion of full-length viral cDNAs into certain plants [Virol J (2011) 8: 488].

(cf. AGROINFECTION.)

AGT O^6-alkylguanine-DNA alkyltransferase: see *Uses of gene fusion* in the entry GENE FUSION.

AHL (*N*-acyl-L-homoserine lactone) See QUORUM SENSING.

***ahpC* gene** See ISONIAZID.

AHT (*N*-acyl-homocysteine thiolactone) See QUORUM SENSING.

AID ACTIVATION-INDUCED CYTIDINE DEAMINASE.

AIDS Acquired immune deficiency syndrome. An HIV^+ person with AIDS has counts of $CD4^+$ T cells below a certain level and, additionally, the presence of one or more types of AIDS-defining disease (such as: candidiasis of the *lower* respiratory tract, retinitis with CMV (cytomegalovirus), *extra*pulmonary infection with *Mycobacterium tuberculosis*, pneumonia due to *Pneumocystis carinii* etc.).

[CD4 cell counts at HIV diagnosis: AIDS Res Treat (2012) doi: 10.1155/2012/869841.]

The causal agent is usually HIV-1 (q.v.); the disease can also be caused by HIV-2. (See RETROVIRUSES for a general background to HIV-1 and other, related, viruses.)

Chemotherapy used in the treatment of AIDS may include various ANTIRETROVIRAL AGENTS (q.v.). (See also HAART.)

One patient was reported to have had long-term remission following a heterologous stem cell transplant from a $CCR5^{-/-}$ donor, even after the discontinuation of conventional therapy. [*Ex vivo* gene therapy for HIV-1: Hum Mol Genet (2011) doi: 10.1093/hmg/ddr160.]

Inhibition of transmission of HIV-1

One approach involves an APTAMER – selected to bind, with high affinity, to the T cell antigen CD4 – linked to an siRNA (see RNA INTERFERENCE); the siRNA targets either the viral genes *gag* and *vif* (see RETROVIRUSES) or the T cell's gene that encodes the CCR5 coreceptor for HIV-1 (see HIV-1). When the aptamer binds to its target (CD4) the construct is internalized so that the siRNA can start to silence the target genes.

It was considered that the constructs described above might be used as the active constituent of a topical microbicide; the constructs might act in two ways: (i) by mechanically blocking the binding of HIV-1 to CD4, and (ii) by silencing genes involved in viral replication. This approach was reported to inhibit infection of (i) primary CD4 cells and macrophages *in vitro*, (ii) human cervicovaginal explants, and (iii) engineered (immunodeficient) mice [J Clin Invest (2011) 121(6):2401–2412, doi: 10.1172/JCI45876].

Quiescent HIV-1

The chemotherapeutic agents currently in use aim, primarily, to break the replicative cycle of the virus (e.g. by inhibiting maturation of the virions). However, this does not address the (covert) problem of viral *persistence* resulting from 'silent' *integrated* HIV genomes that pose an ongoing threat (as they escape the immune system as well as therapeutic agents) [see e.g. Nature Rev Microbiol (2009) 7:798–812].

In one approach to this problem, siRNAs have been used to investigate those particular histone deacetylases (see HDAC) that contribute to HIV-1 repression in latently infected cells. From the results of these studies it was suggested that HDAC inhibitors, specific for particular HDACs, may be useful for the targeted disruption of persistent HIV-1 infection [J Virol (2009) 83(10):4749–4756]. (In an analogous (murine) study, histone acetylation, but not DNA demethylation, was found to reactivate a latent gammaherpesvirus (MHV-68) in a cell line [PLoS ONE (2009) 4(2):e4556].)

In a different approach to the disruption of latency in HIV, an alternatively spliced transcription factor (ΔVII-Ets-1) was found to activate transcription in latent HIV-1 in cells derived from patients on a HAART chemotherapeutic regime. Unlike

some other approaches, this method did not have the major disadvantage of causing significant T cell activation [Proc Natl Acad Sci USA (2009) 106(15):6321–6326].

One study concentrated on the role of histone methylation in promoting latency in HIV-1. In latently infected Jurkat T cells, the long terminal repeat (i.e. LTR) region of the HIV-1 provirus (see the diagram in RETROVIRUSES) was reported to be associated with high levels of a histone methyltransferase: 'Enhancer of Zeste homolog 2' (EZH2 – a member of the Polycomb-group repressor complex 2); the EZH2 was rapidly displaced on reactivation of the provirus. It was reported that knockdown of EZH2 induced reactivation in up to 40% of the latent HIV-1 proviruses; moreover, treatment with the histone methylation inhibitor 3-DEAZANEPLANOCIN A also led to reactivation of latent proviruses. It was suggested that inhibition of histone methylation may be a useful approach in breaking HIV-1 latency [J Virol (2011) doi: 10.1128/JVI.00836-11].

aiRNA Asymmetric interfering RNA: see the entry SIRNA.

alanine scan mutagenesis A method that is used for studying the binding properties (or other characteristics) of particular residues in a protein by replacing them with alanine residues. Replacement of residue(s) may be achieved e.g. by synthesizing the protein from a modified (engineered) mRNA. After insertion of the alanine residues the protein is examined for specific properties/functions.

alarmone Any of various low-molecular-weight molecules that are able to mediate some changes in cellular metabolism as a response to a particular type of stress. One example is ppGpp which is formed in the *stringent response* in *Escherichia coli* (see the entry STRINGENT RESPONSE).

albamycin *Syn*. NOVOBIOCIN.

(See also the entry ANTIBIOTIC (table).)

Alexa Fluor® 488 See XERODERMA PIGMENTOSUM (diagnosis by the EdU method).

AlgR In *Pseudomonas aeruginosa*: the response regulator of a TWO-COMPONENT REGULATORY SYSTEM – FimS/AlgR – which controls biosynthesis of type IV fimbriae (responsible for so-called 'twitching motility'); this regulation involves activating the pilVWXY1Y2E operon [J Bacteriol (2008) 190(6):2023–2030].

AlgR also has roles in regulating (type III) protein secretion genes and alginate biosynthesis.

AlgZ *Syn*. FimS: see the entry ALGR.

ALK granule A cytoplasmic body reported to be found within transformed cells which are expressing anaplastic lymphoma kinase (ALK) constitutively; the constituents of these bodies include polyadenylated mRNAs and various RNA-binding proteins not previously reported in other mammalian foci. An ALK granule differs from a P BODY and a STRESS GRANULE in that it does not have mRNA-degrading components or stress-granule-specific markers [Mol Biol Cell (2011) 22(6):726–735].

AlkA protein See DNA REPAIR.

alkaline phosphatase (AP) An enzyme (EC 3.1.3.1; maximum stability at pH ~7.5–9.5) which is used e.g. for removing 5′ terminal phosphate groups from nucleic acids.

AP is also used in reporter systems. For example, when it is bound to antibodies, AP can act as a label to any molecule of the relevant antigen to which the antibodies bind; the AP is then detectable by using any of various types of substrate that yield a colored product, or light. Substrates that yield colored products include e.g. NBT (nitroblue tetrazolium) + BCIP (5-bromo-4-chloro-3-indolyl phosphate). AP cleaves ATTOPHOS to yield a fluorescent molecule (a fluorophore).

Several 1,2-dioxetanes (e.g. CSPD® and AMPPD®), give rise to CHEMILUMINESCENCE when cleaved by AP.

AP is used as a reporter e.g. in ELISA.

alkaline stripping Stripping of hybridized RNA probes from a DNA MICROARRAY by degradation with buffers that contain NaOH (sodium hydroxide) under carefully regulated conditions (e.g. a temperature of 60–62°C).

A stripped microarray can be re-used – reducing costs – but a microarray cannot be stripped twice without loss of quality. Microarrays which had been stripped once were reported to give results similar to those from virgin (non-stripped) arrays.

***O*^{6}-alkylguanine-DNA alkyltransferase** (AGT) See the subheading *Uses of gene fusion* in the entry GENE FUSION.

allele (allelomorph) Any one of two or more different versions of a particular GENE; the product or function of a given allele may exhibit qualitative and/or quantitative differences from the product or function of other alleles of that gene.

(cf. EPIALLELE.)

In a diploid cell or organism, if an *allelic pair* (i.e. the two alleles of a given gene) consists of two identical alleles then the cell/organism is said to be *homozygous* for that particular gene; if different, the cell/organism is said to be *heterozygous* for the gene.

(See also ALLELE-SPECIFIC GENE EXPRESSION.)

allele-coupled exchange A method for selecting those cells in which a segment from a (circular) plasmid has integrated into the chromosome by a *double* crossover (see also diagram (b) in entry INSERTION–DUPLICATION RECOMBINATION); the method was designed for genetically engineering the (Gram-positive) bacterium *Clostridium*.

The plasmid used in this method was constructed *in vitro* and inserted into cells of *C. acetobutylicum*. This plasmid – which included an antibiotic-resistance gene and an origin of replication – also contained (i) a sequence (300 bp) homologous to a region in the *pyrE* gene, and (ii) a longer sequence of 1200 bp homologous to the region immediately 3′ of the *pyrE* gene.

The procedure involved two stages, essentially as described below:

Following insertion of the plasmid into *C. acetobutylicum*, homologous recombination, involving a single crossover, can integrate the plasmid into the cell's chromosome. (The design of the plasmid was such that the long (1200 bp) sequence of homology directs the *initial* crossover to the location 3′ of the *pyrE* gene in the chromosome, leaving *pyrE* intact.)

The cells were then inoculated onto an antibiotic-containing

medium. A number of clones were isolated and subcultured twice on this medium; in these cells, the presence of a single crossover, at the correct chromosomal site, was confirmed by PCR-based screening.

Subsequently, single-crossover clones were inoculated onto a medium containing 5-fluoro-orotic acid (5-FOA) and uracil. The single-crossover cells, in which the *pyrE* gene (involved in uracil biosynthesis) remains active, are killed by 5-FOA. Double-crossover cells, in which the *second* crossover (in the 300 bp homology region) has inactivated the *pyrE* gene, are not affected by 5-FOA because they lack a complete pathway for uracil biosynthesis; these cells can nevertheless grow, and form colonies, because they can use the exogenous supply of uracil in the medium.

An advantage of this approach is that the *pyrE*-inactivated cells (prepared with the plasmid construct) are amenable to further genetic modification, if required. Thus, it is possible to construct another plasmid containing that part of the *pyrE* gene which is absent in the cells; a single crossover – which integrates this plasmid in the chromosome – is therefore able to create a complete (active) *pyrE* so that these cells can now be selected on a medium that lacks uracil (on which the *pyrE* mutants cannot grow).

[Allele-coupled exchange: Nucleic Acids Res (2012) doi: 10.1093/nar/gkr1321.]

allele drop-out (ADO) The failure of PCR to amplify one of the two alleles of a given gene.

ADO can be problematical e.g. for preimplantation genetic diagnosis (see PGD) in which the sample cell is heterozygous for the relevant gene. In some cases a PGD misdiagnosis has been due to ADO.

ADO may also cause problems in the (forensic) analysis of mixtures of DNA (i.e. DNA from more than one contributor) when only minute amounts of template DNA are available in the sample [Croat Med J (2011) 52(3):314–326].

allele-specific DNA methylation analysis Any method that is used for the assessment of allele-specific methylation. In one method, BISULFITE-treated DNA is amplified by PCR, and this is followed by PYROSEQUENCING of the amplicons, the pyrosequencing using primers that contain allele-specific single-nucleotide polymorphisms (see SNP); this method was used to analyze methylation of the *H19* gene – in which the paternal allele is usually imprinted [BioTechniques (2006) 41(6):734–739].

Using an initial nested PCR, followed by bisulfite-specific PCR, a study of gene *MCHR1* (associated with the regulation of metabolism, food intake etc.) reported allele-specific, age-dependent methylation that affected transcription [PLoS ONE (2011) doi: 10.1371/journal.pone.0017711].

allele-specific gene expression The two alleles of a given gene (in a diploid cell) may be expressed at different levels for a number of reasons – for example, one of the alleles may be transcriptionally silent owing to X-INACTIVATION, or it may be expressed at a different level owing to the presence of one or more polymorphisms (see the entry SNP) affecting transcriptional regulation.

Such differential allelic expression may be detected e.g. by a method in which the levels of mRNA from each of the two alleles are compared – the transcripts from one allele being distinguished from those of the other allele by the presence of a specific polymorphism acting as a marker [PLoS Genetics (2008) 4(2):e1000006]. Other workers screened some 11500 SNPs in order to identify differential allelic expression; they concluded that allele-specific gene expression is widespread across the (human) genome [PLoS ONE (2009) 4(1):e4150].

Allele-specific gene expression patterns were investigated by quantitative genotyping of 2529 genes from patients with acute lymphoblastic leukemia – revealing regulation of gene expression by methylation at CpG sites [Genome Res (2009) 19(1):1–11].

Allele-specific gene expression assays were carried out by using read counts from the Solexa form of massively parallel DNA sequencing [BMC Genomics (2009) 10:422].

(See also EPIGENETIC ALLELIC RATIO ASSAY.)

allele-specific PCR A variant form of PCR designed to amplify a particular allele of a given gene – but no other allele(s) of that gene. One of the two primers is designed with a 3′ terminal nucleotide that pairs with a *specific* base in the required allele – a base which is known to be different from that in the other allele(s) at this location; this primer can be extended on the required allele, which will be amplified. Other alleles are not amplified as the mismatch at the primer's 3′ terminal will inhibit extension.

An essential requirement is the use of a polymerase which *lacks* proofreading ability (i.e. one which lacks 3′-to-5′ exonuclease activity); such an enzyme (e.g. the Taq polymerase) is not able to remove the primer's terminal nucleotide (i.e. it cannot correct the mismatch) and does not amplify unwanted alleles.

It is also important to carry out the reaction with an appropriate level of stringency.

A modified form of this method is found e.g. in SNP GENOTYPING.

allelic pair See the entry ALLELE.

allelic ratio assay See e.g. EPIGENETIC ALLELIC RATIO ASSAY.

allelomorph *Syn.* ALLELE.

allolactose β-D-Galactopyranosyl-(1→6)-D-glucopyranose: the natural inducer of the LAC OPERON in *Escherichia coli*; it is formed as a minor product during the cleavage of lactose by β-galactosidase.

(See also IPTG.)

allosteric effect The effect which is produced when the binding of a ligand to a given target molecule affects the properties of other site(s) on the same molecule; allosteric effects are due to conformational changes that result from the binding of the ligand.

allosteric nucleic acid enzymes Nucleic acid enzymes (see e.g. APTAZYME) whose function can be subject to regulation e.g. by the activity of a low-molecular-weight molecule – or the activity of an oligonucleotide.

(See BINARY DEOXYRIBOZYME LIGASE and MAXIZYME.)

alpha (α, *Lk*) A symbol for LINKING NUMBER.

alpha peptide (α-peptide) See the entry α-PEPTIDE (under 'P').

alpha$_1$-antitrypsin (α_1-antitrypsin; A1AT) In humans: a SERPIN encoded by gene *SERPINA1* – also called *A1AT* – located on chromosome 14. A1AT is a serum glycoprotein of ~52 kDa; it is synthesized in the liver and is a major inhibitor of serine proteases – for example, the enzyme neutrophil elastase (EC 3.4.21.37). A deficiency of A1AT may allow elastase activity to increase to a level that causes damage to lung tissue (leading to the condition known as *pulmonary emphysema*).

Deficiency in A1AT activity can be caused e.g. by smoking or by some point mutations in the *SERPINA1* gene; abnormal (i.e. mutant) forms of A1AT include S and Z mutant forms. Individuals homozygous for the Z mutation exhibit a greatly reduced level of A1AT activity and – particularly if they are also smokers – are at high risk of emphysema.

Those with a deficiency in A1AT activity have been treated by the administration of purified A1AT.

In a proof-of-principle experiment, a biallelic correction of a point mutation in *SERPINA1* has been engineered in human induced pluripotent stem cells; it was proposed that such cells – when differentiated to liver cells – may be suitable for autologous transplantation for the treatment of A1AT deficiency [Nature (2011) doi: 10.1038/nature10424].

Alphanodavirus See the entry NODAVIRUSES.

Alpharetrovirus A genus of viruses (family RETROVIRIDAE, subfamily ORTHORETROVIRINAE).

Species include *Avian leukosis virus*, *Avian myeloblastosis virus* and *Rous sarcoma virus*.

Alphavirus A genus of viruses that include many which cause disease (involving e.g. encephalitis and arthralgia) in humans and animals. The (enveloped) virion is spherical, ~50–70 nm diam.

The (monopartite) genome is linear, positive-sense ssRNA.

Alphaviruses include e.g. SINDBIS VIRUS and *Western equine encephalomyelitis virus*.

alternation of generations See the entry PLOIDY.

alternative end-joining (A-EJ) A process of DNA repair found in some prokaryotes: see NON-HOMOLOGOUS DNA END-JOINING.

alternative polyadenylation See the entry POLYADENYLATION.

alternative splicing SPLICING of a given pre-mRNA which can proceed in at least two different ways, the different modes of splicing producing mRNAs with different overall sequences.

Alternative splicing is a common (i.e. natural) phenomenon [Nucleic Acids Res (2004) 32(13):3977–3983] which allows a given gene to encode extra information. It was reported that – exceptionally – a single gene has the potential to give rise to >100 different transcripts.

In mammals, alternative splicing apparently occurs in transcripts from most genes [Nature Rev Genet (2010) 11(5):345–355] – but it is apparently infrequent or absent in *Saccharomyces cerevisiae*.

A comparative study on a range of eight organisms reported that alternative splicing is more extensive in vertebrates than in invertebrates [Nucleic Acids Res (2007) 35(1):125–131].

Events that may occur during alternative splicing include the splicing out (loss) of an exon (*exon skipping*), inclusion of an intron (*intron retention*) and/or the (aberrant) splicing at a site *within* an exon.

The regulation of (normal) alternative splicing involves a balance between certain factors which promote or inhibit the use of specific splicing sites in pre-mRNA.

Differential, SNP-associated alternative splicing may occur in different tissues [PLoS Biol (2008) 6(12):e1000001].

[Cell-to-cell variability of alternative RNA splicing: Mol Systems Biol (2011) doi: 10.1038/msb.2011.32.]

A typical (U1-*independent*) splicing may be a characteristic feature of some types of alternative splicing [Nucleic Acids Res (2009) 37(6):1907–1914].

Alternative splicing can be involved in the regulation of a particular function – e.g. when a gene encodes two mutually antagonistic messages, each message depending on a specific mode of splicing of the pre-mRNA; in such cases, expression of the two transcripts must clearly be under a suitable level of control.

Aberrant splicing causes many types of disease. Correction of aberrant splicing has been demonstrated both *in vitro* and *in vivo* by using specifically designed *splice-switching oligonucleotides* (SSOs) that can re-direct the splicing machinery to normal splice sites. Positive results were reported with the use of SSOs in patients with Duchenne muscular dystrophy. [Therapeutic potential of splice-switching oligonucleotides (a review): Oligonucleotides (2009) 19(1):1–14.]

Studies on alternative splicing

The alternative splicing of a given gene may be investigated e.g. by initially isolating the mRNAs from the relevant living cells. (For eukaryotic cells, this can be done most easily by exploiting the poly(A) tail which characteristically forms the 3′ end of mRNAs; the cell extract is passed through a column containing the ligand oligo(dT)-cellulose that binds mRNAs (by their poly(A) tails) and allows other types of RNA (e.g. ribosomal RNA) to be eliminated.) When the mRNAs have been eluted, they are subjected to GEL ELECTROPHORESIS and the gel is then used for NORTHERN BLOTTING (q.v.); individual mRNAs can be identified, on the membrane, by using highly specific, labeled PROBES. This procedure can reveal mRNAs *of different sizes* (alternatively spliced mRNAs) derived from a given gene.

Alternative splicing may also be investigated by the use of an EXON ARRAY (q.v.).

The choice of splice site in a transcript can be modulated, *in vitro* and *in vivo*, by using a specific antisense molecule. Thus, splicing of pre-mRNA of gene *bcl-x* normally produces a long anti-apoptotic mRNA as well as a short pro-apoptotic mRNA, and the ratio of these two mRNAs in the cell can be a key determinant of cancer progression. By the use of a short antisense PNA conjugated to an oligopeptide containing eight serine–arginine repeats (cf. SR PROTEINS), it was possible to modify the splicing pattern so that the short (pro-apoptotic)

mRNA became the dominant influence; this method was able to induce APOPTOSIS in HeLa cancer cells [Nucleic Acids Res (2005) 33(20):6547–6554].

siRNA-controlled alternative splicing has been reported in which the siRNAs targeted appropriate sequences in introns or exons [Nature Struct Mol Biol (2009) 16:717–724].

Exon exclusion has been engineered with dsRNA effectors [Nucleic Acids Res (2011) doi: 10.1093/nar/gkr780].

A transcription factor that resulted from alternative splicing was reported to disrupt latency (i.e. to activate transcription) of HIV-1, offering a potential solution to quiescent infection in AIDS [Proc Natl Acad Sci USA (2009) 106:6321–6326].

(See also the entries CRYPTIC SPLICING, EXON TRAPPING, and *alternative polyadenylation* in POLYADENYLATION.)

Alu sequences (*Alu* sequences) In (at least) some mammalian genomes: a family of related sequences, each typically about 300 nt long and commonly having a recognition site for the RESTRICTION ENDONUCLEASE AluI (AG↓CT); the human genome may contain about one million copies. Alu sequences are RETROTRANSPOSONS; owing to their ability to generate insertional mutations they are seen as potential factors in genetic disorders.

Most Alu sequences in the human genome (those from subfamilies S and J) seem to be largely inactive – transpositional activity being essentially confined to a much smaller group of 'younger' Alu sequences (e.g. those in the Y family [Genome Res (2009) 19:545–555].

Some Alu sequences with regions similar to splice sites are found in certain genes and are recognized as exons. (See also EXONIZATION.) Splicing patterns of exonized Alu sequences have been described in (human) tissues [PLoS Genet (2008) 4(10):e1000225].

A study of exonizing and non-exonizing Alu sequences has reported various features required for precise recognition of exons by the splicing machinery [PLoS Comput Biol (2009) 5(3):e1000300].

(See also SINE and LINE.)

AluI A RESTRICTION ENDONUCLEASE from *Arthrobacter luteus*; recognition site: AG↓CT.

α-amanitin A complex, substituted cyclic peptide (one member of a family of toxins produced e.g. by the 'death cap fungus', *Amanita phalloides*) which, at low concentrations, can inhibit (eukaryotic) DNA-dependent RNA polymerase II.

This agent was used e.g. for studies on RNA polymerase II [PLoS ONE (2008) 3(2):e1661; Acta Crystallogr (Section D) (2009) 65(2):112–120; Genome Res (2011) 21(3):390–401].

amantadine (1-adamantanamine hydrochloride) A polycyclic ANTIVIRAL AGENT that is used (e.g.) for prophylaxis and early treatment of infection by *Influenza A virus*.

Rimantadine (α-methyl-1-adamantane methylamine hydrochloride) has similar activity.

Amantadine inhibits viral replication by blocking a proton channel formed by the M2 protein of *Influenza A virus* [Proc Natl Acad Sci USA (2008) 105(5):1483–1488].

[Structure and mechanism of proton transport through the transmembrane tetrameric M2 protein bundle of the influenza virus: Proc Natl Acad Sci USA (2010) 107:15075–15080, doi: 10.1073/pnas.1007071107].

(See also *swine flu* in the entry INFLUENZAVIRUS.)

Amaxa Nucleofector® See the entry NUCLEOFECTION.

amber codon See NONSENSE CODON.

amber mutation A mutation that creates an amber codon (see NONSENSE CODON).

amber suppressor See the entry SUPPRESSOR MUTATION.

ambisense RNA Viral ssRNA in which some gene(s) occur in positive-sense form and other(s) occur in negative-sense form (in the same strand).

Ambisense RNA occurs e.g. in the genome of viruses of the *Arenaviridae* – including *Lassa virus* – and in the genome of viruses of the genus *Phlebovirus*, e.g. the *Rift Valley fever virus*; in *Rift Valley fever virus* the tripartite genome consists of two fragments of negative-sense ssRNA and one fragment of ambisense ssRNA.

In many ambisense viruses, the junction between opposite-sense ORFs in the genome exhibits a hairpin structure which acts as a termination signal. The hairpin structures appear to be absent in the small (S) ambisense fragment in *Rift Valley fever virus*; instead, a conserved motif is reported to act as a termination signal in the ambisense fragment [J Virol (2007) 81(10):5246–5256].

AMD Age-related macular degeneration: any of certain forms of pathologic condition affecting the eyes in the elderly. One form involves the development of new blood vessels (angiogenesis) in retinal tissue. The potential for GENE THERAPY in this condition is being investigated: see e.g. AAV HELPER-FREE SYSTEM, and see also RetinoStat® in the entry GENE THERAPY.

amelanotic melanoma See MELANOMA.

amelogenin A protein associated with dental development. A gene encoding human amelogenin (*AMELX*) occurs on the X chromosome (at location Xp22.3–Xp22.1) and another gene encoding amelogenin (*AMELY*) occurs on the Y chromosome (location Yp11.2).

The amelogenin genes are exploited e.g. in a gender identification assay: see DNA SEX DETERMINATION ASSAY.

***AMELX* gene** See the entry AMELOGENIN.

***AMELY* gene** See the entry AMELOGENIN.

Ames strain (of *Bacillus anthracis*) See BACTERIA (table).

Ames test (Mutatest; *Salmonella*/microsome assay) A test used to determine whether a given agent is mutagenic (and therefore possibly carcinogenic) by investigating its ability to *reverse* an auxotrophic mutation in *Salmonella typhimurium*; the mutation in *S. typhimurium* makes the organism dependent on an exogenous source of histidine, and reversal of the mutation would allow the organism to synthesize its own histidine (i.e. it would revert to prototrophy). Different strains of *S. typhimurium* may be used, each with a different type of mutation in the histidine operon. Some of these test strains may also contain mutations which make them more permeable to certain chemicals and/or which prevent them from carrying out DNA repair. Moreover, the test strains may contain the

plasmid pKM101 which includes genes for so-called error-prone repair and which therefore promotes the mutagenic effects of any DNA-damaging agents present in the reaction.

Because certain chemical agents exhibit mutagenic activity only after their metabolic activation, the test system generally includes microsomal enzymes from a liver homogenate (the 9000 *g* supernatant, fraction 'S9') from rats pre-treated with a carcinogen to induce production of the appropriate enzymes.

When performed as a 'plate incorporation test', a culture of *S. typhimurium*, an S9 preparation and the substance under test are mixed with soft agar (which includes a low level of histidine) and this is poured onto a plate of *minimal agar* – which is then incubated at 37°C in the dark. (Minimal agar permits the growth of prototrophs but does not permit growth of the (auxotrophic) test strain of *S. typhimurium*.) The low level of histidine in the soft agar allows (only) limited growth of the (auxotrophic) *S. typhimurium* and this results in a light, confluent growth of this organism in the upper layer of agar (the 'top agar').

If the test substance had caused reversion to prototrophy in any cells of the test strain, those cells (whose growth would not be limited) can grow and form visible colonies.

When interpreting the results, several factors must be borne in mind. An absence of growth in the top agar would suggest that the substance under test has general antibacterial activity, and that any colonies which develop on the plate are unlikely to be true revertants. Again, before drawing conclusions from a number of *apparent* revertant colonies, it is necessary to take into account the known *spontaneous* reversion rate of the particular mutation in the given test strain.

Various modifications of the basic Ames test are used for specific purposes.

[Ames test with a derivative of carbamic acid: Antimicrob Agents Chemother (2005) 49:1160–1168.]

An Ames test was employed in an assay of mutagenicity on certain sulfur analogs of polycyclic aromatic hydrocarbons [J Org Chem (2007) 72(22):8383–8393].

[Comparison of Ames II and traditional Ames test responses with respect to mutagenicity, strain specificities, need for metabolism and correlation with rodent carcinogenicity: Mutagenesis (2009) 24(4):359–366.]

(See also CELL TRANSFORMATION ASSAY, GENOTOXICITY TEST and SOS CHROMOTEST.)

amethopterin (methotrexate) The agent 4-amino-4-deoxy-10-N-methyl-pteroylglutamic acid – also referred to as 4-amino-10-methylfolic acid: a folic acid analog which blocks nucleotide synthesis; this agent is used e.g. in the chemotherapy of leukemia.

(cf. AMINOPTERIN.)

amikacin See the entry AMINOGLYCOSIDE ANTIBIOTIC.

amino acid A term which (in the context of DNA technology) generally refers to one of 20 compounds (listed in the table) whose residues are common components of oligopeptides, polypeptides and proteins. Each amino acid is represented by at least one CODON (see the table, and see GENETIC CODE).

Ornithine is just one example of an amino acid which is not represented by a CODON but which is nevertheless found e.g. in some oligopeptide antibiotics; this kind of oligopeptide is synthesized by a ribosome-free enzyme system rather than by translation (see NON-RIBOSOMAL PEPTIDE SYNTHETASE).

4-amino-10-methylfolic acid See the entry AMETHOPTERIN.

aminoalkylsilane See the entry the entry AAS.

4-aminofolic acid See the entry AMINOPTERIN.

aminoglycoside antibiotic Any of a group of (broad-spectrum) antibiotics in which the molecular structure typically includes an aminosugar and either 2-deoxystreptamine or streptidine; these antibiotics bind to the bacterial 30S ribosomal subunit and inhibit protein synthesis.

The aminoglycosides include amikacin, framycetin, gentamicin, hygromycin B, kanamycin, neomycin, streptomycin and tobramycin; they are typically bactericidal (at appropriate concentrations) and are active against a wide range of Gram-positive and Gram-negative species.

Resistance to aminoglycosides can arise e.g. by (i) mutation in proteins of the ribosomal 30S subunit (affecting the binding of antibiotics); (ii) inactivation of antibiotics by bacterial enzymes which e.g. carry out *N*-acetylation or *O*-phosphorylation; (iii) decreased uptake by the cell.

(See also G418 SULFATE.)

aminopterin 4-Amino-4-deoxy-pteroylglutamic acid (4-aminofolic acid): an agent which blocks the pathway of nucleotide synthesis. It is used e.g. for preparing a HYBRIDOMA (q.v.).

[Example of the use of aminopterin (for the preparation of a hybridoma): PLoS Pathog (2012) 8(1):e1002474.]

(cf. AMETHOPTERIN.)

amitrole 3-amino-1,2,4-triazole: a NON-GENOTOXIC CARCINOGEN.

AML See ACUTE MYELOID LEUKEMIA.

amniotes Collectively, the reptiles, birds and mammals.

AMO Anti-miRNA oligonucleotide: see e.g. MICRORNAS.

AMP CT Amplified *Chlamydia trachomatis* test: a TMA-based assay used for detecting the pathogen *Chlamydia trachomatis* in clinical specimens (Gen-Probe, San Diego CA). One early study [J Clin Microbiol (1997) 35:676–678] examined urine specimens from female patients as a non-invasive method of diagnosing chlamydial infection; both the AMP CT assay and a PCR-based method were found to be sensitive and specific methods for detecting *C. trachomatis* – and it was concluded that both methods were suitable screening procedures.

ampholyte Any electrolyte with both acidic and basic groups.

ampicillin 6(α-aminobenzylamido)-penicillanic acid – a semi-synthetic PENICILLIN used in media e.g. as a selective agent for bacteria containing a vector with an ampicillin-resistance marker gene.

amplicon (1) A specific (precise) sequence of nucleotides, part of a larger nucleic acid molecule, which is copied (amplified) by an *in vitro* amplification process (e.g. NASBA, PCR or SDA). (2) One of the copies of a sequence of nucleotides which has been copied (amplified) by methods such as NASBA or PCR. (3) One of a number of elements of linear DNA (~100 kb) formed in studies on the *JBP1* gene of *Leishmania tarentolae*

Amino acids: symbols, molecular weights and codons

Amino acid	1-letter symbol	3-letter symbol	Molecular weight	Codons
Alanine	A	Ala	89	GCA, GCC, GCG, GCU
Arginine	R	Arg	174	AGA, AGG, CGA, CGC, CGG, CGU
Asparagine	N	Asn	150	AAC, AAU
Aspartic acid	D	Asp	133	GAC, GAU
Cysteine	C	Cys	121	UGC, UGU
Glutamic acid	E	Glu	147	GAA, GAG
Glutamine	Q	Gln	146	CAA, CAG
Glycine	G	Gly	75	GGA, GGC, GGG, GGU
Histidine	H	His	155	CAC, CAU
Isoleucine	I	Ile	131	AUA, AUC, AUU
Leucine	L	Leu	131	CUA, CUC, CUG, CUU, UUA, UUG
Lysine	K	Lys	146	AAA, AAG
Methionine	M	Met	149	AUG
Phenylalanine	F	Phe	165	UUC, UUU
Proline	P	Pro	115	CCA, CCC, CCG, CCU
Serine	S	Ser	105	AGC, AGU, UCA, UCC, UCG, UCU
Threonine	T	Thr	119	ACA, ACC, ACG, ACU
Tryptophan	W	Trp	204	UGG
Tyrosine	Y	Tyr	181	UAC, UAU
Valine	V	Val	117	GUA, GUC, GUG, GUU

[term used in: Nucleic Acids Res (2005) 33(5):1699–1709].
(4) *Formerly* [Proc Natl Acad Sci USA (1985) 82:694–698]: a defective virus vector.
(5) Within a Y chromosome: a segment with >99% sequence identity to other region(s) in that chromosome (hence adjective *ampliconic*). [Use of term: BMC Genet (2007) 8:11; Hum Reprod Update (2010) 16(5):525–542, doi: 10.1093/humupd/dmq005.]
(6) A construct which, when suitably packaged, can be used as a gene-delivery vehicle: see HSV-1 AMPLICON.
(7) A given sequence of nucleotides *within which* a specific sub-region may be identified as being of special interest and which may be treated as an amplicon (sense 1).

amplicon containment One approach to the minimization of contamination by amplicons from previous assays in methods such as PCR. Essentially, this involves division of the working environment into several dedicated areas, each of which is used for only certain stage(s) of the work. For example, in PCR it is usual to conduct thermal cycling and the analysis of products (e.g. electrophoresis) in separate areas, and separate areas may also be specified for extracting target nucleic acid and for preparing reagents.
(See also AMPLICON INACTIVATION and SUICIDE PCR.)

amplicon inactivation In PCR: any method which avoids contamination by destroying carry-over amplicons from previous assays. Carry-over contamination can be a major problem in clinical laboratories in which samples are examined routinely for only a limited number of target sequences; in these cases, new assays risk contamination if the amplicons are allowed to build up in the laboratory – e.g. in or on equipment or in reagents.

Methods for amplicon inactivation

The uracil-N-glycosylase method. In this method, *all* assays are conducted in the normal way except that deoxythymidine triphosphate (dTTP) is replaced by deoxyuridine triphosphate (dUTP) in the reaction mixture. All the amplicons produced (in every assay) thus contain dUMP instead of dTMP. These amplicons can be analysed in the normal way by gel electrophoresis etc.

In addition to dUTP, the reaction mixture also includes the enzyme URACIL-N-GLYCOSYLASE (UNG). Consequently, if an assay is contaminated with amplicons from a previous assay,

these amplicons will act as substrates for the enzyme – uracil being cleaved from each dUMP; this, in itself, does not bring about strand breakage, but these amplicons are degraded to non-amplifiable pieces by the high temperature used for the initial denaturation of target DNA. The high temperature also inactivates UNG – which is necessary in order to avoid the degradation of amplicons from the current assay. Note that the *target* DNA in the reaction is not affected by UNG as it contains dTMP.

Normally, this method is not used in PCR-based studies of DNA *methylation* in which the sample DNA is treated with BISULFITE; the reason is that bisulfite converts non-methylated cytosines to uracil, so that the template DNA itself would be subjected to degradation. However, unlike the usual method of bisulfite treatment (in which DNA is sulfonated and is subsequently desulfonated), it was found that *non*-desulfonated DNA can be amplified by PCR using the UNG method of decontamination because sulfonated DNA is resistant to UNG. During PCR, the DNA is desulfonated by a prolonged (30-minute) initial stage of denaturation (at 95°C) [Nucleic Acids Res (2007) 35(1):e4].

The isopsoralen method. In this method isopsoralen is added to the reaction mixture. Isopsoralen is a heterocyclic compound which, when bound to DNA, can form covalent interstrand crosslinks when photoactivated by ultraviolet radiation (e.g. 365 nm/15 min at 4°C). Activation of isopsoralen at low temperatures was reported to be more efficient than at room temperature. As the double-stranded amplicons are *covalently* crosslinked they cannot be denatured to single strands; hence, they cannot serve as templates, so that, if they contaminate a subsequent assay the outcome would not be affected.

Amplicons produced by this method are suitable for examination by processes such as gel electrophoresis and staining (e.g. for confirming the presence of a given target sequence in the sample DNA). However, they cannot be used for any process (such as SSCP analysis) that requires single-stranded samples.

APSR. In another approach to amplicon inactivation, all the primers have a 5′ tag which incorporates a binding site for a type IIS restriction endonuclease; this enzyme, in the reaction mixture, cleaves any contaminating amplicons – and is itself inactivated at the initial high-temperature stage (see APSR).

amplicon primer site restriction See the entry APSR.

ampliconic See the entry AMPLICON (sense 5).

amplification (of DNA *in vitro*) See DNA AMPLIFICATION.

amplification (of RNA *in vitro*) See RNA AMPLIFICATION.

amplification-refractory mutation system See ARMS.

amplified fragment length polymorphism (AFLP) See AFLP.

amplified restriction fragment length polymorphism A non-recommended name used for a method for TYPING bacteria – see the entry AFLP.

amplified ribosomal DNA restriction analysis See ARDRA.

Ampligase® See DNA LIGASE.

amplimer Any primer used in PCR.

AmpliTaq™ Gold DNA polymerase A 94-kDa thermostable, recombinant DNA polymerase (Applied Biosystems) used in PCR; its optimal extension temperature is reported to be 72–80°C, with an extension rate of 2–4 kb/min at 72°C.

[Uses (e.g.): Malaria J (2009) 8:154; Mol Vision (2009) 15: 1620–1630; Brain (2012) 135(5):1423–1435.]

AmpliWax™ See the entry HOT-START PCR.

AMPPD® A 1,2-dioxetane substrate that emits light when it is de-phosphorylated by the enzyme ALKALINE PHOSPHATASE. It is used e.g. for detecting AP-labeled probes.

(See also CHEMILUMINESCENCE.)

amprenavir See the entry PROTEASE INHIBITORS.

AMTDT Amplified *Mycobacterium tuberculosis* direct test: a TMA-based assay for detecting *Mycobacterium tuberculosis* in clinical specimens (Gen-Probe, San Diego CA).

AMTDT was approved in ~1995/6 by the American FDA (Food and Drug Administration) for use with *smear-positive* respiratory specimens; a smear-positive specimen is one from which a smear showing ACID-FAST BACILLI can be prepared.

In the original test, the specimen was initially treated with a MUCOLYTIC AGENT and was then decontaminated with NaOH and sonicated (to lyse organisms and release nucleic acids). The specimen was subsequently heated (95°C/15 minutes) to remove intra-strand base-pairing in the rRNA.

The reaction mixture contained 45 µL or 50 µL of sample, and amplification (at 42°C) was conducted for 2 hours. The amplification product was detected by the addition of target-specific probes (for details see entry ACCUPROBE).

An attempt was made to adapt AMTDT for the detection of *Mycobacterium tuberculosis* in *non*-respiratory specimens [J Clin Microbiol (1997) 35:307–310], and studies were made to compare the original and subsequent (improved) versions of AMTDT for the detection of *M. tuberculosis* in respiratory and non-respiratory specimens [J Clin Microbiol (1998) 36: 684–689].

The new-format 'enhanced' AMTDT was approved by the FDA in 1998. Among other changes, this version involved the use of a 450 µL aliquot of the sample (instead of a 40–50 µL sample).

One study, using the original version of the test, reported false-positive results in tests on sputa from patients infected with *Mycobacterium kansasii* and *M. avium*; these species of *Mycobacterium* are not infrequently isolated from infections in immunocompromised (e.g. AIDS) patients. The authors of this study suggested changing the threshold value of luminometer readings that were considered to be an indication of a positive result [J Clin Microbiol (1999) 37:175–178].

anaerobic respiration RESPIRATION (q.v.) which occurs in the absence of oxygen – cf. FERMENTATION (sense 2).

analyte In a test system: that component whose properties are being studied/measured.

anchor primer A primer that binds to an ANCHOR SEQUENCE.

anchor sequence Commonly, a sequence of nucleotides, with a known composition, which is present in a given molecule or which is ligated to another sequence (or added by tailing) in order to serve a particular function – e.g. as a primer-binding

site. For example, in ANCHORED PCR an anchor sequence is used to provide an otherwise unavailable site for priming the amplification of an unknown sequence.

Certain natural sequences, such as the poly(A) tail on many mRNA molecules, have been described as anchor sequences.

anchored PCR A form of PCR used for amplifying an unknown sequence of nucleotides adjacent to a known sequence on a fragment of DNA; this approach addresses the problem of the lack of a primer-binding site in the unknown sequence.

To each end of the fragment is ligated a short segment of DNA of known sequence (e.g. a linker). (If the fragment has 3′ or 5′ overhangs then these can be eliminated, enzymically, in order to prepare the fragment for blunt-end ligation to the linkers.) Following ligation, that linker which is contiguous with the unknown region provides an ANCHOR SEQUENCE that is able to serve as a primer-binding site for one of the PCR primers. The second primer is designed to bind at a site within the known sequence. If PCR is primed in this way, the resulting amplicons will include the unknown sequence and at least part of the known sequence. If the known sequence occurs in the *center* of the fragment, then amplification, as described above, can be carried out for both of the unknown flanking regions.

(See also TAIL-PCR and VECTORETTE PCR.)

anchoring enzyme In SAGE (q.v.): a name sometimes given to the enzyme used for initial cleavage of the cDNAs.

ancient DNA (aDNA) DNA recovered from specimens which are thousands or millions of years old.

(See also PALEOMICROBIOLOGY.)

[Isolation of ancient DNA (optimization of methodology): BioTechniques (2007) 42(3):343–352.]

A method has been described for isolating DNA from fluid inclusions within the mineral halite [PLoS ONE (2011) 6(6): e20683].

(See also SPEX and SUICIDE PCR.)

Studies on (permafrost-derived) mammoth bones provided some indication that mitochondrial DNA is preserved better than nuclear DNA in permafrost [Nucleic Acids Res (2009) doi: 10.1093/nar/gkp159].

[Generating microsatellite data from fossil bones of extinct megafauna: PLoS ONE (2011) 6(1):e16670.]

An assay for *specific* DNA sequences was based on SERRS (surface-enhanced resonance Raman scattering) technology; as this assay is independent of amplication, it was suggested that it may be suitable for detecting ancient or degraded DNA which may be refractory to methods (such as PCR) involving amplification. The method is outlined below.

The (liquid) sample, containing two types of PROBE, is first heated (99°C, 10 minutes) in order to denature target DNA, if present. Probe–target binding occurs at 55°C (3 hours) with gentle agitation. The BIOTIN-labeled *capture probe* binds to one sequence of the target DNA. A 22-base *detection probe*, labeled with rhodamine 6G, binds to another sequence of the target DNA. Addition of streptavidin-coated magnetic beads allows the probe-bound target sequences to be captured (see DYNABEADS) and unbound probes to be removed by washing. The hybridized detection probes are then eluted at 95°C (20 minutes) and the rhodamine 6G detected by Raman spectroscopy; the signal is proportional to the concentration of the target DNA [PLoS ONE (2011) 6(5):e17847, doi: 10.1371/journal.pone.0017847].

ANDENYALAA The (10-amino-acid) tag which functions as a proteolysis signal on an aborted protein in the TRANS TRANSLATION process (q.v.).

aneuploid Refers to a genome that has one or more chromosomes in excess of, or less than, the number characteristic of the species (see e.g. DOWN'S SYNDROME).

Angelman syndrome A disorder that may be caused by any of various genetic mechanisms – see the table in entry GENETIC DISEASE for further details.

angiogenesis (neovascularization) Development of (new) blood vessels – e.g. in an embryo or in a tumor.

(See CANCER THERAPY for approaches to anti-angiogenesis therapy.)

anhidrosis Failure to produce sweat under relevant conditions.

(See also CIPA in the entry EXON SKIPPING, sense 1.)

annealing The hybridization of two complementary (or near-complementary) sequences of nucleotides to form a double-stranded molecule or a double-stranded region within a larger molecule (e.g. the binding of primers to primer-binding sites in PCR).

annotation Information supplied with the database entry of a given sequence or gene.

For an uncharacterized gene, the annotation may include a predicted function and/or an attempted characterization of the gene's product based on sequence homology with a gene of known function present in another organism.

(See also ACCESSION NUMBER.)

antagomir Any of a range of synthetic, chemically engineered oligonucleotides that bind to, and antagonize, specific types of MICRORNA molecule. Intravenous administration (in mice) of antagomirs directed against particular miRNAs resulted in efficient and specific silencing of the given miRNAs [Nature (2005) 438:685–689].

[*Lentivirus*-mediated antagomir expression for the specific inhibition of miRNA function: Nucleic Acids Res (2007) 35: e149.]

Antagomirs have been used to study the role of microRNAs miR-27a and miR-451 in regulating the expression of *MDR*1/P-glycoprotein in ovarian cancer cells [Biochem Pharmacol (2008) 76(5):582–588], and in a study on the TAR miRNA of HIV-1 [Retrovirology (2009) 6:18].

PNA molecules have been used to block the expression of miR-155 in cultured B cells [Nucleic Acids Res (2010) doi: 10.1093/nar/gkq160].

Treatment of tumor-bearing mice with miR-10b antagomirs was reported to suppress breast cancer metastasis [Nature Biotechnol (2010) 28(4):341–347, doi: 10.1038/nbt.1618].

anthrax toxin A toxin, produced by the Gram-positive pathogen *Bacillus anthracis*, which gives rise to the symptoms of

anthrax. It comprises three protein components – each, alone, being unable to function as a toxin; these three proteins are encoded by the plasmid pXO1. (Another plasmid, pXO2, is needed for the pathogenicity of *B. anthracis*; this encodes an essential anti-phagocytic capsule which protects the organism from the host's immune system.)

One component of the toxin localizes in the cell membrane and permits internalization of the other two components – a zinc protease (which disrupts intracellular signaling) and an ADENYLATE CYCLASE (which e.g. promotes edema).

anti Abbreviation for ANTICLINAL.

anti-miRNA oligonucleotide See e.g. the entry MICRORNAS.

anti-oncomir See the entry ONCOMIR.

antibiotic Any of an extensive range of natural, semi-synthetic and fully synthetic compounds which, in low concentrations, are able, selectively, to inhibit or kill specific types of micro-organism and, in some cases, other types of cell – e.g. tumor cells; an antibiotic acts at specific site(s) in a susceptible cell. (Compounds that are active against *viruses* are usually called 'antiviral agents' rather than antibiotics.)

Natural antibiotics (see e.g. BACTERIOCIN) have ecological roles. Some types of antibiotic have medical/veterinary uses in the prevention and/or treatment of infectious diseases, and some (e.g. nisin) are used as food preservatives.

(For some examples of antibiotics see e.g. AMINOGLYCOSIDE ANTIBIOTIC; CHLORAMPHENICOL; β-LACTAM ANTIBIOTICS; OXAZOLIDINONE ANTIBIOTICS; QUINOLONE ANTIBIOTICS, QUINOXALINE ANTIBIOTICS, RIFAMYCINS and VANCOMYCIN.)

Antibiotics in DNA technology

In DNA technology, antibiotics are used in various *selective* procedures. An antibiotic in a growth medium can select for those cells that are expressing a gene conferring resistance to that antibiotic; those cells that are susceptible to the antibiotic – i.e. those which lack the relevant antibiotic-resistance gene – are growth-inhibited or killed by the antibiotic.

An antibiotic-resistance gene may be included in a vector used for transfection of a population of cells; the cells which internalize the vector (and which also express the antibiotic-resistance gene) can then be selected by growth on a medium containing the relevant antibiotic.

General features of antibiotics

An antibiotic may be MICROBICIDAL or MICROBISTATIC (q.v.) – but at lower concentrations, one that is normally microbicidal may behave as a microbistatic agent.

A mixture of antibiotics may behave synergistically or antagonistically (or may not display either effect).

Synergism is shown when different antibiotics, that are acting (simultaneously) on a given organism, produce an effect which is greater than the sum of their individual effects. For example, sulfamethoxazole and trimethoprim block different reactions in the same major metabolic pathway: sulfamethoxazole inhibits the formation of dihydrofolic acid (DHF), and trimethoprim inhibits the conversion of DHF to the important coenzyme tetrahydrofolate (THF); these two antibiotics act synergistically and are used together in the therapeutic agent *cotrimoxazole*.

Antagonism, the converse of synergism, can occur in different ways. In one form, an antibiotic that inhibits growth (e.g. CHLORAMPHENICOL) antagonizes those antibiotics (such as the β-lactam antibiotics) whose activity depends on growth in the target cell. In another form of antagonism, certain antibiotics stimulate cells to produce enzymes that inactivate *other* antibiotics; in one example, the β-lactam imipenem (or cefoxitin) induces synthesis of *β-lactamases* – enzymes that inactivate certain other β-lactam antibiotics.

Modes of action

To be effective at all, an antibiotic must be able to enter, or pass through, the cell envelope in order to reach the relevant target site(s). Moreover, an antibiotic can be effective against a given population of cells only if its concentration is above the appropriate minimum level for that agent under the given conditions.

Modes of action include:

- Interference with DNA gyrase (a topoisomerase), with consequent inhibition of DNA synthesis (e.g. novobiocin, quinolone antibiotics).
- Depletion of guanine nucleotides (by inhibiting synthesis of GMP), affecting the synthesis of nucleic acids (e.g. MYCOPHENOLIC ACID).
- Binding to ribosomes and inhibiting protein synthesis (e.g. aminoglycoside antibiotics, chloramphenicol, macrolide antibiotics (such as erythromycin), tetracyclines, viomycin).
- Binding to RNA polymerase, inhibiting transcription (e.g. rifamycins).
- Disruption of the bacterial cytoplasmic membrane – altered membrane permeability affecting the cell's integrity/survival (e.g. gramicidins, polymyxins).
- Inhibition of synthesis of the bacterial cell wall polymer peptidoglycan, leading to cell lysis (e.g. β-lactam antibiotics, vancomycin).
- Inhibition of the enzyme dihydrofolate reductase, thereby inhibiting tetrahydrofolate-dependent reactions, e.g. synthesis of deoxythymidine – and hence, synthesis of DNA (e.g. pyrimethamine, trimethoprim).
- Interference with DNA function by intercalating agents (e.g. actinomycin D, quinoxaline antibiotics).
- Interaction with sterols in the cytoplasmic membrane (e.g. in yeasts and other fungi), causing leakage (e.g. polyene antibiotics).
- Inhibition of the enzyme chitin synthase (in certain fungi), affecting cell wall synthesis (e.g. polyoxins).

Mechanisms of bacterial resistance to antibiotics

Resistance to a particular type of antibiotic is *constitutive* in cells which (i) lack the antibiotic's specific target, (ii) have a variant form of the target which is not susceptible to the antibiotic, and (iii) are impermeable to the antibiotic. Examples: (i) *Mycoplasma* is resistant to β-lactam antibiotics because it lacks a cell wall; (ii) strains of *Staphylococcus aureus* known as MRSA (methicillin-resistant *S. aureus*) generally contain a modified target PBP that is not susceptible to methicillin; (iii)

Antibiotic: some antibiotics used in DNA technology (e.g. for marker selection)

Antibiotic	Group	Target organisms	Antibiotic action
Actinomycin D	–	Prokaryotic and eukaryotic	Intercalating agent; inhibits DNA-dependent RNA polymerase
Ampicillin	β-Lactams	Bacteria	Blocks synthesis of cell-wall polymer peptidoglycan
Blasticidin S	Nucleoside	Prokaryotic and eukaryotic	Inhibits protein synthesis by inhibiting the peptidyltransferase-mediated reaction at the ribosome
Carbenicillin	β-Lactams	Bacteria	Blocks synthesis of cell-wall polymer peptidoglycan
Cefotaxime	β-Lactams	Bacteria (mainly Gram-negative)	Blocks synthesis of cell-wall polymer peptidoglycan
Chloramphenicol (= chloromycetin)	–	Bacteria (broad spectrum), some eukaryotes	Binds to prokaryotic and mitochondrial ribosomes; inhibits peptidyltransferase and (hence) protein synthesis. (See the entry CHLORAMPHENICOL)
G418 sulfate	Related to gentamicin	Prokaryotes, yeasts, plants, mammalian cells	Inhibits protein synthesis
Gentamicin	Aminoglycosides	Bacteria	Binds to 30S subunit of bacterial ribosomes and inhibits protein synthesis
Hygromycin B	Aminoglycosides	Mammalian and plant cells	Inhibits protein synthesis
Kanamycin	Aminoglycosides	Bacteria	Binds to 30S subunit of bacterial ribosomes and inhibits protein synthesis
Kasugamycin	Aminoglycosides	Bacteria, some fungi	Inhibits polypeptide chain initiation and, hence, protein synthesis
Mycophenolic acid	–	Bacteria (also antitumor agent)	Inhibits synthesis of guanosine monophosphate, inhibiting synthesis of nucleic acids
Nalidixic acid	Quinolones	Bacteria (mainly Gram-negative)	Inhibits function of the A subunit of gyrase; inhibits DNA synthesis
Novobiocin	–	Bacteria	Inhibits binding of ATP to the B subunit of gyrase, inhibiting DNA synthesis
Penicillin G (= benzylpenicillin)	β-Lactams	Bacteria (mainly Gram-positive)	Blocks synthesis of cell-wall polymer peptidoglycan
Polymyxin B	Polymyxins	Bacteria (mainly Gram-negative)	Increases permeability of the cytoplasmic membrane and affects the integrity of the outer membrane
Puromycin	Nucleoside	Prokaryotic and eukaryotic	Inhibits protein synthesis by acting as an analog of part of an aminoacyl-tRNA
Rifampicin	Rifamycins	Bacteria (mainly Gram-positive)	Inhibits DNA-dependent RNA polymerase by binding to the β subunit of the enzyme
Streptomycin	Aminoglycosides	Bacteria, some fungi	Interacts with ribosomes and inhibits protein synthesis
Tetracycline	Tetracyclines	Bacteria	Binds to ribosomes; inhibits protein synthesis by blocking the binding of aminoacyl-tRNAs to the A site
Thiamphenicol	Derivative of chloramphenicol	Bacteria (broad spectrum) and some eukaryotes	As for chloramphenicol. (See the entry THIAMPHENICOL)
Zeocin™	Bleomycin/ phleomycin	Bacteria, yeast and mammalian cells	Binds to, and cleaves, DNA

typically, Gram-negative bacteria are insensitive to penicillin G (a β-lactam antibiotic) because this antibiotic is not able to penetrate their outer membrane.

As well as constitutive resistance (see above) resistance can be acquired e.g. by mutation, or by the acquisition of plasmid (or transposon) gene(s) specifying resistance to one or more types of antibiotic.

[Origins and evolution of antibiotic resistance: Microbiol Mol Biol Rev (2010) 74(3):417–433.]

Examples of resistance mechanisms include:

• Due to mutation, the target of a given antibiotic may be altered so that it fails to bind the antibiotic; consequently, the target (e.g. an enzyme) is not affected by otherwise inhibitory concentrations of that antibiotic. Thus e.g. a mutant form of the ribosomal protein L22 in *Staphylococcus aureus* confers resistance to quinupristin/dalfopristin (Synercid®), a streptogramin, and in *Mycobacterium tuberculosis* point mutations in the *rpoB* gene (encoding the β subunit of RNA polymerase) can confer resistance to rifamycins (such as rifampin) for which RNA polymerase is the target.

A novel mechanism for antibiotic resistance was reported in the Gram-positive pathogen *Streptococcus pneumoniae*; in this organism, resistance to linezolid (an oxazolidinone antibiotic) is linked to mutation in a gene that encodes a methyltransferase which, in *sensitive* strains, methylates a site in the 23S rRNA (the target for linezolid) [Genome Res (2009) 19: 1214–1223].

A mutation can also *increase the level of resistance* to antimicrobial agents. For example, mutation in a single base-pair in *Neisseria gonorrhoeae* creates a new, *stronger* promoter for an OPERON that encodes an efflux pump for antimicrobial agents; enhanced expression of this operon results in a higher level of resistance [mBio (2011) doi: 10.1128/mBio.00187-11].

• Transposon Tn*10* encodes an inducible efflux system that enables certain Gram-negative bacteria to externalize tetracycline via an 'efflux pump' located in the cell envelope.

• Mutant forms of certain envelope proteins are associated with decreased permeability. For example, alteration in outer membrane porins in *Enterobacter aerogenes* increases resistance to certain antibiotics, and in *Pseudomonas aeruginosa* resistance to the aminoglycosides and other antibiotics can be determined through membrane permeability controlled by a TWO-COMPONENT REGULATORY SYSTEM.

• Degradation of antibiotics by plasmid-encoded or chromosome-encoded enzymes. Such enzymes include the inducible and constitutive β-LACTAMASES that cleave the β-lactam ring in, and inactivate, β-lactam antibiotics such as penicillins and cephalosporins. The enzyme chloramphenicol acetyltransferase, which degrades CHLORAMPHENICOL, is another example – as are acetyltransferases, adenylyltransferases and phosphotransferases that inactivate aminoglycoside antibiotics.

• Increased production of an affected metabolite; thus, e.g. synthesis of high levels of *p*-aminobenzoic acid (PABA) may overcome the effect of competitive inhibition by sulfonamide antibiotics.

• Gene amplification. At least some bacteria respond to antibiotics by a gene amplification mechanism which can e.g. upregulate enzymes that hydrolyze antibiotic(s). [Bacterial gene amplification: Nature Rev Microbiol (2009) 7:578–588.]

• In enterococci, the use of antibiotics may have predisposed the organisms to acquire mobile genetic elements that confer multidrug resistance [mBio (2010) 1(4):e00227-10, doi: 10.1128/mBio.00227-10].

[Antibiotic resistance genes (database): Nucleic Acids Res (2009) 37(Database issue):D443–D447.]

Nucleic-acid-based tests for antibiotic resistance

See the entry ANTIBIOTIC RESISTANCE TESTING, below.

antibiotic resistance testing (nucleic-acid-based approaches for bacteria) The traditional, culture-based methods for detecting antibiotic resistance in bacteria are suitable mainly for those species (for example, *Escherichia coli* and *Salmonella* spp) that grow rapidly (within ~24–48 hours) on laboratory media; for these species sensitivity to a particular antibiotic is shown by growth inhibition in the presence of the given antibiotic. Resistance to particular antibiotics in such organisms may be determined e.g. by growing the organisms on agar plates that have antibiotic-impregnated paper disks on the surface; antibiotics diffuse out from the disks, and organisms sensitive to a given antibiotic form a zone of growth-inhibition around the relevant disk. This *disk diffusion* method was reported to be less accurate than the 'agar dilution' method for testing the susceptibility of *Campylobacter* spp [J Clin Microbiol (2012) 50(1):52–56, doi: 10.1128/JCM.01090-11].

Growth-based methods are less satisfactory for some slow-growing species (such as *Mycobacterium tuberculosis*) – and for pathogens such as *Chlamydia trachomatis* (which have a complex life cycle, and which fail to grow on ordinary laboratory media). Moreover, while culture-based methods can, in some cases, indicate the MIC (i.e. the minimum inhibitory concentration) of a given antibiotic (using e.g. the so-called E test) they give no information regarding the precise causation (i.e. mechanism) of resistance.

DNA-based ('genotypic') methods for detecting antibiotic resistance in various organisms have developed over the last few decades. Below is a brief glimpse at some of the methods used for testing two major pathogens: *Staphylococcus aureus* and *Mycobacterium tuberculosis*. (Resistance of the Gram-negative species *Pseudomonas aeruginosa* to tobramycin has been investigated by the TN-SEQ CIRCLE METHOD.)

Staphylococcus aureus

Among early studies a BDNA ASSAY was used for detecting the MECA GENE of *S. aureus* in samples from blood-culture bottles (without the usual prior subculture to solid media) [J Clin Microbiol (1999) 37:4192–4193]; it was suggested that the results of this approach could help the clinician to choose an appropriate antibiotic (β-lactam or vancomycin) to match the actual requirement of an infection.

MULTIPLEX PCR has also been used for detecting the *mecA gene* (and the COA GENE) in *S. aureus*.

A pentaplex assay (targeting five genes) has been designed (a) to detect *S. aureus*, (b) to identify the *mecA* gene, and (c) to help distinguish between *community-acquired* MRSA and hospital-acquired MRSA (see the entry MRSA); for the latter purpose, one of the targeted genes was *lukS* – which encodes the PANTON–VALENTINE LEUCOCIDIN [BMC Microbiol (2009) 9:113].

Mycobacterium tuberculosis

The resurgence of *M. tuberculosis* as a major threat, and the appearance of multidrug-resistant (MDR) strains, has given a strong impetus to the search for suitable nucleic-acid-based methods for detecting antibiotic resistance in this organism. Unlike resistance to β-lactam antibiotics in *S. aureus*, which is commonly due to specific gene products (e.g. PBP 2a or β-lactamase enzymes), the resistance of *M. tuberculosis* to anti-tuberculosis drugs usually arises through mutation(s); these mutations affect the genes whose products are the targets of anti-tuberculosis drugs. While resistance to some drugs (e.g. isoniazid, streptomycin) can be due to mutation in more than one gene, resistance to rifampin (see RIFAMYCINS) is usually due to mutation(s) in only one gene – *rpoB* – which encodes the β-subunit of RNA polymerase. Detecting resistance to rifampin is, therefore, technically simpler. Moreover, strains resistant to rifampin are frequently resistant to various other anti-tuberculosis drugs, so that resistance to rifampin may be a useful marker for multi-resistant strains.

Mutations in the *rpoB* gene are detected in various ways. In some methods the initial step is to use PCR to copy the *rpoB* gene – or a particular region of *rpoB* in which the resistance-associated mutations commonly occur. The PCR products are then examined e.g. by SSCP ANALYSIS or by LINE PROBE ASSAY. Both methods are able to indicate *specific* mutations in the *rpoB* gene. (By identifying specific mutations, methods such as these are valuable e.g. for tracking resistance in a pathogen population and for epidemiological studies.)

In a different approach, *M. tuberculosis* was infected with mycophages carrying a reporter gene encoding either GREEN FLUORESCENT PROTEIN or ZsYellow; infection of the cells was carried out in the presence of either streptomycin or rifampin. Cells that were susceptible (sensitive) to a given drug did not fluoresce because they were unable to synthesize the product of the reporter gene. In contrast, cells resistant to a drug were able to synthesize the reporter gene's product and exhibited fluorescence [PLoS ONE (2009) 4(3):e4870]. [Evaluation of fluoromycobacteriophages for detection of drug resistance in *Mycobacterium tuberculosis*: J Clin Microbiol (2011) 49(5): 1838–1842.]

Rapid identification of mycobacteria to species level, and determination of drug resistance, was reported with a method involving an initial PCR amplification followed by the use of mass spectrometry [J Clin Microbiol (2011) 49(3):908–917]. This method is shown diagrammatically in the figure on page 27.

antibodies (use in gene silencing) See cell-penetrating nucleic-acid-hydrolyzing antibodies in the entry GENE SILENCING.

antibody-based library screening One alternative to screening with a nucleic-acid-based probe (cf. COLONY HYBRIDIZATION).

antibody engineering (with intein-based technology) See entry INTEIN.

antibody-labeling reagents See e.g. the entry ZENON ANTIBODY LABELING REAGENTS.

anti-cancer therapy (*DNA technol.*) See CANCER THERAPY.

anticlinal (*anti*) Of a nucleotide: the conformation in which the oxygen atom within the sugar ring (–O–) is at the maximum distance from the 6-position of a purine (or the 2-position of a pyrimidine). (cf. SYNCLINAL.)

Conversion between *anti* and *syn* conformations in cytosine and guanine nucleotides was reported to be involved during the binding of splicing factor SRSF2 to recognition sites in an HIV-1 transcript [EMBO J (2012) 31:162–174].

anticoagulant (*DNA technol.*) A term that usually refers to an agent which inhibits the coagulation (i.e. clotting) of blood.

See THROMBIN for details of a DNA-based anticoagulant.

The anticoagulants include sodium citrate, sodium oxalate, heparin and SODIUM POLYANETHOLESULFONATE (SPS); the last two agents can inhibit PCR.

anticodon Three consecutive bases in a tRNA molecule which are complementary to a CODON which specifies the particular amino acid carried by that tRNA.

An anticodon is written in the 5′-to-3′ direction; so, too, is a codon.

(See also WOBBLE HYPOTHESIS.)

anti-downstream box (*or* 'antidownstream' box) See DOWNSTREAM BOX.

antigenic drift (in viruses) See the entry GENETIC DRIFT.

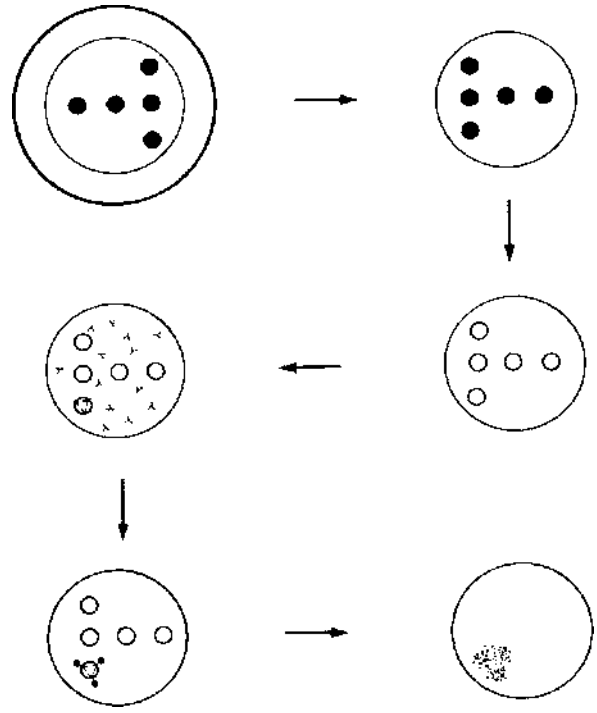
antigenic variation Successive changes in cell-surface antigens which are exhibited by certain types of microorganism (e.g. *Trypanosoma* – see e.g. VSG).

At least two distinct mechanisms are known: (i) the alternative antigens are encoded by specific *pre-existing* genes (see entry PHASE VARIATION), and (ii) the alternative antigens arise by ongoing recombinational events in the genome – i.e. they are encoded by newly formed, rather than pre-existing, genes. An example of the latter mechanism is the formation of new versions of a subunit in the fimbriae of *Neisseria gonorrhoeae*; variant forms of this subunit arise through repeated recombination between the chromosomal subunit gene, *pilE*, and another chromosomal gene, *pilS*, as well as between *pilE* and any homologous DNA received e.g. by transformation.

Some surface proteins of the fungus *Aspergillus fumigatus* may be hypervariable owing to recombination among internal mini- or microsatellite tandem repeat sequences in the genes encoding them [Eukaryotic Cell (2007) 6(8):1380–1391].

Antigenic variation apparently helps a pathogen to evade a host's immunologic defense mechanisms.

antimutator gene Any gene whose activity reduces the rate of spontaneous mutation in a cell. For example, some strains of *Escherichia coli*, with a mutant form of DNA polymerase, have mutation rates below those of wild-type strains; in this case the antimutator activity presumably involves improved



Antibody-based library screening: screening a cDNA expression library (diagrammatic). The cDNA library – consisting of protein-encoding cDNAs within expression vectors – was inserted into a population of bacteria; these bacteria were then inoculated onto agar plates in such a way that each bacterium gave rise to an individual colony. The object now is to determine *which* colony contains the cDNA that encodes (and expresses) the particular protein of interest. While each plate may contain >100 colonies, the plate considered here has only five colonies (for clarity).

The cDNA-containing colonies (*top*, *left*) are lightly overlaid with a nitrocellulose filter; when lifted off, the filter contains a mirror-image replica of the colonies (*top*, *right*). The cells on the filter are lysed, and the proteins they contain (including any encoded by the cDNAs) are bound to the filter (*center*, *right*). The filter is then treated with antibodies (Y) that are specific to the protein of interest (*center*, *left*); antibodies have bound to the given protein (present in *one* of the colonies). Unbound antibodies are washed away. The filter is then treated with *protein A* – a protein (derived from the bacterium *Staphylococcus aureus*) which binds to antibodies. Unbound protein A is washed away, leaving some protein A (•) bound to the specific antibody–protein complex (*bottom*, *left*). Before use, the protein A is labeled with a radioactive source so that its presence can be detected by *autoradiography*; this involves exposing a photographic film to the nitrocellulose filter for an appropriate time and then developing the film. When the film is developed (*bottom*, *right*) it identifies the particular colony on the original plate which contains the cDNA of interest. This colony can then be used as an inoculum to grow more of the cells which contain the specific cDNA.

This procedure clearly depends on efficient and specific protein–antibody binding. A protein synthesized in bacteria from a *eukaryotic* gene may lack the three-dimensional structure and/or post-translational modification that characterizes the native eukaryotic protein; it may therefore fail to bind antibodies raised against the native protein. (Moreover, even if the protein *is* synthesized with normal conformation, the process used to bind it to the filter may alter that conformation.) However, it is possible to produce antibodies that recognise, and bind to, a short, specific run of amino acid residues, even when the target protein lacks the conformation and/or post-translational modification of the native protein.

Finally, a colony containing the *particular* cDNA of interest may not be present on the plate being examined. Hence, it may be necessary to carry out the procedure on more than one plate.

Figure reproduced from *Bacteria in Biology*, *Biotechnology and Medicine*, 6th edition, Figure 8.10, page 222, Paul Singleton (2004) John Wiley & Sons Ltd, UK [ISBN 0-470-09027-8] with permission from the publisher.

fidelity/proof-reading.

anti-oncomir See the entry ONCOMIR.

antiparallel (of strands in dsDNA) The (usual) arrangement in which a 5′-to-3′ strand is hybridized to a 3′-to-5′ strand, i.e. each end of a double-stranded DNA molecule has a 5′ terminal and a 3′ terminal.

(See also the entry DNA.)

antiretroviral agents Agents with activity against retroviruses; some are useful e.g. in chemotherapy against AIDS – see e.g. NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS, NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS and PROTEASE INHIBITORS. Other agents that are useful against AIDS include the INTEGRASE INHIBITORS, the FUSION INHIBITORS, and CHEMOKINE CORECEPTOR ANTAGONISTS.

(See also HAART, HIV-1 and RETROVIRUSES.)

The ability of certain indole derivatives to inhibit synthesis of a retroviral glycoprotein, protecting mice from a challenge with MLV (*Murine leukemia virus*), has suggested a potential use for these compounds as antiretroviral therapeutic agents [PLoS ONE (2009) 4(2):e4533].

Specific HDAC inhibitors (see HDAC) have been suggested as a means to address the problem of *latency* in HIV-1: see *Quiescent HIV-1* in the entry AIDS.

An agent generally associated with treatment of herpesvirus infection, acyclovir, was reported to inhibit HIV-1 replication in $CD4^+$ T cells that lacked detectable herpesvirus infection [J Virol (2011) 85(9):4618–4622].

anti-reverse cap analog (ARCA) A chemically modified form of CAP ANALOG (Ambion, Austin TX) designed to maximize the efficiency of *in vitro* translation by ensuring that the cap analog is incorporated in the transcript in the correct orientation (a cap analog incorporated in the reverse orientation does not support translation).

The use of an anti-reverse cap analog enhanced translation by a factor of 1.5–1.8 in studies on translational efficiency of mRNA encoding the HIV-1 *gag* region [PLoS ONE (2008) 3(6):e2356]. [See also Cancer Res (2010) 70:9053–9061.]

antisense gene In a genetically engineered cell: a gene, inserted into that cell, whose presence is intended to inhibit, or block, the expression of another, endogenous gene.

antisense oligomer For examples of natural and synthetic antisense oligomers, see entries: ANTISENSE RNA and MORPHOLINO ANTISENSE OLIGOMER. (See also PNA.)

antisense RNA Any natural or synthetic RNA whose sequence permits interaction with a given sense sequence (in RNA or in DNA) and which may affect the activity/expression and/or stability of the target molecule: see e.g. FINOP SYSTEM, MICRORNAS, MULTICOPY INHIBITION, POST-SEGREGATIONAL KILLING, R1 PLASMID and RNA INTERFERENCE. (cf. ARNA (sense 1).)

Antisense RNAs of cyanobacterium *Prochlorococcus* were reported to hybridize to certain mRNAs, making the mRNAs resistant to nucleolysis by RNase E – and, hence, increasing their stability [Nucleic Acids Res (2011) doi: 10.1093/nar/gkr037].

Antisense RNAs have been used in a method for studying the *in vivo* processing of RNA precursor molecules by means of a RIBONUCLEASE PROTECTION ASSAY (q.v.).

Other antisense systems

Engineered antisense systems have been devised using PNA or MORPHOLINO ANTISENSE OLIGOMERS.

(See also GENE SILENCING.)

antisense strand (of DNA) The non-CODING STRAND (q.v.).

antisense transcript A transcript which is produced when the CODING STRAND of DNA is used as a template.

Several methods may be used to distinguish between sense and antisense transcripts: see e.g. the entry ASSAGE.

antisense transcriptome See TRANSCRIPTOME.

(See also ASSAGE.)

antisense transcriptome analysis using exon array See entry TRANSCRIPTOME.

α_1-antitrypsin See under 'alpha'.

antiviral agent Any agent with activity against viruses *in vivo* and/or *in vitro*. (cf. ANTIBIOTIC.)

See e.g. ANTIRETROVIRAL AGENTS, ACYCLOVIR, AMANTADINE, GANCICLOVIR, LAMIVUDINE, OSELTAMIVIR, RIBAVIRIN and ZANAMIVIR.

(See also the section: *An assay for −1 frameshifting* in the entry FRAMESHIFTING.)

antizyme Any of a group of proteins associated with regulation of ornithine decarboxylase (ODC) – which is involved in biosynthesis of polyamines. In eukaryotes functional antizyme is expressed in the presence of increased levels of polyamines – antizyme 1 promoting UBIQUITIN-dependent degradation of ODC via the 26S PROTEASOME. Antizymes are regulated by antizyme inhibitor.

[Antizyme in prokaryotes: BMC Biochem (2007) 8:1.]

AOF1 (KDM1B) Amine oxidase (flavin-containing) domain 1: see the entry GENETIC IMPRINTING.

AOX1 In the (methylotrophic) yeast *Pichia pastoris*: a highly regulated, inducible gene which encodes alcohol oxidase – a peroxisomal enzyme involved in the metabolism of methanol.

(See also PPICZ VECTOR.)

AP (1) ALKALINE PHOSPHATASE.

(2) Apurinic or apyrimidinic: refers to a location in a DNA or RNA molecule at which a purine or pyrimidine base has been lost (see e.g. BASE EXCISION REPAIR).

AP endonuclease Any enzyme with endonuclease activity that is involved in the excision of apurinic/apyrimidinic nucleotide residues (see e.g. BASE EXCISION REPAIR).

AP-PCR Arbitrarily primed PCR: any form of PCR which uses primers of arbitrary sequence – and which amplifies random, but discrete, sequences of chromosomal DNA; AP-PCR has been used for TYPING bacteria.

PCR is initially carried out under low stringency, and the primers bind at various sites to each strand of heat-denatured chromosomal DNA; the binding of primers occurs at *best-fit* sequences, and may include mismatches. In some cases two primers bind, with relative efficiency, on opposite strands, at locations separated by a few hundred bases. If synthesis can occur normally from these two primers, then another round of

cycling, under low-stringency conditions, followed by many cycles under high-stringency conditions, may produce copies of an amplicon delimited by the two 'best-fit' sequences. In the phase of high-stringency cycling, not all the primers will bind to their best-fit sequences – so that only a proportion of the amplicons produced under low-stringency conditions will be amplified in the high-stringency phase.

The amplicons from a given sample are subjected to gel electrophoresis, and the stained bands of amplicons form the *fingerprint*. Strains are compared and classified on the basis of their fingerprints.

One advantage of this approach is that there is no need for prior knowledge of the genome sequence; there is no need to design specific primers, and any isolate is potentially typable.

Results are generally reproducible under standardized conditions in a given laboratory, but comparable results will not necessarily be obtained in other laboratories unless the procedures are *identical*; reproducibility of results depends not only on the primer sequence but also e.g. on the particular type of polymerase used and on the initial procedure used for preparing the sample DNA.

Some other named methods are based on the same principle – e.g. RAPD (random amplified polymorphic DNA) analysis and DAF (direct amplification fingerprinting). Such methods may differ e.g. in the length of primers used, in the annealing temperature for primers, and the type of gel used for electrophoresis. The original AP-PCR procedure employed primers of 20 to 50 nucleotides, an annealing temperature of ~40°C, and an agarose gel. In RAPD, the primers are often 10–20 nt, with annealing at ~36°C, and products separated in an agarose gel. DAF uses short primers (5–8 nt) with an annealing temperature of ~30°C; as, in this methiod, there are many more (smaller) products, electrophoresis is carried out in a polyacrylamide gel, and silver staining is used to detect bands in the fingerprint.

AP site (abasic site) In a nucleotide sequence: a site at which the base (purine or pyrimidine) is missing – the remainder of the nucleotide (sugar, phosphate) being present. (cf. GAP.)

APES See the entry AAS.

aphidicolin A tetracyclic diterpenoid, isolated from a fungus, which strongly inhibits eukaryotic DNA polymerase α. The bacterial DNA polymerases are unaffected, but aphidicolin was reported to inhibit DNA synthesis in at least some members of the domain ARCHAEA (e.g. some methanogens).

[Examples of use: Proc Natl Acad Sci USA (2009) 106(3): 803–807; Mol Biol Cell (2012) 23(6):1047–1057.]

Aphthovirus A genus of PICORNAVIRUSES which includes the causal agent of foot-and-mouth disease.

[Inhibition of replication of *Aphthovirus* by siRNA: Virol J (2008) 5:86. Diagnosis of foot-and-mouth disease in Brazil by RT-PCR: BMC Vet Res (2008) 4:53.]

APO-1 (CD95) The cell-surface Fas receptor: see APOPTOSIS.

APOBEC-1 See entries CYTIDINE DEAMINASE and RNA EDITING.

apolipoprotein B See RNA EDITING.

apoptosis In various types of eukaryotic cell: death that occurs in a regulated ('programed') manner, an organized process in which fragmentation of the genome is a characteristic feature. DNA fragmentation can be assessed by the TUNEL ASSAY.

In the vertebrates, apoptosis occurs naturally – for example, during embryogenesis. It occurs during metamorphosis in the invertebrates.

Apoptosis can be a response to damaged DNA in the cell: see e.g. the entry P53.

Apoptosis can be induced by physical agents, such as heat and radiation, and by certain chemicals – e.g. in osteoblasts it was reported to be stimulated by glucocorticoids (leading to osteoporosis).

Ongoing studies of apoptosis have enabled the development of pro-apoptotic receptor agonists that might be useful for the promotion of apoptosis in cancer cells [Nature Rev Drug Discovery (2008) 7:1001–1012].

Apoptosis in the fungal pathogen *Candida albicans* can be induced by the sesquiterpene alcohol farnesol [Antimicrobial Agents Chemother (2009) 53(6):2392–2401].

Apoptosis in (human) lens epithelial cells has been induced by shRNA-mediated downregulation of anti-apoptotic protein Bcl-2 [Mol Vision (2012) 18:74–80].

Other factors that may promote apoptosis include binding of certain cytokines (e.g. TNFα) and cytotoxic ($CD8^+$) T cells to specific cell-surface receptors; in the latter case, Fas ligand (on the T cell) binds to the target cell's Fas receptor (which may also be referred to as CD95 or APO-1).

Inhibition of apoptosis is seen, for example, in B lymphocytes latently infected with the EPSTEIN–BARR VIRUS; in these B cells apoptosis is inhibited by small EBV-encoded RNAs: see EBER.

Caspases

Major players in apoptosis are certain intracellular cysteine proteases (*caspases*) that are synthesized in an inactive form (zymogen) and activated specifically during apoptosis; these enzymes cleave specific protein substrates at a site next to an aspartic acid residue. Cleavage, by a caspase, may inactivate or activate the substrate – e.g. caspase-mediated activation of the nuclease *caspase-activated DNase* (CAD) results in DNA fragmentation. (CAD is normally present in an inactive form, complexed with an inhibitory partner known as ICAD.)

Caspase activation apparently occurs primarily by cleavage of the zymogen. In at least some cases, one caspase may be activated by another, upstream caspase in a caspase cascade.

Fluorophore-labeled probes, which label *active* caspases *in vivo* ('activity-based probes'), allowed researchers to monitor the kinetics of apoptosis in live mice [Nature Med (2009) 15: 967–973].

Apoptosis induced by bacteria

In macrophages which have taken up the bacterium *Shigella flexneri* (by phagocytosis), apoptosis in the macrophage can be promoted by a plasmid-encoded protein, IpaB, secreted by *S. flexneri*; IpaB activates the IL-1β-converting enzyme of the host cell (ICE, a cysteine protease) – which then initiates apoptosis.

(See also *bcl-x* in ALTERNATIVE SPLICING; BARNASE; BINASE; CISPLATIN; MDA-7/IL-24; MYB; MYC and SURVIVIN.)

APSR (amplicon primer site restriction) In PCR, a method for preventing the contamination of a reaction mixture with amplicons from previous assays. In this method, *all* the assays are conducted with primers whose 5′ ends carry a recognition site for a (type IIS) RESTRICTION ENDONUCLEASE that cleaves both strands 3′ of its binding site. In a reaction mixture, the added restriction enzyme will cut any carry-over amplicons but will not cleave the *template* DNA unless (by chance) it contains the recognition site of the given restriction endonuclease; the enzyme is inactivated during PCR temperature cycling.

(See also AMPLICON INACTIVATION.)

APT paper See SOUTHERN BLOTTING.

aptabody A construct, made from multiple RNA APTAMERS, which can function as a protein. The prototype aptabody was a tetravalent construct that was able to mimic an antibody by simultaneously binding two molecules of the *Drosophila* B52 protein and two molecules of streptavidin. The performance of this aptabody was reported to rival that of a monoclonal antibody against the B52 protein [Nucleic Acids Res (2009) doi: 10.1093/nar/gkp243].

[Composite RNA aptamers (functional mimics of proteins): Nucleic Acids Res (2009) doi: 10.1093/nar/gkp243.]

aptamer (1) Any of a large number of (synthetic) oligonucleotides that can adopt (at least one) three-dimensional structure and bind, with high specificity, to a given ligand. Both RNA and DNA aptamers can be synthesized.

(See also APTABODY and INTRAMER.)

Selection of an RNA aptamer for a given target molecule can be achieved by SELEX (systematic evolution of ligands by exponential enrichment). Briefly, in SELEX, the immobilized target ligand – e.g. a protein – is exposed to a large and diverse population of oligonucleotides that were synthesized with random sequences. After removal of unbound oligos, the (relatively few) bound oligos are eluted and then converted to cDNAs. The cDNAs are amplified by PCR using primers that incorporate a promoter. The amplicons are transcribed, and the transcripts are used in another round of selection with the target molecule. This cycle is repeated, target–RNA binding becoming more specific at each round; the range and affinity of the selected aptamers can be determined e.g. by regulating buffer conditions at the binding stage. (A principle similar to this is found in PHAGE DISPLAY.)

In general, SELEX is useful for analyzing protein–nucleic acid binding and e.g. interactions between RNA and various low-molecular-weight molecules.

[Combining SELEX and yeast 3-hybrid system for *in vivo* selection and classification of aptamers: RNA (2007) 13(4): 614–622.]

A 58-nt aptamer sequence (which was developed by the use of SELEX) can – following transcription – adopt *two* distinct structures with different functions; both of the structures are required (jointly) to inhibit a particular receptor. These two structures cannot be interconverted (by unfolding and then refolding) apparently owing to their inherent structural stability [Nucleic Acids Res (2009) doi: 10.1093/nar/gkp284].

Genomic SELEX is an approach which has been used for identifying genome-encoded RNAs of *Escherichia coli* that can bind to protein Hfq (see SRNAS for Hfq), the RNAs being referred to as aptamers [genomic SELEX: Nucleic Acids Res (2010) doi: 10.1093/nar/gkq032].

Studies were carried out on the structural basis of the interaction between RNA aptamers and proteins [Nucleic Acids Res (2010) doi: 10.1093/nar/gkq615].

[Magnetically mediated selection of DNA aptamers: BioTechniques (2007) 43(3):344–353.]

[Cellulose-binding aptamers: Nucleic Acids Res (2007) 35 (19):6378–6388.]

[An *in silico* directed evolution study of DNA aptamers that bind allophycocyanin: Nucleic Acids Res (2009) 37(1):e6.]

[*In silico* selection of (RNA) aptamers: Nucleic Acids Res (2009) doi: 10.1093/nar/gkp408.]

Uses/applications of aptamers

The high-level binding specificity of the aptamers, and their ability to be linked to other molecules, has suggested various uses.

An aptamer–shRNA fusion transcript was used to regulate gene expression within mammalian cells. The activity of the shRNA moiety was controlled by an interaction between the aptamer and its ligand – theophylline (1,3-dimethylxanthine) – the latter being supplied exogenously.

An aptamer – known to bind to prostate tumor cells – was conjugated to an siRNA via a streptavidin bridge; on addition to cells, this conjugate was internalized, and the siRNA was able to inhibit gene expression as efficiently as when it was inserted by a lipid-based method [Nucleic Acids Res (2006) 34(10):e73].

Using a SELEX-based method, five aptamers were selected for their high specificity towards ligands at the surface of the pathogenic Gram-positive bacterium *Staphylococcus aureus* – each of the aptamers recognizing a different target. When used in combination, this set of aptamers constitutes a system for detecting and identifying this species [Nucleic Acids Res (2009) doi: 10.1093/nar/gkp489].

[Aptamers as therapeutics: Nature Rev Drug Disc (2010) 9: 537–550.]

An aptamer–siRNA construct was used to inhibit infection by HIV-1 [J Clin Invest (2011) 121:2401–2412, doi: 10.1172 /JCI45876].

A 15-mer (DNA) aptamer has strong anticoagulant activity – i.e. it inhibits clot formation in blood/plasma by binding to thrombin and inhibiting that enzyme's ability to act on fibrinogen [Nucleic Acids Res (2011) doi: 10.1093/nar/gkq823].

[Aptamers in virology (recent advances, challenges): Front Microbiol (2012) doi: 10.3389/fmicb.2012.00029.]

Broad-spectrum aptamers

It has been suggested that an aptamer which is able to inhibit a broad range of target molecules is less likely (than a highly target-specific one) to be susceptible to the effects of 'escape

mutations' in the target molecules. (An 'escape mutation' in a target molecule is able to inhibit binding by a target-specific aptamer.)

[Broad-spectrum aptamer inhibition of reverse transcriptase of human immunodeficiency virus: Nucleic Acids Res (2011) doi: 10.1093/nar/gkr381.]

(See also APTAZYME and PROXIMITY LIGATION ASSAY.)

(2) A *natural* sequence within a RIBOSWITCH.

(3) A naturally occurring ligand-binding sequence found in genomically encoded RNAs of *Escherichia coli*: see *genomic* SELEX in sense 1, above.

aptazyme (*DNA technol*.) An APTAMER–RIBOZYME construct in which the aptamer – on binding a certain ligand – typically undergoes a conformational change resulting in modification/regulation of the ribozyme.

In one application, ligand-binding by the aptamer promotes the ability of the ribozyme moiety to polymerize ribonucleotides – using another copy of the ribozyme as template. Thus, within the reaction mixture, the ribozymes synthesize copies of each other – so that exponential amplification of the RNA occurs in the presence (although not in the absence) of the particular ligand. As the rate of increase in copies of RNA is governed by the ligand's *concentration*, the concentration of the ligand in a particular sample can be assessed from the increase in RNA; systems can be set up in which an aptamer, in responding to a given ligand, provides a sensitive assay for the ligand. The ligand may be any of a variety of small molecules or proteins – e.g. those that are relevant e.g. in medical or environmental studies. [Nature Biotechnol (2009) 27:288–292.]

One study has examined the performance of an engineered drug-sensing aptazyme made from a theophylline-responsive aptamer fused to a HAMMERHEAD RIBOZYME [see RNA (2009) 15(1):76–84].

apurinic Lacking a purine residue: see AP SITE.

apyrase A nucleotide-degrading enzyme (EC 3.6.1.5) with various applications in technology (see e.g. PYROSEQUENCING).

apyrimidinic Lacking a pyrimidine residue: see AP SITE.

***araBAD* operon** See the entry OPERON.

Arabidopsis thaliana A small cruciferous plant commonly used in plant genetics because of its simple genome and its short generation time. (It is sometimes called *mouse-ear cress*.)

[Genome of *A. thaliana*: Nature (2000) 408:791–826.]

A genome-wide study on *A. thaliana* identified some 1500 putative origins of DNA replication [Nature Struct Mol Biol (2011) doi: 10.1038/nsbm.1988].

For information on *endogenous* siRNAs in *Arabidopsis* see the entry SIRNA.

(See also CHROMATIN and FLORAL DIP METHOD.)

araC See the entry OPERON.

Aranesp® See the entry BIOPHARMACEUTICAL (table).

arbitrarily primed PCR See the entry AP-PCR.

arbitrary degenerate primer (AD primer) See TAIL-PCR.

arboviruses Arthropod-borne viruses: a (non-taxonomic) group which includes those viruses that are able to replicate within a vertebrate host *and* in arthropods (such as mosquitoes and ticks). Many of the arboviruses can cause disease in humans or animals; they include *Bluetongue virus* (genus *Orbivirus*), *Lassa virus* (family *Arenaviridae*), *West Nile virus* (genus *Flavivirus*) and *Yellow fever virus* (genus *Flavivirus*).

Arboviruses that infect mosquitoes can cause damage to the *mosquito* host – damage which may be limited by the insect's antiviral response: RNA INTERFERENCE (q.v.). An experiment to study the role of RNAi in protecting the mosquito used a recombinant SINDBIS VIRUS that expressed a protein (the B2 protein of *Flock House virus*) which inhibits RNAi. In this experiment it was found that expression of the B2 protein in mosquito cells inhibits RNAi. The recombinant *Sindbis virus* (inoculated intrathoracically) was lethal in various mosquito species, and the recombinant virus caused mortality in *Aedes aegypti* in a dose-dependent manner [BMC Microbiol (2009) 9:49].

ARCA See the entry ANTI-REVERSE CAP ANALOG.

Archaea One of the two domains of *prokaryotic* organisms, the other being BACTERIA. (See also PROKARYOTE.) Organisms in these two domains differ e.g. in their 16S rRNA sequences, in composition of the cell-wall macromolecules, composition of cytoplasmic membrane lipids and in flagellar structure; the organisms also differ in their mode of gene expression and in DNA replication – thus, e.g. some archaeans, unlike bacteria, have multiple origins of replication in a given chromosome. [Subcellular localization of DNA replication in *Sulfolobus*: Nucleic Acids Res (2012) doi: 10.1093/nar/gks217.]

Some archaeans are polyploid, *Methanococcus maripaludis* being reported to have up to 55 copies of the genome during rapid growth [J Bacteriol (2011) doi: 10.1128/JB.01016-10].

Most species of Archaea so far examined have a system of acquired immunity to infection by viruses etc. which is based on CRISPRS (q.v.).

(*Eukaryotic* organisms are placed in the domain EUKARYA.)

archaean (*syn*. archaeon) Any organism within the prokaryotic domain ARCHAEA.

Archaebacteria A now-obsolete kingdom of prokaryotes; the organisms formerly placed in this taxon are currently classified in the domain ARCHAEA.

ArchaeMaxx™ A polymerase-enhancing factor marketed by Stratagene (La Jolla CA, USA); it was designed to overcome the so-called DUTP POISONING effect.

[Example of use: PLoS Biol (2006) 4(3):e73.]

archaeon An alternative spelling of ARCHAEAN.

ARCUT Artificial restriction DNA cutter: a system for cutting single-stranded regions which have been induced in double-stranded DNA by the 'invasion' of a double-stranded peptide nucleic acid construct (see entry PNA) *between the strands* of the DNA duplex. (cf. SINGLE-STRAND-SPECIFIC NUCLEASE.)

The PNA construct consists of strands of PNA hybridized together in a staggered fashion such that each remains single stranded at *one* end; each of the single-stranded ends carries a monophosphate group. In these strands the bases thymine and adenine have been replaced by 2-thiouracil and 2,6-diamino-

purine, respectively. This PNA construct can insert between the strands of a DNA duplex *in a highly site-specific way*; the presence of 2-thiouracil and 2,6-diaminopurine in these PNA strands facilitates hybridization between each strand of PNA and a strand of DNA. Insertion of the PNA construct into the DNA duplex produces two regions of single-stranded DNA – each found opposite the region where a single-stranded PNA has hybridized to *one* of the strands of DNA.

With the PNA construct inserted into the DNA duplex (and with regions of single-stranded DNA at each end), the whole is subjected to a complex of cerium ions and EDTA (Ce(IV)/EDTA) at 37°C, pH 7; this hydrolyses a phosphodiester bond in each of the regions of single-stranded DNA. The resulting staggered cuts in the DNA duplex resemble the cuts made by a type IIP RESTRICTION ENDONUCLEASE (such as EcoRI).

By using a pair of ARCUTs, targeted at separate sequences in a DNA duplex, one can cut out the intervening fragment. This can be achieved even when bases in the target sites are methylated and are resistant to cutting by relevant restriction endonucleases.

ARCUT-prepared fragments in homologous recombination

The ARCUT system was used to prepare fragments of DNA for insertion into mammalian cells in studies on homologous recombination; in these studies various chemical and biologic factors were studied for their effect on the efficiency of homologous recombination in these cells. It was found that:

• 3′-overhangs gave a 1.7-fold higher efficiency (compared to 5′-overhangs);

• long regions of homology (in the fragments) were more favorable than shorter regions;

• a ~2-fold increase in homologous recombination occurred if cells were synchronized to the G_2/M phase of the cell cycle (using the agent nocodazole);

• a several-fold increase in efficiency was obtained when the Ku70 and Ku80 proteins (of the NON-HOMOLOGOUS DNA END-JOINING system) were repressed by siRNAs.

[Improving the efficiency of homologous recombination in human cells with ARCUT: Nucleic Acids Res (2012) doi: 10.1093/nar/gks185.]

ARDRA Amplified ribosomal DNA restriction analysis: a technique which has been used e.g. for comparing the populations of microorganisms present in different samples of soil [PLoS ONE (2011) 6(6):e20222]. Essentially, purified DNA extracted from the microbial community in a given sample is first amplified by PCR using BROAD-RANGE PRIMERS targeting 16S rDNA. The PCR products are digested (37°C overnight) with a RESTRICTION ENDONUCLEASE (e.g. HinfI). The resulting fragments are subjected to electrophoresis in a 2% agarose gel at 100 V (for 3 hours); after staining with ethidium bromide, the DNA is photographed under ultraviolet light. Electrophoretograms of all the samples are then compared with appropriate computer software.

(cf. LH-PCR.)

ARES™ See the entry PROBE LABELING.

Argonaute Any of a family of proteins, found in higher eukaryotes, that are involved e.g. as effector molecules in the gene-silencing functions of certain small RNAs such as MICRORNAS (see also RNA INTERFERENCE).

Members of the Ago subfamily of Argonaute proteins are ubiquitous; they are involved e.g. in post-transcriptional gene silencing by miRNAs and siRNAs – in which mRNAs may be either physically degraded or functionally repressed. (See also BIM.)

Proteins of the Piwi subfamily (see the entry PIWI PROTEIN) apparently occur primarily in germ line cells – in which they act in conjunction with small RNAs (piRNAs) e.g. to silence TRANSPOSABLE ELEMENTS.

Various species are known to have several (or many) types of Argonaute protein, and, in a given species, these proteins may carry out different functions. Some Argonaute proteins have endonucleolytic activity, and these, in association with miRNAs or siRNAs, are able to cleave specific mRNAs; this cleavage is reported to occur when there is perfect complementarity between the small RNA and its target sequence on an mRNA. In human cells, only the Ago2 was reported to have nucleolytic capability [Genome Biol (2008) 9(2):210]. Both Ago1 and Ago2 apparently have nucleolytic capability in the cells of *Drosophila* – in which miRNA-directed cleavage of mRNAs appears to involve Ago 1, Ago 2 working mainly in association with siRNAs.

Other types of Argonaute protein may be involved in the repression of translation when miRNAs bind to imperfectly complementary target sites.

Interaction between an Argonaute protein and the so-called SEED REGION (q.v.) of an miRNA has been reported to make the conformation of the seed region optimal for presentation to the target mRNA [Nucleic Acids Res (2011) doi: 10.1093/nar/gkr077].

Ago proteins are also reported to be involved in instances of *transcriptional gene silencing* and *transcriptional gene activation* (see the entry SIRNA).

The Ago2 protein has been detected in body fluids (such as blood plasma) in association with microRNAs; it was thought that these molecules were likely to have been derived largely from dead cells [Nucleic Acids Res (2011) doi: 10.1093/nar/gkr254].

Argonaute proteins in the cytoplasm and nucleus

Argonaute proteins occur in both the cytoplasm and nucleus. However, while Ago2 is usually associated with cleavage of mRNAs in the cytoplasm (e.g in association with miRNAs), one study reported that it can play a role in the nucleus: acting with a targeted dsRNA to promote a change in splicing [Nucleic Acids Res (2011) doi: 10.1093/nar/gkr780].

(See also ARNA (sense 2) and GW182.)

argU In *Escherichia coli*: a tRNA-encoding gene.

ARMS Amplification-refractory mutation system: a procedure used e.g. for demonstrating or detecting a point mutation *at a specific site* in DNA whose wild-type (non-mutant) sequence is known.

Essentially, use is made of a primer in which the 3′-term-

inal nucleotide is complementary to the given *mutant* base at the specific site. After hybridization, extension of the primer by a polymerase signals the presence of the mutation at that site, while the absence of extension indicates the presence of a wild-type (or other) nucleotide.

armyworm The insect *Spodoptera frugiperda*. Cell cultures of this organism are used e.g. for the synthesis of recombinant proteins in BACULOVIRUS EXPRESSION SYSTEMS.

(See also SF9 CELLS.)

aRNA (1) Antisense RNA – see the entry MESSAGEAMP ARNA AMPLIFICATION KIT.

(2) Aberrant RNA: a type of RNA which is produced in cells (under certain conditions) and which can be converted to an effector molecule by modification involving the activity of an RNA-dependent RNA polymerase.

In the fungus *Neurospora crassa*, an aRNA that is induced by damage to DNA acts as a precursor to a small interfering RNA (~20 nt long) referred to as qiRNA. The production of qiRNA (so named because of its interaction with Argonaute protein QDE-2) depends on the activity of an RNA-dependent RNA polymerase and also needs a helicase and the Dicer enzyme [Nature (2009) 459:274–277].

Note. aDNA is used to refer to *ancient* DNA.

array A shortened version of MICROARRAY – but also used to refer to other oligonucleotide- or tissue-based arrangements etc. with analogous or distinct uses (see e.g. MACROARRAY).

array-based CGH See the entry ACGH.

ARS Autonomously replicating sequence: a genomic sequence which, if isolated and linked to a non-replicative fragment of DNA, promotes independent (extrachromosomal) replication of that fragment within the cell.

ARSs were first identified in *Saccharomyces cerevisiae* – an organism that contains, on average, one ARS in every ~40 kb of genomic DNA. ARSs also occur in at least some yeast plasmids.

It appears that some ARSs are active chromosomal origins while others are *silent origins*; some of the silent origins (and some active ones) may function as transcription silencers.

[Genome-wide hierarchy of replication origin usage in the yeast *Saccharomyces cerevisiae*: PLoS Genetics (2006) 2(9): e141.]

Factors reported to contribute to the efficient replication of ARS-containing plasmids in yeast cells include (i) the CEN (centromere) element and (ii) minichromosome maintenance protein 1 (Mcm1).

The circular dsDNA genome of human papillomavirus type 16 can replicate stably in *S. cerevisiae* independently of ARS or CEN; sequences in the viral DNA apparently substitute for both ARS and CEN [J Virol (2005) 79(10):5933–5942].

ARSs were also reported in species of the ARCHAEA.

(See also NUMTS and YEAST ARTIFICIAL CHROMOSOME.)

arsenate (in nucleic acids) Arsenate (in place of phosphate) has been found in both nucleic acids and proteins in a bacterium (GFAJ-1) [Science (2010) doi: 10.1126/science.1197258].

Artemis A DNA sequence viewer and annotation tool (Sanger Institute) used for displaying features of a given sequence of nucleotides and the results of analyses of that sequence (and of its six-reading-frame translation).

Artemis nuclease A multifunctional enzyme involved e.g. in a DNA repair mechanism – *non-homologous DNA end-joining*, NHEJ – used e.g. for repair of double-stranded breaks caused by ionizing radiation; it trims the ends of a double-stranded break, preparing them for subsequent processing and ligation by other components of the NHEJ system [see e.g. Nucleic Acids Res (2008) 36(10):3354–3365].

arthropod-borne viruses See the entry ARBOVIRUSES.

artificial chromosome See e.g. BACTERIAL ARTIFICIAL CHROMOSOME, HUMAN ARTIFICIAL CHROMOSOME and YEAST ARTIFICIAL CHROMOSOME.

artificial restriction DNA cutter See the entry ARCUT.

artificial *trans*-encoded sRNAs See the entry SRNAS.

ascospores See the entry SACCHAROMYCES.

ascus See the entry SACCHAROMYCES.

aseptic technique Measures which avoid the contamination of cultures, sterile media etc. – and/or contamination of persons, animals or plants – by microorganisms which are present in the environment (e.g. in the air) or which may be associated with particular source(s).

In this approach, the vessels used for media etc. must be sterile before use (e.g. pre-sterilized Petri dishes), and sterile material should not be exposed to any non-sterile conditions before use (see also STERILIZATION).

The working surfaces of forceps and other types of metal instrument – such as bacteriological loops etc. – are sterilized by 'flaming' before use, and the rims of bottles etc. used for dispensing sterile (non-flammable) materials are also flamed. (Note that loops and forceps are also flamed after use in order to prevent contamination of the laboratory.)

Benches are regularly treated with disinfectants and/or with ULTRAVIOLET RADIATION (UVR). So-called *germicidal* lamps, which may emit UVR at ~254 nm, are used for disinfecting air and exposed surfaces in enclosed areas. In general, UVR has rather poor powers of penetration; moreover, its effects on microorganisms may be reversible by certain DNA repair processes (see e.g. UVRABC-MEDIATED REPAIR).

Some procedures, e.g. handling specimens likely to contain certain pathogens (such as *Mycobacterium tuberculosis*, or certain highly hazardous viruses such as *Zaire ebolavirus* or *Lassa virus*), are carried out in a SAFETY CABINET.

Asian flu See the entry INFLUENZAVIRUS.

ASLV vectors Avian sarcoma and leukosis virus-based vectors – see e.g. GENE THERAPY (*Viral vectors*).

ASP APOBEC-1-stimulating protein: see RNA EDITING.

aspart See the entry INSULIN ASPART.

Aspergillus A genus of (mycelial) fungi (class Hyphomycetes) which are common in nature. Many species are saprotrophic, but e.g. *A. flavus* and *A. fumigatus* are pathogenic (see also AFLATOXINS).

[*Aspergillus* genome database: Nucleic Acids Res (2009) doi: 10.1093/nar/gkp751.]

A. flavus has been genotyped from its microsatellite DNA [J Clin Microbiol (2010) doi: 10.1128/JCM.01269-09; PLoS ONE (2011) doi: 10.1371/journal.pone.0016086].

(See also INSERTIONAL MUTAGENESIS.)

ASR/GMP oligonucleotides Primers that comply with specifications of the FDA (Food and Drug Administration) in the USA and which are used (in restricted circumstances, and under stated conditions) for specific laboratory tests designed to provide analytical results.

asRNA An abbreviated form of ANTISENSE RNA.

ASSAGE (asymmetric strand-specific analysis of gene expression) A method enabling identification of the template strand (in dsDNA) on which a given transcript was synthesized.

Essentially, this approach involves the initial treatment of transcripts with BISULFITE – thus converting cytidine residues to uridine residues. Reverse transcription follows; this leads subsequently to the formation of double-stranded cDNAs that are then fragmented. Adaptors are added to cDNA fragments (at both ends), followed by massively parallel sequencing-by-synthesis in Illumina flow cells. Any given sequence can be matched to only one of the two possible template strands in a dsDNA molecule; the basic idea is illustrated below:

Gene (sense strand)	5′-T C A G C T A.....
mRNA	5′-UC A G C UA
Gene (antisense strand)	3′-AGT C G AT
mRNA (after bisulfite)	5′-UU A G U UA
cDNA (1st strand)	3′-AA T C A AT
cDNA (2nd strand)	5′-T T A G T T A

Here, the cDNA (2nd strand) clearly corresponds to the sense strand of the gene, bearing in mind that each 'C' in the sense strand of the gene will appear as 'T' in the cDNA 2nd strand owing to the effects of bisulfite; thus, this particular transcript was synthesized on the antisense strand of the DNA.

[ASSAGE: Science (2008) 322:1855–1857, doi: 10.1126/science.1163853.]

assembly of DNA (*in vitro*) See DNA CUTTING AND ASSEMBLY.

assisted reproductive technology See e.g. SCNT (for cloning of domestic animals) and IVF (in humans).

association studies See e.g. entries COPY NUMBER VARIANT and SNP GENOTYPING.

asymmetric DNA synthesis See DNA REPLICATION.

asymmetric interfering RNA See the entry SIRNA.

asymmetric PCR A form of PCR in which the concentration of *one* of the primers is much lower than that of the other (e.g. a ratio of 1:50); during temperature cycling, this primer will be quickly used up – so that only one strand of the target sequence will be significantly amplified.

Uses of asymmetric PCR include the preparation of probes and the preparation of single-stranded DNA for sequencing.

ssDNA products from PCR can also be obtained in a different way. One of the two types of primer can be labeled with BIOTIN and the reaction carried out with both primers in their normal concentrations. When the reaction finishes, STREPTAVIDIN is added; this binds only to the biotin-labeled strands. Subsequent gel electrophoresis (in a denaturing gel) separates the two types of strand: the mobility of a streptavidin-bound strand is much lower. In this approach the biotinylated primer gives rise to the strand which is *not* required.

asymmetric strand-specific analysis of gene expression See the entry ASSAGE.

AT type See the entry BASE RATIO.

ATE 'Antisense transcriptome analysis using exon array': see the entry TRANSCRIPTOME.

ATMS *p*-Aminophenyltrimethoxysilane: a reagent used for covalently binding DNA probes to a solid support when preparing a MICROARRAY. (In an earlier procedure, DNA was bound *non*-covalently to glass slides by the reagent poly-L-lysine.) [Method: Nucleic Acids Res (2001) 29:e107.]

(See also DENDRICHIP.)

atomic force microscopy (AFM; or scanning force microscopy) A method for imaging *surfaces*, including those of molecules and of (living) cells, in e.g. air or liquid, at nanometer-scale resolution. The object's surface is scanned, in a raster pattern, with a fine probe located underneath a traveling cantilever; a laser, reflected from the cantilever – thus giving information on cantilever's movements – is detected by a photodiode, and incoming signals are converted, by computer, into a surface profile.

Atomic force microscopy was used e.g. to study chromatin structure and nucleosome remodeling [Methods (2007) 41(3): 333–341]; to analyze repetitive α-satellite DNA [Eur Biophys J (2007) 37(1):81–93]; and for the characterization of an antibody scFv [Nanomedicine (2008) 4(1):1–7].

Atomic force microscopy was used for direct visualization of G-quadruplexes in DNA [Nucleic Acids Res (2009) doi: 10.1093/nar/gkp679].

AFM has been used for characterizing RNA from satellite tobacco mosaic virus [Nucleic Acids Res (2010) doi: 10.1093/nar/gkq662].

[Atomic force microscopy for the imaging of viruses and virus-infected cells: Microbiol Mol Biol Rev (2011) 75:268–285, doi: 10.1128/MMBR.00041-10.]

ATP:GTP pyrophosphotransferase See the entry RELA/SPOT HOMOLOG (RSH) SUPERFAMILY.

ATPase An enzyme which cleaves phosphate from ATP in an energy-converting event.

(See also AAA ATPASES and NTPASE.)

atsRNAs Artificial *trans*-encoded sRNAs: see the entry SRNAS.

***att* sites** Chromosomal sites at which SITE-SPECIFIC RECOMBINATION occurs e.g. when the genome of PHAGE LAMBDA integrates into a bacterial chromosome.

Lambda *att* sites are used in commercial DNA technology systems: see e.g. the GATEWAY SITE-SPECIFIC RECOMBINATION SYSTEM, MULTISITE GATEWAY TECHNOLOGY, BP CLONASE and LR CLONASE.

To facilitate the use of φC31 recombinase for site-specific

recombination in *Saccharopolyspora erythraea* (an organism used for producing erythromycin A), artificial *attB* sites have been inserted into the organism's chromosome [Appl Environ Microbiol (2011) doi: 10.1128/AEM.06034-11].

(See also *att*Tn*7* in the entry TN7.)

attaching and effacing lesion See PATHOGENICITY ISLAND.

***att*B, *att*P** See the entry PHAGE LAMBDA. (See also ATT SITES and GATEWAY SITE-SPECIFIC RECOMBINATION SYSTEM.)

attenuator control See the entry OPERON.

***att*I sites** See the entry TN4655.

***att*L, *att*R** See the entry PHAGE LAMBDA. (See also ATT SITES and GATEWAY SITE-SPECIFIC RECOMBINATION SYSTEM.)

atto- A prefix meaning 10^{-18}. (See also *Ready reference* at the front of the dictionary.)

AttoPhos™ A reagent (Promega, Madison WI, USA) that can be cleaved by ALKALINE PHOSPHATASE to yield a fluorophore.

Attophos™ has been used e.g. in studies on the staging of trypanosomiasis [PLoS Negl Trop Dis (2009) 3(6):e459] and in immunoblotting in studies on prion proteins [Mol Biol Cell (2009) 20(1):233–244]. Other uses include studies on DNA and (modified) vaccinia vaccines [J Infect Dis (2011) 203(5): 610–619] and enzyme activation PLoS ONE (2012) doi: 10.1073/journal.pone.0033350].

att*Tn*7 See the entry TN7.

Aubergine A member of the Piwi subfamily of ARGONAUTE proteins which is found in *Drosophila*. It is reported to be essential e.g. for germ cell formation.

(See also PIWI PROTEIN.)

Augmentin A combined formulation of the β-lactam antibiotics clavulanic acid (see β-LACTAMASES) and amoxycillin; its uses include e.g. the treatment of urinary tract infections.

autoactivation (*syn*. self-activation) (two-hybrid systems) Activation of a reporter system without prior interaction between the bait and prey proteins.

autocatalytic aptazyme See APTAZYME.

autocatalytic splicing See SPLICING.

autoclave An apparatus within which objects and/or materials are sterilized by saturated (air-free) steam under pressure; the conditions in a working autoclave are commonly within the range 115°C (~69 kPa; 10 lb/inch^2) to 134°C (~207 kPa; 30 lb/inch^2).

STERILIZATION in an autoclave is carried out e.g. when preparing certain types of media. The heat-labile constituents of a medium (e.g. a solution of an antibiotic) may be membrane-filtered before being added to a sterile (autoclaved) medium.

Some steam-impermeable items that cannot be sterilized by autoclaving may be sterilized in a hot-air oven at 160–170°C for ~1 hour.

autoclave tape A paper strip (usually self-adhesive) which is included with the objects being sterilized in an autoclave; it exhibits a visible change (e.g. in color) when it is subjected to appropriate sterilizing conditions, and can therefore act as a check on the correct operation of the autoclave.

autogenous regulation The regulation of expression of a gene, or operon, by its own product(s).

***Autographa californica* NPV** A member of the NUCLEAR POLYHEDROSIS VIRUSES.

autoinducer (in quorum sensing) See QUORUM SENSING.

autointegration During infection of cells by human immunodeficiency virus 1 (HIV-1): the aberrant interaction of the end regions of HIV DNA with *viral* DNA (rather than interaction with the chromosome), i.e. the contrary of what is needed for integration of viral DNA into the chromosome. Such an event appears to be inhibited by the high proportion of uridines in viral DNA (>500 uracils/genome) [Proc Natl Acad Sci USA (2012) 108(22):9244–9249, doi: 10.1073/pnas.1102943108].

(Overexpression of UNG was reported to inhibit replication of human immunodeficiency virus [Nucleic Acids Res (2009) doi: 10.1093/nar/gkp673].)

autologous transplantation Transplantation involving the cells of an individual which have been removed, modified *ex vivo*, and then returned to that individual. This approach has been used in GENE THERAPY (q.v. for examples) for treating certain disorders.

(An alternative approach that has been used in gene therapy uses cells from an immunologically compatible donor.)

automated sequencing (of DNA) A method used for rapidly sequencing DNA fragments of up to ~800 nt. Essentially, the process involves conventional chain-termination (i.e. Sanger) sequencing (see DIDEOXY METHOD) with fluorophore-labeled ddNTPs – each type of ddNTP (A, G, C, T) being labeled with a fluorophore that emits a distinctive color on excitation. The sequencing products are separated by polyacrylamide gel electrophoresis and the bands of products are scanned by a laser; the positions of individual nucleotides, identified by the color of the fluorescence, are recorded automatically.

(See also DNA SEQUENCING and PYROSEQUENCING.)

autonomous ZNFs See the entry ZINC-FINGER NUCLEASE.

autonomously replicating sequence See the entry ARS.

autoplast A PROTOPLAST or SPHEROPLAST which develops as a result of activity of an organism's own autolytic enzymes.

autoradiography A procedure in which a radioactive source is detected or quantitated by its effect on a photographic film; a film is exposed to the radioactive source, in the dark, and for an appropriate period of time, and is subsequently processed.

Autoradiography is used e.g. for investigating intracellular processes (radioactive isotopes being incorporated into biomolecules), and is also used for detecting bands of products (fragments of DNA), following gel electrophoresis, by means of radioactively labeled probes (see PROBE LABELING).

In general, optimal resolution may require the use of those isotopes which have relatively low-energy emission (such as tritium, ^{3}H) rather than those (such as ^{32}P) which have high-energy emission.

autosomal dominant disorder Refers to a genetic disorder in which the phenotypic manifestation arising from expression of an abnormal autosomic allele occurs in the presence of the corresponding normal allele – that is, the influence of the abnormal allele overrides that of the normal allele. This type of disorder tends to exhibit a so-called *vertical* pattern of trans-

mission from one generation to the next; in such cases, an abnormal trait is more likely (than in an autosomal recessive condition) to affect each successive generation.

Both males and females can be affected – and, unlike the situation in X-linked dominant disorders, father-to-son transmission can occur.

Examples of these disorders: AXENFELD–RIEGER SYNDROME, LI–FRAUMENI SYNDROME, PEUTZ–JEGHERS SYNDROME (see also CHARCOT–MARIE–TOOTH DISEASE).

(cf. AUTOSOMAL RECESSIVE DISORDER, X-LINKED DISORDER.)

autosomal recessive disorder Refers to a genetic disorder in which manifestation of the abnormal phenotype is exhibited when an abnormal allele is not accompanied by the presence of the corresponding normal, wild-type allele; heterozygous individuals with one normal allele do not usually exhibit the abnormal phenotype.

Both males and females can be affected.

When mating occurs between two (homozygously) affected individuals the trait is found in all offspring; mating between heterozygous individuals – or between one heterozygous and one normal individual – tends to spare some of the offspring. An autosomal recessive disorder may miss generation(s); it is said to exhibit a *horizontal* mode of transmission.

Autosomal recessive disorders include: BERNARD–SOULIER SYNDROME, citrullinemia type II, CRIGLER–NAJJAR SYNDROME type I, FRIEDREICH'S ATAXIA, GLANZMANN'S THROMBASTHENIA, ICF SYNDROME, PHENYLKETONURIA, SMITH–LEMLI–OPITZ SYNDROME, TAY–SACHS DISEASE, WERNER SYNDROME and XERODERMA PIGMENTOSUM.

(cf. AUTOSOMAL DOMINANT DISORDER, X-LINKED DISORDER.)

autosome Any chromosome other than a HETEROSOME.

autotransporter See the entry OMPT GENE.

auxins Phytohormones (plant hormones) which promote stem elongation and other aspects of plant development; the auxins are derivatives of tryptophan. Indole 3-acetic acid (IAA; also referred to as 'auxin' or 'heteroauxin') is a major auxin; it is synthesized from the precursor indole 3-acetonitrile (IAN).

Abnormally high levels of auxins (*hyperauxiny*) are found in some plant diseases (e.g. CROWN GALL).

auxotrophic mutant Any microorganism which, as a result of a mutation, is unable to synthesize an essential nutrient and which therefore can grow only if provided with an exogenous source of that nutrient. (An organism which does *not* contain such a mutation, and which can synthesize all of its essential nutrients, is called a *prototroph*.)

One example of an auxotrophic mutant is mentioned in the entry AMES TEST.

An auxotrophic strain can be used e.g. in BACTOFECTION.

Isolation of auxotrophic bacteria

The usual selective procedures are not suitable for isolating auxotrophic bacteria from a mixture of prototrophs and auxotrophs: a medium that supports the growth of auxotrophs will also permit the growth of the corresponding prototrophs.

The *limited enrichment* method uses an agar-based *minimal medium* enriched with *small* amounts of nutrients. A minimal medium is one which supports the growth of prototrophs but – because it lacks one or more essential nutrients – does not support the growth of auxotrophs. Any colony of auxotrophic cells will quickly exhaust the small amount of nutrients in its vicinity – so that the colony will remain small; however, the unrestricted growth of prototrophs on the medium means that colonies of prototrophs will be larger than those of the auxotrophs. Hence, the small colonies indicate presumptive auxotrophs.

The *delayed enrichment* technique employs an agar-based minimal medium for initial growth, so that prototrophs (only) form colonies in the initial incubation. Complete medium is then poured onto the plate and allowed to set; the nutrients in this medium diffuse into the minimal medium below, allowing the growth of auxotrophs. Again, small colonies indicate presumptive auxotrophs.

For (penicillin-sensitive) bacteria, auxotrophic mutants can be isolated by virtue of their inability to grow in a (penicillin-containing) minimal medium; penicillin is an antibiotic that acts only on *growing* cells. In this technique, a well-washed population of bacteria (that includes auxotrophs) is exposed to penicillin in a minimal medium; the prototrophs (which are able to grow) are killed by the penicillin. The remaining cells are washed and re-plated on a complete medium in order to recover any auxotrophs that may be present. It's important to note that, if the auxotrophs had developed through an *in vitro* process of mutagenization, the cells must be allowed to grow for several generations in complete medium prior to exposure to penicillin; this is because newly mutated cells will contain a full complement of (prototrophic) enzymes – auxotrophy developing only after several rounds of cell division, during which the prototrophic enzymes are 'diluted out'. A failure to observe this requirement would cause the death of any newly mutagenized auxotrophs on exposure to penicillin. A further requirement in this method is that only a low concentration of cells be used; the reason for this is that auxotrophs should not be allowed to grow on nutrients released by lysed prototrophs as this would render them susceptible to lysis by penicillin. For this reason, STREPTOZOTOCIN (q.v.) may be used in place of penicillin.

Auxotrophs may also be isolated by REPLICA PLATING.

Avian erythroblastosis virus See the entry ERB.

Avian leukosis virus See the entry ALPHARETROVIRUS.

Avian myeloblastosis virus See the entry ALPHARETROVIRUS.

avirulence gene See the entry GENE-FOR-GENE CONCEPT.

Avulavirus A genus of viruses in the family PARAMYXOVIRIDAE; it includes the *Newcastle disease virus*.

Axenfeld–Rieger syndrome An autosomal dominant disorder involving eye defects and certain systemic abnormalities. The syndrome has been associated with mutations in the *PITX2* gene – which encodes a transcription factor – or mutation in other genes (e.g. *FOXC1*, *PAX6*). [A novel *PITX2* mutation: Mol Vision (2008) 14:2205–2210.]

In some patients the disorder is reported to involve aberrant splicing of pre-mRNA; it was suggested that variability in the

extent of the splicing fault may be reflected in the variability of phenotypic manifestations [BMC Med Genet (2006) 7:59].

5-aza-2′-deoxycytidine (decitabine) A nucleoside analog used for studying DEMETHYLATION and as a therapeutic agent in the treatment of (e.g.) myelodysplastic syndrome and myeloid leukemia. In cells, 5-aza-2′-deoxycytidine is phosphorylated and incorporated into DNA; it then inhibits methyltransferase activity – for example, it has been shown to reactivate tumor suppressor genes silenced by methylation of promoter DNA. Although effective against leukemias, this agent is generally less effective against solid tumors.

Studies on MELANOMA cells suggest that the activity against this type of cancer could be made more effective with better knowledge of the epigenetic and genetic details of individual tumors [PLoS ONE (2009) 4(2):e4563]. (These studies also suggested that HDAC and proteasomal inhibitors might act synergistically with a methyltransferase inhibitor in a subset of patients.)

Studies to determine the optimal therapeutic dosing of 5-aza-2′-deoxycytidine have been carried out in cultured cells [BMC Cancer (2008) 8:128]. Together with various HDACs, 5-aza-2′-deoxycytidine has been studied in Ewing's sarcoma cells [Cancer Cell Int (2008) 8:16]. This agent has also been used in studies on promoter methylation in breast tumor cell lines [BMC Cancer (2009) 9:80], and for identifying hypermethylated genes [BMC Med Genomics (2009) 2:11].

5-aza-2dC The nucleoside analog 5-AZA-2′-DEOXYCYTIDINE.

5-aza-CdR The nucleoside analog 5-AZA-2′-DEOXYCYTIDINE.

5-azacytidine A nucleoside analog that is used e.g. for inhibiting DNA methyltransferases; its activity is similar to that of 5-AZA-2′-DEOXYCYTIDINE (q.v.).

azaserine (*O*-diazoacetyl-L-serine) An agent with antimicrobial and antitumor activity produced by *Streptomyces* sp (a Gram-positive bacterium). It inhibits the activity of phosphoribosylformylglycinamidine synthetase (and certain other enzymes), inhibiting biosynthesis of purines (and hence nucleotides). (cf. DON; see also HADACIDIN.)

AZT See the entry ZIDOVUDINE.