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Science, Genetics

Use RESTRICTED to schools where students have purchased this manual Molecular Genetics IB SL IB HL IB Options AP Biology Complete nos: Complete nos: Complete nos: Complete nos: 1, 3-4, 7, 9(a), 11, 13(a)-(d), 14-15, 20-22 Extension: 2, 12 1-26, 28-29, 3132, 34 Extension: 27, 30, 33 Option D: 30 1-34 Some numbers as extension as appropriate L earning Objectives 1. Compile your own glossary from the KEY WORDS displayed in bold type in the learning objectives below. The genetic blueprint Nucleic acid structure (pages 128-130, 132-135, also see 150) 2. Name some examples of nucleic acids and describe their role in biological systems. 3. Describe the components of a (mono)nucleotide: a 5C sugar (ribose or deoxyribose), a nitrogenous base (purine or pyrimidine), and a phosphate. Identify the bases that form nucleotides. 4. Understand the role of condensation reactions in joining the components of nucleotides and in the formation of di- and polynucleotides (nucleic acids). 5. Outline the structure of nucleosomes, including reference to the role of histone proteins in packaging of the DNA in the nucleus. 6. Understand that DNA contains repetitive sequences and that only a small proportion constitutes genes. Appreciate the role of repetitive sequences in DNA technologies such as DNA profiling. 7. Describe the Watson-Crick double-helix model of DNA structure and the base pairing rule. Explain the importance of complementary base pairing to the conservation of the base sequence in DNA. Contrast the structure and function of DNA and RNA. 8. In more detail than #7 above, describe the structure of DNA including the antiparallel strands, the 3’—5’ linkages, and the role of the hydrogen bonding between purines and pyrimidines. DNA replication (pages 136-137) 9. Describe the semi-conservative replication of DNA, and interpret

experimental evidence for this process. Explain the role of the following in DNA replication: (a) DNA polymerase, helicase, DNA ligase. (b) DNA polymerase III, RNA primase, DNA polymerase I, Okazaki fragments, and deoxynucleoside triphosphates. 10. Understand that DNA replication proceeds only in the 5’ â†’ 3’ direction and explain the significance of this. Explain the term: replication fork, and explain its significance in eukaryotic chromosomes. 11. Demonstrate an understanding of the base-pairing rule for creating a complementary strand from a template strand. 12. Appreciate the role of polymerase chain reaction (PCR) as an artificially induced form of DNA replication, used as a tool in molecular biology (see the topic Aspects of Biotechnology for coverage of this technique). Photocopying Prohibited The genetic code (page 131) 13. Explain the main features of the genetic code, including reference to the following: (a) The 4-letter alphabet and the 3-letter triplet code (codon) of base sequences. (b) The non-overlapping, linear nature of the code. (c) The universal nature of the code. (d) The degeneracy of the code. (e) The way in which the code is always read from a start point to a finish point in a 3’ â†’ 5’ direction. (f) Specific punctuation codons and their significance. Gene expression (pages 138-143) 14. Outline the basis by which information is transferred from DNA to protein. Distinguish clearly between allele and gene. Explain what is meant by gene expression and define its two distinct stages: transcription and translation. Note that gene expression is sometimes used to refer just to transcription. 15. Recall the structure and role of messenger RNA (mRNA). In simple terms, describe the process of transcription, identifying the role of RNA polymerase. 16. In more detail than in #15 above, describe the process of transcription. Demonstrate

an understanding of the direction of transcription (5’ â†’ 3’ direction). 17. Distinguish between the coding (sense) strand, template (antisense) strand. Relate the base sequence on each of these strands to the sequence on the mRNA molecule. 18. Distinguish between introns and exons. Explain the significance of introns with the respect to the production of a functional mRNA molecule. 19. Understand how reverse transcriptase catalyzes the production of DNA from RNA. Explain how this enzyme is used by retroviruses. Appreciate the use of reverse transcriptase in molecular biology. 20. Recall the structure of proteins as polypeptides with a complex (post-translational) structure. 21. Explain how the 4-letter alphabet of bases provides the code for the 20 amino acids needed to assemble proteins. Explain the relationship between one gene and one polypeptide. 22. In simple terms, describe the process of translation. Describe the role of transfer RNA (tRNA) molecules in translation, with reference to the significance of the anticodons. Understand and explain the general role of ribosomes in translation. 23. With respect to the process of translation, describe how the structure of transfer RNA (tRNA) molecules allows recognition by a tRNA-activating enzyme. Explain the role of this enzyme in binding specific amino acids to their tRNAs and identify the role of ATP in this process. © Biozone International 2001-2003 Use RESTRICTED to schools where students have purchased this manual 127 Molecular Genetics 24. Outline the structure of ribosomes with reference to: small and large subunits, RNA and protein, tRNA binding sites, and mRNA binding sites. Relate the functional role of ribosomes to their specific structure. 25. Describe translation as a process involving initiation, elongation, and

termination, occurring in a 5’ â†’ 3’ direction. In more detail than in #22 above, explain the process of translation including more detailed reference to ribosomes, polysomes (polyribosomes), start codons, and stop codons. 26. Distinguish between protein synthesis on free ribosomes and on those bound to the endoplasmic reticulum. Explain why proteins are synthesized in these different locations in the cell. 27. Contrast gene expression in prokaryotic and eukaryotic cells, identifying differences in mRNA processing after transcription, movement of the mRNA to the site of translation, and the speed at which translation can take place. Control of metabolic pathways Metabolic Pathways (pages 144-145) 28. Recognize enzymes as proteins whose synthesis is controlled by DNA. Appreciate the role of enzymes in the control of metabolic pathways and in determining the phenotype of an organism. 29. Explain clearly how enzymes control metabolic pathways as illustrated by specific examples e. g. oxidoreductases, anabolism and catabolism. With respect to this control, explain how the amount or activity of an enzyme regulating a metabolic pathway can itself be controlled. Define the terms: end-product and end-product inhibition. 30. Identify major metabolic disorders that are inherited in humans. Explain, using an example, how the malfunction of enzymes are responsible in many cases. Exemplar case study: metabolism of phenylalanine. Describe the metabolic breakdown of the essential amino acid phenylalanine by liver enzymes. Describe how malfunctioning of specific enzymes can interrupt this metabolic pathway, causing a variety of metabolic defects e. g. phenylketonuria (PKU). Regulation of gene action (pages 146-147) 31. Understand the term operon as being a unit of genes in prokaryotes that function in a coordinated way

under the control of an operator gene. Comment on the extent to which the operon model is universally applicable. 32. Explain how simple metabolic pathways are regulated in bacteria, as illustrated by the lac operon in E. coli. Outline the principles involved in gene induction in the lac operon, identifying how lactose activates transcription and how metabolism of the substrate is achieved. Explain the adaptive value of gene induction. 33. Appreciate that the end-product of a metabolic pathway can activate a repressor and switch genes off (gene repression). Appreciate the adaptive value of gene repression for the control of a metabolic end-product. 34. Describe the regulation of gene action (transcriptional control only) in eukaryotes. Identify the roles of the promoter region, RNA polymerase, and the terminator (not to be confused with terminator codons in translation). Appreciate that the energy for the incorporation of the nucleotides into the mRNA strand in mRNA synthesis is provided by the hydrolysis of nucleoside triphosphates (ATP, GTP, CTP, and UTP). NOTE: In DNA replication, the nucleoside triphosphates are dATP, dGTP, dCTP, and dTTP. For simplicity, often the nucleotide only is shown). â– Control Centre New Scientist, 17 July 1999, (Inside Science). The organization of DNA in eukaryotic cells, the nucleus, how genes code for proteins, and the role of ribosomes and RNA. Metabolic pathways and their control Textbooks See the ‘ Textbook Reference Grid’ on pages 8-9 for textbook page references relating to material in this topic. Supplementary Texts See pages 5-6 for additional details of these texts: â– Adds, J., et al., 2000. Molecules and Cells, (NelsonThornes), pp. 19-32. â– Clegg, C. J., 1999. Genetics & Evolution, (John Murray), pp. 40-42, 44-47. â– Jones, N., et al., 2001. Essentials of Genetics,

(John Murray), pp. 123-155 as required. Periodicals See page 6 for details of publishers of periodicals: STUDENT'S REFERENCE Gene structure and expression â– Gene Structure and Expression Biol. Sci. Rev., 12 (5) May 2000, pp. 22-25. An account of gene function, including a comparison of gene regulation in pro- and eukaryotes. â– What is a Gene? Biol. Sci. Rev., 15(2) Nov. 2002, pp. 9-11. A good synopsis of genes and their role in heredity, mutations, and transcriptional control of gene expression. â– Transfer RNA Biol. Sci. Rev., 15(3) Feb. 2003, pp. 26-29. A good account of the structure and role of tRNA in protein synthesis. â– DNA in a Spin Biol. Sci. Rev., 11(3) Jan. 1999, pp. 15-17. A short account of the methods used to establish the mechanism for DNA replication. â– Molecular Machines that Control Genes Scientific American, Feb. 1995, pp. 38-45. How gene action is regulated by protein complexes that assemble on DNA. â– A Discovery Lab for Studying Gene Regulation The American Biology Teacher, 59(8), Oct. 1997, pp. 522-526. Investigating gene regulation in prokaryotes: a how-to-do-it account. â– Tyrosine Biol. Sci. Rev., 12 (4) March 2000, pp. 29-30. The central metabolic role of the amino acid tyrosine (includes errors in tyrosine metabolism). â– Genes that Control Genes New Scientist, 3 Nov. 1990 (Inside Science). The control of gene expression in prokaryotes by gene induction and repression. The operon model is explained. TEACHER'S REFERENCE â– DNA 50 SSR, 84(308), March 2003, pp. 17-80. A special issue celebrating 50 years since the discovery of DNA. There are various articles examining the practical and theoretical aspects of teaching molecular genetics and inheritance. â– DNA: 50 Years of the Double Helix New Scientist, 15 March 2003, pp. 35-51. A special issue on DNA: structure and

function, repair, the new-found role of histones, and the functional significance of chromosome position in the nucleus. â– Modeling the Classic Meselson and Stahl Experiment The American Biology Teacher, 63(5), May 2001, pp. 358-361. An account of how to model the experiments of Meselson and Stahl to demonstrate semi-conservative replication of DNA. â– A Working Model of Protein Synthesis using Lego™ Building Blocks The American Biology Teacher, 64(9), Nov. 2002, pp. 673-678. Using a hands-on project to demonstrate the various stages of protein synthesis. Internet See pages 10-11 for details of how to access Bio Links from our web site: www. thebiozone. com. From Bio Links, access sites under the topics: GENERAL BIOLOGY ONLINE RESOURCES > Online Textbooks and Lecture Notes: - S-Cool! A level biology revision guide - Learn. co. uk - Mark Rothery's biology web site ... and others CELL BIOLOGY AND BIOCHEMISTRY: - Cell and molecular biology online - MIT biology hypertextbook ... and others GENETICS: - DNA basics - MIT biology hypertextbook - Gene almanac - Virtual library on genetics - Prokaryotic genetics and gene expression chapter ... and others > Molecular Genetics (DNA): - Beginners guide to molecular biology - Basic genetics - DNA and molecular genetics - DNA from the beginning - DNA workshop - E! Mouse - Primer on molecular genetics - Protein synthesis - Model of Lac operon (animation) - Induction of the Lac operon - Molecular genetics of prokaryotes â– Deciphering the Code of Life Scientific American, December 1999, pp. 50-55. An exploration of what will be gained from the study of the genomes of humans and other organisms. â– Stuff or Nonsense New Scientist, 1 April 2000, pp. 38-41. The functional and evolutionary role of introns (junk DNA) in the genomes of organisms.

Photocopying Prohibited © Biozone International 2001-2003 Software and video resources are now provided in the Teacher Resource Handbook Use RESTRICTED to schools where students have purchased this manual Molecular Genetics 128 Nucleic Acids A Nucleic acids are a special group of chemicals in cells concerned with the transmission of inherited information. They have the capacity to store the information that controls cellular activity. The central nucleic acid is called deoxyribonucleic acid (DNA). DNA is a major component of chromosomes and is found primarily in the nucleus, although a small amount is found in mitochondria and chloroplasts. Other ribonucleic acids (RNA) are involved in the ‘ reading’ of the DNA information. All nucleic acids are made up of simple repeating units called nucleotides, linked together to form chains or strands, often of great length (see the activity DNA Molecules). The strands vary in the sequence of the bases found on each nucleotide. It is this sequence which provides the ‘ genetic code’ for the cell. In addition to nucleic acids, certain nucleotides and their derivatives are also important as suppliers of energy (ATP) or as hydrogen ion and electron carriers in respiration and photosynthesis (NAD, NADP, and FAD). Chemical Structure of a Nucleotide Bases Purines: N P O OCH 2 G Guanine NH 2 OH OH A Adenine N N O O Pyrimidines: C N T U H H OH Phosphate Cytosine H Uracil (RNA only) H Sugar The two-ringed bases above are purines and make up the longer bases. The single-ringed bases are pyrimidines. Although only one of four kinds of base can be used in a nucleotide, uracil is found only in RNA, replacing thymine. DNA contains: A, T, G, and C, while RNA contains A, U, G, and C. Base Symbolic Form of a Nucleotide A Phosphate: Links neighboring sugars together. Thymine (DNA only) H Sugars Base: One of four types

possible (see box on right). This part of the nucleotide comprises the coded genetic message. Sugar: One of two types possible: ribose in RNA and deoxyribose in DNA. OH Ribose Nucleotides are the building blocks of DNA. Their precise sequence in a DNA molecule provides the genetic instructions for the organism to which it governs. Accidental changes in nucleotide sequences are a cause of mutations, usually harming the organism, but occasionally providing benefits. RNA Molecule H Deoxyribose Deoxyribose sugar is found only in DNA. It differs from ribose sugar, found in RNA, by the lack of a single oxygen atom (arrowed). DNA Molecule G DNA Molecule C G Deoxyribose sugar U In RNA, uracil replaces thymine in the code. T A C G C A Ribose sugar Hydrogen bonds hold the two strands together. Only certain bases can pair. A T Symbolic representation Ribonucleic acid (RNA) comprises a single strand of nucleotides linked together. Space filling model Deoxyribonucleic acid (DNA) comprises a double strand of nucleotides linked together. It is shown unwound in the symbolic representation (left). The DNA molecule takes on a twisted, double helix shape as shown in the space filling model on the right. Photocopying Prohibited © Biozone International 2001-2003 Use RESTRICTED to schools where students have purchased this manual 129 Molecular Genetics Formation of a nucleotide Formation of a dinucleotide Condensation (water removed) A H2O H 2O T H2O A Two nucleotides are linked together by a condensation reaction between the phosphate of one nucleotide and the sugar of another. Hydrolysis (water added) C A nucleotide is formed when phosphoric acid and a base are chemically bonded to a sugar molecule. In both cases, water is given off, and they are therefore condensation reactions. Double-stranded DNA molecule 3'

5' The double-helix structure of DNA is like a ladder twisted into a corkscrew shape around its longitudinal axis. It is ‘ unwound’ here to show the relationships between the bases. C - The way the correct pairs of bases are attracted to each other to form hydrogen bonds is determined by the number of bonds they can form and the shape (length) of the base. G G A T - The template strand is the side of the DNA molecule that stores the information that is transcribed into mRNA. - The other side (sometimes called the coding strand) has the same nucleotide sequence as the mRNA except that T in DNA substitutes for U in mRNA. The coding strand is also called the sense strand. T A C 5' 3' 1. The diagram above depicts a double-stranded DNA molecule. Label the following parts on the diagram: (a) Sugar (deoxyribose) (b) Phosphate (c) Hydrogen bonds (points of attraction between bases) (d) Purine bases (e) Pyrimidine bases 2. State the ‘ base-pairing rule’ which describes which bases can pair up opposite each other to form a double-stranded DNA molecule: 3. State the functional role of the following nucleic acids: (a) Nucleotides: (b) ATP: (c) NAD/NADP: (d) Coenzyme A: 4. Complete the following table that summarizes the differences between DNA and RNA molecules: DNA RNA Sugar present Bases present Number of strands Relative length Photocopying Prohibited © Biozone International 2001-2003 Use RESTRICTED to schools where students have purchased this manual Molecular Genetics 130 DNA Molecules D Even the smallest DNA molecules are extremely long. The DNA from the small Polyoma virus, for example, has a length of 1. 7µm (about 3 times longer than the longest proteins). The DNA comprising a bacterial chromosome is 1000 times longer than the cell into which it has to fit. The amount of DNA

present in the nucleus of the cells of eukaryotic organisms varies widely from one species to another. The quantity of DNA in vertebrate sex cells ranges from 40 000 kb to 80 000 000 kb, with humans in the middle of the range. There is good reason to believe that most proteins (or polypeptide chains) are coded for by only one gene in each set of chromosomes. Proteins that are found in relatively large concentrations within the cell usually have multiple copies of their gene. About 50-75% of the DNA consists of base sequences that are long enough to code for proteins (around 1000 bases). Current estimates suggest that as little as 10% of the human genome (the total DNA complement of a cell) encodes proteins or structural RNA and is therefore made up of genes. Of the remaining 90% of the DNA, some is used for the structural aspects of gene expression, DNA replication, chromosome division, and organizing chromatin within the chromosome. Some regions of the DNA appear to have no function, although this view may change with further research. Kilobase (kb) Sizes of DNA Molecules Group Base pairs Organism Viruses Length (in 1000s, or kb) Polyoma or SV40 5. 1 1. 7 µm 48. 6 Lambda phage 17 µm T2 phage 166 190 DNA 65 µm Mycoplasma 760 Drosophila (fruit fly) Human 260 µm 4 600 1. 56 mm 13 500 4. 6 mm 165 000 5. 6 cm 2 900 000 E. coli (from human gut) Yeast Eukaryotes Exons: coding regions 56 µm Vaccinia Bacteria A unit of length equal to 1000 base pairs of a double-stranded nucleic acid molecule (or 1000 bases of a single-stranded molecule). One kilobase of double stranded DNA has a length of 0. 34 µm. (1 µm = 1/1000 mm) 99 cm Intron Intron: edited out during protein synthesis Intron Most genes in eukaryotic DNA are not continuous and may be interrupted by ‘ intrusions’ of other pieces of DNA. Coding regions (exons)

are interrupted by non-coding regions called introns. Introns range in frequency from 1 to over 30 in a single gene and also in size (100 to more than 10 000 bases). They are edited out of the genetic instructions during protein synthesis. Giant lampbrush chromosomes Lampbrush chromosomes are large chromosomes found in amphibian eggs, with lateral loops of DNA that produce a brushlike appearance under the microscope. The two scanning electron micrographs (below and right) show minute strands of DNA giving a fuzzy appearance in the high power view. Loops of DNA EII EII Enlarged 1. Consult the table above and make the following comparisons. Determine how much more DNA is present in: (a) The bacterium E. coli compared to the Lambda phage virus: (b) Human cells compared to the bacteria E. coli: 2. State what proportion of DNA in a eukaryotic cell is used to code for proteins or structural RNA: 3. List three functions for some of the remaining (noncoding) DNA: (a) (b) (c) 4. State the length of all the DNA (genome) from a single human cell: Photocopying Prohibited © Biozone International 2001-2003 Use RESTRICTED to schools where students have purchased this manual 131 Molecular Genetics The Genetic Code A The genetic information that codes for the assembly of amino acids is stored as three-letter codes, called codons. Each codon represents one of 20 amino acids used in the construction of polypeptide chains. The mRNA amino acid table (bottom of page) can be used to identify the amino acid encoded by each of the mRNA codons. Note that the code is degenerate in that for each amino acid, there may be more than one codon. Most of this degeneracy involves the third nucleotide of a codon. The genetic code is universal; all living organisms on Earth, from viruses and bacteria, to plants and humans,

share the same genetic code book (with a few minor exceptions representing mutations that have occurred over the long history of evolution). Codons that code for this amino acid No. GCU, GCC, GCA, GCG 4 Amino acid Codons that code for this amino acid Amino acid Leu Leucine Arg Arginine Lys Lysine Asn Asparagine Met Methionine Asp Aspartic acid Phe Phenylalanine Cys Cysteine Pro Proline Gln Glutamine Ser Serine Glu Glutamic acid Thr Threonine Gly Glycine Try Tryptophan His Histidine Tyr Tyrosine Iso Isoleucine Val No. Valine Ala Alanine 1. Use the mRNA amino acid table (below) to list in the table above all the codons that code for each of the amino acids and the number of different codons that can code for each amino acid (the first amino acid has been done for you). 2. (a) State how many amino acids could be coded for if a codon consisted of just TWO bases: (b) Explain why this number of bases is inadequate to code for the 20 amino acids required to make proteins: 3. There are multiple codons for a single amino acid. Comment on the significance of this with respect to point mutations: Read second letter here Read third letter here Second Letter Read first letter here U C A G U UUU UUC UUA UUG Phe Phe Leu Leu UCU UCC UCA UCG Ser Ser Ser Ser UAU UAC UAA UAG Tyr Tyr STOP STOP UGU UGC UGA UGG Cys Cys STOP Try U C A G C CUU CUC CUA CUG Leu Leu Leu Leu CCU CCC CCA CCG Pro Pro Pro Pro CAU CAC CAA CAG His His Gln Gln CGU CGC CGA CGG Arg Arg Arg Arg U C A G A AUU AUC AUA AUG Iso Iso Iso Met ACU ACC ACA ACG Thr Thr Thr Thr AAU AAC AAA AAG Asn Asn Lys Lys AGU AGC AGA AGG Ser Ser Arg Arg U C A G G GUU GUC GUA GUG Val Val Val Val GCU GCC GCA GCG Ala Ala Ala Ala GAU GAC GAA GAG Asp Asp Glu Glu GGU GGC GGA GGG Gly Gly Gly Gly U C A G Example: Determine CAG C on

the left row, A on the top column, G on the right row CAG is Gln (glutamine) Photocopying Prohibited © Biozone International 2001-2003 Third Letter How to read the table: The table on the right is used to 'decode' the genetic code as a sequence of amino acids in a polypeptide chain, from a given mRNA sequence. To work out which amino acid is coded for by a codon (triplet of bases) look for the first letter of the codon in the row label on the left hand side. Then look for the column that intersects the same row from above that matches the second base. Finally, locate the third base in the codon by looking along the row from the right hand end that matches your codon. First Letter mRNA-Amino Acid Table Use RESTRICTED to schools where students have purchased this manual Molecular Genetics 132 PA Creating a DNA Model Although DNA molecules can be enormous in terms of their molecular size, they are made up of simple repeating units called nucleotides. A number of factors control the way in which these nucleotide building blocks are linked together. These factors cause the nucleotides to join together in a predictable way. This is referred to as the base pairing rule and can be used to construct a complementary DNA strand from a template strand, as illustrated in the exercise below: DNA Base Pairing Rule Adenine is always attracted to Thymine A T Thymine is always attracted to Adenine T A Cytosine is always attracted to Guanine C G Guanine is always attracted to Cytosine G C 1. Cut out the facing page and separate each of the 24 nucleotides by cutting along the columns and rows (see arrows indicating 2 such cutting points). Although drawn as geometric shapes, these symbols represent chemical structures. 2. Place one of each of the four kinds of nucleotide on their correct spaces below: Place a cut-out symbol for thymine

here from the facing page Place a cut-out symbol for cytosine here from the facing page Thymine Cytosine Place a cut-out symbol for adenine here from the facing page Place a cut-out symbol for guanine here from the facing page Adenine Guanine 3. Identify and label each of the following features on the adenine nucleotide immediately above: phosphate, sugar, base, hydrogen bonds 4. Create one strand of the DNA molecule by placing the 9 correct 'cut out' nucleotides in the labeled spaces on the now facing page (DNA Molecule). Make sure these are the right way up (with the P on the left) and are aligned with the left hand edge of each box. Begin with thymine and end with guanine. 5. Create the complementary strand of DNA by using the base pairing rule above. Note that the nucleotides have to be arranged upside down. 6. Under normal circumstances, it is not possible for adenine to pair up with guanine or cytosine, nor for any other mismatches to occur. Describe the two factors that prevent a mismatch from occurring: Factor 1: Factor 2: 7. Once you have checked that the arrangement is correct, you may glue, paste or tape these nucleotides in place. NOTE: There may be some value in keeping these pieces loose in order to practise the base pairing rule. For this purpose, removable tape would be best. Photocopying Prohibited © Biozone International 2001-2003 Use RESTRICTED to schools where students have purchased this manual 133 Molecular Genetics Nucleotides Tear out this page along the perforation and separate each of the 24 nucleotides S Thymine Cytosine P P P S S Thymine Cytosine S P P P S S Thymine Cytosine by cutting along the columns and rows (see arrows indicating the cutting points). P S Adenine Guanine S P P S Adenine Guanine S P S P P S Adenine Guanine Cut S Thymine Cytosine P P P S S Thymine

Cytosine S P P P S S Thymine Cytosine Cut Cut Cut Photocopying Prohibited Cut Cut © Biozone International 2001-2003 P S Adenine Guanine S P P S Adenine Guanine S P S P P S Adenine Guanine Cut Cut Use RESTRICTED to schools where students have purchased this manual Molecular Genetics 134 This page is deliberately left blank Photocopying Prohibited © Biozone International 2001-2003 Use RESTRICTED to schools where students have purchased this manual 135 Molecular Genetics DNA Molecule P Adenine Adenine S Thymine S P P Put the named nucleotides on the left hand side to create the template strand Thymine Cytosine Adenine Adenine Guanine Thymine Thymine Cytosine Guanine Photocopying Prohibited © Biozone International 2001-2003 Put the matching complementary nucleotides opposite the template strand Use RESTRICTED to schools where students have purchased this manual Molecular Genetics 136 DNA Replication A The replication of DNA is a necessary preliminary step for cell division (both mitosis and meiosis). This process creates the two chromatids that are found in chromosomes that are preparing to divide. By this process, the whole chromosome is essentially 3' duplicated, but is still held together by a common centromere. Enzymes are responsible for all of the key events. The diagram below shows the essential steps in the process. The diagram on the facing page shows how enzymes are involved at each stage. Step 1: Unwinding the DNA molecule 5' Single-armed chromosome as found in non-dividing cell. A normal chromosome consists of a single DNA molecule packed into a single chromatid. The long molecule of double stranded DNA must be untwisted at high speed at its replication fork by two enzymes: helicase unwinds the parental strands; DNA gyrase then relieves the strain

that this generates by cutting, winding and rejoining the DNA strands. Temporary break to allow swivel. Step 2: Making new DNA strands Free nucleotides are used to construct the new DNA strand. The formation of new DNA is carried out mostly by an enzyme complex called DNA polymerase, and a series of proteins that cause the two strands to break apart. On one side (the leading strand), nucleotides are assembled in a continuous fashion. On the other side (the lagging strand) fragments of single-stranded DNA between 1000—2000 nucleotides long are created (Okazaki fragments). These will be later joined together to form one continuous length. Parent strand of DNA is used as a template to match nucleotides for the new strand. The new strand of DNA is constructed from free nucleotides, using the parent strand as a template. Each of the two newly formed DNA double helix molecules will go into creating a chromatid. 3' 5' 3' 5' The two new strands of DNA coil up into a helix. Step 3: Rewinding the DNA molecule Replicated chromosome ready for cell division. Photocopying Prohibited Each of the two new double-helix DNA molecules has one strand of the original DNA (dark gray and white) and one strand that is newly synthesized (patterned). The two DNA molecules rewind into their 'corkscrew' double-helix shape again. Each double-helix is then coiled around histone proteins and further wrapped up to form separate chromatids (still joined by a common centromere). The new chromosome has actually twice as much DNA as a regular (non-replicated) chromosome. The two chromatids will become separated in the cell division process to form two separate chromosomes. © Biozone International 2001-2003 Use RESTRICTED to schools where students have purchased this manual 137 Molecular Genetics Enzyme Control of DNA

Replication 3' Overall direction of replication 5' This process of DNA replication occurs at an astounding rate. As many as 4000 nucleotides per second are replicated. This explains how under ideal conditions, bacterial cells with as many as 4 million nucleotides, can complete a cell cycle in about 20 minutes. See the section on polymerase chain reaction for a useful application of this process. Double strand of original (parental) DNA Helicase: This enzyme splits and unwinds the 2-stranded DNA molecule. RNA polymerase: Synthesizes a short RNA primer which is later removed. Swivel point The leading strand is synthesized continuously in the 5' to 3' direction by DNA polymerase III. DNA polymerase III: Extends RNA primer with short lengths of complementary DNA. Parental strand provides a 'template' for the new strand's synthesis The lagging strand is formed in fragments, between 1000 and 2000 nucleotides long. Called Okazaki fragments, they are later joined together. RNA primers Replication fork re Di ct is n sy of DNA polymerase I: Digests RNA primer and replaces it with DNA. 5' 3' that one new strand is constructed as a continuous length (the leading strand) while the other new strand is made in short segments to be later joined together (the lagging strand). NOTE that the nucleotides are present as deoxynucleoside triphosphates. When hydrolyzed, these provide the energy for incorporating the nucleotide into the strand. 1. Briefly summarize the steps involved in DNA replication (on the facing page): (a) Step 1: (b) Step 2: (c) Step 3: 2. Explain the role of the following enzymes in DNA replication: (a) Helicase: (b) DNA polymerase I: (c) DNA polymerase III: (d) Ligase: 3. Briefly explain the purpose of DNA replication: 4. Determine the time it would take for a bacteria to replicate its DNA (see note in diagram above): Photocopying

Prohibited sis The sequence of enzyme controlled events in DNA replication is shown above. Although shown as separate, many of the enzymes are found clustered together as enzyme complexes. These enzymes are also able to ‘ proof-read’ the new DNA strand as it is made and correct mistakes. The polymerase enzyme can only work in one direction, so he 5' nt DNA ligase: Joins neighboring fragments together into longer strands. 3' sy of i ct re Di on io es h nt © Biozone International 2001-2003 Use RESTRICTED to schools where students have purchased this manual Molecular Genetics 138 Genes Code For Proteins A The genetic code is responsible for the construction of proteins, which may be structural components of cells or metabolism controlling enzymes. The various levels of genetic instructions are illustrated below, together with their 'protein equivalents'. Nucleotides are the simplest basic unit of genetic information, that are read in groups of three (called triplets). One triplet provides information to bring in a single amino acid during protein construction. Series of triplets in a long string allow the synthesis of polypeptide chains and are called genes. Some triplets have a special controlling function in the making of a polypeptide chain. The equivalent of the triplet on the mRNA molecule is the codon. Three codons can signify the end point of polypeptide chain construction in the mRNA: UAG, UAA and UGA (also called STOP codons). The triplet ATG is found at the beginning of every gene (codon AUG on mRNA) and marks the starting position for reading the gene. Several polypeptide chains may be needed to form a functional protein. The genes required to do this are collectively called a transcription unit. This polypeptide chain forms one part of the functional protein. Polypeptide chain aa aa aa This polypeptide chain forms

the other part of the functional protein. Functional protein aa aa Polypeptide chain aa aa A triplet codes for one amino acid aa aa aa aa aa aa Amino acids Protein synthesis: transcription and translation START Triplet Triplet Triplet Triplet Triplet Triplet Triplet STOP START Triplet Triplet Triplet Triplet Triplet Triplet STOP 5' 3' DNA Gene Gene Transcription unit Note: This start code is for the coding strand of the DNA. The template DNA strand from which the mRNA is made would have the sequence: TAC. Three nucleotides make up a triplet A G In models of nucleic acids, nucleotides are denoted by their base letter. Nucleotide 1. The following exercise is designed to establish an understanding of the terms used in describing protein structure and the genetic information that determines them. Your task is to consult the diagram above and match the structure in the level of protein organization with its equivalent genetic information: (a) Nucleotide codes for: (b) Triplet codes for: (c) Gene codes for: (d) Transcription unit codes for: 2. Name the basic building blocks for each of the following levels of genetic information: (a) Nucleotide is made up of: (b) Triplet is made up of: (c) Gene is made up of: (d) Transcription unit is made up of: Photocopying Prohibited © Biozone International 2001-2003 Use RESTRICTED to schools where students have purchased this manual 139 Molecular Genetics Gene Expression RA The process of protein synthesis is fundamental to the understanding of how a cell can control its activities. Genetic instructions, in the form of DNA, are used as a blueprint for designing and manufacturing proteins. Some of these proteins are the enzymes that control the complex biochemical reactions in the cell, while others take on a variety of other roles. The Chromosomal DNA DNA contains the master copy of all the genetic information to produce

proteins for the cell. Most eukaryotic genes contain segments of coding sequences (exons) interrupted by noncoding sequences (introns). Intron DNA process of transferring the information encoded in a gene to its functional gene product is called gene expression. It is divided up into two distinct stages: transcription and translation. These are summarized below and detailed in the following pages. For the sake of simplicity, the involvement of introns in gene expression has been omitted from the following pages. Intron Intron Intron Intron Double stranded molecule of genomic DNA Exon Exon Exon Exon Exon Exon Exon Reverse transcription occurs when retroviruses (e. g. HIV) invade host cells. Their viral RNA is converted to DNA and spliced into the host’s genome by an enzyme called reverse transcriptase. Transcription Primary RNA Transcript Both exons and introns are transcribed to produce a long primary RNA transcript. Primary RNA Introns are removed Exons are spliced together Introns Messenger RNA Introns in the DNA (also copied to the primary RNA) are long sequences of codons that have (as yet) no apparent function. They may be the remnants of now unused ancient genes. It has been suggested that they might facilitate recombination between protein-coding regions (exons) of different genes; a process known as exon shuffling. This may accelerate evolution. mRNA The introns are then removed by splicing to form a mature mRNA. Messenger RNA is an edited copy of the DNA molecule (now excluding the introns) that codes for the making of a single protein. Structural proteins Translation Protein Regulatory proteins Contractile proteins Immunological proteins Transport proteins Catalytic proteins 1. The hypothesis known as the central dogma of biology states that: “ genetic information can only flow in the direction of DNA to

proteins and not in the opposite direction". Accounting for the ideas in the diagram above, form a discussion group with 2-3 of your classmates and discuss the merits of this statement. Summarize your group’s response below: 2. Explain the significance of introns and exons found in DNA and primary RNA: (a) Intron: (b) Exon: Photocopying Prohibited © Biozone International 2001-2003 Use RESTRICTED to schools where students have purchased this manual Molecular Genetics 140 Transcription A Transcription is the process by which the code contained in the DNA molecule is transcribed (rewritten) into a mRNA molecule. Transcription is under the control of the cell's metabolic processes which must activate a gene before this process can begin. The enzyme that directly controls the process is RNA polymerase, which makes a strand of mRNA using the single antisense (template) strand of DNA as a template. The enzyme 5' DNA transcribes only a gene length of DNA at a time and therefore recognizes start and stop signals (codes) at the beginning and end of the gene. Only RNA polymerase is involved in mRNA synthesis; it causes the unwinding of the DNA as well. It is common to find several RNA polymerase enzyme molecules on the same gene at any one time, allowing a high rate of mRNA synthesis to occur. 3' A copy of the genetic information for making a protein is made in the form of messenger RNA (mRNA). Many mRNA copies may be made from a single gene on the DNA molecule. Once the mRNA is complete and has been released from the chromosome, it travels to the edge of the nucleus where it gains access to the cytoplasm through a tiny hole called a nuclear pore. In prokaryotic cells (bacteria) there is no nucleus, and the chromosomes are in direct contact with the cytoplasm. This means that the next stage

(translation) can begin immediately, with the mRNA still being synthesized by enzymes on the DNA molecule. Free nucleotides used to construct the mRNA strand. Single-armed chromosome as found in non-dividing cell. RNA polymerase enzyme 3' Template strand of DNA contains the information for the construction of a protein. of n io is ct es re th Di syn Pore (hole) in the nuclear membrane through which the mRNA passes to enter the cytoplasm. Coding strand of DNA has a nucleotide sequence complementary to the template strand. mRNA 5' Once in the cytoplasm, the mRNA will engage ribosomes to begin the next stage in protein synthesis: translation Formation of a single strand of mRNA that is complementary to the template strand (therefore the same “ message" as the coding strand). The two strands of DNA coil up into a helix. Nuclear membrane that encloses the nucleus. 3' Nucleus 5' Cytoplasm 1. Explain the role of messenger RNA (mRNA) in protein synthesis: 2. The genetic code contains punctuation codons to mark the starting and finishing points of the code for synthesis of polypeptide chains and proteins. Consult the mRNA—amino acid table earlier in this manual and state the codes for: (a) Start codon: (b) Stop (termination) codons: 3. For the following triplets on the DNA, determine the codon sequence for the mRNA that would be synthesized: (a) Triplets on the DNA: TAC TAG CCG CGA TTT TAC AAG CCT ATA AAA Codons on the mRNA: (b) Triplets on the DNA: Codons on the mRNA: Photocopying Prohibited © Biozone International 2001-2003 Use RESTRICTED to schools where students have purchased this manual 141 Molecular Genetics Translation A The diagram below shows the translation phase of protein synthesis. The scene shows how a single mRNA molecule can be 'serviced' by many ribosomes at

the same time. The ribosome on the right is in a more advanced stage of constructing a polypeptide chain because it has 'translated' Unloaded Thr-tRNA more of the mRNA than the ribosome to the left. The anticodon at the base of each tRNA must make a perfect complementary match with the codon on the mRNA before the amino acid is released. Once released, the amino acid is added to the growing polypeptide chain by enzymes. Lys Activating Lys-tRNA Ser Met Thr Polypeptide chain This chain is in an advanced stage of synthesis. Phe Unloaded Arg-tRNA Arg Polypeptide chain in an early stage of synthesis Val Activated Tyr-tRNA Unloaded Thr-tRNA Tyr Lys Tyr Met Cys Arg Thr Asn Phe Start codon Ribosome 5' 3' mRNA Ribosomes moving in this direction Amino acid attachment site tRNA molecules move into the ribosome, bringing in amino acids to add to the polypeptide chain under construction. Transfer RNA molecule Ribosome Ribosome attachment point Large subunit Small subunit Ribosomes are made up of a complex of ribosomal RNA (rRNA) and proteins. They exist as two separate sub-units until they are attracted to a binding site on the mRNA molecule, when they join together. Ribosomes have binding sites that attract tRNA molecules loaded with amino acids. The transfer RNA Anticodon The anticodon is the site of the 3-base sequence that 'recognizes' and matches up with the codon on the mRNA molecule. (tRNA) molecules are about 80 nucleotides in length and are made under the direction of genes in the chromosomes. There is a different tRNA molecule for each of the different possible anticodons (there may be up to six different tRNAs carrying the same amino acid). 1. For the following codons on the mRNA, determine the anti-codons for each tRNA that would deliver the amino acids: Codons on the

mRNA: UAC UAG CCG CGA UUU Anti-codons on the tRNAs: 2. There are many different types of tRNA molecules, each with a different anti-codon (HINT: see the mRNA table). (a) State how many different tRNA types there are, each with a unique anticodon: (b) Give a reason for your answer in (a) above: Photocopying Prohibited © Biozone International 2001-2003 Use RESTRICTED to schools where students have purchased this manual Molecular Genetics 142 Protein Synthesis Summary A Thr Phe E A Asn Tyr Cys Arg B Lys Val Met Lys 8 2 1 Met Tyr Thr Phe Arg C Val Lys Tyr 7 Met Arg Thr Cys Asn Phe 3 4 D 6 F Nucleus Cytoplasm The diagram above shows an overview of the process of protein synthesis. It is a combination of the diagrams from the previous two pages. Each of the major steps in the process are numbered, while structures are labeled with letters. 1. Write a brief description of each numbered process in the diagram above: (a) Process 1: (b) Process 2: (c) Process 3: (d) Process 4: (e) Process 5: (f) Process 6: (g) Process 7: (h) Process 8: 2. Identify each of the structures marked with a letter and write their names below in the spaces provided: (a) Structure A: (f) Structure F: (b) Structure B: (g) Structure G: (c) Structure C: (h) Structure H: (d) Structure D: (i) Structure I: (e) Structure E: (j) Structure J: 3. Explain the purpose of protein synthesis (gene expression): Photocopying Prohibited © Biozone International 2001-2003 Use RESTRICTED to schools where students have purchased this manual 143 Molecular Genetics Analyzing a DNA Sample A The nucleotide (base sequence) of a section of DNA can be determined using DNA sequencing techniques. The base sequence determines the amino acid sequence of the resultant protein therefore the DNA tells us what type of protein that gene encodes. This

exercise reviews the areas of DNA replication, transcription, and translation using an analysis of a gel electrophoresis column. Attempt it after you have completed the rest of this topic. Remember that the gel pattern represents the sequence in the synthesized strand. 1. Determine the amino acid sequence of a protein from the nucleotide sequence of its DNA, with the following steps: (a) Determine the sequence of synthesized DNA in the gel (b) Convert it to the complementary sequence of the sample DNA (c) Complete the mRNA sequence (d) Determine the amino acid sequence by using the 'mRNA-amino acid table' in this manual. NOTE: The nucleotides in the gel are read from bottom to top and the sequence is written in the spaces provided from left to right (the first four have been done for you). Triplet Triplet Triplet Triplet Triplet Triplet Triplet Triplet Triplet Triplet Triplet CGTA (DNA sequence read from the gel; comprises radioactive nucleotides that bind to the coding strand DNA in the sample). Replication Synthesized DNA Read in this direction GCAT DNA sample (This is the DNA that is being investigated) Transcription CGUA mRNA Translation A T G Arginine Amino acids C Part of a polypeptide chain TCGA 2. For each single strand DNA sequence below, write the base sequence for the complementary DNA strand: (a) DNA: TAC TAG CCG CGA TTT ACA ATT TAC GCC TTA AAG GGC CGA ATC DNA: (b) DNA: DNA: (c) Name the cell process that this exercise represents: 3. For each single strand DNA sequence below, write the base sequence for the mRNA strand and the amino acid that it codes for (refer to the mRNA-amino acid table to determine the amino acid sequence): (a) DNA: TAC TAG CCG CGA TTT ACA ATT TAC GCC TTA AAG GGC CGA ATC mRNA: Amino acids: (b) DNA: mRNA: Amino acids: (c) Name the cell process that

this exercise represents: Photocopying Prohibited © Biozone International 2001-2003 Use RESTRICTED to schools where students have purchased this manual Molecular Genetics 144 Metabolic Pathways RA Metabolism is all the chemical activities of life. The myriad enzyme-controlled metabolic pathways that are described as metabolism form a tremendously complex network that is necessary in order to 'maintain' the organism. Errors in the step-wise regulation of enzyme-controlled pathways can result in metabolic disorders that in some cases can be easily identified. An example of a well studied metabolic pathway, the metabolism of phenylalanine, is described below. A Metabolic Pathway Gene A Expression of Gene A (by protein synthesis) produces enzyme A Expression of Gene B (by protein synthesis) produces enzyme B Enzyme A Precursor chemical Gene B Enzyme B Enzyme A transforms the precursor chemical into the intermediate chemical by altering its chemical structure Intermediate chemical Enzyme B transforms the intermediate chemical into the end product End product Case Study: The Metabolism of Phenylalanine Protein Phenylketonuria Proteins are broken down to release free amino acids, one of which is phenylalanine. Symptoms: Mental retardation, mousy body odor, light skin color, excessive muscular tension and activity, eczema. Phenylalanine This in turn causes: Faulty enzyme causes buildup of: Phenylalanine hydroxylase a series of enzymes Thyroxine Tyrosinase Tyrosine Faulty enzymes cause: Phenylpyruvic acid Melanin Faulty enzyme causes: Transaminase Albinism Cretinism Symptoms: Complete lack of the pigment melanin in body tissues, including skin, hair, and eyes. Hydroxyphenylpyruvic Symptoms: acid Dwarfism, mental retardation, low levels of thyroid hormones, retarded sexual development,

Hydroxyphenylpyruvic yellow skin color. acid oxidase Carbon dioxide & water Faulty enzyme causes: Tyrosinosis Symptoms: Death from liver failure, or (if surviving) chronic liver and kidney disease. Homogentisic acid Homogentisic acid oxidase Faulty enzyme causes: Alkaptonuria Symptoms: Dark urine, pigmentation of cartilage and other connective tissues. In later years, arthritis. Maleylacetoacetic acid A well-studied metabolic pathway is the metabolic breakdown of the essential amino acid phenylalanine. The first step is carried out by an enzyme produced in the liver, called phenylalanine hydroxylase. This enzyme converts phenylalanine to the amino acid tyrosine. Tyrosine, in turn, through a series of intermediate steps, is converted into melanin, the skin pigment, and other substances. If phenylalanine hydroxylase is absent, phenylalanine is in part converted into phenylpyruvic acid, which accumulates, together with phenylalanine, in the blood stream. Phenylpyruvic acid and phenylalanine are toxic to the central nervous system Photocopying Prohibited and produce some of the symptoms of the genetic disease phenylketonuria. Other genetic metabolic defects in the tyrosine pathway are also known. As indicated above, absence of enzymes operating between tyrosine and melanin, is a cause of albinism. Tyrosinosis is a rare defect that causes hydroxyphenylpyruvic acid to accumulate in the urine. Alkaptonuria makes urine turn black on exposure to air, causes pigmentation to appear in the cartilage, and produces symptoms of arthritis. A different block in another pathway from tyrosine produces thyroid deficiency leading to goiterous cretinism (due to lack of thyroxine). © Biozone International 2001-2003 Use RESTRICTED to schools where students have purchased this manual 145 Molecular Genetics 1. Explain what is

meant by a metabolic pathway: 2. Describe the role that enzymes play in metabolic pathways: 3. List three final products of the metabolism of phenylalanine: 4. Name the enzyme failures (faulty enzymes) responsible for the following conditions: (a) Albinism: (b) Phenylketonuria: (c) Cretinism: (d) Tyrosinosis (e) Alkaptonuria: 5. Explain why people with phenylketonuria have light skin coloring: 6. Explain the role of the hormone thyroxine in causing the symptoms of cretinism: 7. The five conditions illustrated in the diagram are due to too much or too little of a chemical in the body. For each condition listed below, state which chemical (absent or in excess), causes the problem: (a) Albinism: (b) Phenylketonuria: (c) Cretinism: (d) Tyrosinosis (e) Alkaptonuria: 8. If you suspected that a person suffered from phenylketonuria, suggest how could you test for the condition: 9. The diagram at the top of the previous page represents the normal condition for a simple metabolic pathway. A starting chemical, called the precursor, is progressively changed into a final chemical called the end product. Consider the effect on this pathway if gene A underwent a mutation and the resulting enzyme A did not function: (a) Name the chemicals that would be present in excess: (b) Name the chemicals that would be absent: Photocopying Prohibited © Biozone International 2001-2003 Use RESTRICTED to schools where students have purchased this manual Molecular Genetics 146 Control of Metabolic Pathways A structural genes called the operator. A gene outside the operon, called the regulator gene, produces a repressor molecule that can bind to the operator and block the transcription of the structural genes. It is the repressor that switches the structural genes on or off and controls the metabolic pathway. Two mechanisms operate in the operon model: gene

induction and gene repression. Gene induction occurs when genes are switched on by an inducer binding to the repressor molecule and deactivating it. In the Lac operon model based on E. coli, lactose acts as the inducer, binding to the repressor and permitting transcription of the structural genes for the utilization of lactose. Gene repression occurs when genes that are normally switched on (e. g. genes for synthesis of an amino acid) are switched off by activation of the repressor. The operon mechanism was proposed by Jacob and Monod to account for the regulation of gene activity in response to the needs of the cell. Their work was carried out with the bacterium Escherichia coli and the model is not applicable to eukaryotic cells where the genes are not found as operons (see opposite for the eukaryote model). An operon consists of a group of closely linked genes that act together and code for the enzymes that control a particular metabolic pathway. These may be for the metabolism of an energy source (e. g. lactose) or the synthesis of a molecule such as an amino acid. The structural genes contain the information for the production of the enzymes themselves and they are transcribed as a single transcription unit. These structural genes are controlled by a promoter, which initiates the formation of the mRNA, and a region of the DNA in front of the Control of Gene Expression Through Induction: the Lac Operon Structure of the operon RNA polymerase At least one structural gene is present. The structural gene codes for the creation of an enzyme in a metabolic pathway. Transcription begins Regulator gene Promoter The regulator gene, on another part of the DNA, produces the repressor molecule by protein synthesis. In the lac operon the regulator gene is located next to the promoter. Structural gene A Operator

The promoter site is where the RNA polymerase enzyme first attaches itself to the DNA to begin synthesis of the mRNA. DNA The operator is the potential blocking site. It is here that an active repressor molecule will bind, stopping mRNA synthesis from proceeding. OPERON The operon consists of the structural genes and the promoter and operator sites Structural genes switched off RNA polymerase enzyme may not be able to bind to the promoter, or it may be blocked along the DNA. Lactose is not a common energy source for E. coli and the genes for the metabolism of lactose by the cell are normally switched off. With lactose absent, the repressor molecule binds tightly to the operator. This prevents RNA polymerase from transcribing the adjacent structural genes and the enzymes for lactose metabolism are not produced. An active repressor molecule binds to the operator site and suppresses its activity (the gene is " switched off"). Transcription is stopped Repressor Regulator gene Gene induction Promoter Operator Structural gene A The inducer binds to the repressor altering its shape. It can no longer bind to the DNA, permitting the operator gene to become active (i. e. the gene is " switched on"). DNA When lactose is available, some of it is converted into the inducer allolactose. Allolactose binds to the repressor molecule, altering its shape and preventing it from binding to the operator. The structural genes can then be transcribed, and the enzymes for the metabolism of lactose are produced. Inducer Repressor Repressor Regulator gene Transcription occurs Promoter Operator Photocopying Prohibited Structural gene A 147 Molecular Genetics Control of Gene Expression in Eukaryotes

Although all the cells in your body contain identical copies of your genetic instructions, these cells appear very different. Morphological differences between cell types reflect profound differences in gene expression. For example, nerve cells express proteins responsible for propagating electrical signals, whereas muscle cells express the proteins that make up the contractile elements. This variety of cell structure and function reflects the precise control over the time, location and extent of expression of a huge variety of genes. The role of transcription factors: RNA polymerase requires additional proteins called transcription factors in order to recognize and bind to the promoter region at the upstream end of the gene. According to one hypothesis, transcription is activated when a hairpin loop in the DNA brings the transcription factors attached to the enhancer in contact with the transcription factors bound to RNA polymerase at the promoter. Transcription is deactivated when a terminator sequence is encountered. Terminators are nucleotide sequences that function to stop transcription. Do not confuse these with terminator codons, which are the stop signals for translation. Transcription factors that bind to enhancer RNA polymerase Transcription factors that bind to RNA polymerase Promoter Coding region of gene Enhancer sequence Transcription factors and RNA polymerase bind Transcription begins and will continue until a terminator is encountered. A range of transcription factors and enhancer sequences throughout the genome may selectively activate the expression of specific genes at appropriate stages in cell development. 1. Explain the functional role of each of the following in relation to gene regulation in a prokaryote e. g. E. coli: (a) Operon: (b) Regulator gene: (c) Operator: (d) Promoter: (e) Structural genes:

2. (a) Explain the advantage in having an inducible enzyme system that is regulated by the presence of a substrate: (b) Suggest when it would not be adaptive to have an inducible system for metabolism of a substrate: 3. With reference to eukaryotes, briefly explain why the control of gene expression is necessary: Photocopying Prohibited © Biozone International 2001-2003 Use RESTRICTED to schools where students have purchased this manual Terms of Use 1. Schools MAY NOT place this file on any networked computer. 2. Schools MAY NOT place this file on any student computer (including student laptops), unless they have entered into a specific licensing agreement to do so with BIOZONE International Ltd. 3. This file may ONLY be placed on teaching staff computers (including teaching staff laptops). 4. Projection of these pages using a data projector is permitted ONLY if each student in the class has purchased a current edition of the manual. Please report any abuse of these terms of use to: copyright@biozone. co. nz or Phone: +64 7-8568104 (USA/Canada: 011 64 7-8568104) or Fax: +64 7-8569243 (USA/Canada: 011 64 7-8569243)