Central dogma of molecular biology ppt pdf

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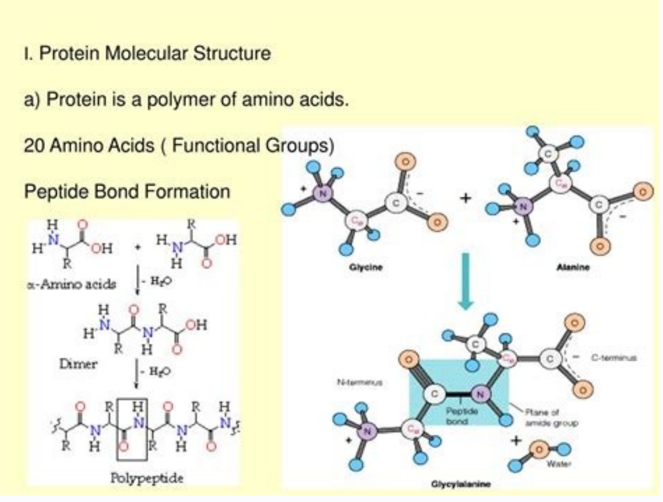
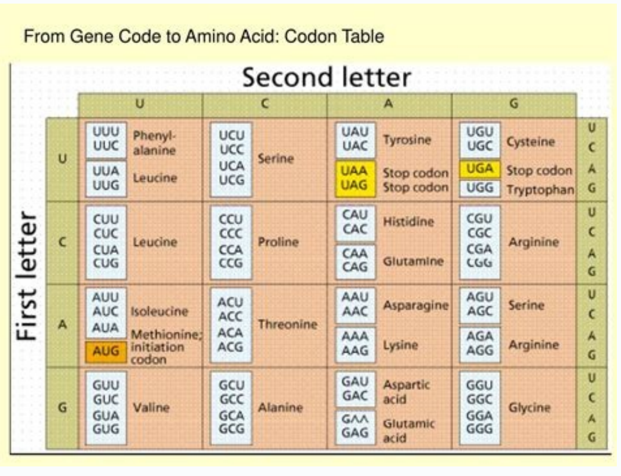

I. Protein Molecular Structure

a) Protein is a polymer of amino acids.

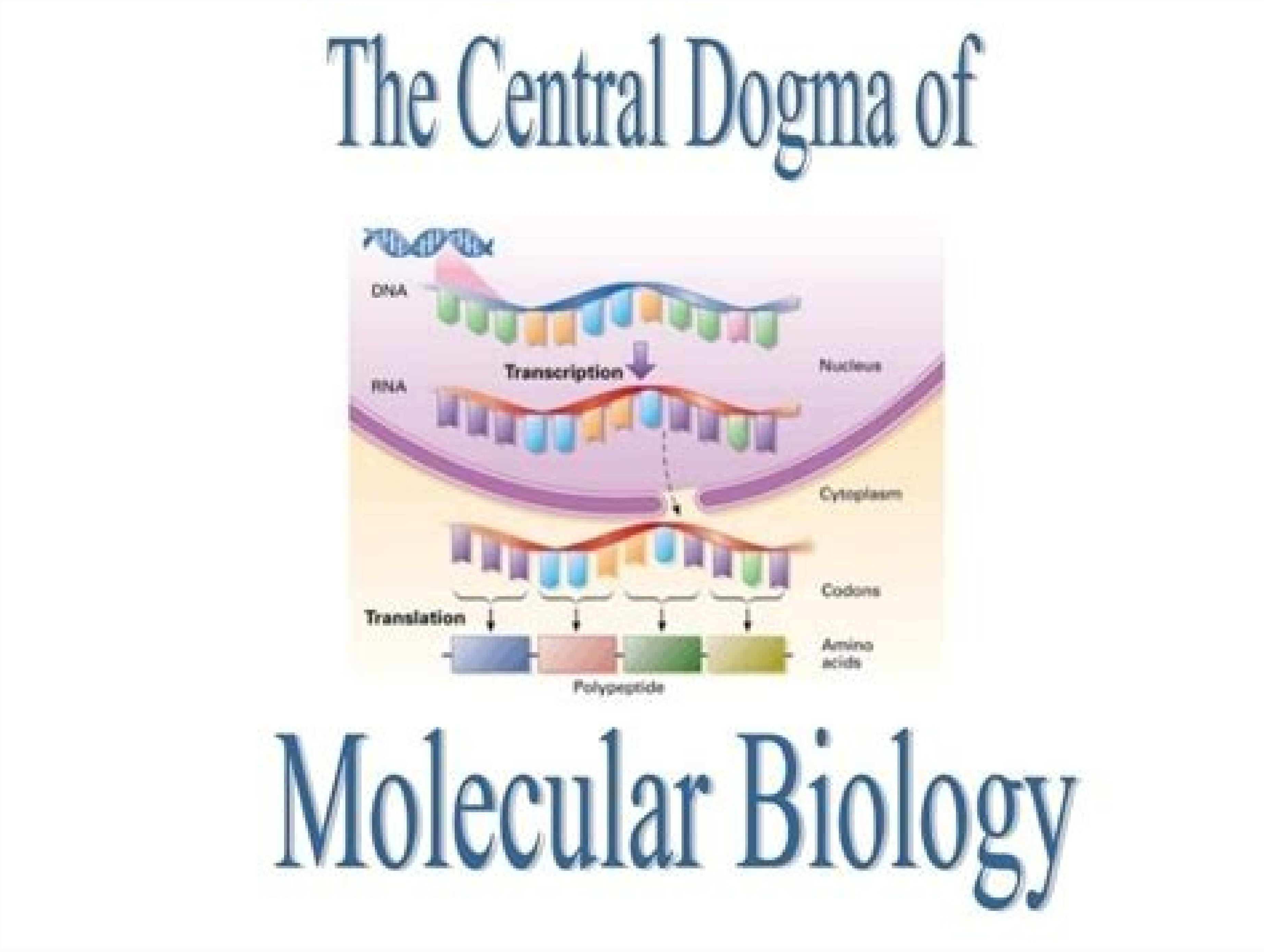
20 Amino Acids (Functional Groups)

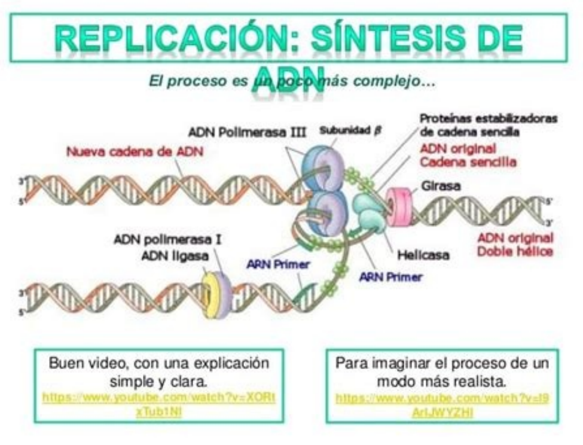
Peptide Bond Formation


From Gene Code to Amino Acid: Codon Table

		Second letter				
		U	C	A	G	
First letter	U	UUU UUC Phenylalanine UUA UUG Leucine	UCU UCC UCA UCG Serine	UAU UAC Tyrosine UAA Stop codon UAG Stop codon	UGU UGC Cysteine UGA Stop codon UGG Tryptophan	U C A G
	C	CUU CUC CUA CUG Leucine	CCU CCC CCA CCG Proline	CAU CAC Histidine CAA CAG Glutamine	CGU CGC CGA CGG Arginine	U C A G
	A	AUU AUC AUA Isoleucine AUG Methionine; initiation codon	ACU ACC ACA ACG Threonine	AAU AAC Asparagine AAA AAG Lysine	AGU AGC Serine AGA AGG Arginine	U C A G
	G	GUU GUC GUA GUG Valine	GCU GCC GCA GCG Alanine	GAU GAC Aspartic acid GAA GAG Glutamic acid	GGU GGC GGA GGG Glycine	U C A G


DOGMA CENTRAL DE LA BIOLOGÍA MOLECULAR


The Central Dogma of Molecular Biology


REPLICACIÓN: SÍNTESIS DE ADN

El proceso es un poco más complejo...

Buen video, con una explicación simple y clara. https://www.youtube.com/watch?v=XORtxTub1NI

Para imaginar el proceso de un modo más realista. https://www.youtube.com/watch?v=I9ArLJWYZHI

What is a central dogma of molecular biology. Example of central dogma of molecular biology. Central dogma of molecular biology ppt pdf. What is central dogma of molecular biology pdf. What do you mean by central dogma of molecular biology.

1 The Central Dogma of Molecular Biology DNA RNA Protein Trait 2 RNA vs. DNA Study the images of the two molecules and observe their similarities & differences. 3 The Genetic Code How are the instructions for assembling amino acids into proteins encoded into DNA? There are 20 amino acids, but there are only four nucleotide bases in DNA How many bases correspond to an amino acid? 4 Codons: Triplets of Bases Example: Base triplet 3’-ACC-5’ on DNA Provides a template for 5’-UGG-3’ on mRNA UGG is the codon for the amino acid tryptophan 5 Central Dogma of Molecular Biology 6 The Central Dogma of Molecular Biology DNA RNA Protein Trait Transferring genetic information into protein. 7 Transcription: Rewriting DNA into mRNA Enzymes add nucleotides to mRNA from 5’ to 3’ Transcription is initiated at a promoter, a sequence of DNA that signals the start of a gene 8 Enzymes Modify the “pre-mRNA” Enzymes attach a “cap” to the mRNA which binds the mRNA to the ribosome Enzymes attach a tail of nucleotides to the mRNA, this controls the “lifespan” of the mRNA 9 mRNA is Spliced Introns: Non-coding regions of DNA Exons: Coding regions of DNA 10 The Functional and Evolutionary Importance of Introns Some genes can encode more than one kind of polypeptide, depending on which segments are treated as exons during RNA splicing The number of different proteins an organism can produce is much greater than its number of genes Copyright © 2008 Pearson Education Inc., publishing as Pearson Benjamin Cummings 11 Translation: The RNA directed synthesis of a polypeptide 12 The Genetic Code 13 Molecules of tRNA are not identical: –Each carries a specific amino acid on one end –Each has an anticodon on the other end; the anticodon base-pairs with a complementary codon on mRNA Copyright © 2008 Pearson Education Inc., publishing as Pearson Benjamin Cummings 14 Translation mRNA codons are translated into a polypeptide chain 15 Analysis Questions Compare and contrast transcription and translation in prokaryotic and eukaryotic cells. Compare and contrast DNA replication with transcription 1 Introduction The Central Dogma of Molecular BiologyCell DNA mRNA Transcription Polypeptide (protein) Translation Ribosome 2 Protein Synthesis Flow of Information: DNA RNA ProteinsTranscription Translation Transcription is the process by which a molecule of DNA is copied into a complementary strand of RNA. This is called messenger RNA (mRNA) because it acts as a messenger between DNA and the ribosomes where protein synthesis is carried out. 3 Protein Synthesis TranscriptionTranscription process RNA polymerase (an enzyme) attaches to DNA at a special sequence that serves as a “start signal”. The DNA strands are separated and one strand serves as a template. The RNA bases attach to the complementary DNA template, thus synthesizing mRNA. 4 Protein Synthesis: TranscriptionTranscription process continued The RNA polymerase recognizes a termination site on the DNA molecule and releases the new mRNA molecule. (mRNA leaves the nucleus and travels to the ribosome in the cytoplasm.) 5 Protein Synthesis: Transcription 6 Eukaryotic TranscriptionDNA Cytoplasm Nucleus Nuclear pores RNA Transcription G AAAAAA RNA Processing mRNA Export G AAAAAA 7 Protein Synthesis: TranslationTranslation is the process of decoding a mRNA molecule into a polypeptide chain or protein. Each combination of 3 nucleotides on mRNA is called a codon or three-letter code word. Each codon specifies a particular amino acid that is to be placed in the polypeptide chain (protein). 8 Protein Synthesis: Translation 9 A Codon Guanine Arginine Adenine B A S E S SUGAR-PHOSPHATE BACKBONE OCH2 NH2 N NH OH Guanine Adenine Arginine 10 Protein Synthesis: TranslationA three-letter code is used because there are 20 different amino acids that are used to make proteins. If a two-letter code were used there would not be enough codons to select all 20 amino acids. That is, there are 4 bases in RNA, so 42 (4x 4)=16; where as 43 (4x4x4)=64. 11 Protein Synthesis: Translation 12 Protein Synthesis: TranslationTherefore, there is a total of 64 codons with mRNA, 61specify a particular amino acid. This means there are more than one codon for each of the 20 amino acids. The remaining three codons (UAA, UAG, & UGA) are stop codons, which signify the end of a polypeptide chain (protein). Besides selecting the amino acid methionine, the codon AUG also serves as the “initiator” codon, which starts the synthesis of a protein 13 Protein Synthesis: Translation 14 Protein Synthesis: TranslationTransfer RNA (tRNA) Each tRNA molecule has 2 important sites of attachment. One site, called the anticodon, binds to the codon on the mRNA molecule. The other site attaches to a particular amino acid. During protein synthesis, the anticodon of a tRNA molecule base pairs with the appropriate mRNA codon. 15 Protein Synthesis: Translation 16 Met-tRNA Anticodon Methionine 9 26 22 23 16 12 10 25 A 17 13 20 G 50U* 9 26 22 23 Pu 16 12 Py 10 25 20:1 G* 17:1 A 20:2 17 13 20 G 50 51 65 64 63 62 52 C 59 y A* T 49 39 41 42 31 29 28 Pu* 43 1 27 U 35 38 36 Py* 34 40 30 47:1 47:15 46 47:16 45 44 47 73 70 71 72 66 67 68 69 3 2 7 6 5 4 A U C Anticodon 17 Protein Synthesis: TranslationRibosome: Are made up of 2 subunits, a large one and a smaller one, each subunit contains ribosomal RNA (rRNA) & proteins. Protein synthesis starts when the two subunits bind to mRNA. The initiator codon AUG binds to the first anticodon of tRNA, signaling the start of a protein. 18 Protein Synthesis: TranslationRibosome: The anticodon of another tRNA binds to the next mRNA codon, bringing the 2nd amino acid to be placed in the protein. As each anticodon & codon bind together a peptide bond forms between the two amino acids. 19 Protein Synthesis: TranslationRibosome: The protein chain continues to grow until ribosome reaches the stop codon, which results in the release of the new protein and mRNA, completing the process of translation. 20 Protein Synthesis: Translation 21 Translation - InitiationfMet UAC A E Large subunit P GAG...CU-AUG--UUC--CUU--AGU--GGU--AGA--GCU--GUA--UGA-AT GCA...TAAAAAA 5’ mRNA 3’ Small subunit 22 Translation - ElongationPhe Leu Met Ser Gly Polypeptide CCA UCU Arg Aminoacyl tRNA A E Ribosome P GAG...CU-AUG--UUC--CUU--AGU--GGU--AGA--GCU--GUA--UGA-AT GCA...TAAAAAA 5’ mRNA 3’ 23 Translation - ElongationPhe Leu Met Ser Gly Polypeptide Arg CCA UCU Aminoacyl tRNA A E Ribosome P GAG...CU-AUG--UUC--CUU--AGU--GGU--AGA--GCU--GUA--UGA-AT GCA...TAAAAAA 5’ mRNA 3’ 24 Protein Synthesis Amino Acid H2O H C O OH R N C H O OH N C H O OH N HOAMINE H C O OH R N Amino Acid ACID C H O OH N Alanine C H O OH N HO Serine ANYTHING H2O C O OH N H HO 25 Translation - ElongationArg UCU Phe Leu Met Ser Gly Polypeptide CCA A E Ribosome P GAG...CU-AUG--UUC--CUU--AGU--GGU--AGA--GCU--GUA--UGA-AT GCA...TAAAAAA 5’ mRNA 3’ 26 Translation - ElongationArg UCU Phe Leu Met Ser Gly Polypeptide Aminoacyl tRNA CGA Ala CCA A E Ribosome P GAG...CU-AUG--UUC--CUU--AGU--GGU--AGA--GCU--GUA--UGA-AT GCA...TAAAAAA 5’ mRNA 3’ 27 Translation - ElongationArg UCU Phe Leu Met Ser Gly Polypeptide CCA CGA Ala A E Ribosome P GAG...CU-AUG--UUC--CUU--AGU--GGU--AGA--GCU--GUA--UGA-AT GCA...TAAAAAA 5’ mRNA 3’ 28 Transcription And Translation In Prokaryotes3’ 5’ 5’ mRNA RNA Pol. Ribosome Ribosome 1,271 views Qualification: BDS, BDS, B.Tech/B.E. Teaches: Biology, Botany, Zoology, Chemistry, EVS, Geograph... Contact this tutor 1. Chapter 12: From DNA to Protein: Genotype to Phenotype Central Dogma in Molecular Biology 2. Chapter 12: From DNA to Protein: Genotype to Phenotype DNA and Its Role in Heredity DNA to Protein: Genotype to Phenotype 3. Chapter 12: From DNA to Protein: Genotype to Phenotype The central dogma DNA structure DNA replication RNA structure RNA synthesis (Transcription) The genetic code Protein synthesis (Translation) Mutation Consequences of mutation Lecture 1 Lecture 2 Lecture 3 Lecture 4 4. Chapter 12: From DNA to Protein: Genotype to Phenotype The Central Dogma The Flow of Information: DNA → RNA → protein DNA Replication Transcription Translation A gene is expressed in two steps: DNA is transcribed to RNA Then RNA is translated into protein. 5. DNA ReplicationDNA Replication 6. Chapter 12: From DNA to Protein: Genotype to Phenotype DNADNA Discovery of the DNA double helixDNA double helix A. 1950’s B. Rosalind Franklin - X-ray photo of DNA. C. Watson and Crick - described the DNA molecule from Franklin’s X-ray. 7. Chapter 12: From DNA to Protein: Genotype to Phenotype Question:Question: What isWhat is DNADNA?? 8. Chapter 12: From DNA to Protein: Genotype to Phenotype Deoxyribonucleic AcidDeoxyribonucleic Acid (DNA)(DNA) Made up of nucleotidesnucleotides (DNA molecule) in a DNADNA double helix.double helix. NucleotideNucleotide:: 1. Phosphate groupPhosphate group 2. 5-carbon sugar5-carbon sugar 3. Nitrogenous baseNitrogenous base ~2 nm wide~2 nm wide 9. Chapter 12: From DNA to Protein: Genotype to Phenotype DNA NucleotideDNA Nucleotide O O=P-O O PhosphatePhosphate GroupGroup N Nitrogenous baseNitrogenous base (A, G, C, or T)(A, G, C, or T) CH2 O C1 C4 C3 C2 5 SugarSugar (deoxyribose)(deoxyribose) 10. Chapter 12: From DNA to Protein: Genotype to Phenotype DNA Double HelixDNA Double Helix NitrogenousNitrogenous Base (A,T,G or C)Base (A,T,G or C) ““Rungs of ladder”Rungs of ladder” ““Legs of ladder”Legs of ladder” Phosphate &Phosphate & Sugar BackboneSugar Backbone 11. Chapter 12: From DNA to Protein: Genotype to Phenotype DNA Double HelixDNA Double Helix P P P O O O 1 2 3 4 5 5 3 3 5 P P P O O O 1 2 3 4 5 5 3 5 3 G C T A 12. Chapter 12: From DNA to Protein: Genotype to Phenotype Nitrogenous BasesNitrogenous Bases PURINESPURINES 1. Adenine (A)Adenine (A) 2. Guanine (G)Guanine (G) PYRIMIDINESPYRIMIDINES 3. Thymine (T)Thymine (T) 4. Cytosine (C)Cytosine (C) T or C A or G 13. Chapter 12: From DNA to Protein: Genotype to Phenotype BASE-PAIRINGSBASE-PAIRINGS Base # of Purines Pyrimidines Pairs H-Bonds Adenine (A)Adenine (A) Thymine (T)Thymine (T) A = T 2 Guanine (G)Guanine (G) Cytosine (C)Cytosine (C) C G 3 CG 3 H-bonds 14. Chapter 12: From DNA to Protein: Genotype to Phenotype BASE-PAIRINGSBASE-PAIRINGS CG H-bonds T A 15. Chapter 12: From DNA to Protein: Genotype to Phenotype Chargaff’s RuleChargaff’s Rule AdenineAdenine must pair with ThymineThymine GuanineGuanine must pair with CytosineCytosine Their amounts in a given DNA molecule will be about the sameabout the same. G CT A 16. Chapter 12: From DNA to Protein: Genotype to Phenotype Question:Question: If there is 30% AdenineAdenine, how much CytosineCytosine is present? 17. Chapter 12: From DNA to Protein: Genotype to Phenotype Answer:Answer: There would be 20% CytosineCytosine. Adenine (30%)Adenine (30%) == Thymine (30%)Thymine (30%) Guanine (20%)Guanine (20%) == Cytosine (20%)Cytosine (20%) (50%) = (50%)(50%) = (50%) 18. Chapter 12: From DNA to Protein: Genotype to Phenotype Question:Question: When and where doesWhen and where does DNA ReplicationDNA Replication take place?take place? 19. Chapter 12: From DNA to Protein: Genotype to Phenotype Synthesis Phase (S phase)Synthesis Phase (S phase) S phase in interphase of the cell cycle. Nucleus of eukaryotes Mitosis -prophase -metaphase -anaphase -telophase G1 G2 S phase interphase DNA replication takesDNA replication takes place in the S phase.place in the S phase. 20. Chapter 12: From DNA to Protein: Genotype to Phenotype DNA ReplicationDNA Replication Origins of replicationOrigins of replication 1. Replication ForksReplication Forks: hundredshundreds of Y-shapedY-shaped regions of replicating DNA moleculesreplicating DNA molecules where new strands are growing. ReplicationReplication ForkFork Parental DNA MoleculeParental DNA Molecule 3’ 5’ 3’ 5’ 21. Chapter 12: From DNA to Protein: Genotype to Phenotype DNA ReplicationDNA Replication Origins of replicationOrigins of replication 2. Replication BubblesReplication Bubbles: a. HundredsHundreds of replicating bubbles (Eukaryotes)(Eukaryotes). b. SingleSingle replication fork (bacteria).(bacteria). Bubbles Bubbles 22. Chapter 12: From DNA to Protein: Genotype to Phenotype DNA ReplicationDNA Replication Strand SeparationStrand Separation: 1.1. HelicaseHelicase: enzyme which catalyze the unwindingunwinding and separationseparation (breaking H- Bonds) of the parental double helix. 2.2. Single-Strand Binding ProteinsSingle-Strand Binding Proteins: proteins which attach and help keep the separated strands apart. 23. Chapter 12: From DNA to Protein: Genotype to Phenotype DNA ReplicationDNA Replication Strand SeparationStrand Separation: 3.3. TopoisomeraseTopoisomerase: enzyme which relievesrelieves stressstress on the DNA moleculeDNA molecule by allowing free rotation around a single strand. Enzyme DNA Enzyme 24. Chapter 12: From DNA to Protein: Genotype to Phenotype DNA ReplicationDNA Replication Priming:Priming: 1.1. RNA primersRNA primers: before new DNA strands can form, there must be small pre-existing primers (RNA)primers (RNA) present to start the addition of new nucleotides (DNA Polymerase)(DNA Polymerase). 2.2. PrimasePrimase: enzyme that polymerizes (synthesizes) the RNA Primer. 25. Chapter 12: From DNA to Protein: Genotype to Phenotype DNA ReplicationDNA Replication Synthesis of the new DNA Strands:Synthesis of the new DNA Strands: 1.1. DNA PolymeraseDNA Polymerase: with a RNA primerRNA primer in place, DNA Polymerase (enzyme) catalyze the synthesis of a new DNA strand in the 5’synthesis of a new DNA strand in the 5’ to 3’to 3’ directiondirection. RNARNA PrimerPrimerDNA PolymeraseDNA Polymerase NucleotideNucleotide 5’ 5’ 3’ 26. Chapter 12: From DNA to Protein: Genotype to Phenotype Remember!!!!Remember!!!! O O=P-O O PhosphatePhosphate GroupGroup N Nitrogenous baseNitrogenous base (A, G, C, or T)(A, G, C, or T) CH2 O C1 C4 C3 C2 5 SugarSugar (deoxyribose)(deoxyribose) 27. Chapter 12: From DNA to Protein: Genotype to Phenotype Remember!!!!!Remember!!!!! P P P O O O 1 2 3 4 5 5 3 3 5 P P P O O O 1 2 3 4 5 5 3 5 3 G C T A 28. Chapter 12: From DNA to Protein: Genotype to Phenotype DNA ReplicationDNA Replication Synthesis of the new DNA Strands:Synthesis of the new DNA Strands: 2.2. Leading StrandLeading Strand: synthesized as a single polymersingle polymer in the 5’ to 3’ direction5’ to 3’ direction. RNARNA PrimerPrimerDNA PolymeraseDNA PolymeraseNucleotidesNucleotides 3’5’ 5’ 29. Chapter 12: From DNA to Protein: Genotype to Phenotype DNA ReplicationDNA Replication Synthesis of the new DNA Strands:Synthesis of the new DNA Strands: 3.3. Lagging StrandLagging Strand: also synthesized in the 5’ to 3’ direction5’ to 3’ direction, but discontinuouslydiscontinuously against overall direction of replication. RNA PrimerRNA Primer Leading StrandLeading Strand DNA PolymeraseDNA Polymerase 5 ’ 5’ 3’ 3’ Lagging StrandLagging Strand 5’ 5’ 3’ 3’ 30. Chapter 12: From DNA to Protein: Genotype to Phenotype DNA ReplicationDNA Replication Synthesis of the new DNA Strands:Synthesis of the new DNA Strands: 4.4. Okazaki FragmentsOkazaki Fragments: series of short segments on the lagging strand.lagging strand. Lagging Strand RNARNA PrimerPrimer DNADNA PolymerasePolymerase 3’ 3’ 5’ 5’ Okazaki FragmentOkazaki Fragment 31. Chapter 12: From DNA to Protein: Genotype to Phenotype DNA ReplicationDNA Replication Synthesis of the new DNA Strands:Synthesis of the new DNA Strands: 5.5. DNA ligaseDNA ligase: a linking enzyme that catalyzes the formation of a covalent bond from the 3’ to 5’ end3’ to 5’ end of joining stands. Example: joining two Okazaki fragments together.Example: joining two Okazaki fragments together. Lagging Strand Okazaki Fragment 2Okazaki Fragment 2 DNA ligaseDNA ligase Okazaki Fragment 1Okazaki Fragment 1 5’ 5’ 3’ 3’ 32. Chapter 12: From DNA to Protein: Genotype to Phenotype DNA ReplicationDNA Replication Synthesis of the new DNA Strands:Synthesis of the new DNA Strands: 6.6. ProofreadingProofreading: initial base-pairing errors are usually corrected by DNA polymeraseDNA polymerase. 33. Chapter 12: From DNA to Protein: Genotype to Phenotype DNA ReplicationDNA Replication Semiconservative Model:Semiconservative Model: 1. Watson and Crick showed:Watson and Crick showed: the two strands of the parental molecule separate, and each functions as a template for synthesis of a new complementary strand. Parental DNA DNA Template New DNA 34. Chapter 12: From DNA to Protein: Genotype to Phenotype DNA RepairDNA Repair Excision repair:Excision repair: 1. Damaged segment is excisedexcised by a repairrepair enzymeenzyme (there are over 50 repair enzymes). 2. DNA polymeraseDNA polymerase and DNA ligaseDNA ligase replace and bond the new nucleotides together. 35. Chapter 12: From DNA to Protein: Genotype to Phenotype Question: What would be the complementary DNA strand for the following DNA sequence? DNA 5’-GCGTATG-3’DNA 5’-GCGTATG-3’ 36. Chapter 12: From DNA to Protein: Genotype to Phenotype Answer:Answer: DNA 5’-GCGTATG-3’DNA 5’-GCGTATG-3’ DNA 3’-CGCATAC-5’DNA 3’-CGCATAC-5’ 37. Chapter 12: From DNA to Protein: Genotype to Phenotype The central dogma DNA structure DNA replication RNA structure RNA synthesis (Transcription) The genetic code Protein synthesis (Translation) Mutation Consequences of mutation Lecture 1 Lecture 2 Lecture 3 Lecture 4 TOPICS 38. Chapter 12: From DNA to Protein: Genotype to Phenotype DNA and RNA differ RNA differs from DNA in three ways: RNA is single-stranded (but it can fold back upon itself to form secondary structure, e.g. tRNA) In RNA, the sugar molecule is ribose rather than deoxyribose In RNA, the fourth base is uracil rather than thymine. 39. Chapter 12: From DNA to Protein: Genotype to Phenotype DNA RNA 1 OH OH OH OH 2 U H 3 40. Chapter 12: From DNA to Protein: Genotype to Phenotype The Central Dogma The Flow of Information: DNA → RNA → protein DNA Replication Transcription Translation RNA is synthesized via a process called Transcription mRNA, rRNA and tRNA are transcribed by similar mechanisms Transcription 41. Chapter 12: From DNA to Protein: Genotype to Phenotype Three types of RNA are involved in protein synthesis Messenger RNA [mRNA] - the template Ribosomal RNA [rRNA] - structural component of the ribosome Transfer RNA [tRNA] - the adapter 42. Chapter 12: From DNA to Protein: Genotype to Phenotype 43. Chapter 12: From DNA to Protein: Genotype to Phenotype Figure 12.7 Transfer RNA - the adapter RNA is single-stranded but it can fold back upon itself to form secondary structures. 44. Chapter 12: From DNA to Protein: Genotype to Phenotype Transcription has three phases: Initiation Elongation Termination RNA is transcribed from a DNA template after the bases of DNA are exposed by unwinding of the double helix. In a given region of DNA, only one of the two strands can act as a template for transcription. Transcription: DNA-Directed RNA Synthesis 45. Chapter 12: From DNA to Protein: Genotype to Phenotype Figure 12.4 – Part 1 46. Chapter 12: From DNA to Protein: Genotype to Phenotype Three phases: Initiation, Elongation, Termination Unwind the DNA template: template and complementary strands Initiation: RNA polymerase recognizes and binds to a promoter sequence on DNA Transcription: DNA-Directed RNA Synthesis - Initiation 47. Chapter 12: From DNA to Protein: Genotype to Phenotype Figure 12.4 – Part 1 48. Chapter 12: From DNA to Protein: Genotype to Phenotype Initiation Elongation: RNA polymerase elongates the nascent RNA molecule in a 5’-to-3’ direction, antiparallel to the template DNA • Nucleotides are added by complementary base pairing with the template strand • The substrates, ribonucleoside triphosphates, are hydrolyzed as added, releasing energy for RNA synthesis. Transcription: DNA-Directed RNA Synthesis - Elongation 49. Chapter 12: From DNA to Protein: Genotype to Phenotype Figure 12.4 – Part 1 50. Chapter 12: From DNA to Protein: Genotype to Phenotype (DNA Replication figure adapted for Transcription) OH OH OH OH OH OH OH OH OH OH RNA RNA DNA U U 51. Chapter 12: From DNA to Protein: Genotype to Phenotype Initiation Elongation Termination: Special DNA sequences and protein helpers terminate transcription. The transcript is released from the DNA. This Primary Transcript is called the “pre- mRNA” The pre-mRNA is processed to generate the mature mRNA Transcription: DNA-Directed RNA Synthesis - Termination 52. Chapter 12: From DNA to Protein: Genotype to Phenotype Figure 12.4 – Part 2 53. Chapter 12: From DNA to Protein: Genotype to Phenotype The central dogma DNA structure DNA replication RNA structure RNA synthesis (Transcription) The genetic code Protein synthesis (Translation) Mutation Consequences of mutation Lecture 1 Lecture 2 Lecture 3 Lecture 4 Topics 54. Chapter 12: From DNA to Protein: Genotype to Phenotype Translation 55. Chapter 12: From DNA to Protein: Genotype to Phenotype The Central Dogma The Flow of Information: DNA → RNA → protein DNA Replication Transcription Translation A gene is expressed in two steps: DNA is transcribed to RNA Then RNA is translated into protein. 56. Chapter 12: From DNA to Protein: Genotype to Phenotype Translation- the synthesis of protein from an RNA template. Five stages:Pre-initiation Initiation Elongation Termination Post-translational modification Complicated: In eukaryotes, ~300 molecules involved Translation 57. Chapter 12: From DNA to Protein: Genotype to Phenotype mRNA- serves as a template code tRNA- serves as an adapter molecule rRNA- holds molecules in the correct position, protein portion also catalyze reactions Functions of the Types of RNA 58. Chapter 12: From DNA to Protein: Genotype to Phenotype Shine-Dalgarno sequence ~10 nt upstream of initiation codon Positions ribosome at correct start site mRNA Structure 59. Chapter 12: From DNA to Protein: Genotype to Phenotype All tRNA molecules have a similar but not identical structure- “cloverleaf” Acceptor arm- CCA-3’ an amino acid will be esterified to 3’ OH of A TΨC arm - named for ribothymidine- pseudouridine-cytidine sequence Extra arm - variable in size ~3-~20 nt tRNA Structure 60. Chapter 12: From DNA to Protein: Genotype to Phenotype anti-codon arm named for 3 bases which base-pair with mRNA codon D arm- dihydro-uridine base modification Sequence differs for the different amino acid- not just in the anticodon arm tRNA Structure, cont’d 61. Chapter 12: From DNA to Protein: Genotype to Phenotype Triplet codons Universal (almost) Commaless Degenerate- wobble Unambiguous Reading frames Embedded genes The Genetic Code 62. Chapter 12: From DNA to Protein: Genotype to Phenotype Pre-initiation - Charging the tRNA 63. Chapter 12: From DNA to Protein: Genotype to Phenotype Aminoacyl-tRNA Synthetase One for each amino acid 2 step mechanism attach a.a. to AMP transesterify to 3’ (or 2’ and then rearrange) Proofread identity elements “sieve” Modify Met-tRNAfmet to fMet-tRNAfmet 64. Chapter 12: From DNA to Protein: Genotype to Phenotype Pre-initiation 1. Charging the tRNA 2. Formylation of met-tRNAfmet 65. Chapter 12: From DNA to Protein: Genotype to Phenotype Pre-initiation 1. Charging the tRNA 2. Formylation of met-tRNAfmet 3. Dissociation of ribosomes (IF-1 and IF-3) 4. IF-2:GTP binary complex formation 5. IF-2:GTP:charged tRNA ternary complex formation 6. IF4F, 4A and 4B bind mRNA to place it on small subunit 7. 40S initiation complex 66. Chapter 12: From DNA to Protein: Genotype to Phenotype Initiation Preinitiation complexes form an 80S complex: small subunit, ternary complex (GDP + Pi leave), mRNA, large subunit, aminoacyl tRNA P-site- only thing that can enter is a peptide In prokaryotes, f-met “tricks” the ribosome A-site- only thing that can enter is an aminoacyl tRNA 67. Chapter 12: From DNA to Protein: Genotype to Phenotype Each ribosome contains 3 binding sites for tRNA molecules: A-site = aminoacyl-tRNA P-site = peptidyl-tRNA E-site = exit 68. Chapter 12: From DNA to Protein: Genotype to Phenotype 07_32_initiation.jpg 69. Chapter 12: From DNA to Protein: Genotype to Phenotype Ribosome composed of 2 subunits: Small subunit – matches the tRNAs to the codons of the mRNA Large subunit – catalyzes the formation of the peptide bonds between amino acids in the growing polypeptide chain The two subunits come together near the 5’ end of the mRNA to begin synthesis of a protein Then ribosome moves along, translating codons, until 2 subunits separate after finishing 70. Chapter 12: From DNA to Protein: Genotype to Phenotype 07_28_ribosome.jpg 71. Chapter 12: From DNA to Protein: Genotype to Phenotype 07_29_binding.site.jpg 72. Chapter 12: From DNA to Protein: Genotype to Phenotype Elongation 1. EF-1:GTP: aminoacyl- tRNA ternary complex enters A-site; GDP + Pi leave (EF-Tu and EF-Ts involved with GTP metabolism in prokaryotes) 2. Peptide bond forms as P-site content is transferred onto A-site occupant 3. Translocation requires GTP; GDP + Pi are products 73. Chapter 12: From DNA to Protein: Genotype to Phenotype 07_34_stop codon.jpg 74. Chapter 12: From DNA to Protein: Genotype to Phenotype 07_30_3_step_cycle.jpg Peptidyl transferase catalyzes peptide bond formation 75. Chapter 12: From DNA to Protein: Genotype to Phenotype 07_35_polyribosome.jpg A polyribosome from a eucaryotic cell 76. Chapter 12: From DNA to Protein: Genotype to Phenotype Termination 1. UAA, UAG, UGA is enveloped by A-site of ribosome 2. RF-1 enters A site 3. GTP is hydrolyzed, H2O is used to cleave protein off tRNA 4. Components are recycled to synthesize another protein molecule 77. Chapter 12: From DNA to Protein: Genotype to Phenotype The ribosome is a ribozyme Determination of its 3-D structure in 2000 showed that the rRNAs are responsible for: -- ribosome’s overall structure -- its ability to position tRNAs on the mRNA -- its catalytic function in forming peptide bonds (via a highly structured pocket that precisely orients the elongating peptide and the charged tRNA) RNA rather than protein served as first catalysts, and ribosome is a relic of an earlier time 78. Chapter 12: From DNA to Protein: Genotype to Phenotype 07_31_ribos_shape.jpg 79. Chapter 12: From DNA to Protein: Genotype to Phenotype Codons in mRNA signal where to start and stop protein synthesis Translation begins with codon AUG and a special tRNA required for initiation— The initiator tRNA always carries methionine (Met) or a modified form of it All new proteins begin with Met, although it is usually removed later by a protease 80. Chapter 12: From DNA to Protein: Genotype to Phenotype The initiator tRNA is loaded into the P site of ribosome along with translation initiation factors The loaded ribosomal small subunit binds to the 5’ end of the mRNA, recognized by the cap Then moves forward along the mRNA searching for the AUG Once found, large subunit associates Protein synthesis begins with next tRNA binding to the A site, etc. 81. Chapter 12: From DNA to Protein: Genotype to Phenotype Mechanism for finding start codon is different in bacteria Instead of a 5’ cap, mRNA has specific ribosome- binding sequence located upstream of AUG = Shine-Dalgarno sequence Bacterial ribosome can also bind to this sequence when it is internal on the mRNA – important difference between procaryotes and eucaryotes Necessary for translation of polycistronic mRNAs – found only in bacteria 82. Chapter 12: From DNA to Protein: Genotype to Phenotype 07_33_mRNA.encode.jpg Ribosomes initiate translation at ribosome-binding sites in polycistronic procaryotic mRNAs, which can encode more than one protein **Note mistake in the legend to this figure in your text – Figure 7-33 83. Chapter 12: From DNA to Protein: Genotype to Phenotype One of three stop codons (UAA, UAG, UGA) signals the end of translation A protein release factor, rather than a tRNA, binds to a stop codon This signals peptidyl transferase to add water rather than an amino acid to the end of the growing polypeptide This releases that last amino acid from the tRNA, and thus the polypeptide from the ribosome The ribosome releases the mRNA and disassociates into its 2 subunits 84. Chapter 12: From DNA to Protein: Genotype to Phenotype Most proteins begin folding into their 3-D shape as they are being made Some require molecular chaperones to help them fold correctly (review this term) – these bind to the partially folded chain 85. Chapter 12: From DNA to Protein: Genotype to Phenotype Proteins are made on polyribosomes (or polysomes)– several to many ribosomes spaced as close as 80 nucleotides along a single mRNA **Thus, many more proteins can be made in a given time period Remember too that translation is coupled to transcription in bacteria – both are going on at the same time 86. Chapter 12: From DNA to Protein: Genotype to Phenotype Inhibitors of procaryotic protein synthesis are used as antibiotics There are some important differences between protein synthesis in bacteria v. eucaryotes, which can be exploited Why are these differences important in treating bacterial infections? 87. Chapter 12: From DNA to Protein: Genotype to Phenotype Inhibitors of procaryotic protein synthesis are used as antibiotics There are some important differences between protein synthesis in bacteria v. eucaryotes, which can be exploited Why are these differences important in treating bacterial infections? Need to be able to inhibit bacterial translation, but not eucaryotic translation (or would be toxic to humans) 88. Chapter 12: From DNA to Protein: Genotype to Phenotype Many antibiotics are isolated from fungi! Why? 89. Chapter 12: From DNA to Protein: Genotype to Phenotype Number of copies of a protein in a cell depends on both how many are made, and how long they survive (like human population) **An important type of regulation on the amount of protein available in the cell is carefully controlled protein breakdown e.g. structural proteins may last for months or years, enzymatic proteins for hours or seconds Proteases act by hydrolyzing the peptide bonds between individual amino acids 90. Chapter 12: From DNA to Protein: Genotype to Phenotype Functions of proteolytic pathways: 1) To rapidly degrade those proteins whose lifetimes must be short 2) To recognize and eliminate proteins that are damaged or misfolded (neurodegenerative diseases like Alzheimer’s, Huntington’s, and Creutzfeldt-Jacob disease are caused by aggregation of misfolded proteins) 91. Chapter 12: From DNA to Protein: Genotype to

Phenotype Most damaged proteins degraded in cytosol by large complexes of proteolytic enzymes called proteasomes Contain a central cylinder formed of proteases whose active sites face inward Cylinder is stoppered on ends by large protein complex – binds the proteins to be degraded, unfolds them, and then feeds them into cylinder, using ATP 92. Chapter 12: From DNA to Protein: Genotype to Phenotype 07_36_proteasome.jpg The proteasome degrades unwanted proteins cap cylinder 93. Chapter 12: From DNA to Protein: Genotype to Phenotype Proteasomes recognize proteins to be degraded by the attachment of a small protein called ubiquitin Ubiquitin added to special amino acid sequences, or to abnormal amino acids or motifs that are normally buried 94. Chapter 12: From DNA to Protein: Genotype to Phenotype 07_37_Protein.produc.jpg All of these steps can be regulated by the cell 95. Chapter 12: From DNA to Protein: Genotype to Phenotype RNA and the Origins of Life One view is that an RNA world existed on Earth before modern cells arose In primitive cells, RNA both 1) stored genetic information 2) catalyzed chemical reactions Eventually, DNA took over as genetic material Proteins became major catalysts and structural components 96. Chapter 12: From DNA to Protein: Genotype to Phenotype 07_38_RNA world.jpg 97. Chapter 12: From DNA to Protein: Genotype to Phenotype Some RNA catalysts carry out fundamental reactions in modern-day cells = molecular fossils of an earlier world For example: ribosomes RNA splicing machinery The arguments in support of the RNA world hypothesis…….. 98. Chapter 12: From DNA to Protein: Genotype to Phenotype Life requires autocatalysis The origin of life requires molecules with the ability to catalyze the production of more molecules like themselves These would out compete others What molecules have autocatalytic properties? 99. Chapter 12: From DNA to Protein: Genotype to Phenotype Life requires autocatalysis The origin of life requires molecules with the ability to catalyze the production of more molecules like themselves These would out compete others What molecules have autocatalytic properties? Best catalysts are proteins, but can’t reproduce themselves directly 100. Chapter 12: From DNA to Protein: Genotype to Phenotype Life requires autocatalysis The origin of life requires molecules with the ability to catalyze the production of more molecules like themselves These would out compete others What molecules have autocatalytic properties? Best catalysts are proteins, but can’t reproduce themselves directly **But RNA can both store information and catalyze reactions 101. Chapter 12: From DNA to Protein: Genotype to Phenotype RNA can specify the sequence of a complementary polynucleotide, which in turn can specify the sequence of the original molecule 102. Chapter 12: From DNA to Protein: Genotype to Phenotype 07_39_copy_itself.jpg RNA can make an exact copy of itself Results in “multiplication” of the original sequence 103. Chapter 12: From DNA to Protein: Genotype to Phenotype But efficient synthesis also requires catalysts to promote fast, efficient, error-free reactions Today, the protein RNA and DNA polymerases do that What did it before proteins had appeared? Even today, have ribozymes with catalytic activity – what? 104. Chapter 12: From DNA to Protein: Genotype to Phenotype But efficient synthesis also requires catalysts to promote fast, efficient, error-free reactions Today, the protein RNA and DNA polymerases do that What did it before proteins had appeared? Even today, have ribozymes with catalytic activity – what? 1) the rRNA that catalyzes the peptidyl transferase reaction on the ribosome 2) the snRNAs in the snRNPs that catalyze splicing 105. Chapter 12: From DNA to Protein: Genotype to Phenotype A single-stranded RNA molecule can base-pair to itself (with both conventional and “non- conventional” hydrogen bonding, thus folding into complex 3-D structure These too can act as catalysts, because of their surface with unique contours and chemical properties But since have only 4 types of nucleotides, the range of chemical reactions, and efficiency, is limited 106. Chapter 12: From DNA to Protein: Genotype to Phenotype 07_40_ribozyme.jpg Ribozyme = an RNA molecule with catalytic activiites 107. Chapter 12: From DNA to Protein: Genotype to Phenotype The processes in which catalytic RNAs play a role are some of the most fundamental steps in the expression of genetic information--- **especially those steps where RNA molecules themselves are spliced or translated into proteins 108. Chapter 12: From DNA to Protein: Genotype to Phenotype 109. Chapter 12: From DNA to Protein: Genotype to Phenotype Thus, RNA has all the properties required of a molecule that could catalyze its own synthesis Self-replicating systems of RNA molecules not yet found in nature, but scientists believe they can be constructed in the lab 110. Chapter 12: From DNA to Protein: Genotype to Phenotype 07_41_catalyze_synt.jpg A hypothetical RNA molecule that could catalyze its own synthesis 111. Chapter 12: From DNA to Protein: Genotype to Phenotype RNA is thought to predate DNA in evolution Evidence that RNA arose before DNA found in chemical differences between them: 1) Ribose is readily formed from formaldehyde (HCHO), one of principal products of experiments simulating conditions on primitive earth Deoxyribose made from ribose, catalyzed by a protein today Thus, suggestion that ribose came first 112. Chapter 12: From DNA to Protein: Genotype to Phenotype Once DNA appeared, it proved more suitable for permanent storage of genetic information--- 1) It’s chemically more stable than RNA (because of the deoxyribose), so can maintain longer chains without breakage 2) It’s double-stranded, so a damaged nucleotide on one strand can be easily repaired by using the other strand as template 3) Using thymine rather than uracil makes deamination easier to repair (deam. C → U) 113. Chapter 12: From DNA to Protein: Genotype to Phenotype Eventually in cells, DNA took over for information storage Proteins took over as catalysts because of greater chemical complexity RNA remains as the intermediary connecting them And cells could become ever more complex, evolving great diversity of structure and function 114. Chapter 12: From DNA to Protein: Genotype to Phenotype 07_42_RNA_DNA.jpg 115. Chapter 12: From DNA to Protein: Genotype to Phenotype How We Know – Cracking the Genetic Code Researchers began by perfecting the isolation of a cell-free system that could synthesize proteins from added synthetic RNAs Could only use polynucleotide phosphorylase at first, which randomly joined together ribonucleotides present in the test tube First tested poly-UUUUUUUU → phenylalanine 116. Chapter 12: From DNA to Protein: Genotype to Phenotype 07_24_UUU codes.jpg 117. Chapter 12: From DNA to Protein: Genotype to Phenotype And, poly-AAAAAAAAA → lysine poly-CCCCCCCC → proline poly-GGGGGGG base-paired and didn’t work 118. Chapter 12: From DNA to Protein: Genotype to Phenotype Eventually figured out how to make mixed polynucleotides, which were harder to interpret: e.g. UGUGUGUGUG → cysteine and valine, but which is which, since have both UGU and GUG codons? 119. Chapter 12: From DNA to Protein: Genotype to Phenotype 07_25_coding.jpg 120. Chapter 12: From DNA to Protein: Genotype to Phenotype Eventually figured out how to make RNA fragments only 3 nucleotides in length These would bind to ribosomes and attract the appropriate charged tRNA Had only to to capture these on filter paper, and then identify the attached amino acid Within a year, the entire code was deciphered! 121. Chapter 12: From DNA to Protein: Genotype to Phenotype The central dogma DNA structure DNA replication RNA structure RNA synthesis (Transcription) The genetic code Protein synthesis (Translation) Mutation Consequences of mutation Lecture 1 Lecture 2 Lecture 3 Lecture 4 Topics 122. Chapter 12: From DNA to Protein: Genotype to Phenotype Mutations Mutation- change in DNA sequence leading to a different protein sequence being produced -same codon produced Missense- different codon introduced Silent (acceptable) Partially acceptable Nonsense-stop codon introduced Usually unacceptable 123. Chapter 12: From DNA to Protein: Genotype to Phenotype Energetics Each amino acid residue requires 4 ATP equivalents ATP AMP + PPi to “charge” tRNA 1 GTP is used to place aminoacyl-tRNA into A-site 1 GTP is used to translocate after each peptide bond formation 124. Chapter 12: From DNA to Protein: Genotype to Phenotype Regulation of Translation 1. Elongation factor 2- a. phosphorylated under stress b. when phosphorylated, doesn’t allow GDP- GTP exchange and protein synthesis stops 2. eIF-4E/4E-BP complex can be phosphorylated 125. Chapter 12: From DNA to Protein: Genotype to Phenotype Post-translational Modifications 1. Proteolytic cleavage (most common) a. Direction into the ER and signal sequence cleavage b. Other signal sequences exist for other organelles c. Activation 2. Disulfide bond formation 126. Chapter 12: From DNA to Protein: Genotype to Phenotype Post-translational Modifications, contd. 3. Group addition a. Glycosylation (most complex known) b. Acetylation or phosphorylation, etc. 4. Amino acid modification a. Hydroxylation of Pro (in ER) b. Methylation of Lys This list is not exhaustive 127. Chapter 12: From DNA to Protein: Genotype to Phenotype Genetic Regulation Constitutive vs. Inducible Expression Constitutive- A gene is expressed at the same level at all times. AKA housekeeping gene. Inducible- A gene is expressed at higher level under the influence of some signal. 128. Chapter 12: From DNA to Protein: Genotype to Phenotype Genetic Regulation - The Operon Operon- an operator plus two or more genes under control of that operator Occurs only in prokaryotes (in eukaryotes, each gene is under separate control). Best known is the lac operon of Jacob and Monod 129. Chapter 12: From DNA to Protein: Genotype to Phenotype The Operon Under Normal Expression 130. Chapter 12: From DNA to Protein: Genotype to Phenotype The Operon Under Induced Expression 131. Chapter 12: From DNA to Protein: Genotype to Phenotype Eukaryotic Transcriptional Regulation TATA box- where to start CAAT box and Enhancer- how often to start Enhancer CAAT TATA Gene 132. Chapter 12: From DNA to Protein: Genotype to Phenotype Post-Transcriptional Regulation 1. mRNA stability can be altered by signal molecules PEPCK +Insulin = 30 min -Insulin = 3 h

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