

DNA structure and function

I. Introduction

- DNA holds the genetic information of a cell -- heritable information

II. DNA structure

- a polymer of nucleotides -- two strands of nucleotides twisted around each other in a double helix, held together by hydrogen bonds
 - three types of nucleotides
 - adenine nucleotides
 - guanine nucleotides
 - thymine nucleotides
 - cytosine nucleotides
 - analogy of a ladder twisted about itself
 - each side of ladder formed by alternating sugar-phosphate units
 - rungs of ladder formed by nitrogenous bases hydrogen bonding with each other -- hold two nucleotide strands together
- principle of complementary base pairing:
 - adenine always hydrogen bonds thymine
 - cytosine and guanine always hydrogen bond
- reason for such pairing:
 - available hydrogen bonding sites
 - one ring base pairs with two ring base
- hereditary information in DNA is encoded in the sequence of nucleotides that make up DNA molecule
- a chromosome consists of a single DNA molecule
- consequences of complementary of bases:
 - molecule easily replicated
 - molecule translated to RNA sequence

III. DNA replication

- process is semiconservative

- need following:

- unwinding enzyme -- helicase
- enzyme that adds nucleotides, matching them to template strand -- DNA polymerase
- a supply of nucleotides (deoxyribonucleoside triphosphates)

III. DNA expression -- an outline

- the process of taking the information in a particular sequence of the DNA molecule and using it to produce a protein

A. DNA expression occurs in two steps:

- transcription: information of a DNA sequence (gene) copied into corresponding information in RNA sequence
- translation: information in RNA converted into amino acid sequence in a polypeptide

B. RNA structure

- single strand of nucleotides

- phosphate/ribose/nitrogenous base

- bases are A, U, G, C

- produced from a DNA template

- three types

- mRNA
- rRNA
- tRNA

C. Central dogma (Francis Crick)

1. how does genetic information get from nucleus to cytoplasm?

- messenger hypothesis:
 - RNA forms complementary copy of one DNA strand comprising specific gene, messenger RNA (mRNA) -- travels to cytoplasm, a template for synthesis of proteins

- there are as many kinds of mRNA as genes
- 2. what is relationship between specific nucleotide sequence in DNA and a specific amino acid (a.a.) sequence in proteins?
 - adapter hypothesis:
 - an adapter molecule that binds a specific a.a. at one end and recognizes a specific mRNA sequence at other end
 - transfer RNA -- recognize the genetic message of mRNA and place specific a.a. in a certain sequence next to one another -- translation of the mRNA
 - tRNAs produced by transcription
 - ribosome -- ribosomal RNA (rRNA) and protein form structure where translation occurs
 - rRNAs produced by transcription

IV. Transcription

A. Molecules required:

- enzyme that mediated process: RNA polymerase
- supply of nucleotides (ribonucleotides) ATP, GTP, CTP, UTP
- DNA template -- within one gene only one DNA strand transcribed, template strand

B. Initiation

- RNA polymerase binds promoter
 - promoter -- a specific sequence of DNA, at least one per gene to be transcribed to mRNA
 - contains initiation site, exact location where transcription begins

C. Elongation

- upon binding promoter RNA polymerase unwinds DNA (20 base pairs)
 - reads template strand
 - adds new nucleotides to end of the growing strand
 - moving transcription complex:
 - after unwinded region is transcribed along template strand, DNA rewinds into helix -- RNA polymerase unwinds next 20 or so bases of DNA, moves along and transcribes template strand

D. Termination

- a particular base sequence in DNA template strand specifies end of transcription
- RNA polymerase unbinds template strand, transcript falls off transcription complex

V. The genetic code

- sequences of three nucleotides that provide specificity for protein synthesis
 - each sequence of three nucleotides along mRNA (and thus DNA template strand) specifies a particular a.a.
 - each of these three sequences of nucleotides is called a codon -- complementary to DNA template from which it was transcribed
 - how did scientists figure out how four bases (letters) could code for 20 amino acids?
 - one letter code: $4^1 = 4$ a.a.
 - two letter code: $4^2 = 16$ a.a.
 - three letter code $4^3 = 64$ a.a.
 - one start codon: AUG (methionine)
 - three stop codons: UAA, UAG, UGA
 - thus 60 codons left over to code for 20 a.a.
 - genetic code is redundant -- one a.a. may be represented by more than one codon
 - however one codon represents one and only one a.a.

VI. Translation overview

A. basically involves having an adapter molecule (tRNA) that recognizes a specific sequence of mRNA (a specific codon) and bind the a.a. specified by that codon.

- tRNA must recognize specific codon
- tRNA must carry a.a. that is correct for its reading of codon
- tRNA thus interacts with ribosomes, carries an a.a., associates with mRNA
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B. for each of the 20 a.a. there is at least one specific type of tRNA

C. tRNA structure:

- one end of molecule has a.a. covalently bound to it (high energy bond)
- midway through molecule there is group of three bases, anticodon
 - complementary to the mRNA codon for that tRNA's a.a.
 - codon and anticodon unite by complementary base pairing (H-bonding); antiparallel
- note that 61 codon encode 20 a.a. in proteins; however cell does not need 61 different tRNA species
 - pairing with third base of codon not always strictly observed -- wobble phenomenon, does not compromise specificity of genetic code

D. ribosome is cellular structure where translation occurs

- ribosomes comprised of two subunits, large and small
- ribosomes not specific for specific mRNAs or tRNAs -- not specific for production of one kind of protein
 - can combine with any mRNA or tRNAs, ribosome just a factory where translation occurs
 - allows for interactions between mRNA and tRNA

VI. Translation

A. Initiation

- formation of an initiation complex:

- small ribosomal subunit binds mRNA
- charged tRNA binds start codon (AUG) at P site -- carries methionine (N-terminus of future p.p. chain)
- large ribosomal subunit joins complex so that charged tRNA with methionine are at P-site
- A site aligned with second codon

B. Elongation of polypeptide chain

- charged tRNA specific for second codon enters free A site
- a.a. carried by this tRNA aligned next to methionine
- large ribosomal subunit catalyzes two reactions:
 - breaks bond between tRNA at P site and its a.a. (methionine)

- peptide bond formation between this a.a. (methionine) and one at A site
- ribosome shifts along mRNA
 - first tRNA dissociates from ribosome
 - second tRNA now bearing a dipeptide shifts to P site
 - A site aligned with next codon
 - process repeats itself

C. Termination

- when a specific termination codon enters A-site, a specific protein binds at A site
- mRNA and forming polypeptide chain released from ribosome

VII. Mutations

- heritable changes in genes
- although errors in pairing of complementary bases occur least often in replication (as opposed to transcription and translation), these errors are most severe as only they are heritable

A. mutations in multicellular organisms:

- somatic mutations -- occur in nongamete body cells
- germ-line mutations -- occur in cells that give rise to gametes; potentially passed on to new organisms

B. mutations may lead to observable changes in phenotype

- certain types of dwarfism -- mutations in GH receptor
- thyroid hormone resistance – ADD

C. mutations may lead to relatively unobservable changes in phenotype

- mutation that lowers levels of glucose-6-phosphate dehydrogenase in RBC -- makes them sensitive to antimalarial drugs

D. point mutations: mutations in single genes

- result from addition or subtraction of a nucleotide base, or the substitution of one base for another in the DNA and hence mRNA
 - missense mutations -- some base substitution mutations may change the genetic message such that one amino acid substitutes for another in the protein

- sickle cell anemia -- people homozygous for recessive allele have defective red blood cells
- nonsense mutation -- bases substituted causes a stop codon to be produced
 - shortened, nonfunctional protein product
- frame-shift mutation -- base pairs inserted or deleted from DNA
 - interfere with decoding of the genetic message by throwing it out of register