Genetic transfer of information

Where does the information come from to produce proteins?

DNA is ________________ in all known cellular life forms

___________________________ of DNA information to make proteins

DNA sequence (bases) dictates __________________________
DNA

double helix structure

- overall DNA structure very complex
  - interaction with ____________
  - coiling
  - coiling of coil
  - allows for packing of huge amounts

- ~3 m of DNA in _______________
DNA Structure
double helix structure

History

Gregor Mendel
- Austrian priest and scientist,
- 1853 - 1856 discovered the inheritance of traits follow laws (Mendelian genetics) using pea plants.
- his work not fully appreciated until 1900

Friedrich Miescher
- Swiss physician, worked at University of Tübingen, Germany
- 1869, discovered DNA in pus on discarded surgical bandages.
- found it in nucleus and called it “nuclein”

Phoebus Levene
- Russian born, worked at Rockefeller Institute of Medical Research
- 1919, identified the base, sugar and phosphate nucleotide unit of DNA

Alfred Hershey and Martha Chase
- 1953 confirmed DNA as hereditary genetic material
DNA Structure
double helix structure
James D. Watson and Francis Crick

History
Watson - American
Crick - English
- Worked at University of Cambridge
- 1953, determined the double helix structure of DNA
- Controversially, they used the DNA x-ray diffraction images of Rosalind Franklin (Kings College, London) without her permission
- 1957, Crick presented the “Central Dogma” that laid out framework of DNA to RNA to protein, laying the foundation of modern molecular biology
- 1962 Watson and Crick awarded Nobel Prize in Physiology or Medicine
DNA Structure

History

James Watson
- in 1988 initiated the Human Genome Project
- led project until 1992
- May 31, 2007 became the second person to have his full genome sequence published
monomer units - as with proteins, DNA is made up of monomer units - ________________

DNA Structure

double helix structure

___________________________ chains in a helix

Each polynucleotide chain made up of:

backbone - ___________ (ribose) _____________________ (PO$_4$)
nucleotide base - ____ containing ring structure that H- bonds across _____

monomer units - as with proteins, DNA is made up of monomer units - ________________
DNA Structure

double helix structure

Nucleotide bases - made up of a nucleic acid, ribose sugar, and a phosphate
- “base” refers to a ____________________, not as in pH

Nucleotide bases:

Pyrimidines - ____________________
________________________

Purines - ____________________
________________________

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DNA Structure
double helix structure

Nucleotides - made up of a base, ribose sugar, and a phosphate
- “base” refers to a N ring structure, not as in pH

Nucleoside - a base and a sugar
_______________ to each other
- ________________

Ribonucleoside - ________________

______________________________
DNA Structure
double helix structure

**Nucleotides** - made up of a base, ribose sugar, and a phosphate
- “base” refers to a N ring structure, not as in pH

**Nucleotide** - phosphate group (phosphoric acid) esterified to the ________________
- ________________

- ![Deoxyadenosine 5'-monophosphate](image1)
  - **dAMP**
  - Deoxyadenosine 5'-monophosphate

- ![Deoxyguanosine 5'-monophosphate](image2)
  - **dGMP**
  - Deoxyguanosine 5'-monophosphate

- ![Deoxythymidine 5'-monophosphate](image3)
  - **dTMP**
  - Deoxythymidine 5'-monophosphate

- ![Deoxycytidine 5'-monophosphate](image4)
  - **dCMP**
  - Deoxycytidine 5'-monophosphate
DNA Structure
double helix structure

Formation of sugar-phosphate backbone

Individual nucleotides are connected through linking the 3’ OH ribose group with ________________
__________________________

Sugar-phosphate backbone _____________
_____________________

Identity of the bases determines DNA sequence

T G C A

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DNA Structure
double helix structure

Directionality of a single DNA strand

5' - T G C A - 3'

5' end = __________

3' end = __________

Ultimately 5' end of a gene = ________________

3' end of a gene = ________________
DNA Structure
double helix structure

Bases on one strand are complementary to _______________________________

Adenine - Thymine
(purine)         (pyrimidine)

Guanine - cytosine
(purine)         (pyrimidine)

Strands run in antiparallel (opposite) directions

5’ - _________ - 3’
3’ - _________ - 5’

Early experiments showed that the amount of _____________________ indicated that:

_______________________________ in a double helix
DNA Structure  
double helix structure

What is the sequence of the complimentary strand?

When writing sequence of one strand, ________________

$5’ - A G C T C C G T A A G - 3’$

1. $5’ - T C G A G G C A T T C - 3’$
2. $5’ - U C G A G G C A U U C - 3’$
3. $5’ - C T T A C G G A G C T - 3’$
4. $5’ - C U U A C G G A G C U - 3’$
DNA Structure

double helix structure

Outside diameter = 2.0 nm
Inside diameter = 1.1 nm

Length of one turn = 10 base pairs
= 3.4 nm

Empty spaces in helix not filled by atoms
_________________ , 2.2 nm
_________________ , 1.2 nm

places where ________________
bases of DNA
DNA Structure

double helix structure

Base pairs

2 H-bonds

purine - pyrimidine base pairing allows for___________
_____________ with out bulges.
gives consistent _____________
_____________________.

H-bonds are _____________
to the helix axis

Double Helix Structure

(http://www.youtube.com/watch?v=ZGHkHMoyC5I)
DNA Structure

double helix structure

Other forms of double helix

B-DNA - form we have discussed
- predominant ______________
- ________________ form of DNA

A-DNA - base pair H-bonds at __________
- ________________ per helix turn
- more compact than B-DNA
- forms under ________________
- not found in ________________

Z-DNA - forms in regions of DNA with
- alternating ________________
- ________________ : CGCGCGCGCG
- is in physiological DNA
- ________________ than B-DNA
- ________________ per helix turn
DNA Structure

double helix structure

Other forms of double helix

Both B- and A-DNA ____________
__________________________________.

Helix winds ______ in the direction
the _________ of right hand curl

Z-DNA is a _________________
DNA Structure

double helix structure

left-handed

right-handed

Left-Handed Helix

Right-Handed Helix

twists ________________
twists ________________
DNA Structure

How does so much DNA fit into a cell or nucleus?

DNA Supercoiling

Supercoiling - [Diagram of supercoiled DNA]
DNA Structure

DNA Supercoiling

**Supercoiling** - twisting of double helix in space about its axis

Prokaryotic DNA supercoiling:
- prokaryotic DNA is ________________
- twists in circular structure give extra twist to DNA
- positive supercoil - “right-handed” ________________
- negative supercoil - “left-handed” ________________
- naturally occurring form of circular DNA
DNA Structure

DNA Supercoiling

Eukaryotic DNA supercoiling - more complex than _______________________
- ______________________
- DNA has an overall ______________________
- DNA complexes with positively ______________________

Histones - ______________________
- basic proteins with large amounts of basic ______________________
- 5 main types:
  H1, H2A, H2B, H3, and H4
**DNA Structure**

**Eukaryotic DNA Supercoiling**

**Chromatin** - the complex of ________________ that make up chromosomes
- resembles ________________________________
- is coiled into tight packing to form chromosome

**Nucleosome** - __________________________ histone core
- histone core = octamer of \((H2A)_2(H2B)_2(H3)_2(H4)_2\)
- H1 holds ____________________

- packing of nucleosomes ____________________________
DNA Structure

Eukaryotic DNA Supercoiling

**Nucleosome** - ___________________________ wrapped around histone core

- 30 - 50 base pairs of ___________________________

[Diagram of DNA structure with nucleosomes]

**chromatin formation**
http://youtube.com/watch?v=Pj9cdVeIntY

**chromatin formation 2**
http://www.youtube.com/watch?v=N5zFOScowqo
DNA Replication

Differences in details of DNA replication between eukaryotes and prokaryotes
But, basic mechanism is the same.

DNA replication takes place ________
______________________________

RNA and protein synthesis occur _____
_______________________________.

Differences in details of DNA replication between eukaryotes and prokaryotes
But, basic mechanism is the same.
DNA Replication

3 possible modes of DNA replication

1. Semiconservative - each strand is copied and resulting DNA ____________________________

2. Conservative - only new strand copies associate with ____________ and only original strands associate ___________________________

3. Dispersive - resulting DNA has ____________

Three postulated methods of DNA Replication

- Semi-Conservative
- Conservative
- Dispersive

Newly, synthesized strand
Original template strand
DNA Replication
Meselson - Stahl Experiment

Semiconservative Replication Experiments
- 1958, at Cal Tech
- used $^{15}$N, natural isotope $^{14}$N
- Fed $^{15}$N, traced incorporation into DNA over generations
- Used bacteria *E. coli*

Both American born scientists
Start with $^{15}$N labeled DNA

**Semiconservative Replication Experiments**

**RED** = $^{15}$N

**BLUE** = $^{14}$N

$^{14}$N – ___ protons, ___ neutrons

$^{15}$N – ___ protons, ___ neutrons

After first replication each DNA double helix should be ________________

After second replication ________________ should be 50 - 50%

$^{15}$N - $^{14}$N
DNA Replication

DNA has **origins of replication** - locations where ______________

DNA replication is ______________

**Replication fork** – point at which ______________
DNA Replication

Directionality - new DNA is always produced in ___________________
- copied DNA is always read in ___________________

DNA replication is **Semidiscontinuous** - one strand is copied in one
_______________________, one strand is copied in _________________.

**Leading strand** - strand of DNA being _______________________

**Lagging strand** - strand of DNA being replicated _______________

**Okazaki fragments** - __________________________ used to copy lagging

strand

**Replication loop** - because lagging strand runs _____, it must be looped
around to be read ________ for replication.
DNA Replication

DNA Polymerase - enzyme that catalyzes the addition of nucleotides to the growing DNA chain

- ________________

- 5 different DNA polymerases:
  - prokaryotes: ________________
  - eukaryotes: ________________
Helicase: enzyme that separates ________________

Problem: if two strands of DNA duplex are separated, the DNA duplex ahead of separation ________________. Creates tension.

Overcome by the enzyme:

Prokaryotes:

DNA gyrase: enzyme that ________________, relaxes DNA ahead of ______ ________________, then rejoins duplex.

Eukaryotes:

Topoisomerase: performs same function in eukaryotes.
DNA Replication

Proofreading and Mutations

DNA replication error: mismatched base pairs

_______ or _______

Errors occur one in every $10^9$ (_______) to $10^{10}$ (_______) base pairs

DNA polymerase ________________________________

Can fix ________________________________
Prokaryotic DNA Replication:

- DNA polymerase
- DNA gyrase
- Helicase
- Template
- Newly synthesized strand
- Replication fork

Eukaryotic DNA Replication:

- DNA polymerase
- Topoisomerase
- Helicase
- Template
- Newly synthesized strand
- Replication fork
DNA Replication

When does DNA replication take place?

Prior to ________________________________
____________________ is needed for new cells

DNA replication is complex process in ________________________________.

System has built in correction systems ex: proof reading of DNA polymerase