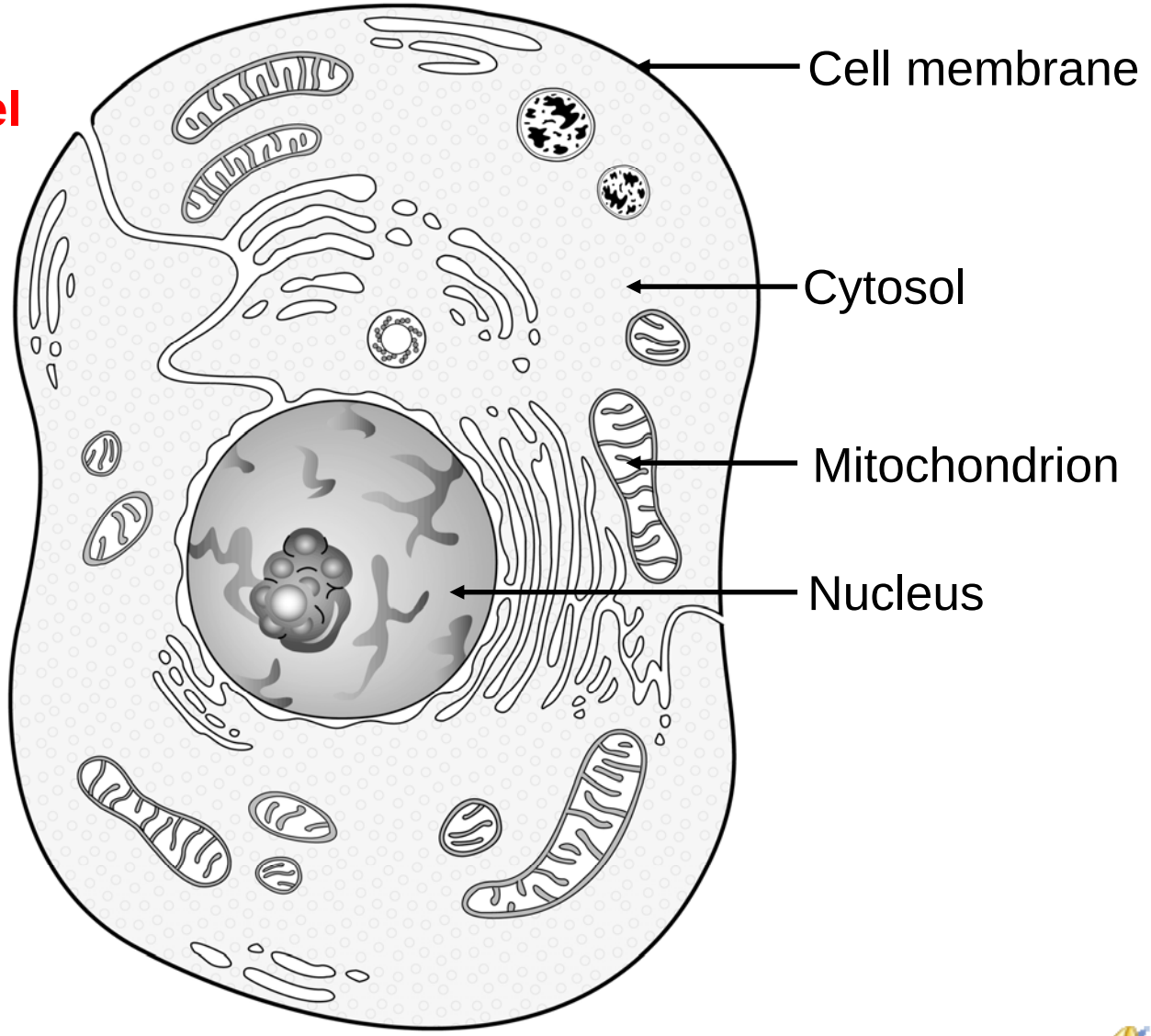
Nuclear DNA and Chromosomes

- Most (but not all) DNA in eukaryotic cells is in the nucleus

Eukaryotic Cell: Model

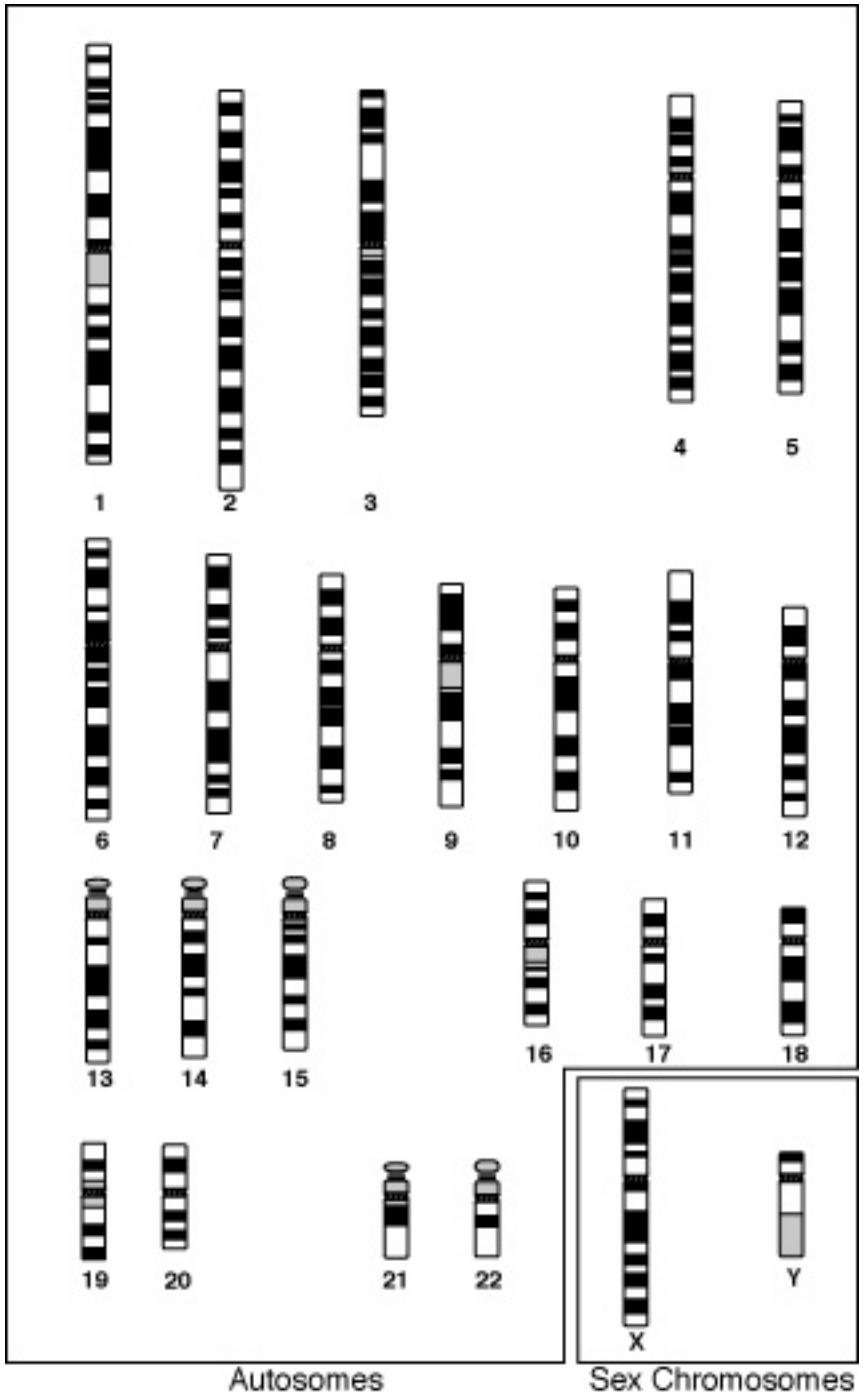


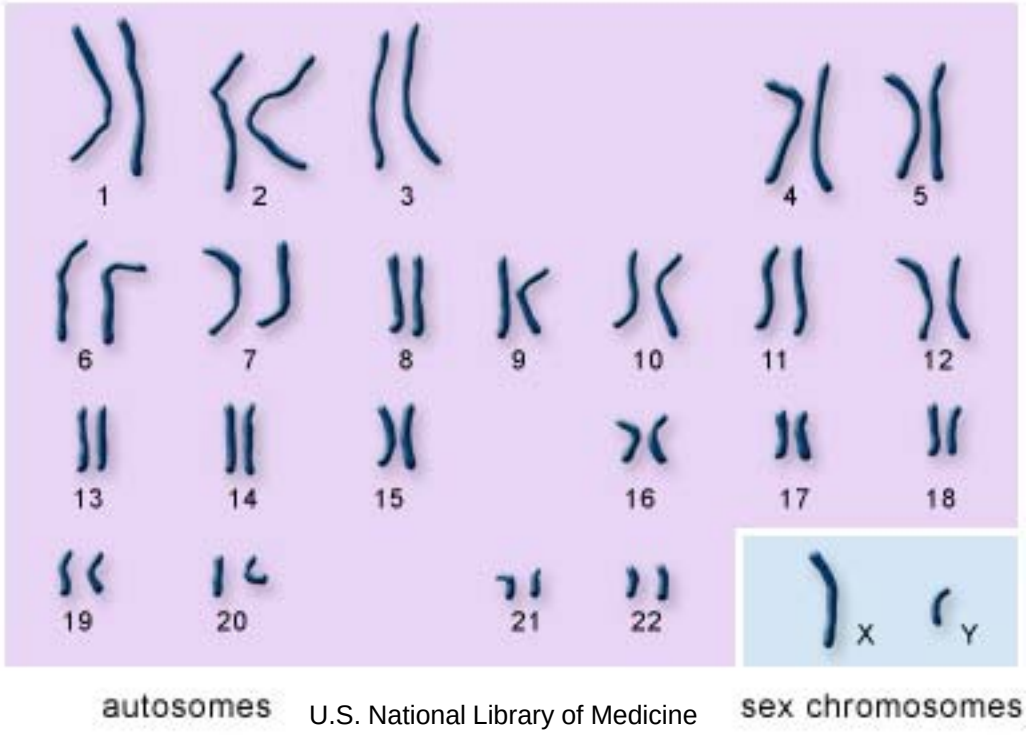
Nuclear DNA and Chromosomes

- Most DNA in eukaryotic cells is in the nucleus
- Nuclear DNA packaged in chromosomes
  - Humans have 23 sets of chromosomes (= "homologous" chromosomes)
    - 22 pairs of autosomal (= non-sex) chromosomes (= autosomes)
      - Numbered 1 to 22 in order of decreasing length
    - 1 pair of sex chromosomes
      - Males: 1 X chromosome, 1 Y chromosome
      - Females: 2 X chromosomes
    - Present in all cells
- Diploid = presence of both copies of each homologous chromosome in the nucleus (= 46 chromosomes total in human cells)
  - From Greek "dis" = twice
- Haploid = presence of only one copy of each homologous chromosome in the nucleus (= 23 chromosomes total in human cells)
  - From Greek "haplos" = once
- Examples of human chromosomes on the next slides

The 22 Autosomal Chromosomes and 2 Sex Chromosomes in a Human Cell

There are 2 copies of each autosome in a diploid cell. A male has one X chromosome and one Y chromosome; a female has two X chromosomes.





U.S. National Library of Medicine

http://www.genome.gov/10002096
http://ghr.nlm.nih.gov/handbook/illustrations/chromosomes

The Largest and Smallest Human Autosomal Chromosomes

1

246 million base pairs

Cataracts
Malignant transformation suppression
Ehlers-Danlos syndrome, type VI
Glaucoma, primary infantile
Hirschsprung disease, cardiac defects
Schwartz-Jampel syndrome
Hypophosphatasia, infantile, childhood
Breast cancer, ductal
Cutaneous malignant melanoma/dysplastic nevus
p53-related protein
Serotonin receptors
Schnyder crystalline corneal dystrophy
Kostmann neutropenia
Oncogene MYC, lung carcinoma-derived
Deafness, autosomal dominant
Porphyria
Epiphyseal dysplasia, multiple, type 2
Intervertebral disc disease
Lymphoma, non-Hodgkin
Breast cancer, invasive intraductal
Colon adenocarcinoma
Maple syrup urine disease, type II
Atrioventricular canal defect
Fluorouracil toxicity, sensitivity to
Zellweger syndrome
Stickler syndrome, type III
Marshall syndrome
Stargardt disease
Retinitis pigmentosa
Cone-rod dystrophy
Macular dystrophy, age-related
Fundus flavimaculatus
Hypothyroidism, nongoitrous
Exostoses, multiple
Pheochromocytoma
Psoriasis susceptibility
Limb-girdle muscular dystrophy, autosomal dominant
Pycnodysostosis
Vohwinkel syndrome with ichthyosis
Erythrokeratoderma, progressive symmetric
Anemia, hemolytic
Elliptocytosis
Pyropoikilocytosis
Spherocytosis, recessive
Schizophrenia
Lupus nephritis, susceptibility to
Migraine, familial hemiplegic
Emery-Dreifuss muscular dystrophy
Cardiomyopathy, dilated
Lipodystrophy, familial partial
Dejerine-Sottas disease, myelin P-related
Hypomyelination, congenital
Nemaline myopathy, autosomal dominant
Lupus erythematosus, systemic, susceptibility
Neutropenia, alloimmune neonatal
Viral infections, recurrent
Antithrombin III deficiency
Atherosclerosis, susceptibility to
Glaucoma
Tumor potentiating region
Nephrotic syndrome
Sjogren syndrome
Coagulation factor deficiency
Alzheimer disease
Cardiomyopathy
Factor H deficiency
Membroproliferative glomerulonephritis
Hemolytic-uremic syndrome
Nephropathy, chronic hypocomplementemic
Epidermolysis bullosa
Popliteala pterygium syndrome
Ectodermal dysplasia/skin fragility syndrome
Usher syndrome, type 2A
Kenny-Caffey syndrome
Diphenylhydantoin toxicity

Homocystinuria
Neuroblastoma (neuroblastoma suppressor)
Rhabdomyosarcoma, alveolar
Neuroblastoma, aberrant in some
Exostoses, multiple-like
Opioid receptor
Hyperprolinemia, type II
Bartter syndrome, type 3
Prostate cancer
Brain cancer
Charcot-Marie-Tooth neuropathy
Muscular dystrophy, congenital
Erythrokeratodermia variabilis
Deafness, autosomal dominant and recessive
Glucose transport defect, blood-brain barrier
Hypercholesterolemia, familial
Neuropathy, paraneoplastic sensory
Muscle-eye-brain disease
Medulloblastoma
Basal cell carcinoma
Corneal dystrophy, gelatinous drop-like
Leber congenital amaurosis
Retinal dystrophy
B-cell leukemia/lymphoma
Lymphoma, MALT and follicular
Mesothelioma
Germ cell tumor
Sezary syndrome
Colon cancer
Neuroblastoma
Glycogen storage disease
Osteopetrosis, autosomal dominant, type II
Waardenburg syndrome, type 2B
Vesicoureteral reflux
Choreoathetosis/spasticity, episodic (paroxysmal)
Hemochromatosis, type 2
Leukemia, acute
Gaucher disease
Medullary cystic kidney disease, autosomal dominant
Renal cell carcinoma, papillary
Insensitivity to pain, congenital, with anhidrosis
Medullary thyroid carcinoma
Hyperlipidemia, familial combined
Hyperparathyroidism
Lymphoma, progression of
Porphyria variegata
Hemorrhagic diathesis
Thromboembolism susceptibility
Systemic lupus erythematosus, susceptibility
Fish-odor syndrome
Prostate cancer, hereditary
Chronic granulomatous disease
Macular degeneration, age-related
Epidermolysis bullosa
Chitotriosidase deficiency
Pseudohypoaldosteronism, type II
Hypokalemic periodic paralysis
Malignant hyperthermia susceptibility
Glomerulopathy with fibronectin deposits
Metastasis suppressor
Measles, susceptibility to
van der Woude syndrome (lip pit syndrome)
Rippling muscle disease
Hypoparathyroidism-retardation-dysmorphism syndrome
Ventricular tachycardia, stress-induced polymorphic
Fumarase deficiency
Chediak-Higashi syndrome
Muckle-Wells syndrome
Zellweger syndrome
Adrenoleukodystrophy, neonatal
Endometrial bleeding-associated factor
Left-right axis malformation
Prostate cancer, hereditary
Chondrodysplasia punctata, rhizomelic, type 2

22

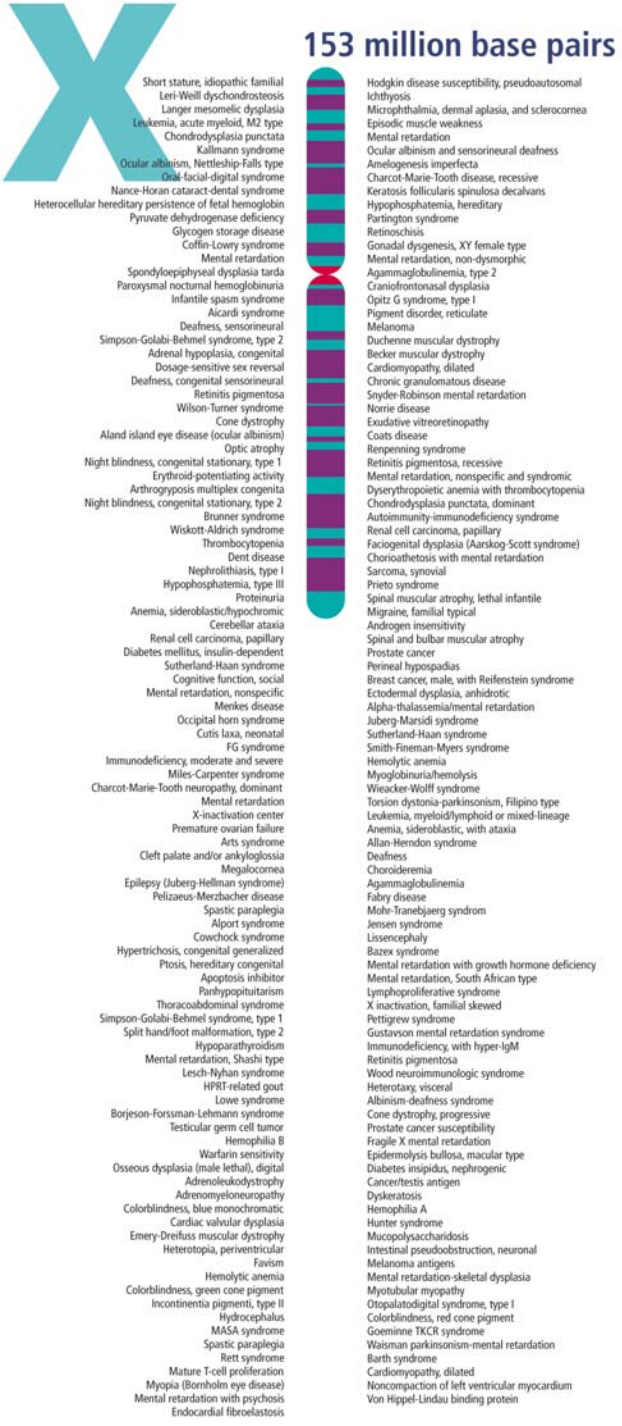
49 million base pairs

Cat eye syndrome
Thrombophilia
Rhabdoid predisposition syndrome, familial
Schizophrenia susceptibility locus
Bernard-Soulier syndrome, type B
Giant platelet disorder, isolated
Hyperprolinemia, type I
Cataract, cerulean, type 2
Leukemia, chronic myeloid
Ewing sarcoma
Neuroepithelioma
Li-Fraumeni syndrome
Fechtner syndrome
Amyotrophic lateral sclerosis
Pulmonary alveolar proteinosis
Meningioma, SIS-related
Dermatofibrosarcoma protuberans
Giant-cell fibroblastoma
Spinocerebellar ataxia
Waardenburg-Shah syndrome
Yemenite deaf-blind hypopigmentation syndrome
Debrisoquine sensitivity
Polycystic kidney disease
Leukodystrophy, metachromatic
Myoneurogastrointestinal encephalomyopathy
Leukoencephalopathy

DiGeorge syndrome
Velocardiofacial syndrome
Schindler disease
Kanzaki disease
NAGA deficiency, mild
Epilepsy, partial
Glutathioninuria
Opitz G syndrome, type II
Ubiquitin fusion degradation
Transcobalamin deficiency
Heme oxygenase deficiency
Manic Fringe
Leukemia inhibitory factor
Sorsby fundus dystrophy
Neurofibromatosis, type 2
Meningioma, NF2-related, sporadic
Schwannoma, sporadic
Neurolemmomatosis
Malignant mesothelioma, sporadic
Deafness, autosomal dominant
Colorectal cancer
Cardioencephalomyopathy, fatal infantile
Adenylosuccinase deficiency
Autism, succinylpurinemic
Glucose/galactose malabsorption
Benzodiazepine receptor, peripheral type
Methemoglobinemia, types I and II

http://genomics.energy.gov/gallery/chromosomes/detail.np/detail-01.html

The Two Human Sex Chromosomes



50 million base pairs

Short stature homeo box, Y-linked
Short stature
Leri-weill dyschondrosteosis
Langer mesomelic dysplasia
Interleukin-3 receptor, Y chromosomal
Sex-determining region Y (testis-determining)
Gonadal dysgenesis, XY type
Protocadherin 11, Y-linked
Azoospermia factors
Male infertility due to spermatogenic failure
Growth control, Y-chromosome influenced
Chromodomain proteins
Retinitis pigmentosa, Y-linked

http://genomics.energy.gov/gallery/chromosomes/detail.np/detail-01.html

The Genome of an Organism

- = the total hereditary information encoded in nucleic acid
  - In most organisms, the genetic material is DNA
  - In some viruses, it is RNA
  - Genome structure of many (100's) organisms has been determined
    - Major technique used: DNA sequencing
    - Will not cover DNA sequencing in this course. It has become routine (but not easy or cheap)
    - Good URL on DNA sequencing if interested: http://www.ornl.gov/sci/techresources/Human_Genome/faq/seqfacts.shtml#whatis > Sanger Sequencing > Play
      - Fred Sanger, 1980 Nobel Prize for developing this method (his 2nd Nobel Prize)

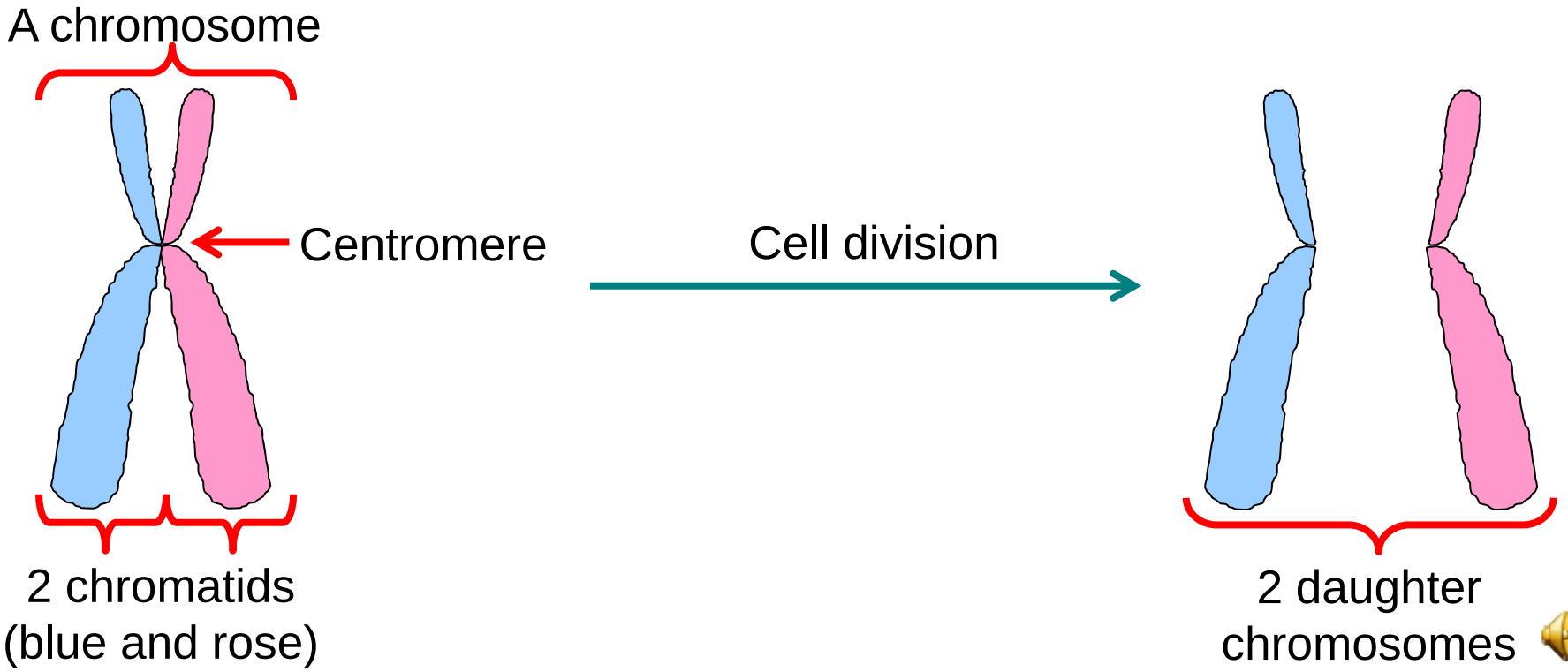
The Human Genome and The Human Genome Project

- Human DNA is ~6 feet long (in every cell!!!!!)
- Encodes ~25,000 genes (estimated)
- If each letter (b.p.) of the human genome were printed in book form, the book would have to:
  - Be 1,000,000,000 words long in 5,000 volumes of 300 pages each

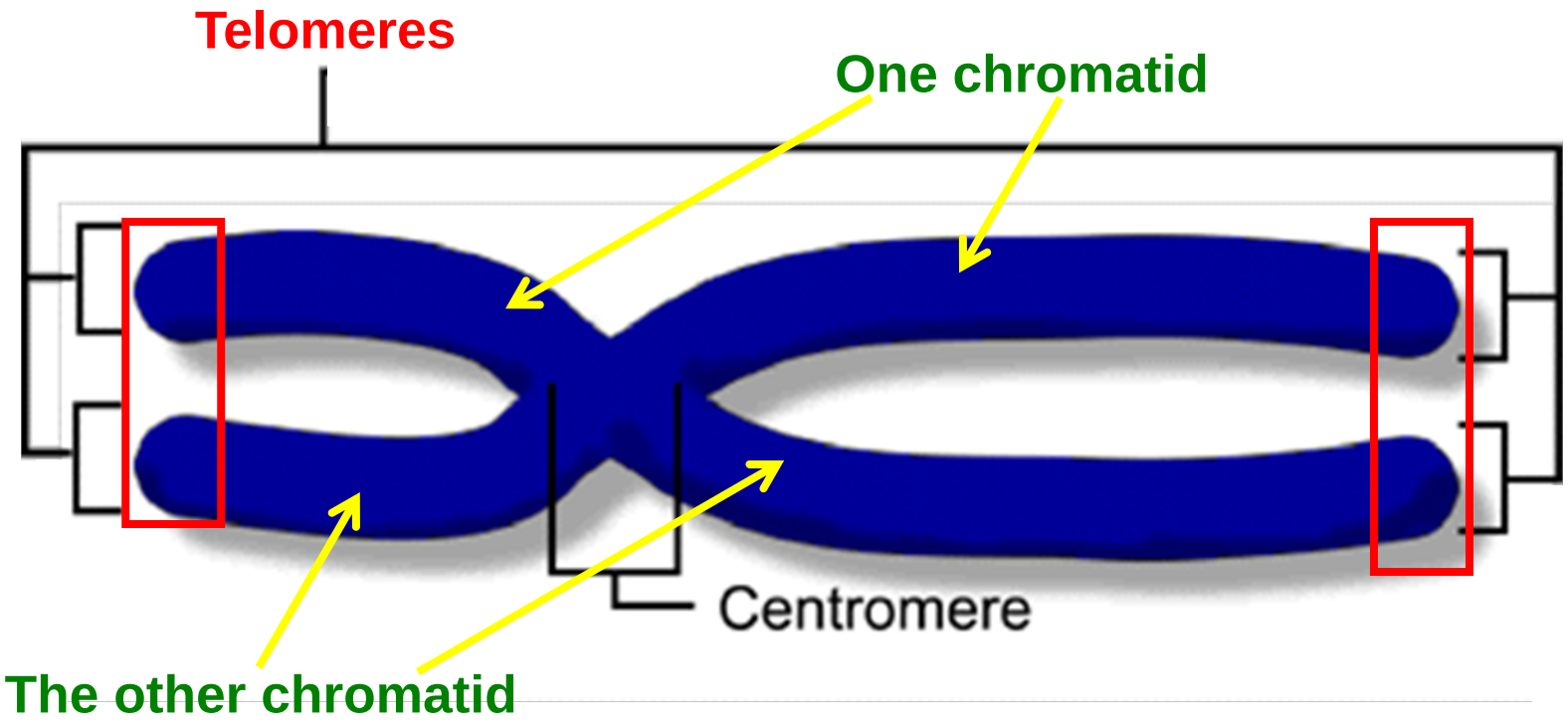
    and
  - Fit in the nucleus of every cell

Cell Division: Mitosis and Meiosis

- Sex cells = egg and sperm = germ cells
- Non-sex cells = somatic cells
- Chromatid = one of the two identical copies of DNA making up a replicated chromosome
  - Both chromatids are joined at their centromeres for the process of cell division (mitosis or meiosis)
  - When the chromatids separate, are termed "daughter chromosomes"



A Chromosome Containing 4 Strands of DNA (= 2 dsDNA)



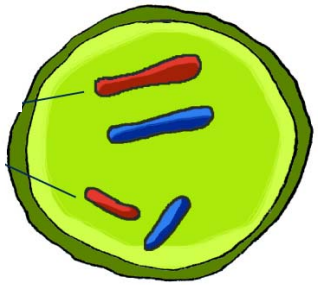
http://www.ncbi.nlm.nih.gov/About/primer/genetics_genome.html

Cell Division: Mitosis and Meiosis

- Sex cells = egg and sperm = germ cells
- Non-sex cells = somatic cells
- Chromatid = one of the two identical copies of DNA making up a replicated chromosome
  - Both chromatids are joined at their centromeres for the process of cell division (mitosis or meiosis)
  - When the chromatids separate, are termed "daughter chromosomes"
- Mitosis:
  - = somatic cell division: one cell division, one DNA replication
  - From Greek "mitos" = thread (referring to the appearance of a chromosome in the light microscope)

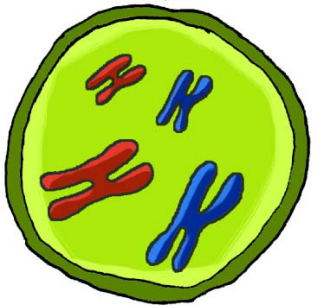
Somatic (non-sex) Cell Division (mitosis) Showing 2 Sets of Chromosomes in the Cell Nucleus

Red (with 2 lines pointing to them) = from mother
Blue = from father



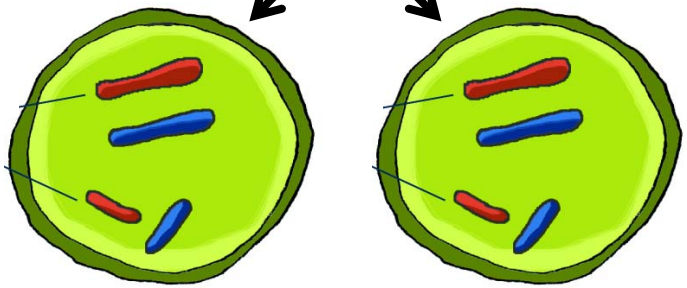
Diploid cell with 2 sets of homologous chromosomes (long and short)

DNA replication



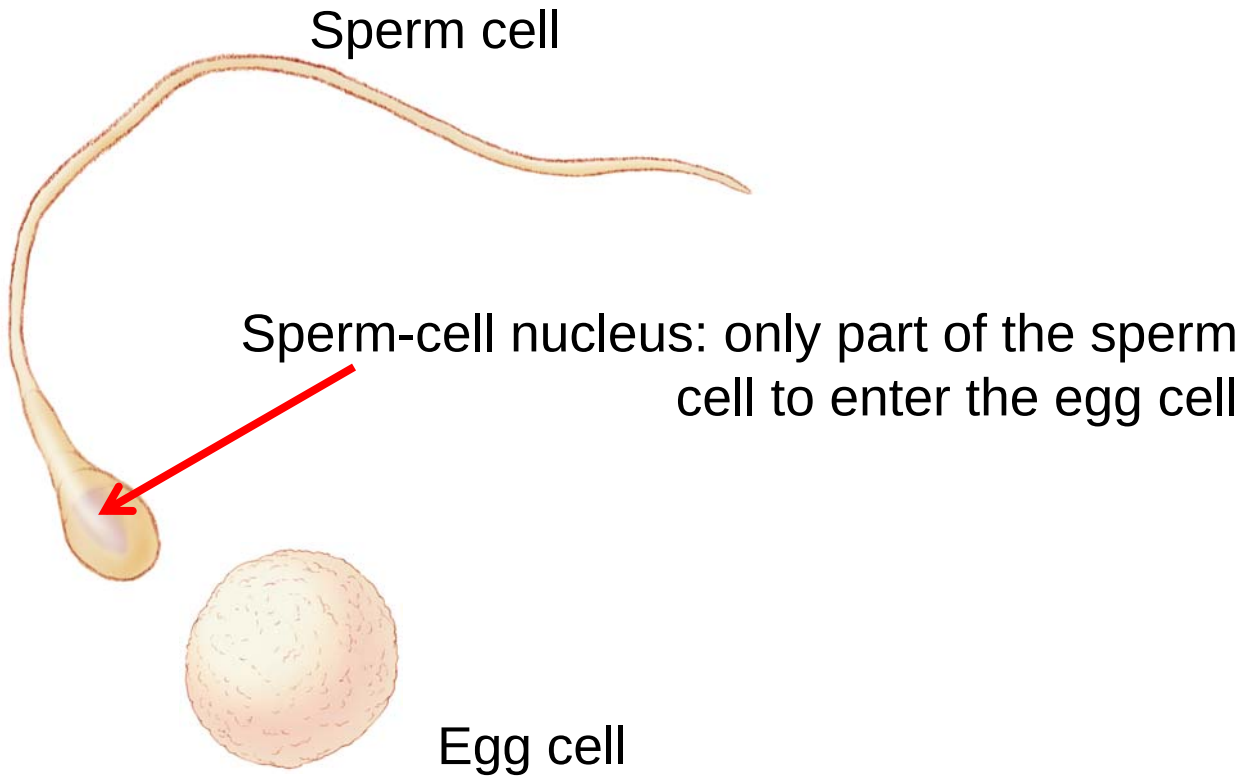
8 chromatids: 4 for each of the 2 sets of homologous chromosomes

Cell division



2 diploid cells with 2 sets of homologous chromosomes (long and short)

What About Sex?

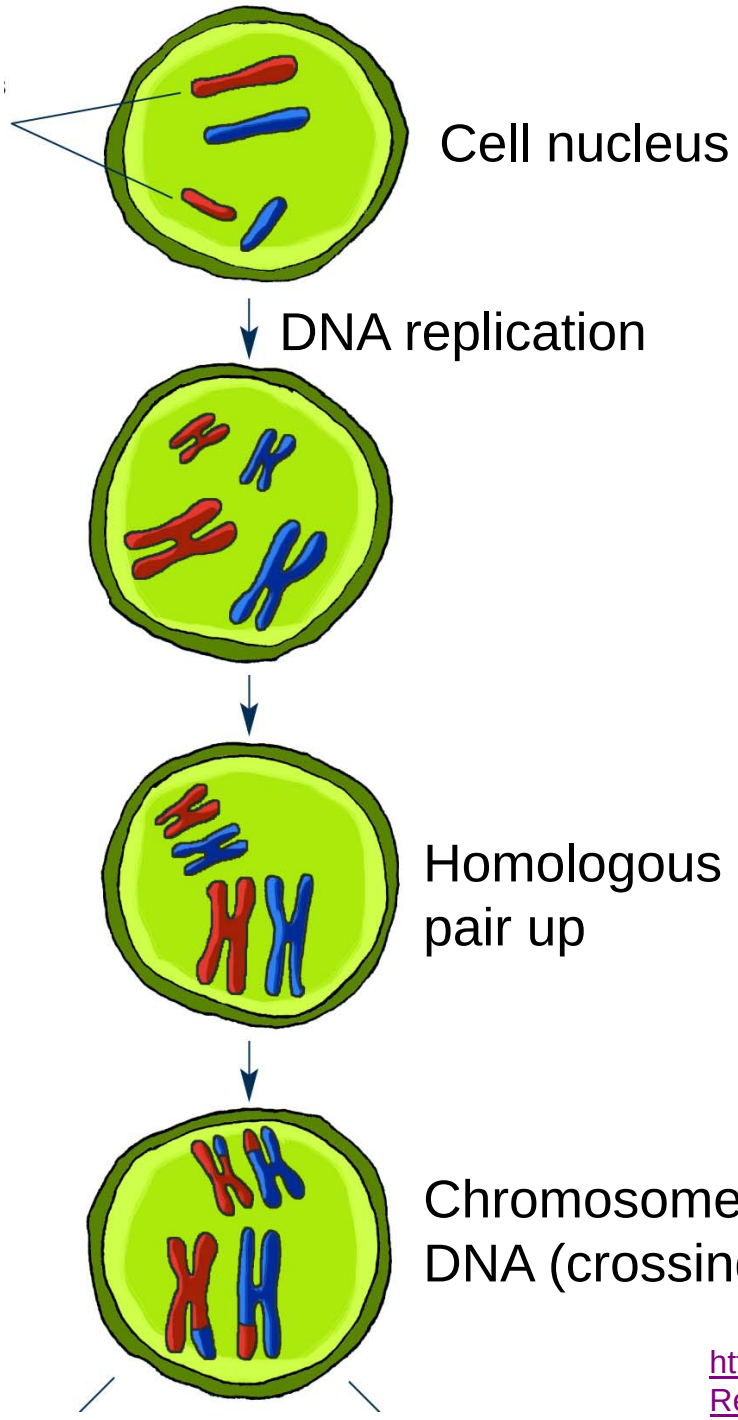


Actual question asked of a reference librarian at SE Kentucky Community and Technical College:
"I need a book about the history of sex. You know, when people first found out about it."

Cell Division: Mitosis and Meiosis

- Mitosis:
  - = somatic cell division: one cell division, one DNA replication
  - From Greek "mitos" = thread (referring to the appearance of a chromosome in the light microscope)
- Meiosis:
  - = sex cell division: two cell divisions, one DNA replication
  - From Greek "meion" = less (referring to a diploid cell resulting in haploid cells, i.e., cells with fewer chromosomes)
  - We are almost neglecting crossing-over during meiosis, even though it is extremely important in redistributing genes

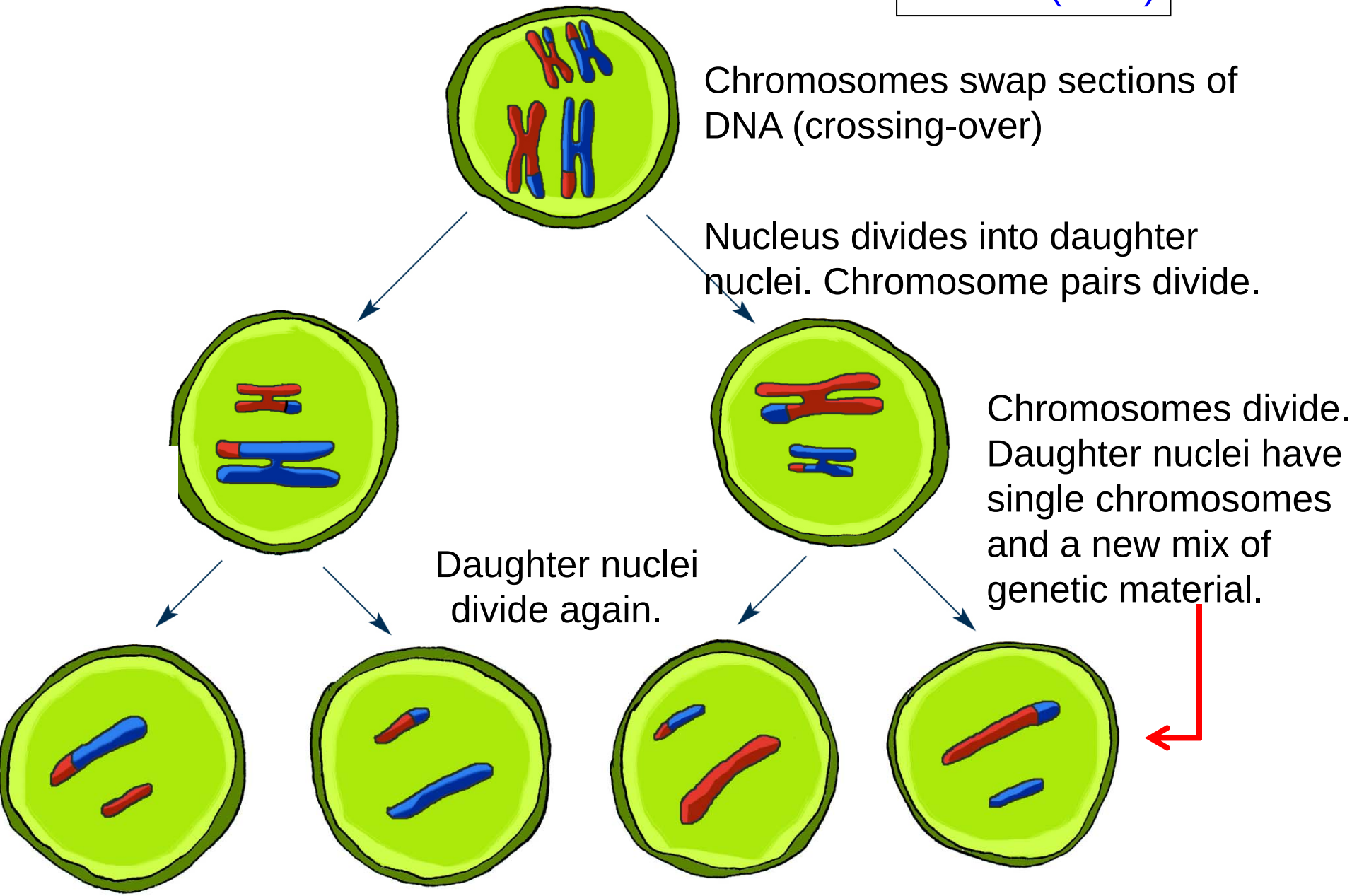
Meiosis



Red (with 2 lines pointing to them) = from mother
Blue = from father
Shown are 2 homologous chromosomes (large and small)

http://images.nigms.nih.gov/imageRepository/2546/Meiosis_with_labels.jpg

Meiosis (cont.)



http://images.nigms.nih.gov/imageRepository/2546/Meiosis_with_labels.jpg

Mitosis vs. Meiosis

	Mitosis	Meiosis
# of DNA replications	1	1
# of cell divisions	1	2
Start with:	1 diploid cell	1 diploid cell
End with:	2 diploid somatic cells	4 haploid gametes (= germ cells)

Reminder:

- Diploid = presence of both homologous chromosomes in the nucleus (= 46 chromosomes total in humans)
- Haploid = presence of only one homologous chromosome in the nucleus (= 23 chromosomes total in humans)

Excellent visual presentation:
http://www.pbs.org/wgbh/nova/miracle/divide.html

There's a lot to be said for patience. In time, even an egg will walk.

Hardy-Weinberg Principle

- In a large randomly breeding population, allelic frequencies will remain the same from generation to generation assuming no:
  - mutation (the genes stay the same)
  - gene migration (no one immigrates or emigrates)
  - selection (no environmental pressures)
  - genetic drift (no random chance selection of a gene)
- No need to memorize the above. Main point: Our discussion is limited to large randomly mating populations with no flow into or out of the population and nothing "happens by chance"
- Punnett squares = convenient graphic method to look at inheritance patterns
  - Very good URL on Punnett squares: http://anthro.palomar.edu/mendel/mendel_2.htm

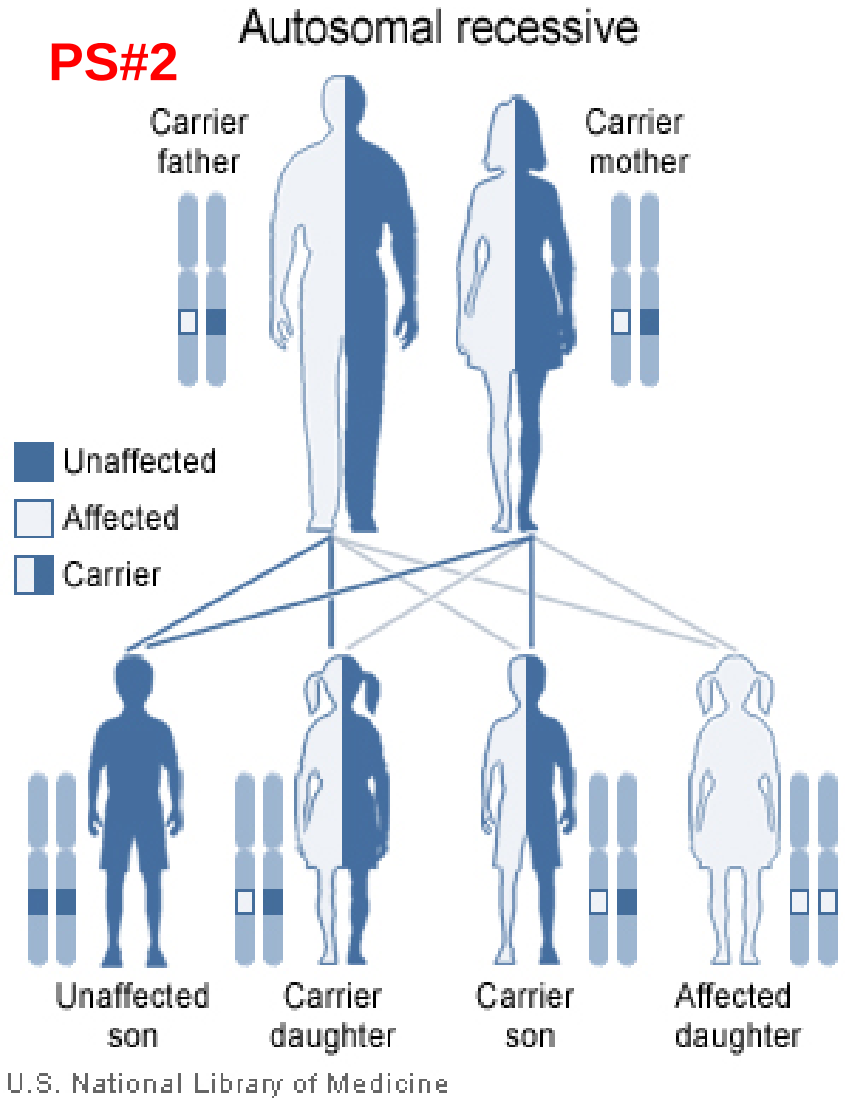
Inheritance Patterns

- Genotype = genetic constitution of an organism = what genes are expressed
- Phenotype = obervable properties of an organism resulting from interaction of the genotype and the environment
- Autosomal dominant gene = a gene on one of the non-sex chromosomes that is always expressed, even if only one copy is present
  - Represented with a capital letter; e.g., A
- Autosomal recessive gene = a gene on one of the non-sex chromosomes that is expressed only if there are 2 identical copies
  - Represented with a small letter; e.g., a
- Example -- at a single allele with a copy of the allele on each of the two autosomal chromosomes:
  - Dominant = **purple**, recessive = **orange**

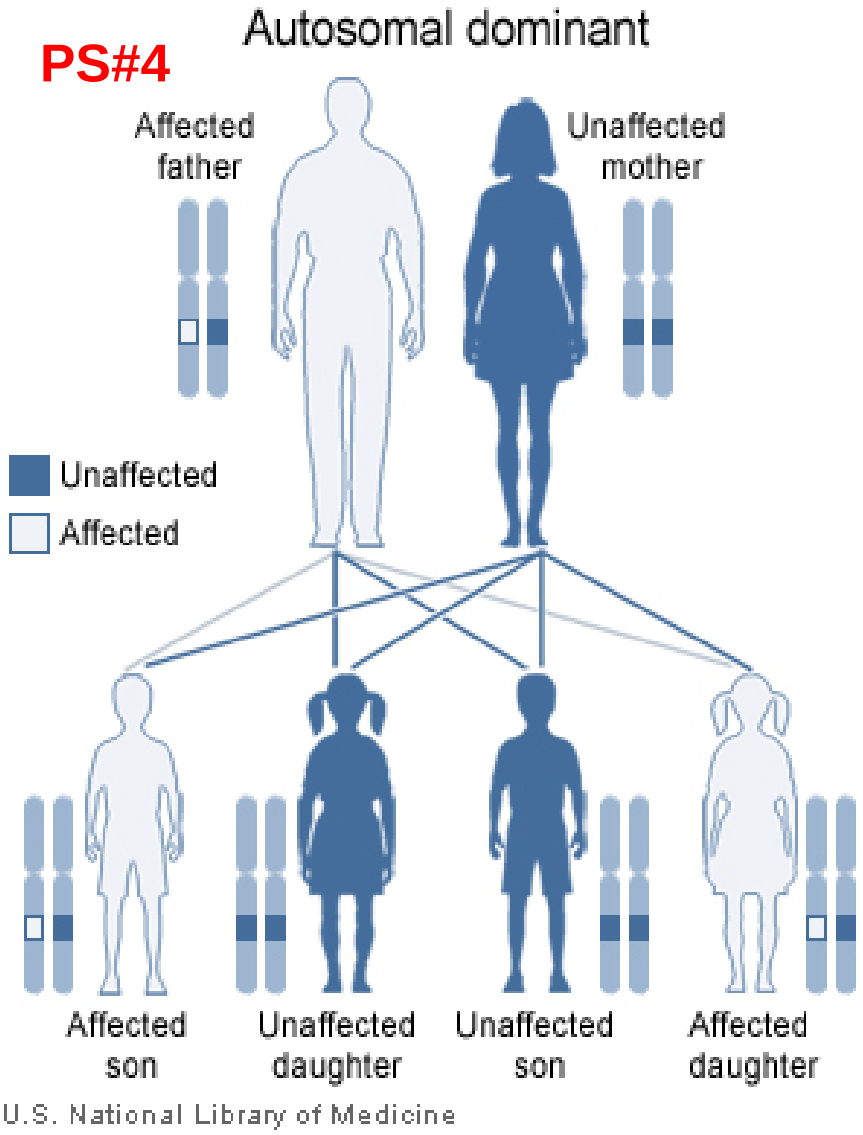
Genotype	Phenotype
AA	**Purple**
Aa	**Purple**
aa	**Orange**

Autosomal Inheritance Patterns

PS#2



PS#4



Think: Affected = "disease-causing"; see Punnett squares in following slide

http://ghr.nlm.nih.gov/handbook/illustrations/

Punnett Squares (autosomal inheritance)

PS#1

		Male	
		A	A
Fe-male	A	AA	AA
	A	AA	AA

Only phenotype is A

AA = 1

PS#2

		Male	
		A	a
Fe-male	A	AA	Aa
	a	Aa	aa

Since A is dominant, the phenotype ratio is A:a = 3:1

AA:Aa:aa = 1:2:1

PS#3

		Male	
		A	a
Fe-male	A	AA	Aa
	A	AA	Aa

Only phenotype is A

AA:Aa = 1:1

PS#4

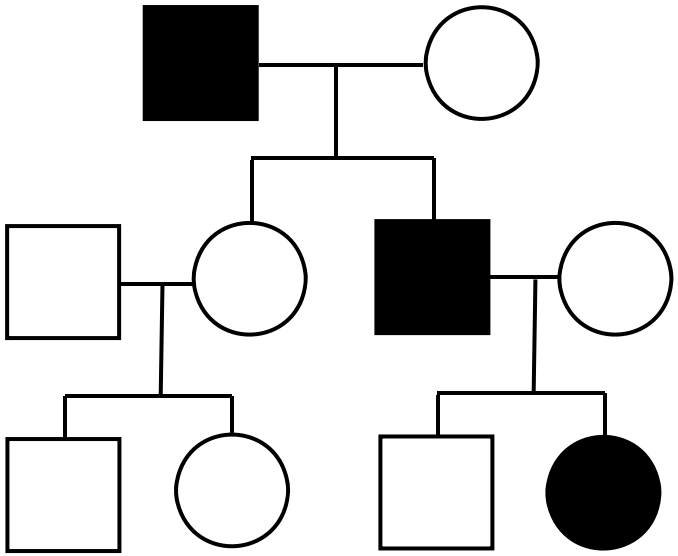
		Male	
		A	a
Fe-male	a	Aa	aa
	a	Aa	aa

Since A is dominant, the phenotype ratio is A:a = 1:1

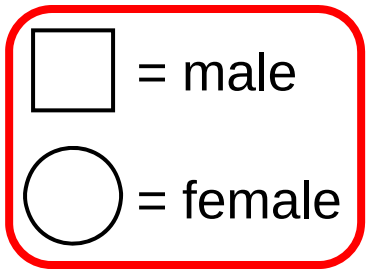
Aa:aa = 2:2

Mendelian Disorders (I)

- Autosomal dominant inheritance
  - A disorder appears in several generations of a family.
  - Affected parents have a 50% risk of an affected child with each pregnancy.
  - Variability and reduced penetrance can complicate predictions of prognosis.



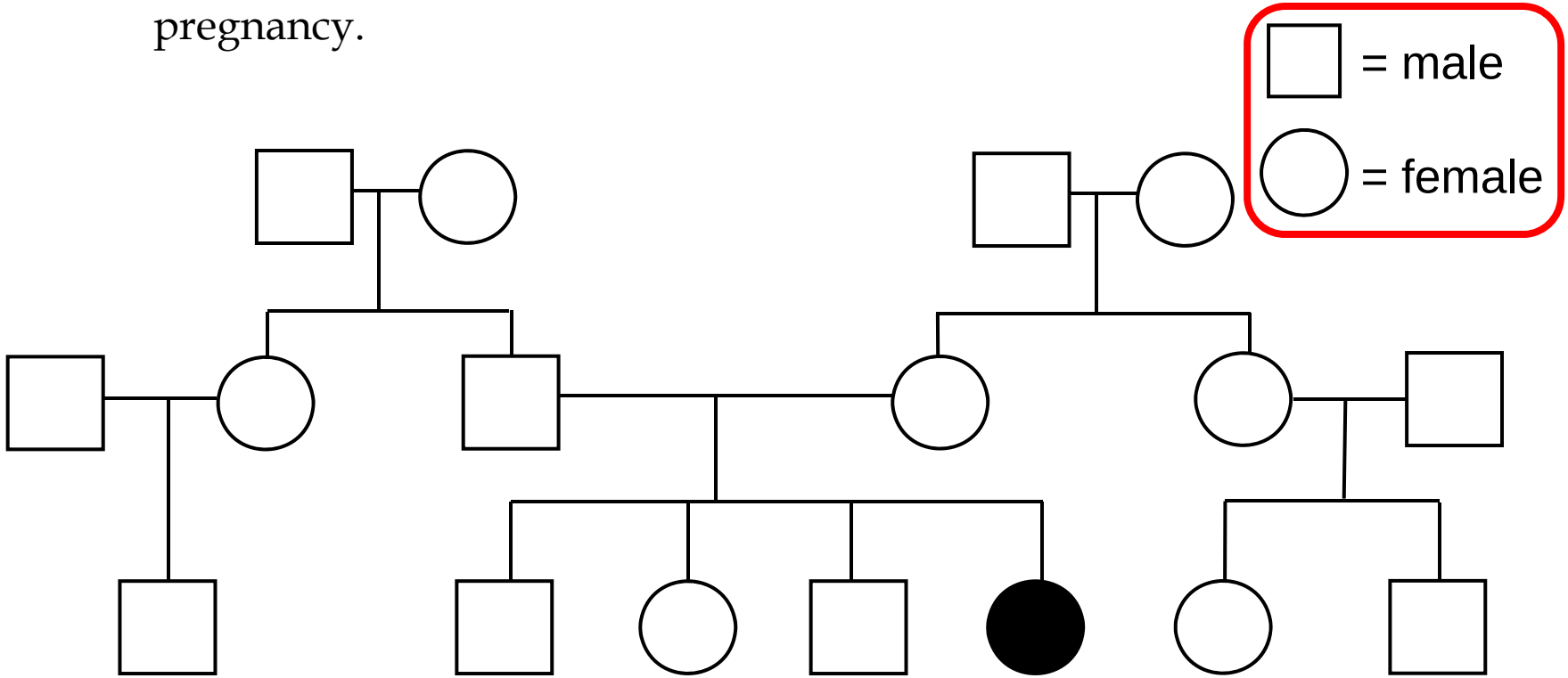
PS#4



Mendelian Disorders (II)

- Autosomal recessive inheritance
  - Disorders often appear in only one generation of a family.
  - Carrier couples have a 25% risk of an affected child with each pregnancy.

PS#2



Punnett Squares (X-linked inheritance)

Fe-ale	Male: X	Male: Y
X	XX	XY
X	XX	XY

Ms and Fs normal

XX:XY = 1

Fe-ale	Male: X	Male: Y
X	XX	XY
x	Xx	xY

1/2 Ms affected
1/2 Fs carriers

XX:Xx:XY:xY = 1:1:1:1

Fe-ale	Male: x	Male: Y
X	Xx	XY
X	Xx	XY

Fs carriers
Ms normal

Xx:XY = 1:1

Fe-ale	Male: X	Male: Y
x	Xx	xY
x	Xx	xY

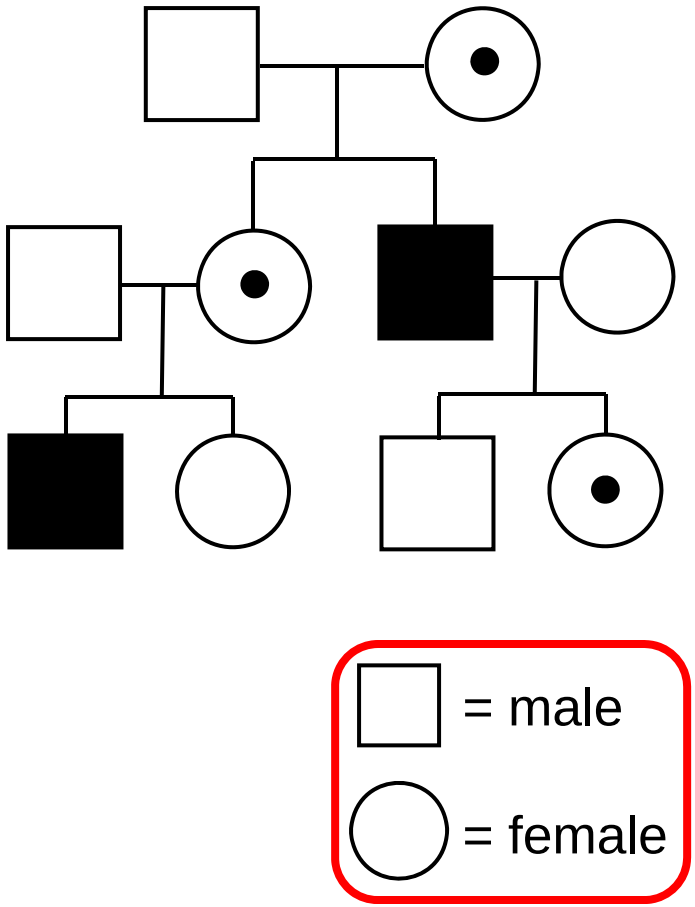
Fs carriers
Ms affected

Xx:xY = 1:1

Mendelian Disorders (III)

Example of:
Male = XY
Female = Xx

- X-linked inheritance
  - X-linked dominant disorders are few in number.
  - Male to male transmission of X-linked disorders is not seen.
  - Carrier females may show mild to moderate symptoms of certain X-linked disorders.



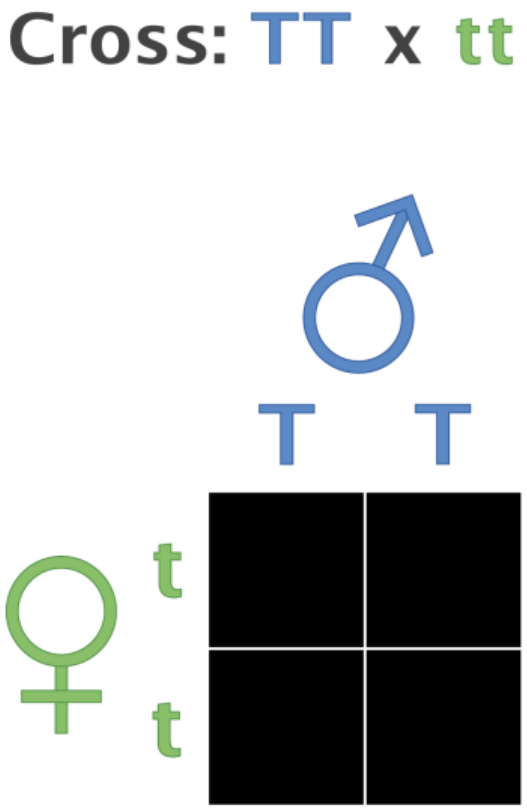
The next 5 slides are included only as an aid; they are not required. You may be asked to determine an inheritance pattern on an exam, but it will be straightforward.

The 5 slides are courtesy of:

at: http://www.bioedonline.org/slides/slide01.cfm?tk=30

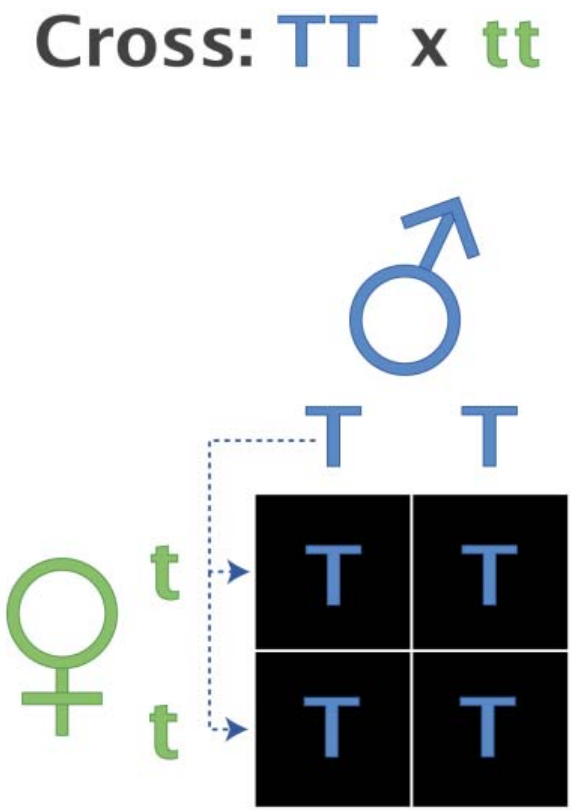
Working out Mendelian Genetics

- A Punnet square is bookkeeping tool.
- The allele is the **specific form of** hereditary particle passed on through male or female gametes.
- Allele capital letter **T** confers tallness. In this case, the tall parental line has all **T**'s.
- Allele lower case letter **t** confers shortness. The short parental line has all **t**'s.
- Cross a tall male with a short female.



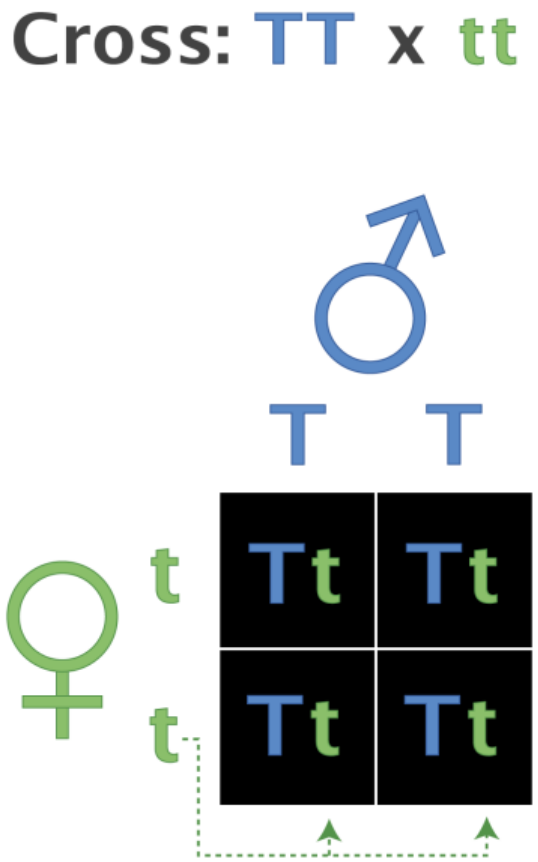
Crossing the Parental Lines: Male Contribution

- First, the male passes on his alleles, one per gamete (reproductive cell).



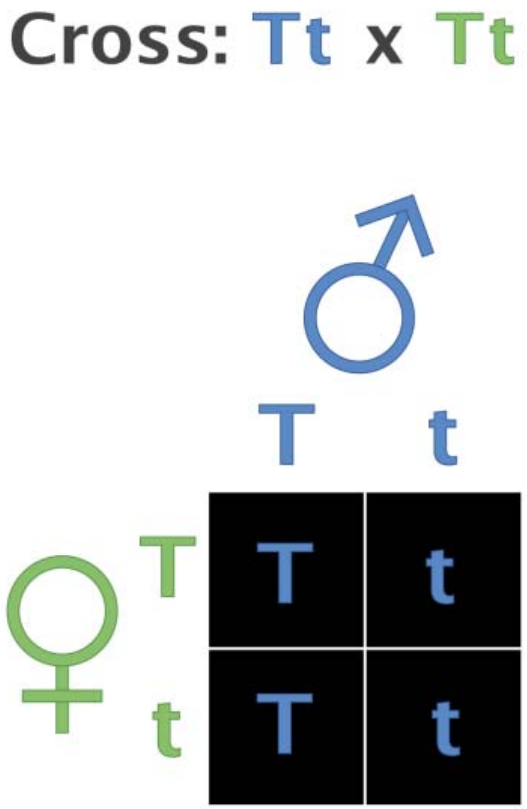
Crossing the Parental Lines: Female Contribution

- Then, the female passes on her alleles, one per egg.
- Crossing these two parents yields all **Tt** offspring.
- Since **T** is dominant to **t**, all of the offspring are tall pea plants.



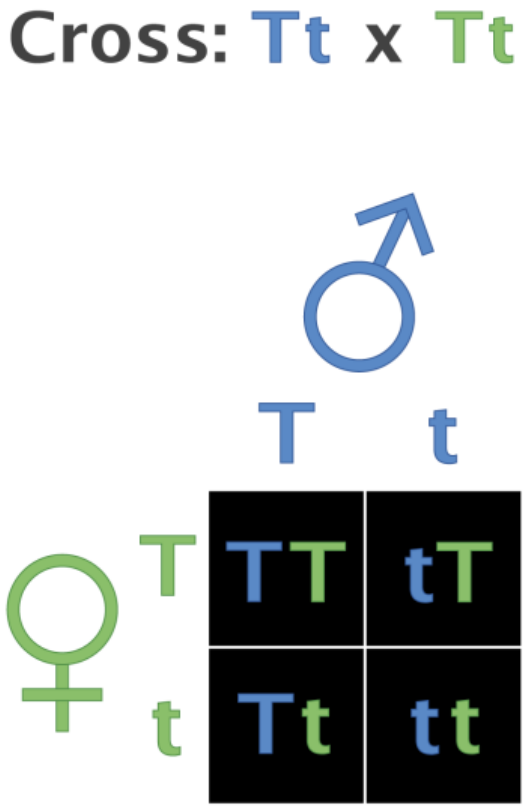
Crossing the F_1 Generation

- Crossing two homozygous individuals, **TT** and **tt**, yields all heterozygous offspring, **Tt**. This generation is referred to as **F_1**.
- Now, cross two individuals from the F_1 generation (Tt x Tt).
- First, the male pea plant passes on its alleles, one per gamete.



Crossing the F_1 Generation

- Now, the female passes on her alleles, one per egg.
- Genotypes of the F_2
  - ¼ of the offspring are **TT**.
  - ½ of the offspring are heterozygotes (one **T** and one **t**).
  - ¼ of the offspring are **tt**.
- Phenotypes of the F_2
  - ¾ are tall (at least one **T**).
  - ¼ are short (homozygous for **t**).



The Central Dogma (How Genetic Information Is Transferred)

DNA ⟶ RNA ⟶ Protein

- DNA = Deoxyribonucleic acid = genetic material of cells
- RNA = Ribonucleic acid = intermediate in information transfer; genetic material of some viruses

Transcription Translation

DNA ⟶ RNA ⟶ Protein

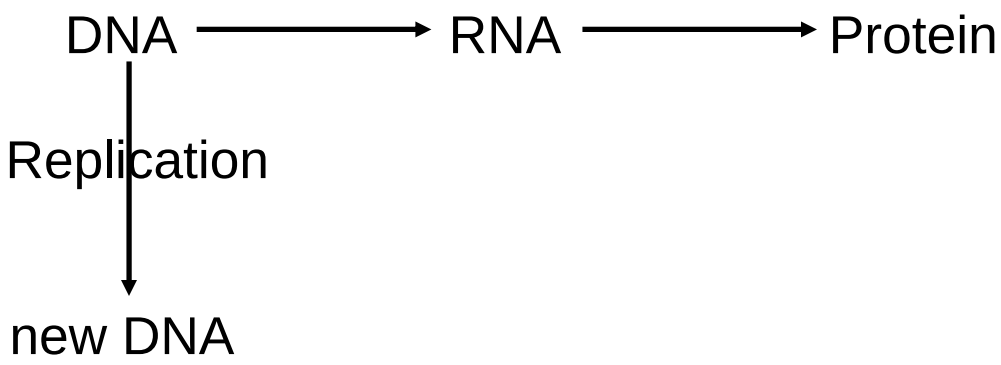
- Transcription = synthesis of RNA (nucleotides to nucleotides)
- Translation = synthesis of protein (nucleotides to amino acids)

Reverse transcription

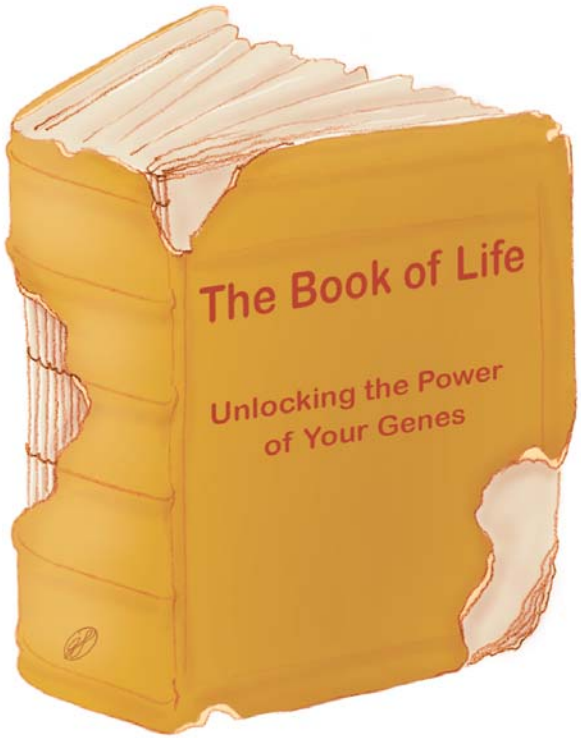
DNA ⟷ RNA ⟶ Protein

- In some RNA viruses must first make DNA copies of the RNA before making protein

The Central Dogma (cont.)



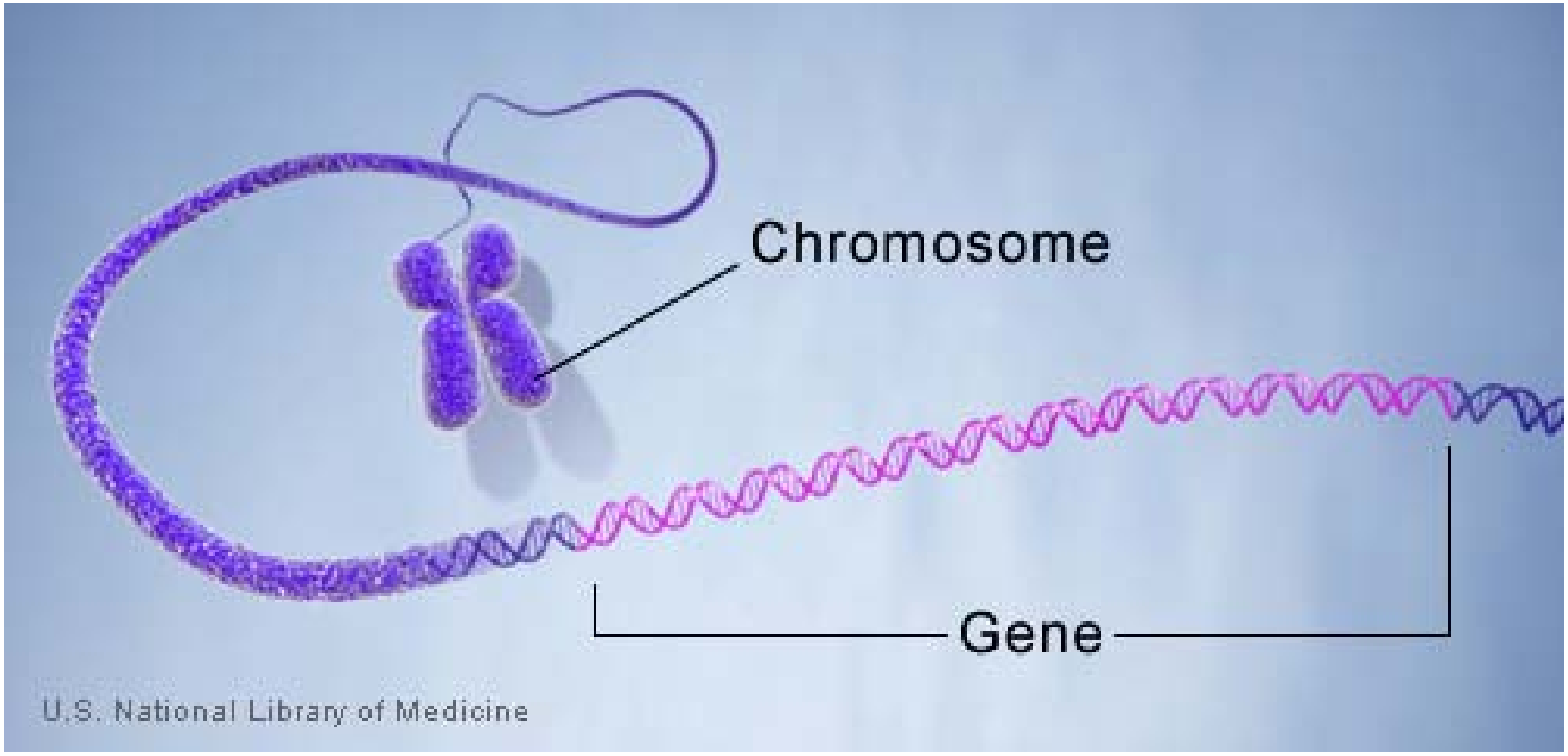
- Replication = synthesis of new (daughter) DNA from old (parental) DNA



In spring, if your fancy turns to the opposite sex, you've been wasting the winter.

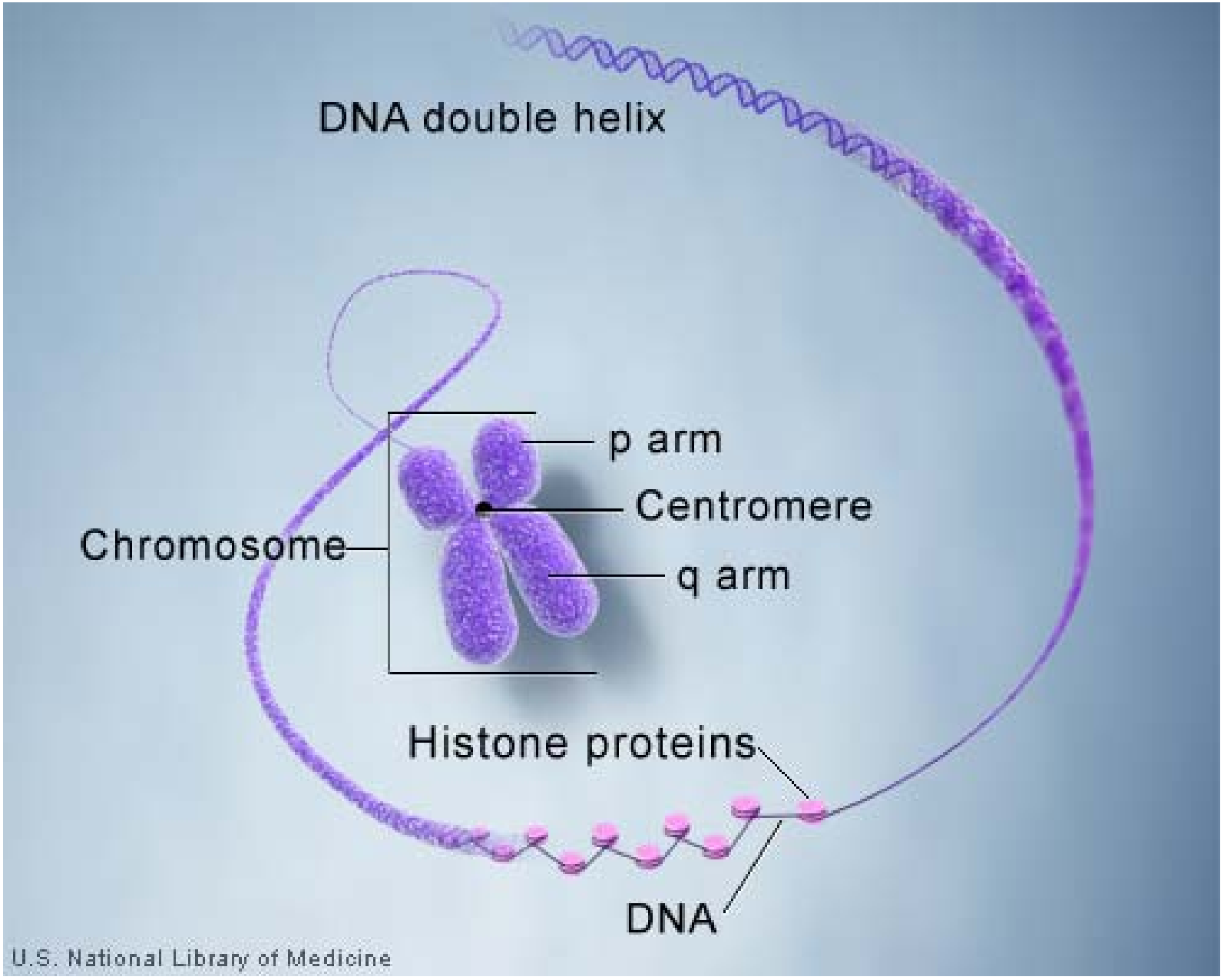
Gene

- A unit of hereditary information = a segment of DNA in a cell that carries the information for the synthesis of a specific protein or RNA.
  - Sometimes regulatory segments of DNA are included within the definition of a gene



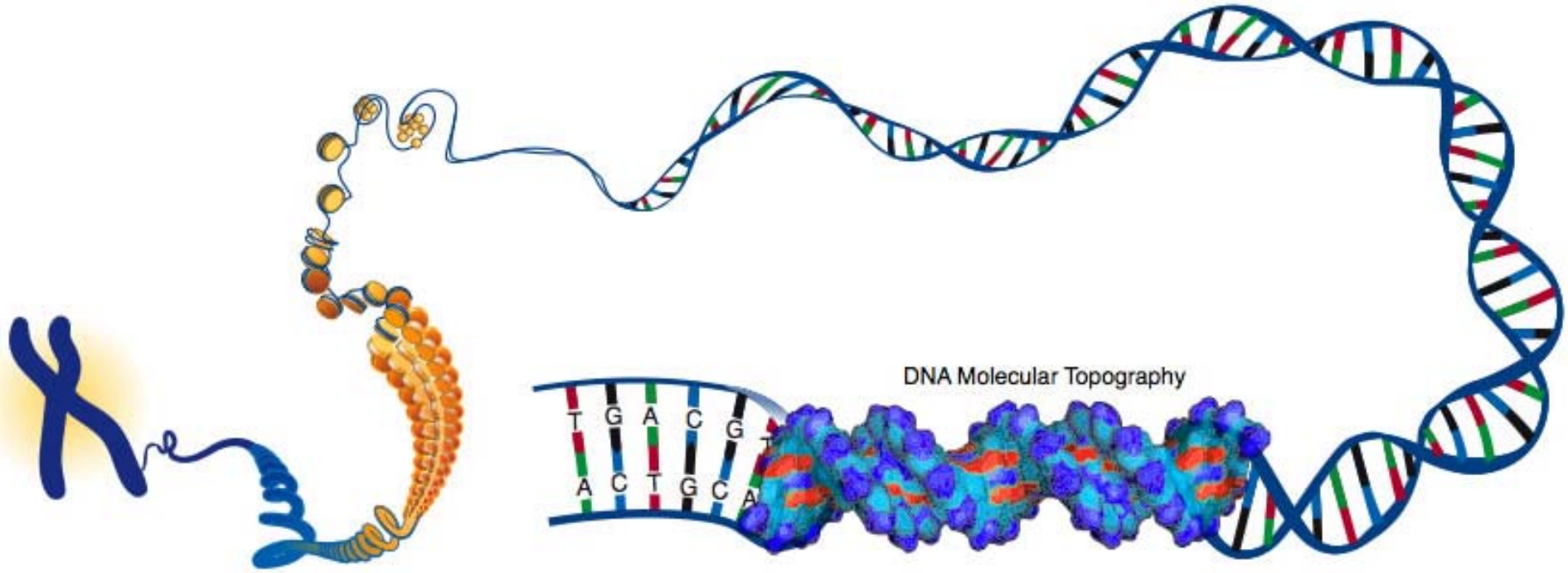
http://ghr.nlm.nih.gov/handbook/illustrations/geneinchromosome

Chromosome Structure



http://ghr.nlm.nih.gov/handbook/illustrations/chromosomestructure

Chromosome Structure



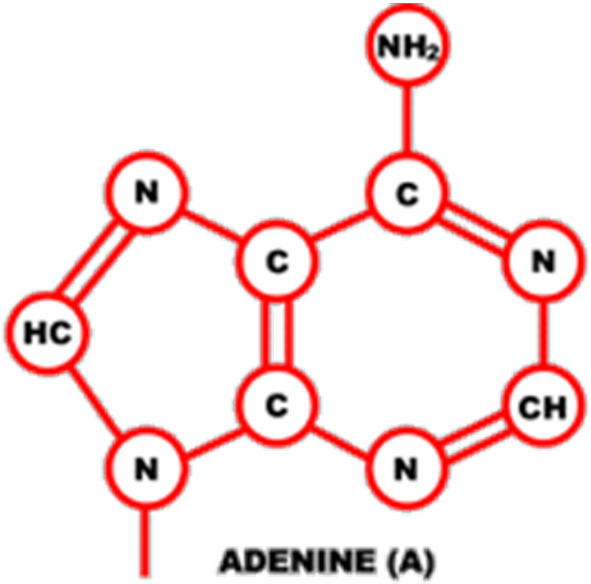
http://www.genome.gov/Images/press_photos/highres/20150-300.jpg

Heredity is something all believe in until their children start acting like fools.

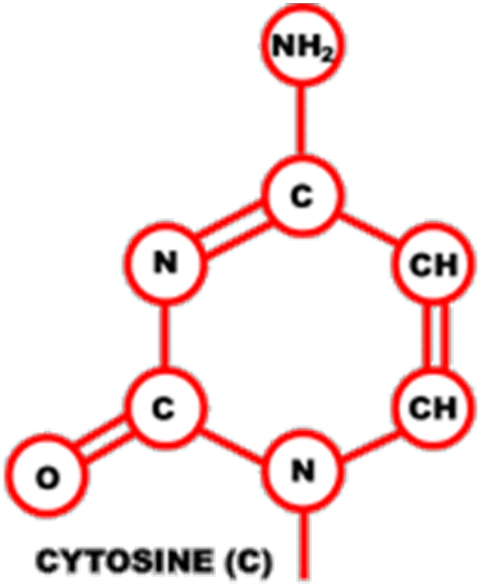
Structure of dsDNA (= Watson-Crick Model)

- Helical structure with 2 strands = double-stranded DNA = dsDNA
- Strands run antiparallel; i.e., one strand runs in the 5' to 3' direction and the other strand runs in the 3' to 5' direction
- Backbone consists of alternating deoxyribose (sugar) groups and phosphate groups
- The N-bases are attached to the deoxyribose groups and point inward to the center of the helix
  - Bases pointed inward allows base pairing
- Base pairing between the two strands:
  - A (adenine) base-pairs with T (thymine) via 2 hydrogen bonds
  - G (guanine) base-pairs with C (cytosine) via 3 hydrogen bonds
- DNA is a polymer of deoxynucleotides (often lazily called simply nucleotides)
  - Deoxynucleotides contain one of the N-bases (A, G, C, or T) attached to the sugar group deoxyribose. A phosphate group is also attached to the deoxyribose, albeit at a different site

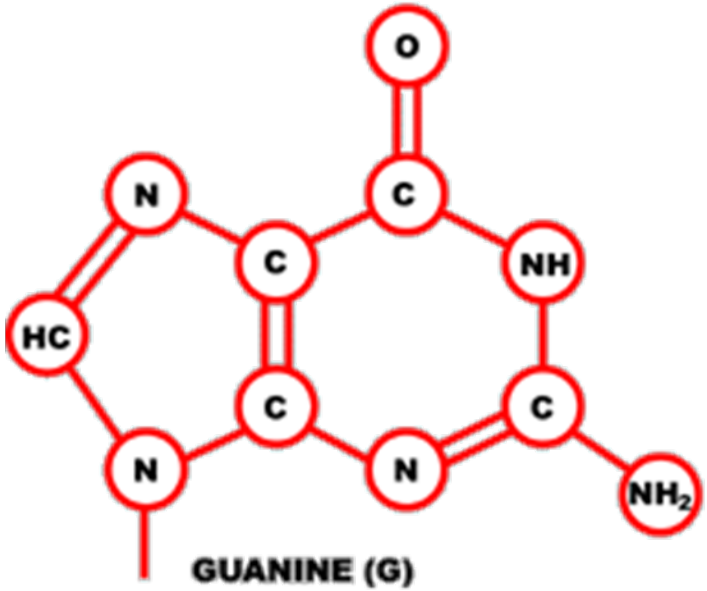
Structure of the 4 N-bases in DNA



ADENINE (A)



CYTOSINE (C)

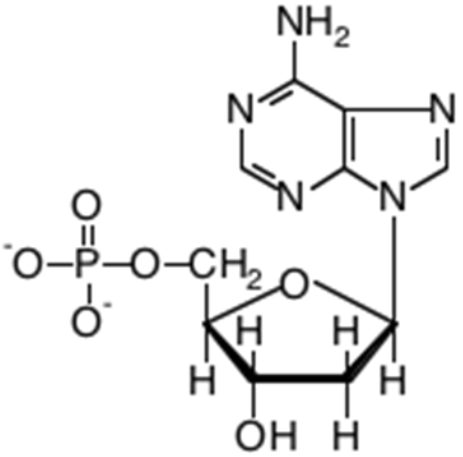


GUANINE (G)

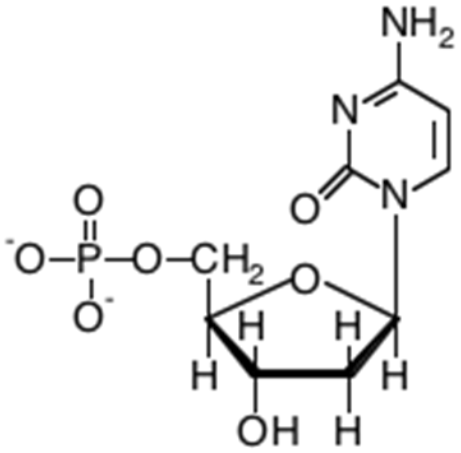
THYMINE (T)

http://ghr.nlm.nih.gov/handbook/basics/cell

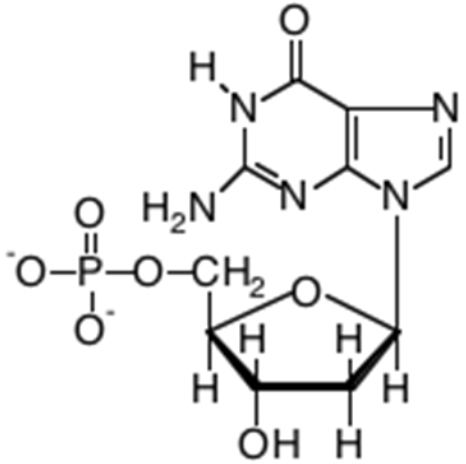
Structure of the Four Deoxynucleotides



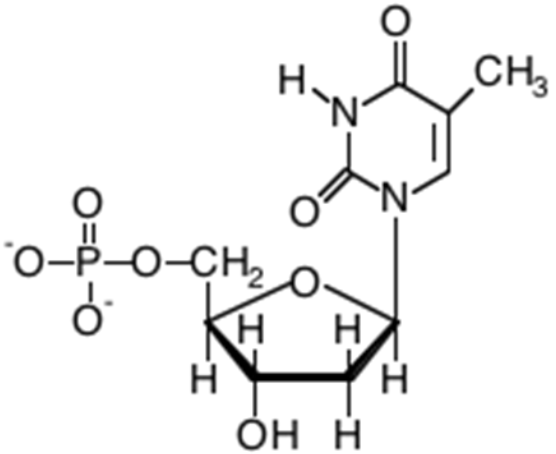
Deoxyadenosine monophosphate (dAMP)



Deoxycytidine monophosphate (dCMP)

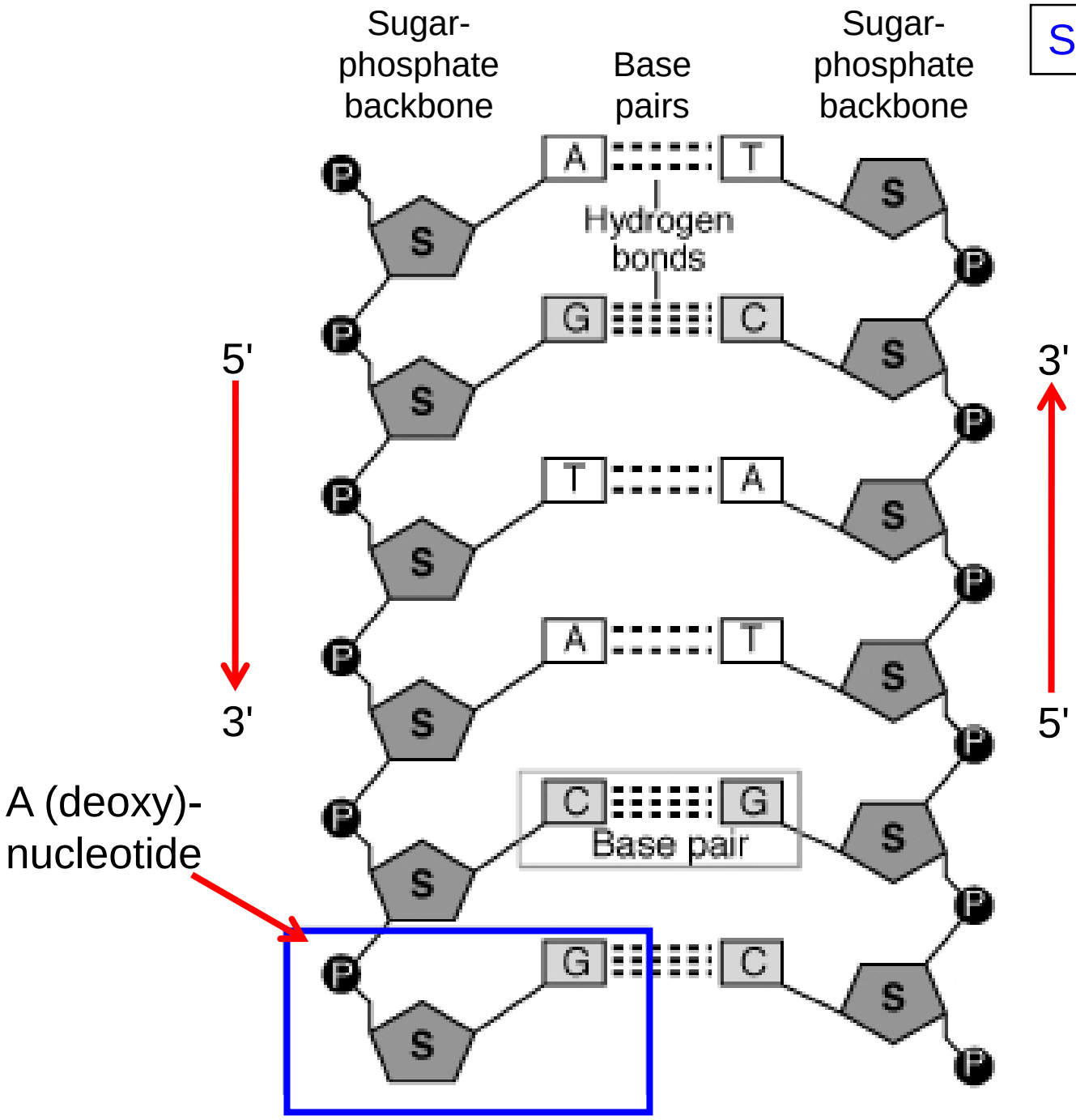


Deoxyguanosine monophosphate (dGMP)

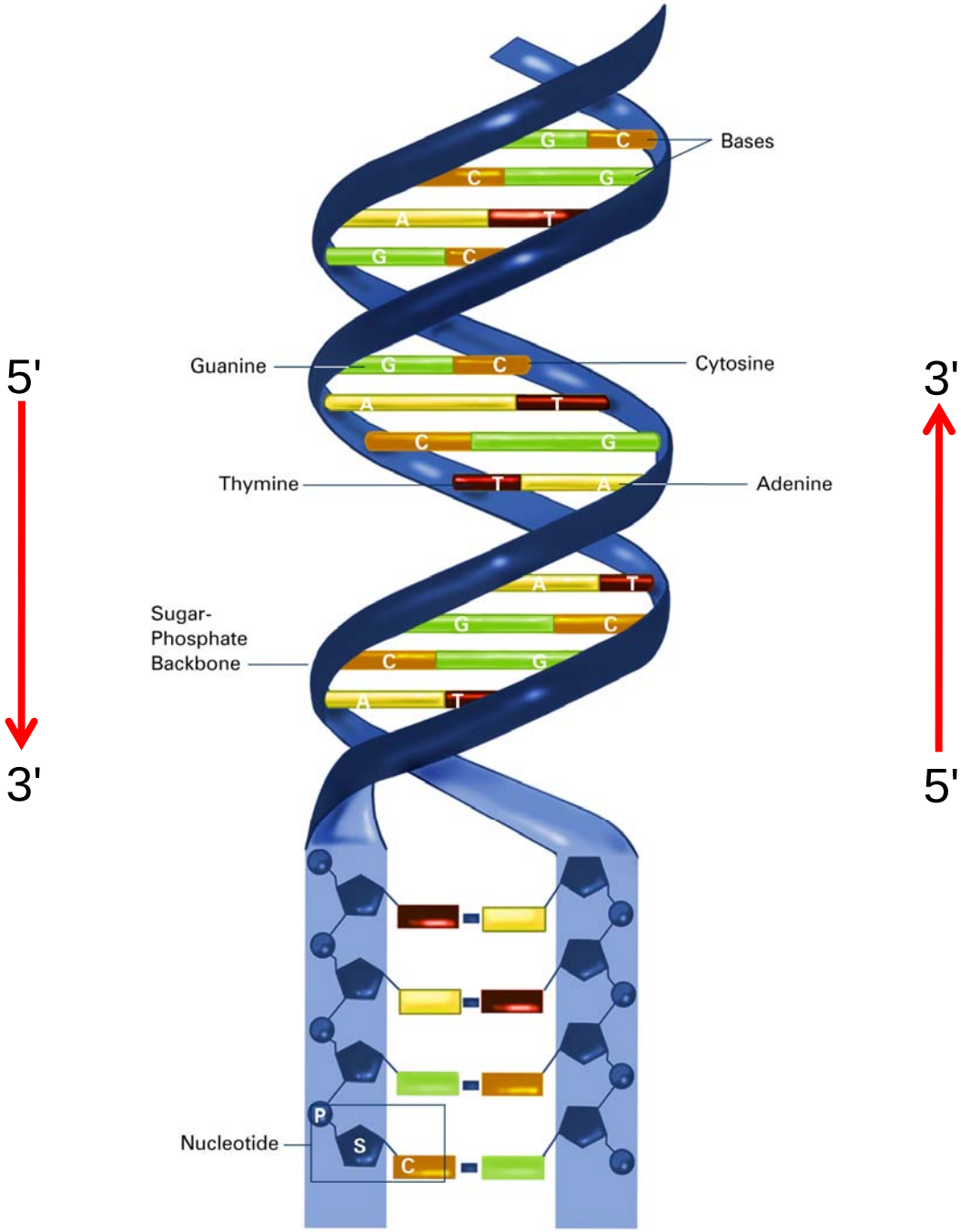


(Deoxy)thymidine monophosphate [(d)TMP]

Structure of dsDNA

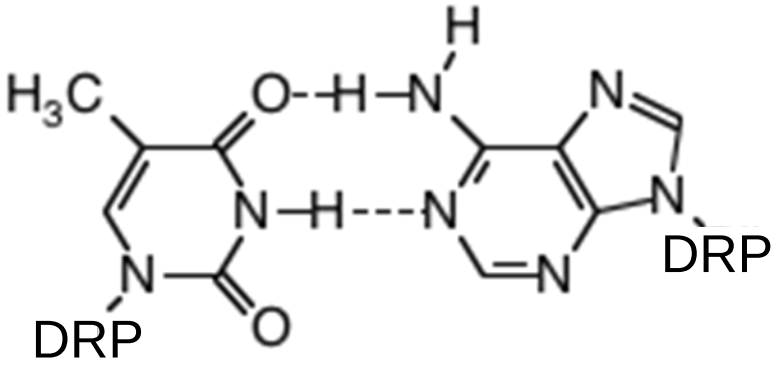


http://www.genome.gov/Pages/Hyperion/DIR/VIP/Glossary/Illustration/nucleotide.cfm?key=nucleotide



http://images.nigms.nih.gov/imageRepository/2542/Nucleotides_with_labels.jpg

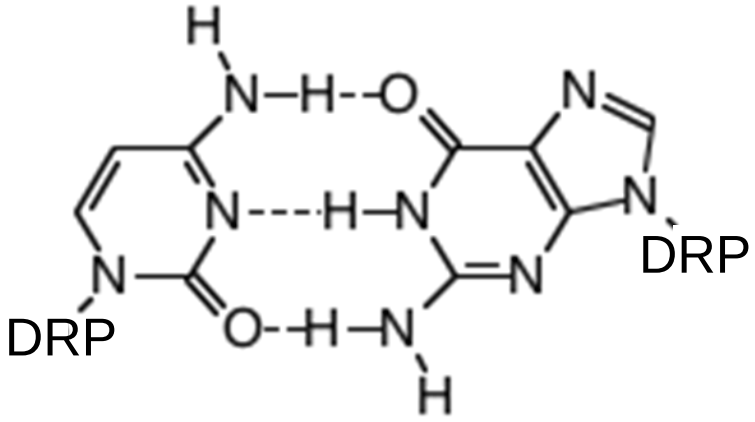
Complementary Base Pairing



Thymine Adenine

AT

(2 hydrogen bonds)



Cytosine Guanine

GC

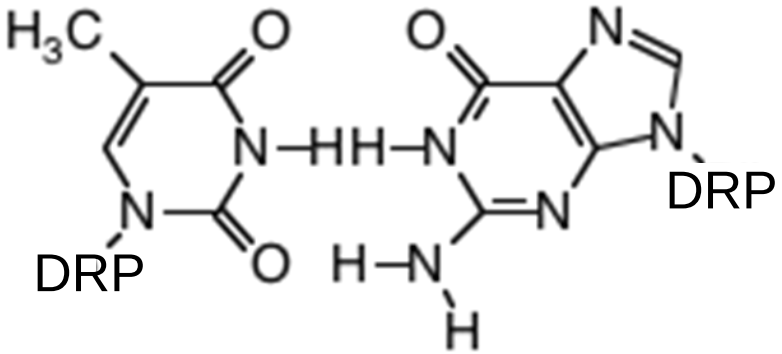
(3 hydrogen bonds)

DRP = deoxyribose-phosphate backbone

A pair of complementary deoxynucleotides in DNA = "base pairs" or "b.p."

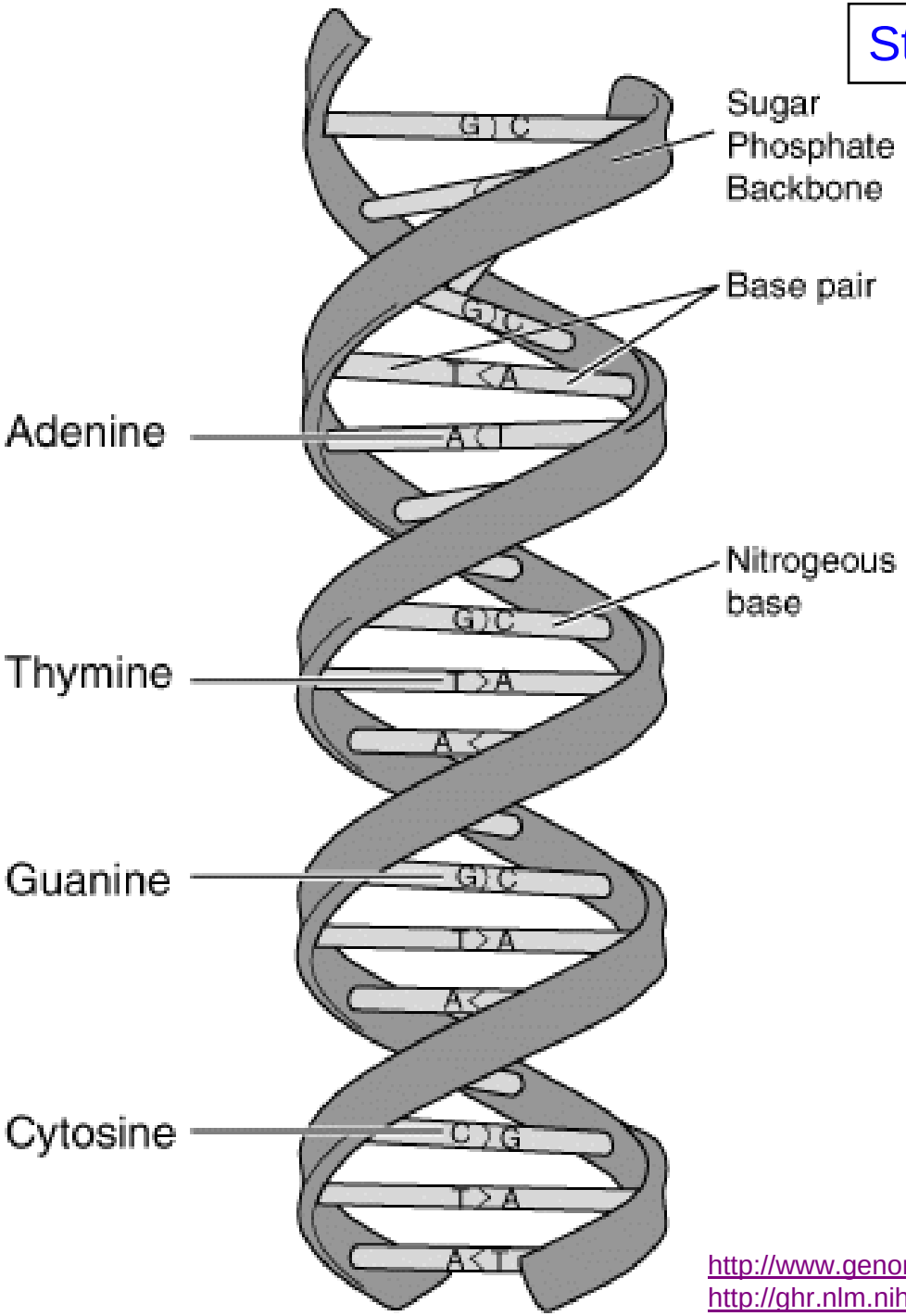
"Base" refers to the fact that the N-containing ring structures are alkaline; i.e., they are "basic" as opposed to "acidic"

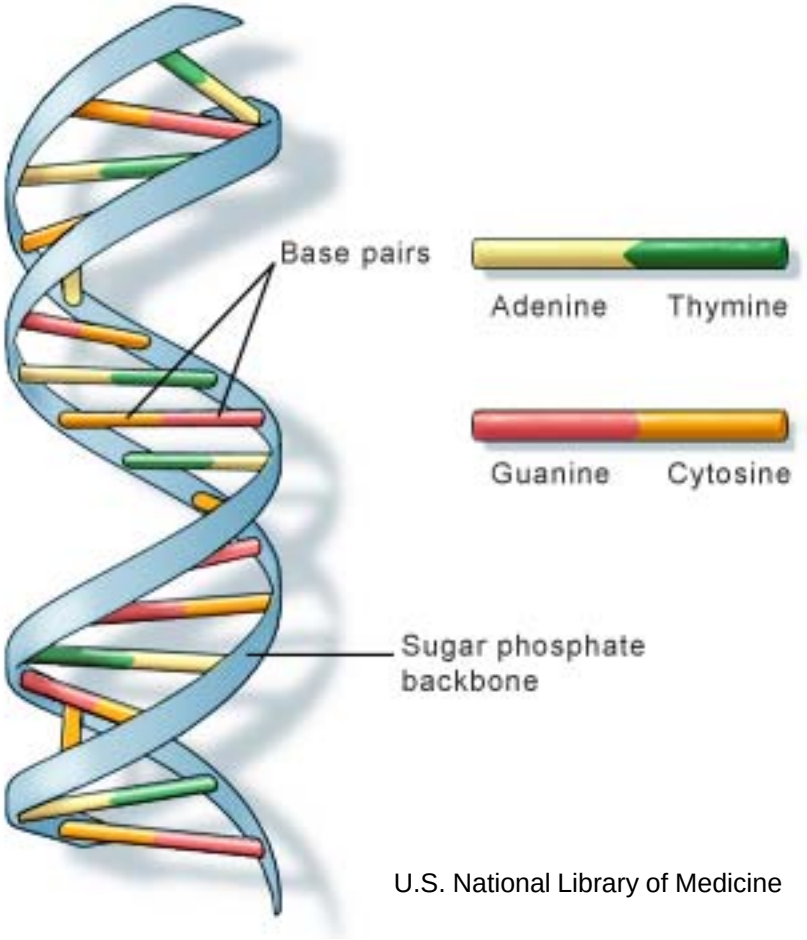
Example of Verboten Base Pairing



Thymine Guanine

Structure of dsDNA





U.S. National Library of Medicine

http://www.genome.gov/Pages/Hyperion/DIR/VIP/Glossary/Illustration/Images/d[illegible].gif
http://ghr.nlm.nih.gov/handbook/illustrations/dnastructure

Very Good URLs on the Structure of DNA

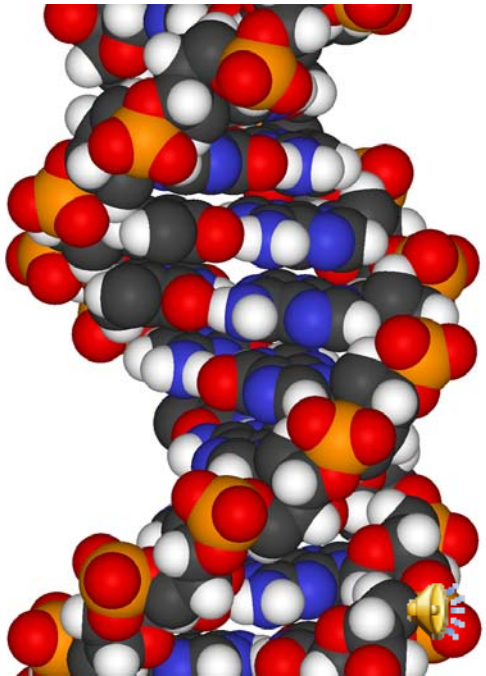
- http://www.umass.edu/molvis/tutorials/dna/ > Bottom of page

  > A. Double helix by element: base pairs, hydrogen bonding > Look at AT (DNA -> AT icon) and GC base pairing (DNA -> GC icon) > Select Spacefill icon if you want to see what the molecule really looks like

  > C. Strands and helical backbone

  > D. Ends, Antiparallelism > Look at the 5'- and 3'- ends (icons at the bottom of the page)

- http://biomodel.uah.es/en/model3/index.htm > DNA and RNA

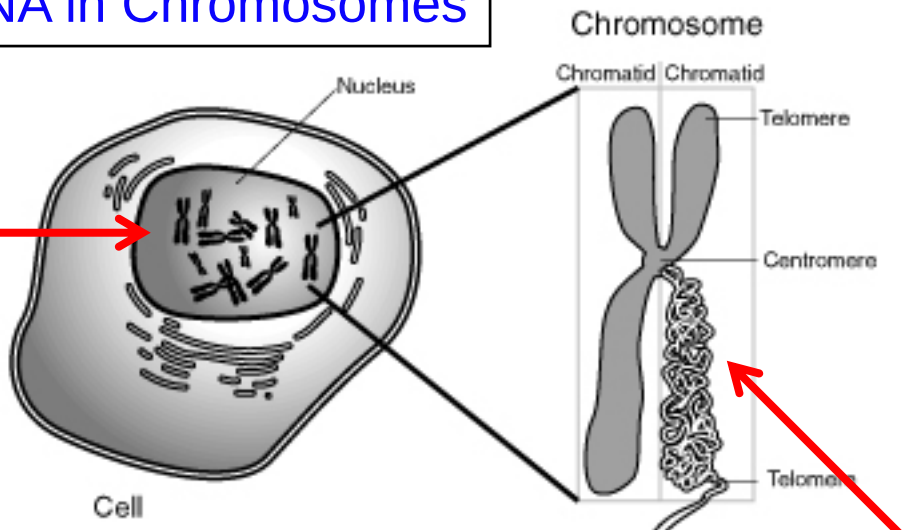


Fairly Good Movies on DNA Structure

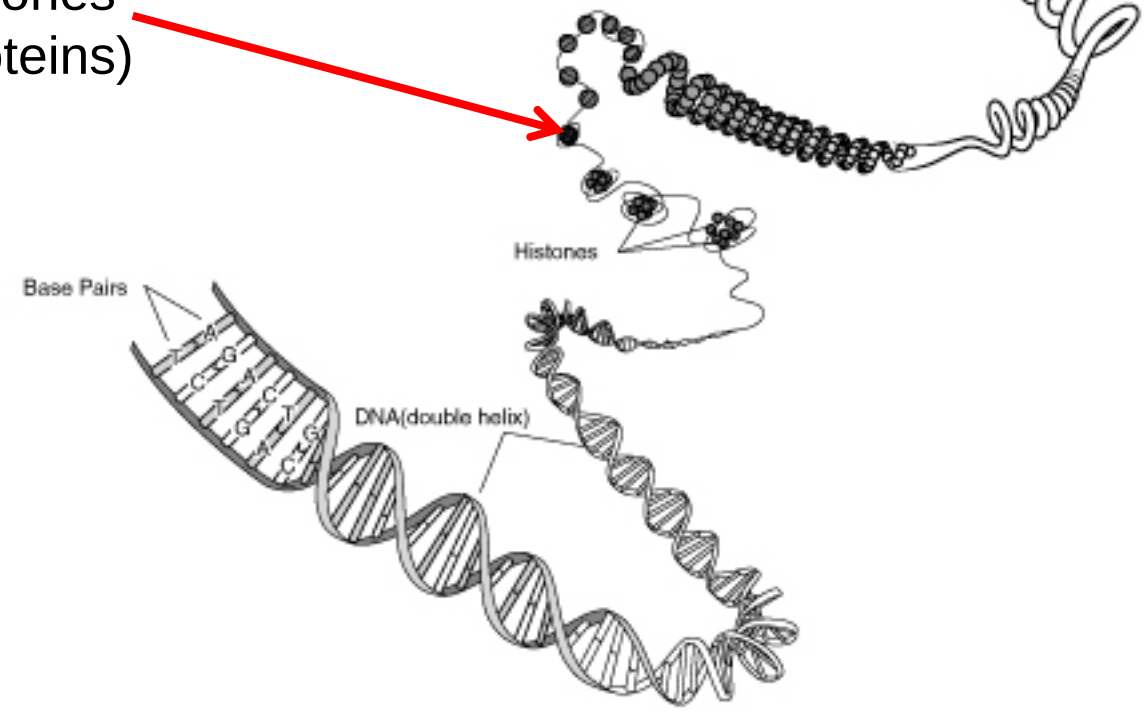
- http://www.biotechnologyonline.gov.au/biotec/whatisdna.html: Low resolution is sufficient
  - First movie shows James Watson describing his "wow" breakthrough
  - Second movie shows unzipping of dsDNA to 2 ssDNA

Packaging of DNA in Chromosomes

Nucleus inside a cell



Histones (proteins)



Chromosome with one centromere (center) and two telomeres (ends)

http://www.genome.gov/Pages/Hyperion/DIR/VIP/Glossary/Illustration/chromosome.cfm?key=chromosome

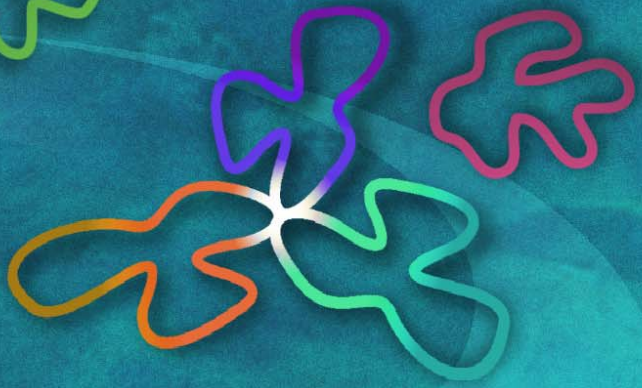
From DNA to Humans

CGTTCTCTATTAACA...

GCAAGAGATAATTGT...

3 billion DNA subunits in the cell nucleus

DNA Codes for ~80,000 different proteins in trillions of cells

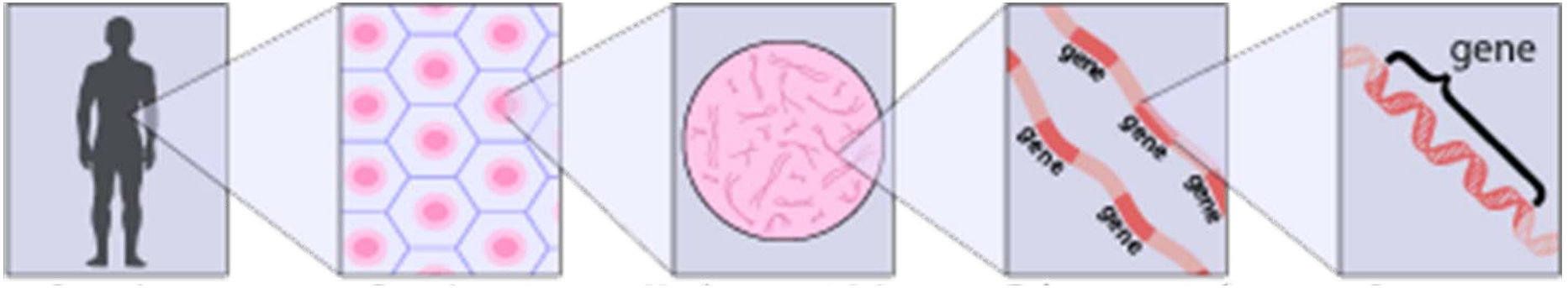


Cells respond to environment

YGG-00-0482

http://genomics.energy.gov/gallery/basic_genomics/detail.np/detail-22.html

You to Your Genes



Organism (human)

Constituent cells

Nucleus containing two sets of 23 chromosomes (each set constitutes a genome)

Enlargement of part of a pair of chromosomes

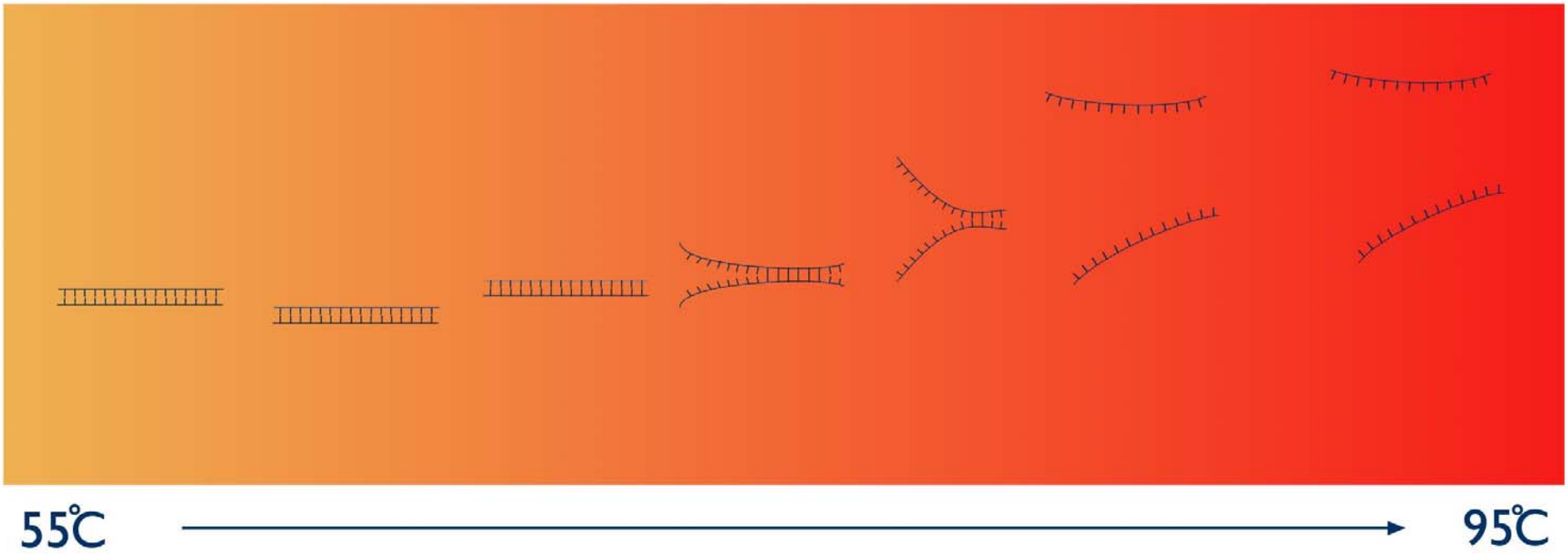
One gene, a functional region of chromosomal DNA

http://populations.dna.gov/m01/01/a/

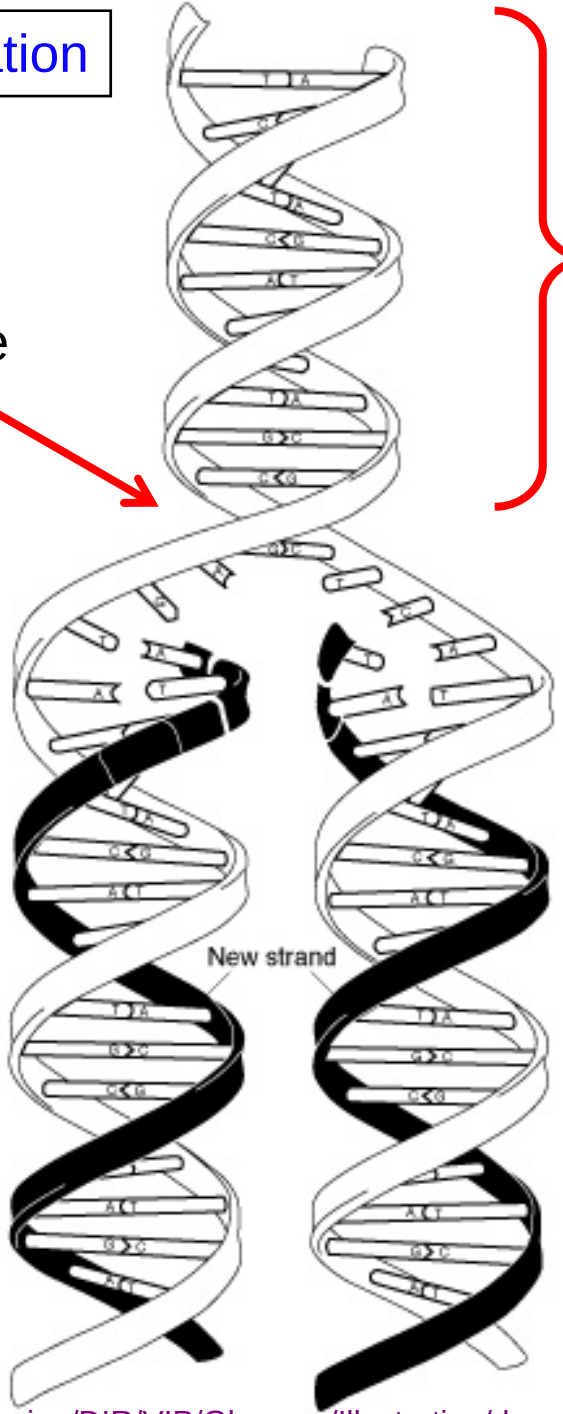
Melting of dsDNA

- dsDNA = double-stranded DNA; ssDNA = single-stranded DNA
- The "melting" of DNA is not the same as the "melting" of ice
  - dsDNA melts to give 2 ssDNA molecules (also termed "denatures")
    - The hydrogen bonds holding the complementary bases together are broken
  - Solid ice "melts" to give liquid water
- Usual way to melt DNA: increase temperature until the hydrogen bonds begin to break
  - Temperature at which dsDNA melts (denatures) to 2 ssDNA depends upon many factors
    - E.g., the more the GC content of the DNA, the higher the melting temperature
      - 3 H bonds between G-C, only 2 between A-T
- Partial melting of dsDNA occurs during DNA replication

Melting of dsDNA



DNA Replication



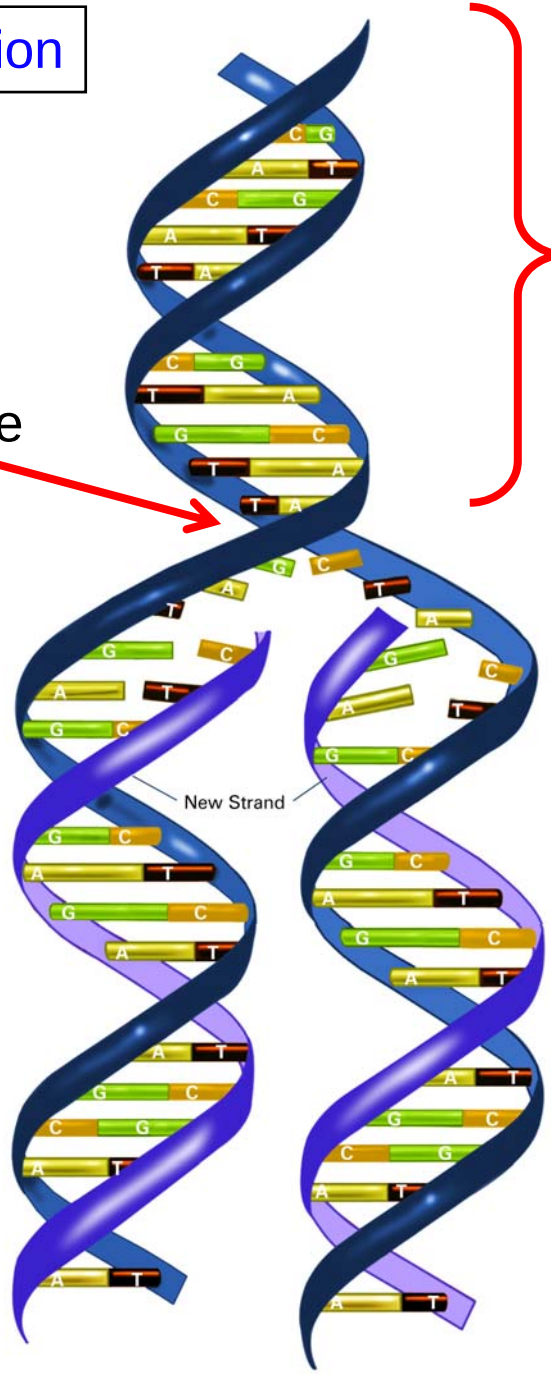
DNA polymerase acts here

Parent ("old") DNA strands

Daughter (1/2 "new" & 1/2 "old") DNA strands

http://www.genome.gov/Pages/Hyperion/DIR/VIP/Glossary/Illustration/dna_replication.cfm?key=DNA%20replication

DNA Replication

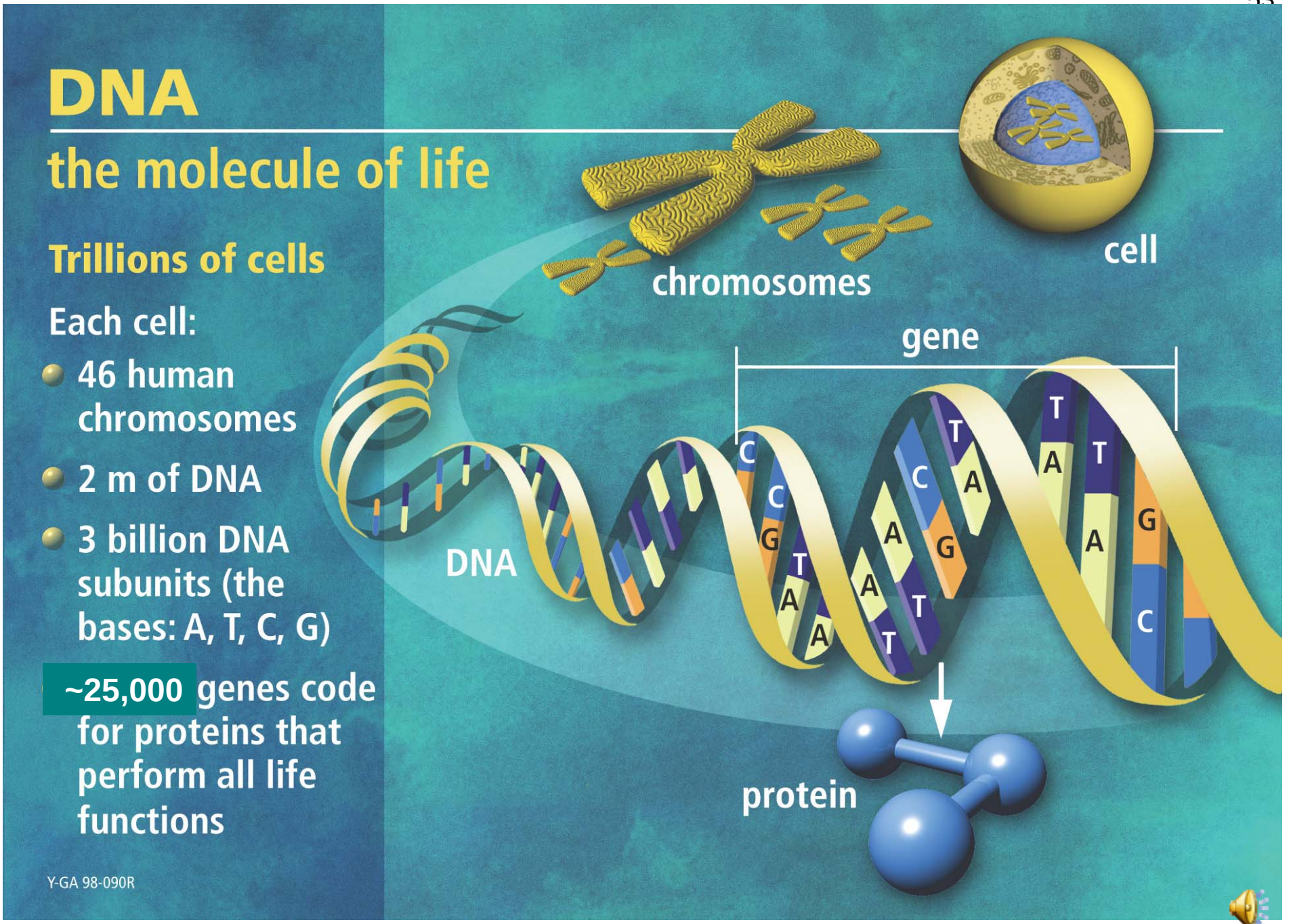


Parent ("old") DNA strands

DNA polymerase acts here

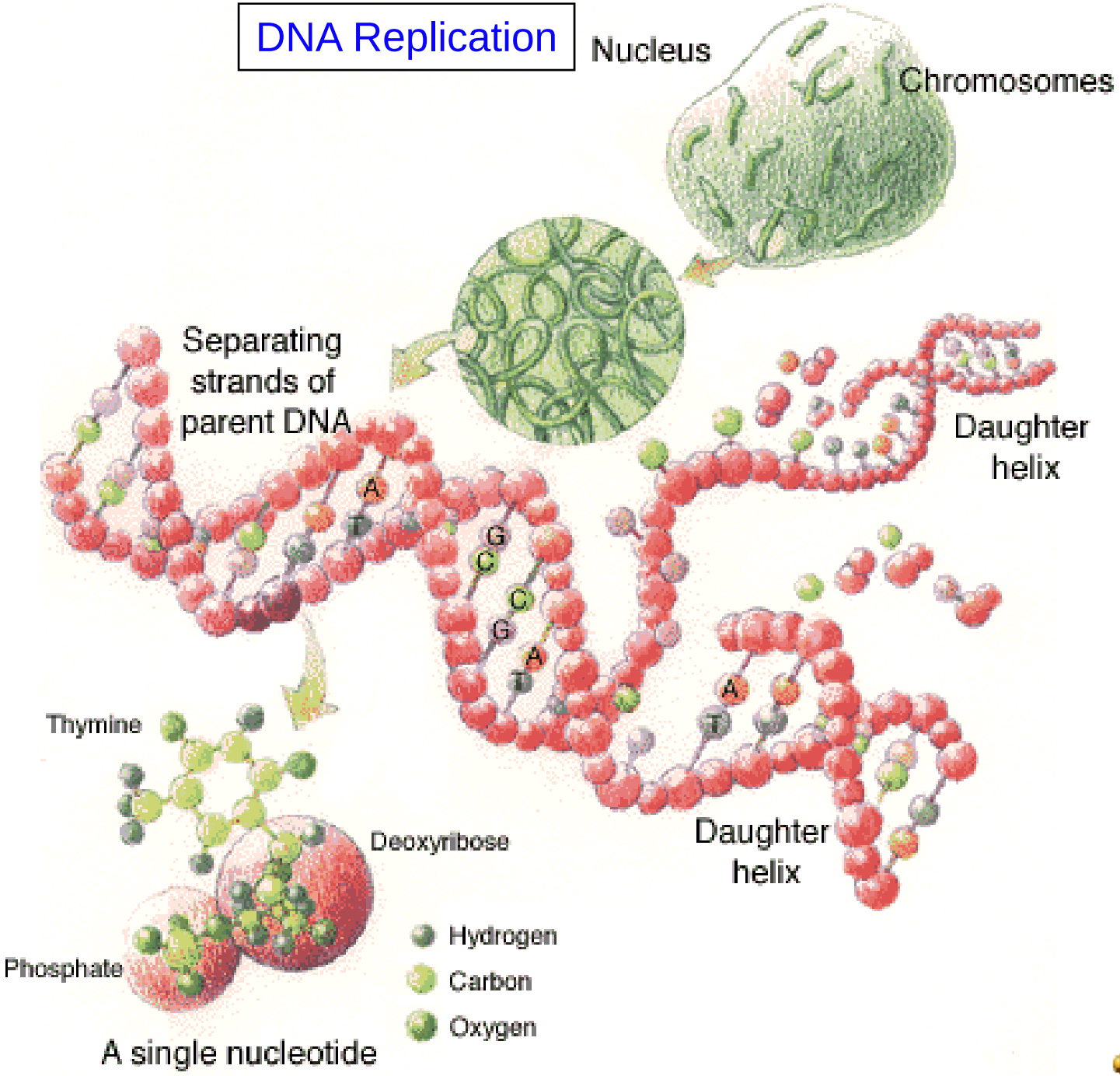
Daughter (1/2 "new" & 1/2 "old") DNA strands

http://www.genome.gov/Pages/Hyperion/DIR/VIP/Glossary/Illustration/dna_replication.cfm?key=DNA%20replication



http://genomics.energy.gov/gallery/basic_genomics/detail.np/detail-18.html

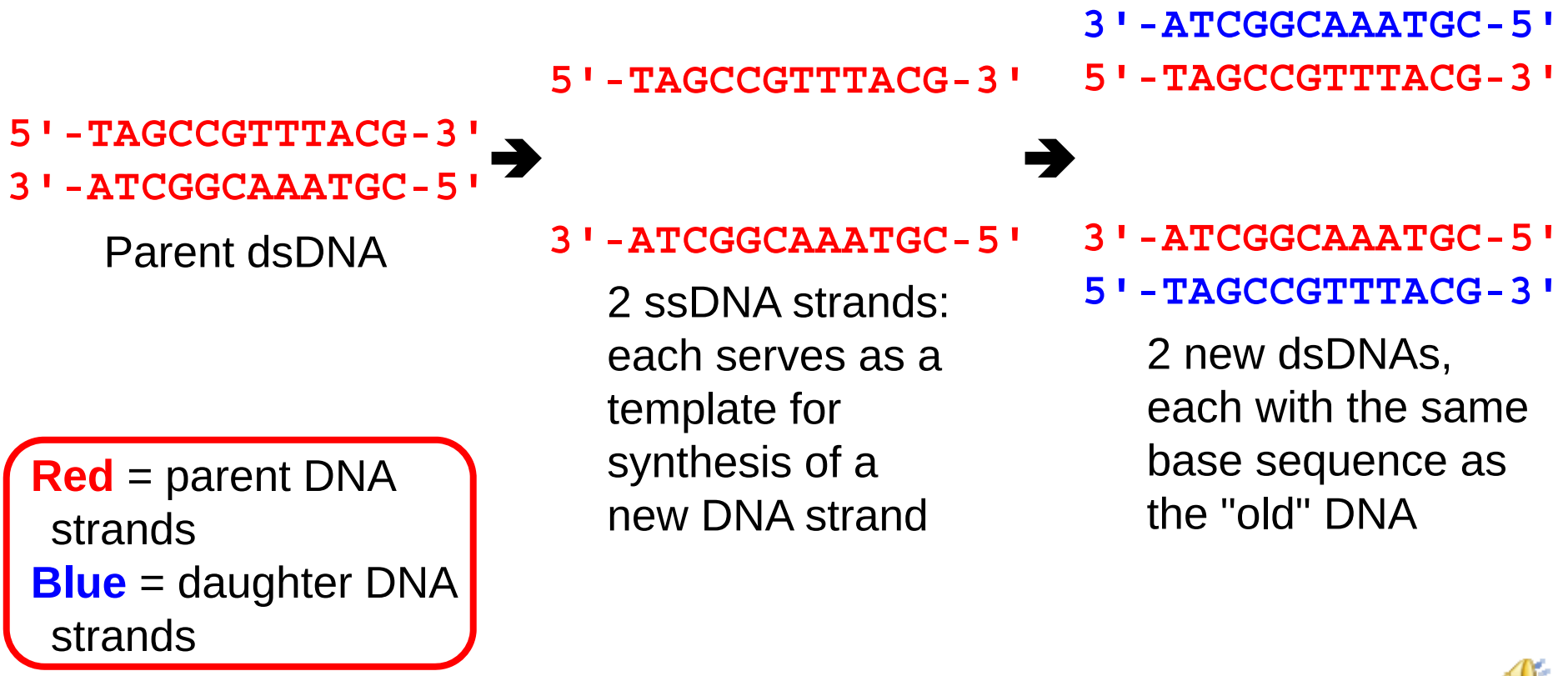
DNA Replication



http://www.ornl.gov/sci/techresources/Human_Genome/publicat/tko/03_introducing.html

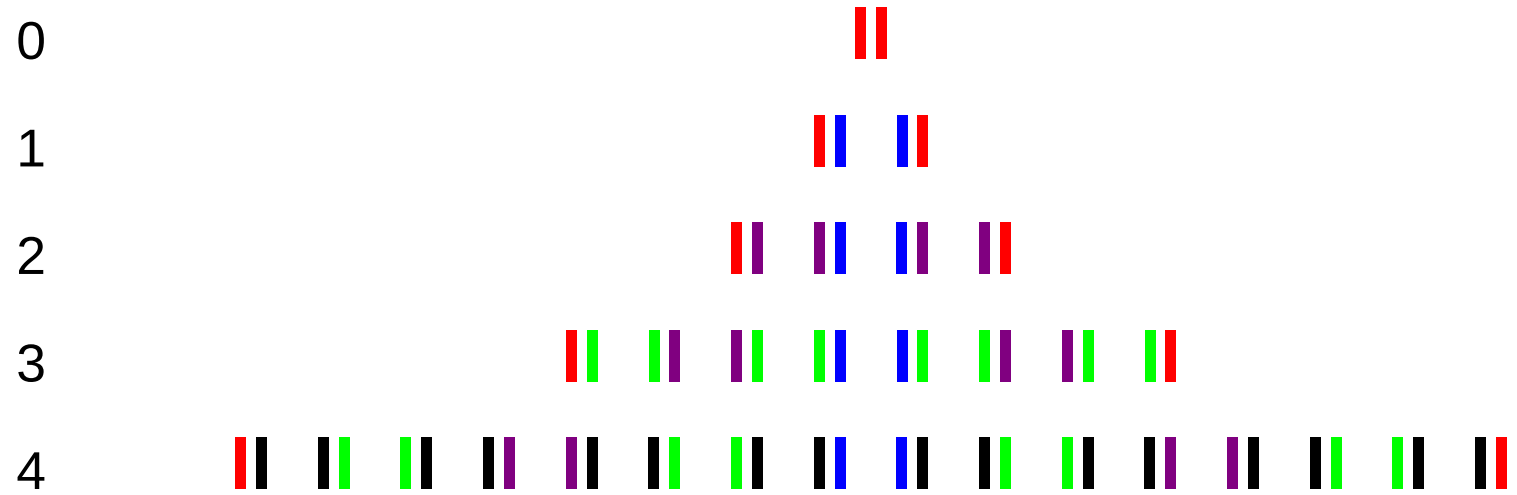
DNA Replication

- DNA replicates itself; i.e., it makes (almost) identical copies of itself
  - dsDNA partially unwinds (i.e., partially melts) to two ssDNA strands
  - Each ssDNA serves as a template to make a complementary daughter strand
- Oversimplified version:



Red = parent DNA strands
Blue = daughter DNA strands

DNA Replication



Red = original strands

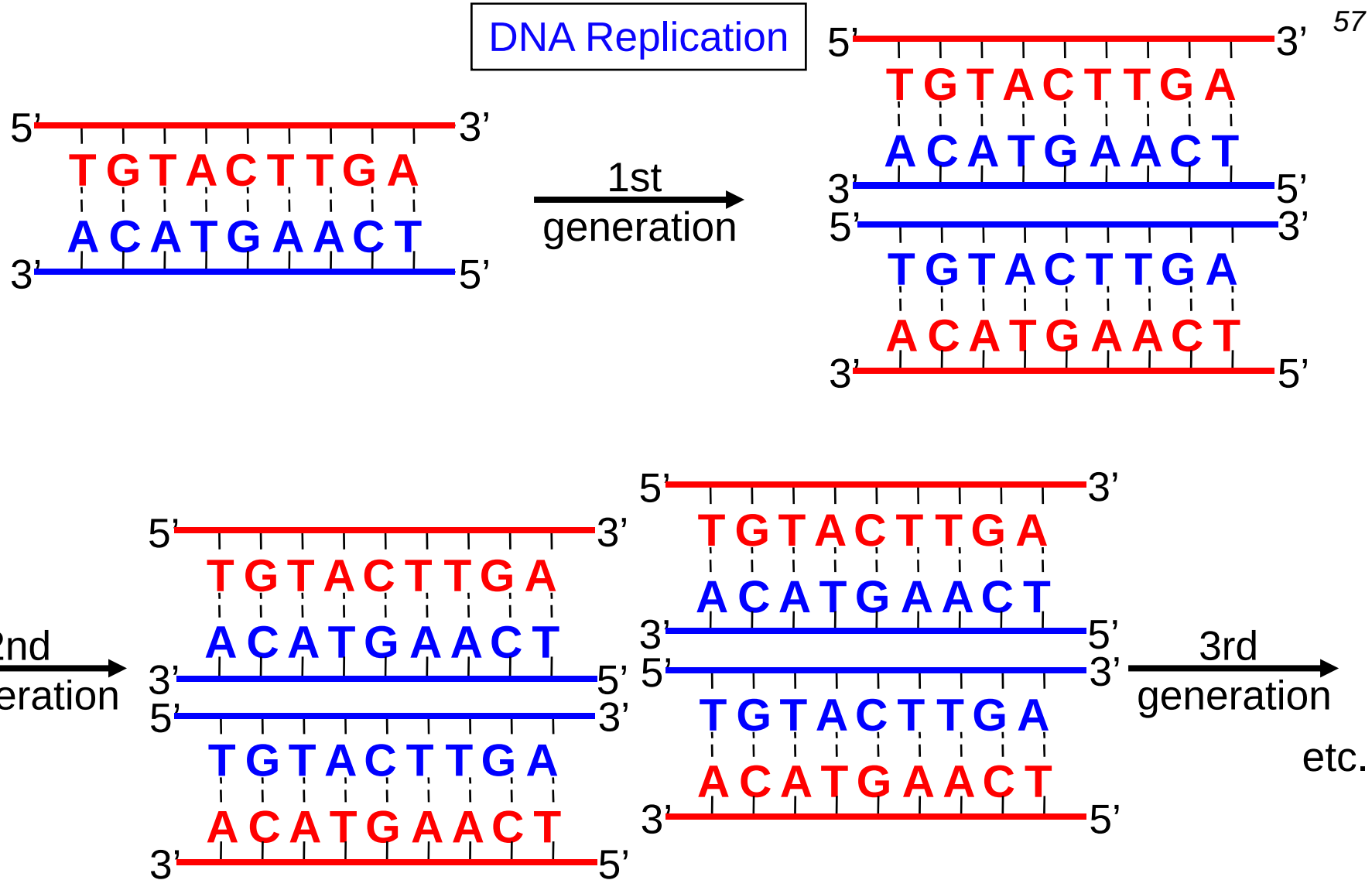
Blue = strands synthesized during 1st generation

Purple = strands synthesized during 2nd generation

Green = strands synthesized during 3rd generation

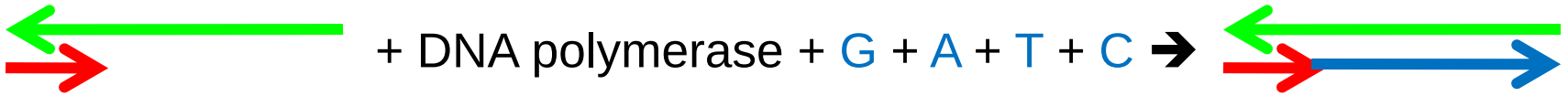
Black = strands synthesized during 4th generation

DNA Replication

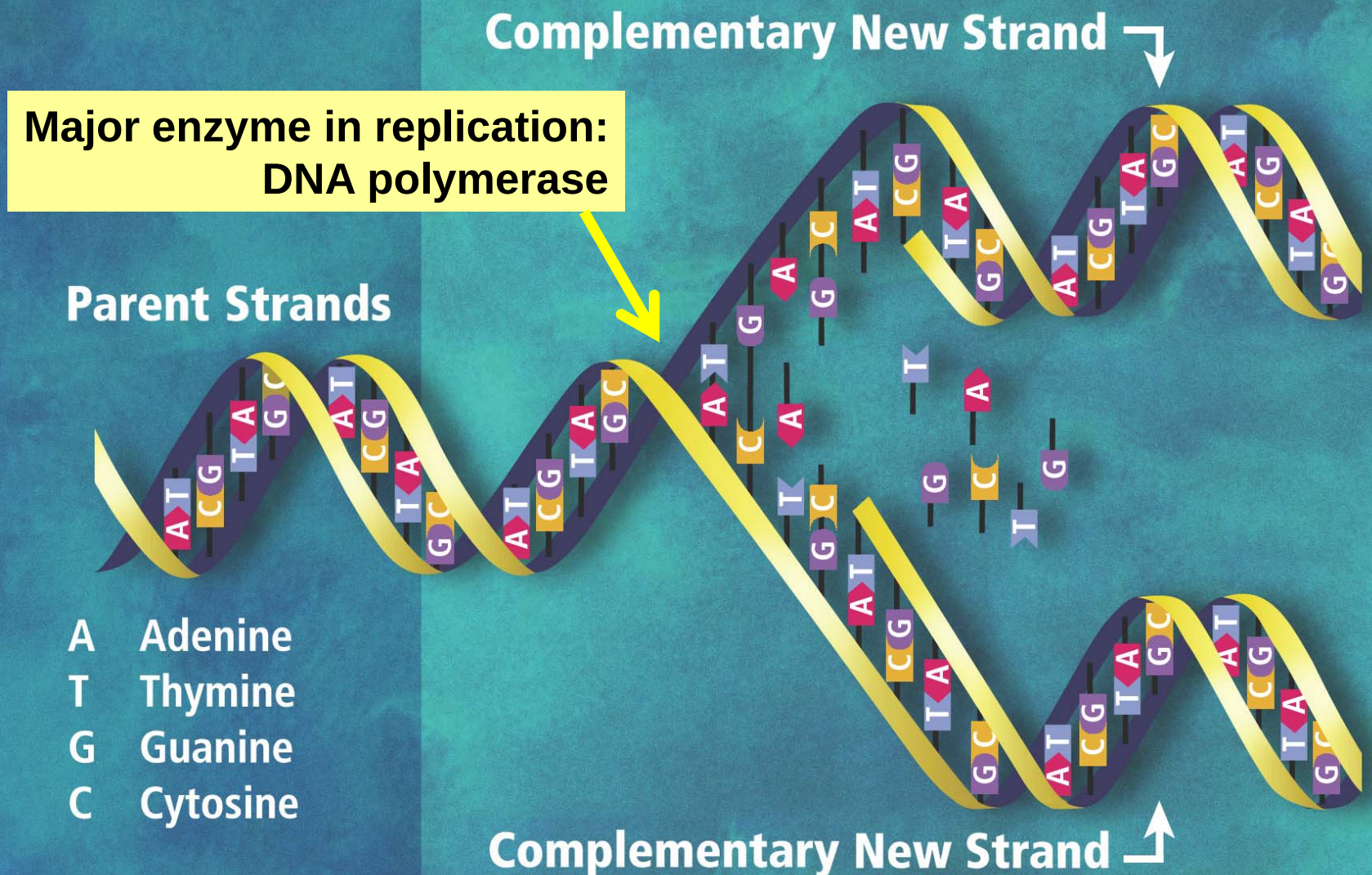


DNA Polymerase

- Major enzyme involved in DNA replication (1959 Nobel Prize)
  - Several other enzymes involved -- very complex. We ignore these other enzymes (such as helicase, ligase, gyrase, primase)
- Template ssDNA + the 4 deoxynucleotides (A, T, G, C) + primer ssDNA ➔ dsDNA
  - The new DNA strand is complementary to the template DNA strand
- DNA polymerase requires a primer (in addition to the template)
  - DNA polymerase can only add nucleotides to a pre-existing strand of DNA; it cannot start from scratch. E.g.:



DNA Replication Prior to Cell Division



http://genomics.energy.gov/gallery/basic_genomics/detail.np/detail-12.html

Closer to "the Real Story" of DNA Replication (not responsible for this)