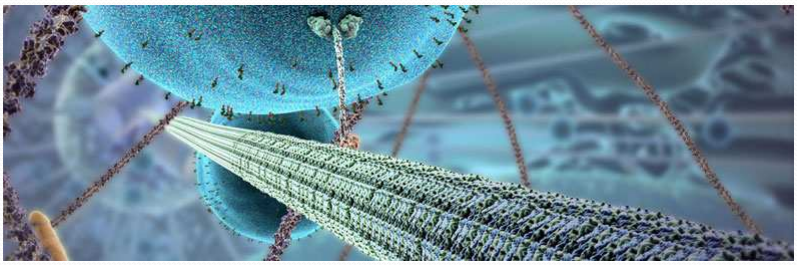
Inner Life of a Cell

- Video
- http://www.studiodaily.com/main/searchlist/6850.html



S3690 The Biology of Cancer

HSSP @ Harvard Fall 2010

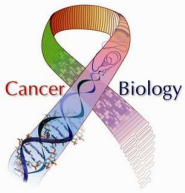
Lecture 1: Framing the Problem

10/2/2010

Zhi Dong

Lecture 1 Outline

- Introduction to the course
  - Course content, format and expectations
- Framing the problem: What is cancer?
  - Treatment and Research
  - Molecular Biology and Disease
- Fundamental building blocks of the cell
  - Macromolecules and organelles
- Discussion: The RNA World Hypothesis



Course Objectives

- Understand fundamental principles in molecular and cellular biology.
- Familiarize with basic building blocks and processes inside cells.
- Conceptualize what cancer is and how it arises.
- Develop scientific inquiry through discussions of current research and discoveries.
- Focus on understanding how biological principles operate in cancer. Less emphasis on clinical management.

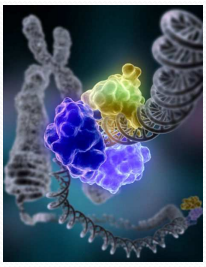
Class Format and Logistics

- Lectures
  - Biological principle
  - Examples in cancer
- Discussions
- Weekly readings

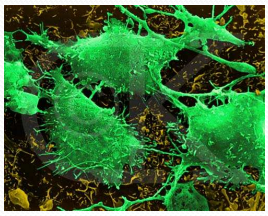
- Media (videos, animations and applets)
- Final Project

- Meet in Lyman 330
  Time: Sat 10:00am--12:00pm

http://genegenie.wordpress.com/2007/05/06/gene-genie-the-first-issue-at-scienceroll/



DNA and Protein

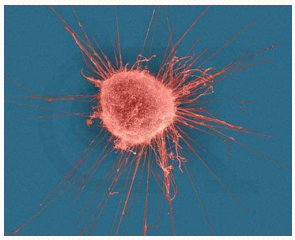


Brain Cancer Cell

Background and Expectations

- No background in biology is necessary!
- Do the weekly reading
- Preview and Review key terms and concepts
- Actively engage in discussion

http://www.alternative-cancer.net/Cell_photos.htm



Breast Cancer Cell

About me

- Phoenix, Arizona
- Junior at Harvard College
- Molecular and Cellular Biology Concentrator
- Secondary in East Asian Studies
- Mather House
- Research on Medulloblastoma at Children's Hospital Boston

What is cancer?

- Perspective from patients
- Perspective from researchers
- Current state of cancer research
- A look at the molecular biology of cancer

Bibliography- Cancer Videos

- **Two best friends, one form of cancer**
- http://www.youtube.com/watch?v=NFJAqNS627Q&feature=related
- **It's Our Time - American Association for Cancer Research (AACR)**
- http://www.youtube.com/watch?v=3pobQRfzoNo
- **Pamela Martin, Cancer Biology Lab Manager**
- http://www.youtube.com/watch?v=PppO4rKzOko
- **Cancer Research Laboratory**
- http://www.youtube.com/watch?v=tcrf2wCOicw&feature=related
- **Cancer Treated with Radiation Therapy**
- http://www.youtube.com/watch?v=6soM9N3cgwA&feature=related

What is cancer?

- Discussion: What are the features of cancer? What do you notice from the last video?

Cell, Vol. 100, 57–70, January 7, 2000, Copyright ©2000 by Cell Press

The Hallmarks of Cancer

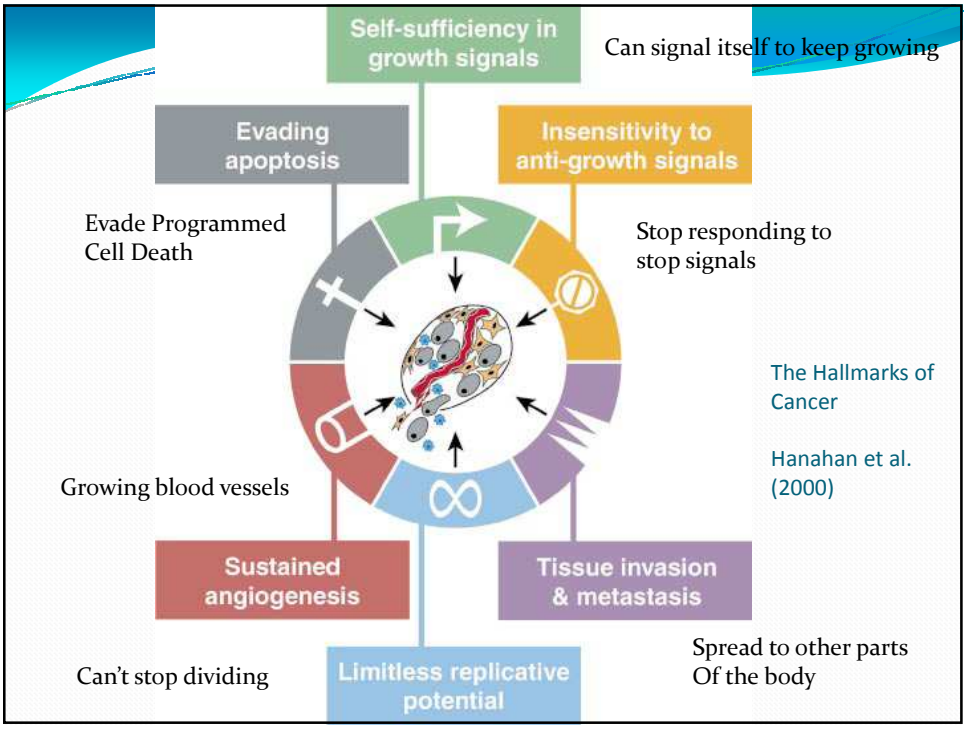
Review

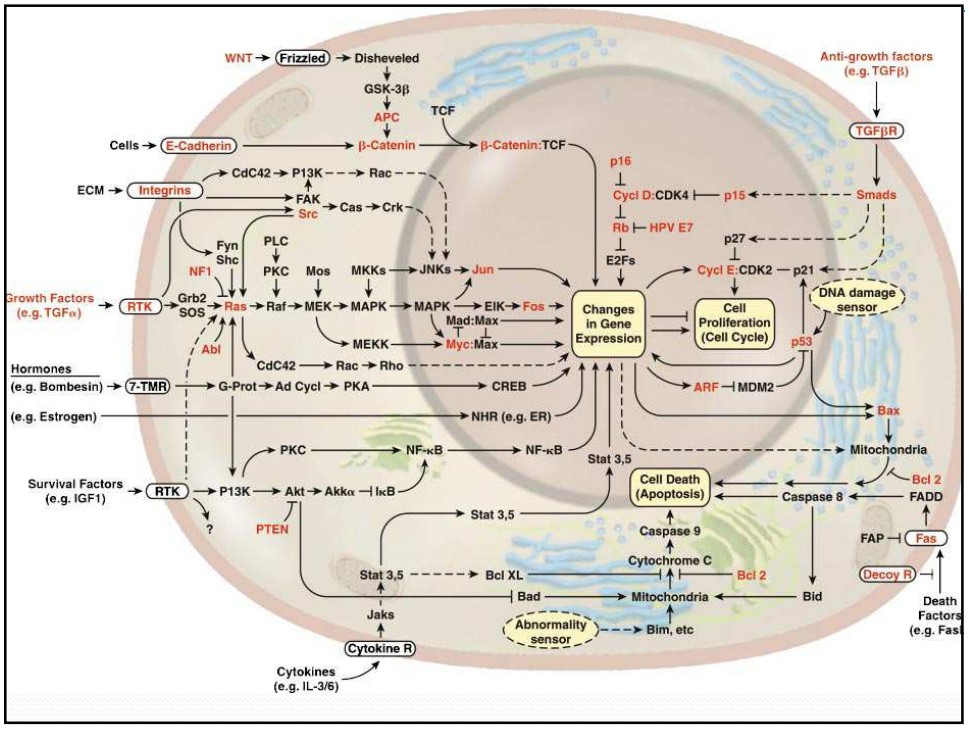
Douglas Hanahan* and Robert A. Weinberg†
*Department of Biochemistry and Biophysics and Hormone Research Institute
University of California at San Francisco
San Francisco, California 94143
†Whitehead Institute for Biomedical Research and Department of Biology
Massachusetts Institute of Technology
Cambridge, Massachusetts 02142

After a quarter century of rapid advances, cancer research has generated a rich and complex body of knowledge, revealing cancer to be a disease involving dynamic changes in the genome. The foundation has been set in the discovery of mutations that produce oncogenes with dominant gain of function and tumor suppressor genes with recessive loss of function; both classes of cancer genes have been identified through their alteration in human and animal cancer cells and by their elicitation of cancer phenotypes in experimental models (Bishop and Weinberg, 1996).

evolve progressively from normalcy via a series of premalignant states into invasive cancers (Foulds, 1954).

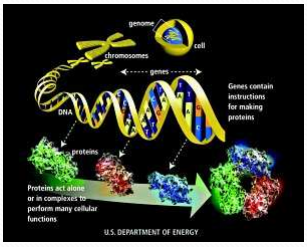
These observations have been rendered more concrete by a large body of work indicating that the genomes of tumor cells are invariably altered at multiple sites, having suffered disruption through lesions as subtle as point mutations and as obvious as changes in chromosome complement (e.g., Kinzler and Vogelstein, 1996). Transformation of cultured cells is itself a multistep process: rodent cells require at least two introduced genetic changes before they acquire tumorigenic competence, while their human counterparts are more difficult to transform (Hahn et al., 1999). Transgenic models of tumorigenesis have repeatedly supported the conclusion that tumorigenesis in mice involves multiple rate-limiting steps (Bergers et al., 1998; see *Oncogene*, 1999, R. DePinho and T. E. Jacks, volume 18[38], pp. 5248–5362). Taken together, observations of human cancers and animal models argue that tumor development proceeds via a process formally analogous to Darwinian evolution, in which a succession of genetic changes, each conferring one or another type of growth





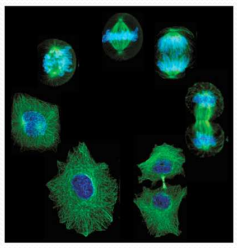
Lecture 2

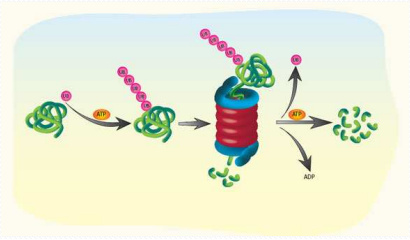
- What's wrong with the cancer cell?
- Principle: Central Dogma, introduction to molecular genetics, gene regulation, epigenetic regulations
- Cancer: Mutation, gene regulation, repair, p53 gene



Lecture 3

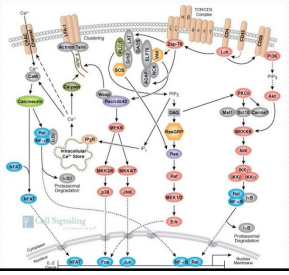
- Why can't they stop dividing?
- Principle: Cell cycle, regulation of cellular processes, protein degradation.
- Cancer: limitless replicative potential, current therapy, retinoblastoma, Rb gene

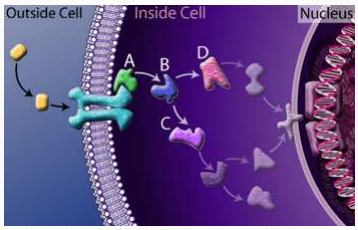




Lecture 4

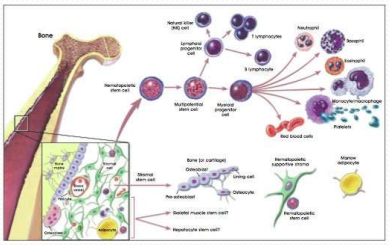
- How do the cells know what to do?
- Principles of cell signaling, phosphorylation
- Cancer: self-sufficiency in growth signals and insensitivity to anti-growth signals. Chronic Myelogenous Leukemia, Philadelphia chromosome

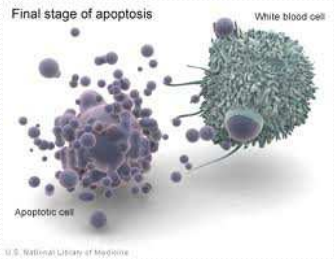




Lecture 5

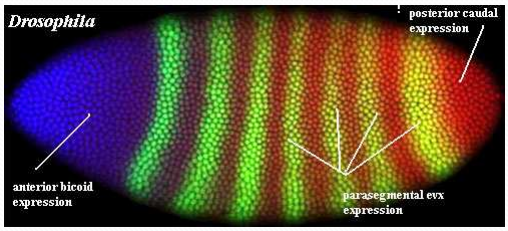
- The life story of a cell called George.
- Differentiation, cell aging, and apoptosis.
- Cancer: Evading apoptosis, cancer stem cell theory, Multiple Myeloma, Medulloblatoma, Bcl gene, SHH gene

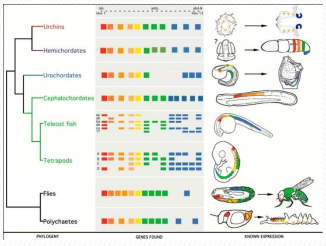




Lecture 6

- How do your arms and legs know where to grow?
- Principles of development, organogenesis, morphogenesis.
- Cancer: sustained angiogenesis, tissue invasion and metastasis, Bicoid to Hox genes. Teratocarcinoma.



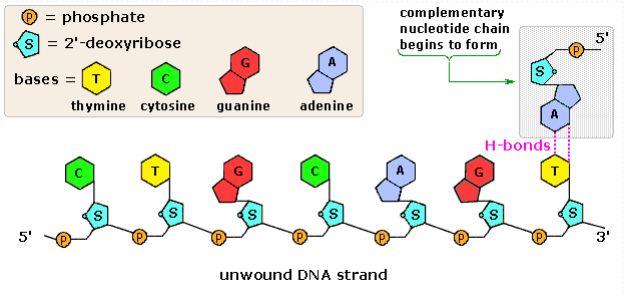


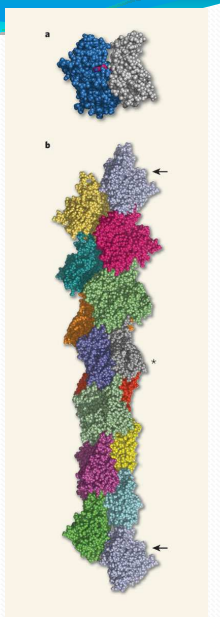
Lecture 7

- Final Project
- We will see an example soon…

Macromolecules

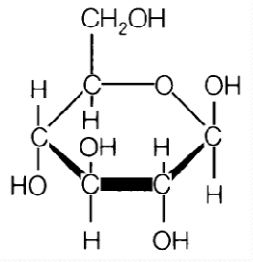
- Monomer vs. Polymer

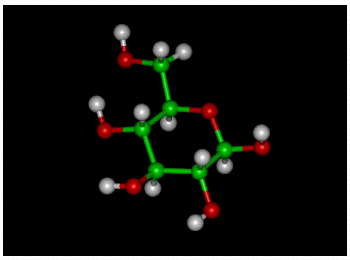


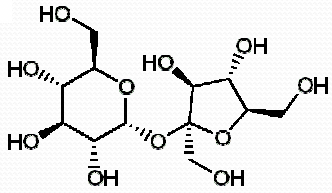


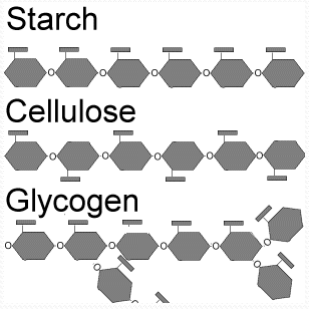
Macromolecules

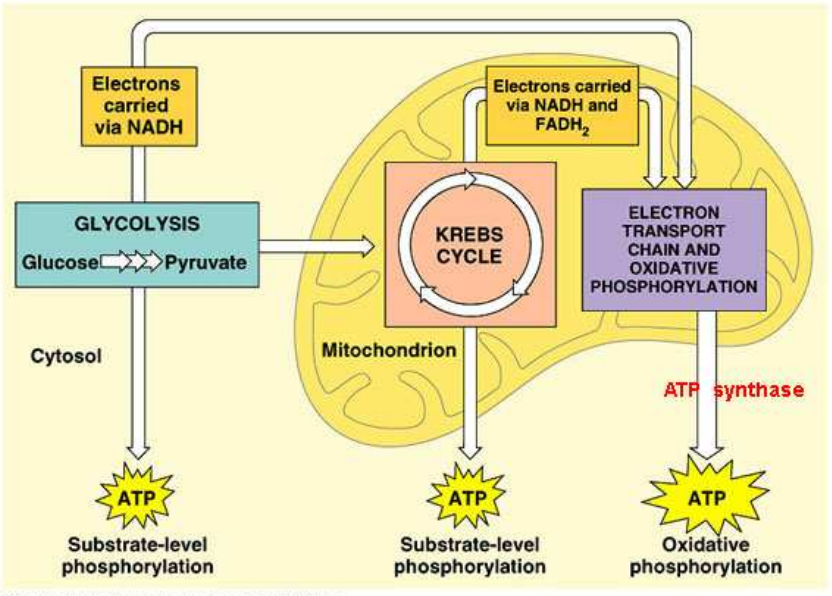
- Carbohydrates (sugar)

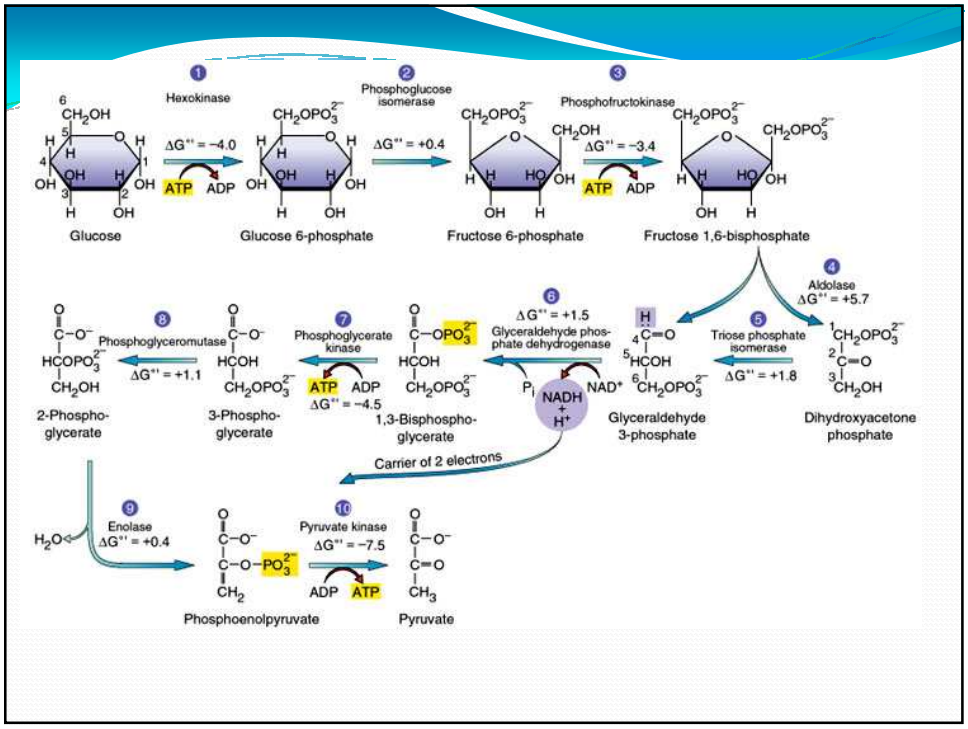


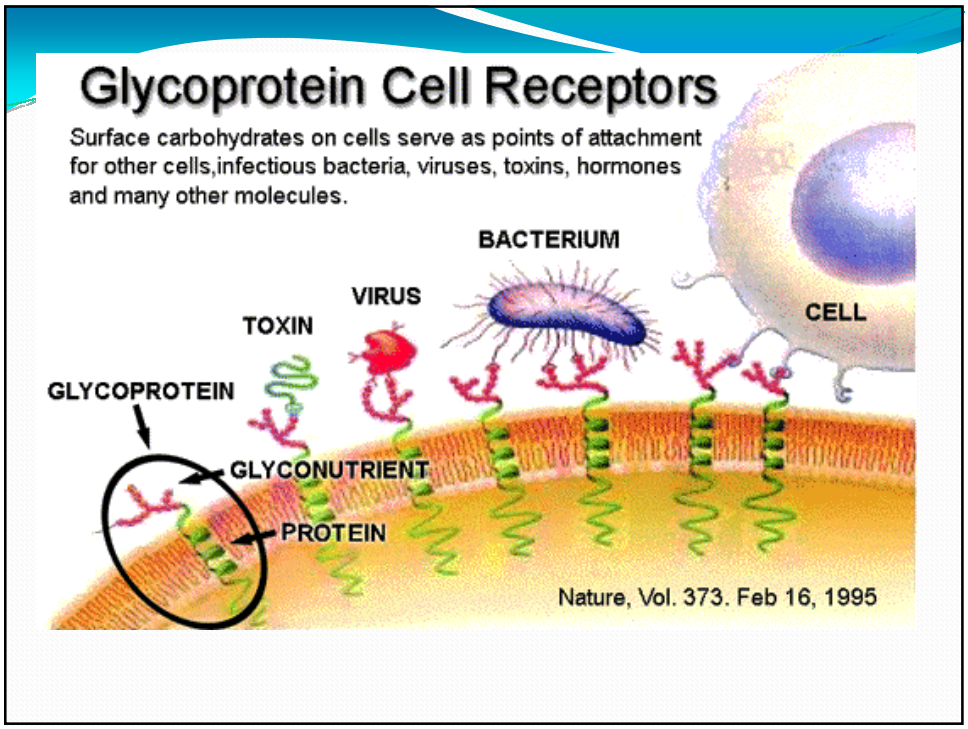


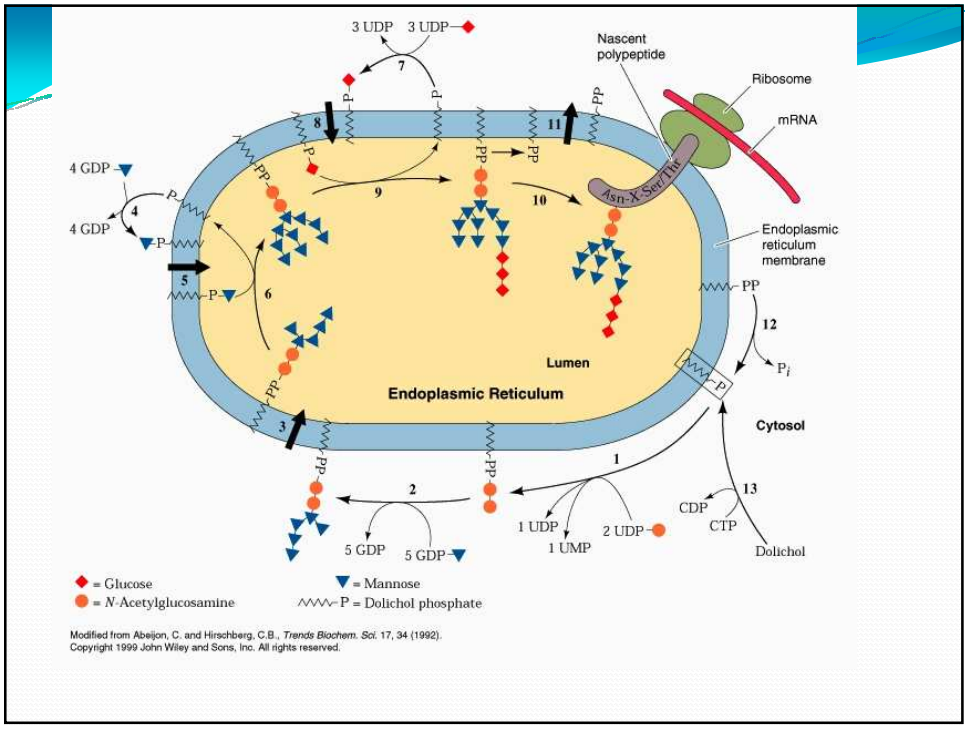







1
Hexokinase
2
Phosphoglucose isomerase
3
Phosphofructokinase
ΔG°' = −4.0
ATP
ADP
ΔG°' = +0.4
ΔG°' = −3.4
ATP
ADP
Glucose
Glucose 6-phosphate
Fructose 6-phosphate
Fructose 1,6-bisphosphate
4
Aldolase
ΔG°' = +5.7
5
Triose phosphate isomerase
ΔG°' = +1.8
6
ΔG°' = +1.5
Glyceraldehyde phosphate dehydrogenase
NADH + H+
NAD+
Pi
Glyceraldehyde 3-phosphate
Dihydroxyacetone phosphate
7
Phosphoglycerate kinase
ATP
ADP
ΔG°' = −4.5
1,3-Bisphospho-glycerate
8
Phosphoglyceromutase
ΔG°' = +1.1
2-Phospho-glycerate
3-Phospho-glycerate
Carrier of 2 electrons
9
Enolase
ΔG°' = +0.4
H2O
10
Pyruvate kinase
ΔG°' = −7.5
ADP
ATP
Phosphoenolpyruvate
Pyruvate

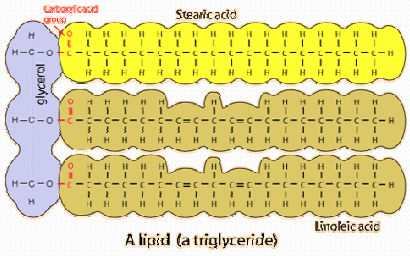

Glycoprotein Cell Receptors
Surface carbohydrates on cells serve as points of attachment for other cells,infectious bacteria, viruses, toxins, hormones and many other molecules.
BACTERIUM
VIRUS
TOXIN
CELL
GLYCOPROTEIN
GLYCONUTRIENT
PROTEIN
Nature, Vol. 373. Feb 16, 1995



Modified from Abeijon, C. and Hirschberg, C.B., *Trends Biochem. Sci.* 17, 34 (1992).

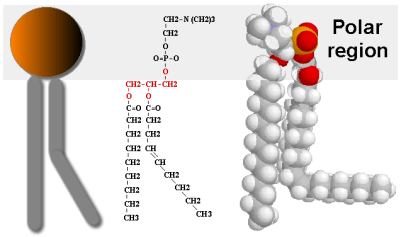
Macromolecules

- Lipids



A lipid (a triglyceride)

Phospholipids



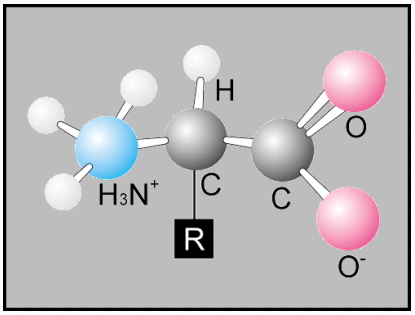
Macromolecules

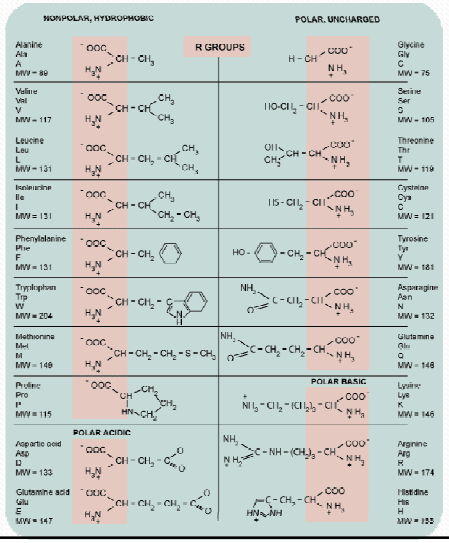
Phospholipid bilayer

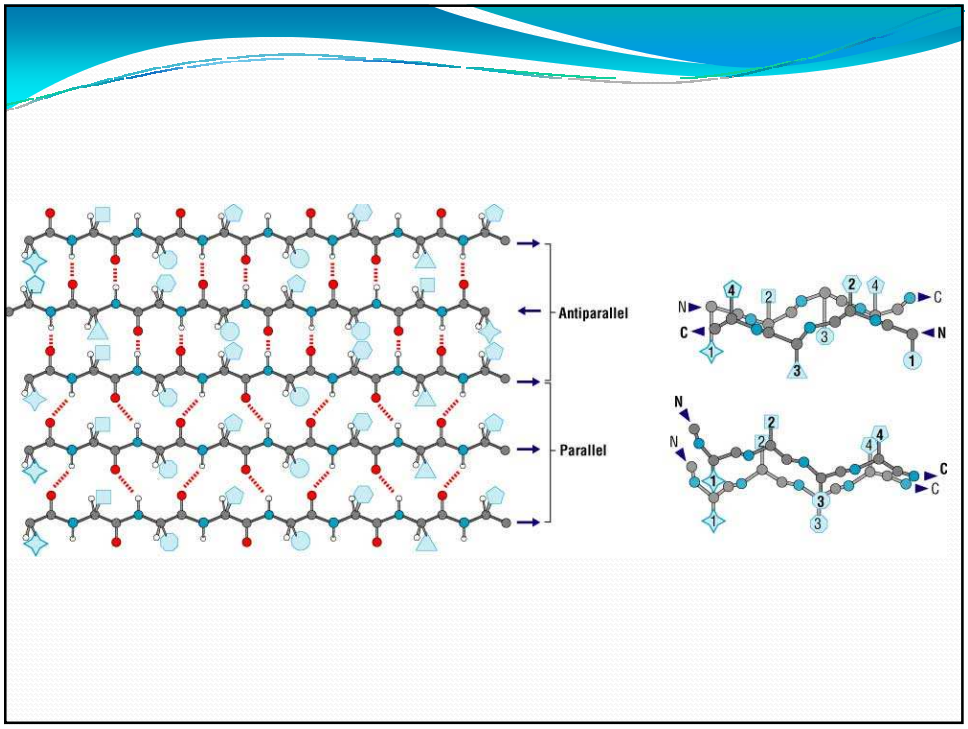
- http://www.youtube.com/watch?v=7k2KAfRsZ4Q
- http://www.youtube.com/watch?v=LKN5sq5dtW4&feature=related
- http://www.youtube.com/watch?v=JShwXBWGMyY&feature=fvw

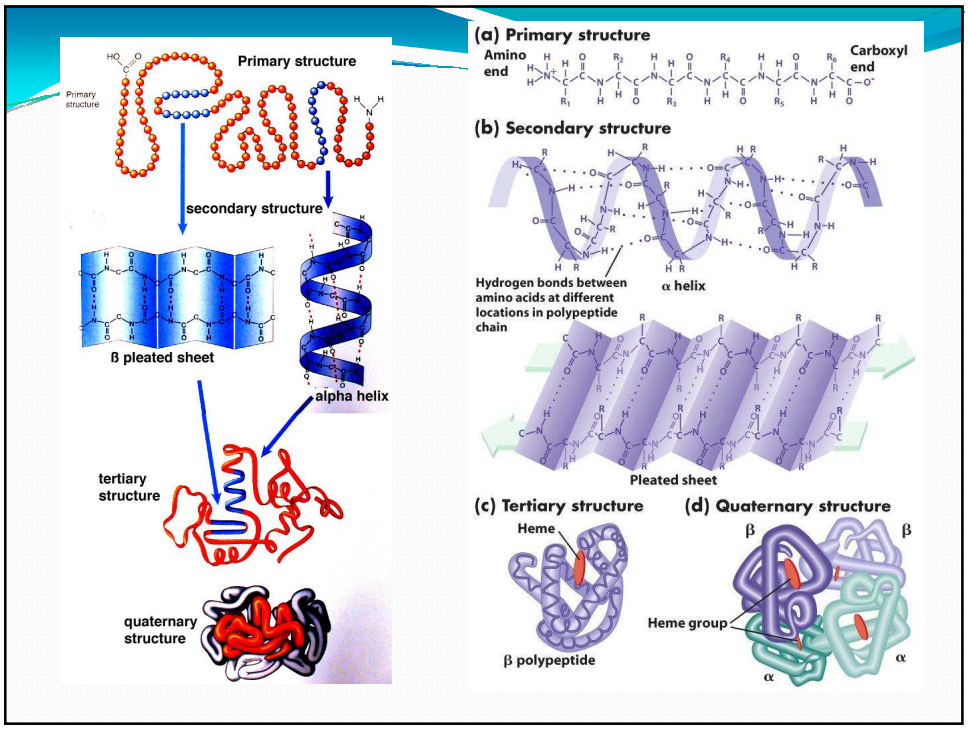
Macromolecules

- Proteins






Antiparallel
Parallel
N
C
C
N
N
C
C

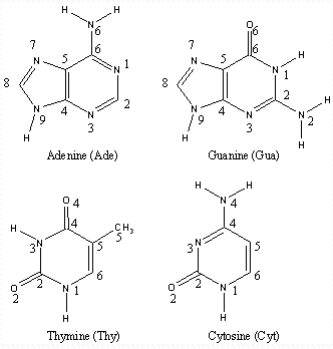

Primary structure
Primary structure
secondary structure
ß pleated sheet
alpha helix
tertiary structure
quaternary structure
(a) Primary structure
Amino end
Carboxyl end
(b) Secondary structure
Hydrogen bonds between amino acids at different locations in polypeptide chain
α helix
Pleated sheet
(c) Tertiary structure
Heme
β polypeptide
(d) Quaternary structure
β
β
Heme group
α
α

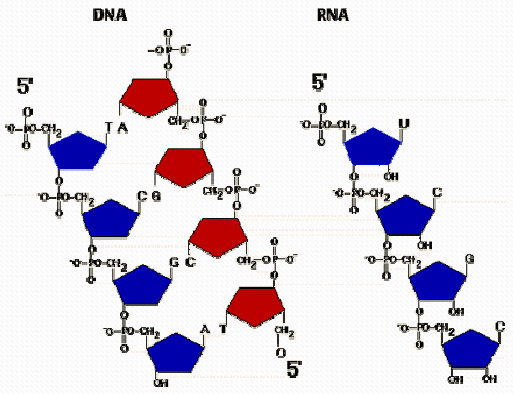
Proteins

- http://www.youtube.com/watch?v=lijQ3a8yUYQ
- http://www.youtube.com/watch?v=iaHHgEoa2c8
- http://www.youtube.com/watch?v=Ms_ehUVvKKk

Macromolecules

- Nucleic Acid

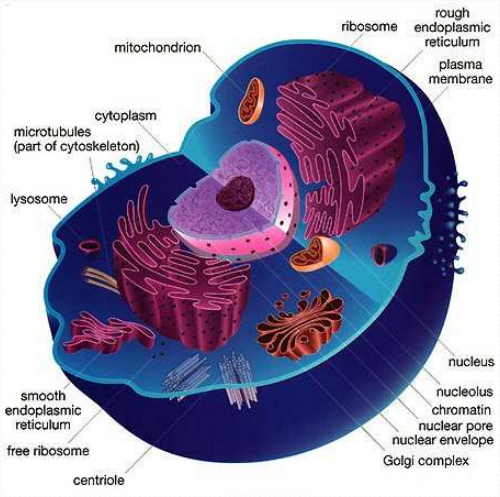




Nucleic acid

- http://www.youtube.com/watch?v=vJSmZ3DsntU&feature=related
- http://www.youtube.com/watch?v=70aoOUpMswc
- http://www.youtube.com/watch?v=oLz-IIoeZvk&feature=fvw

Structure of Cells

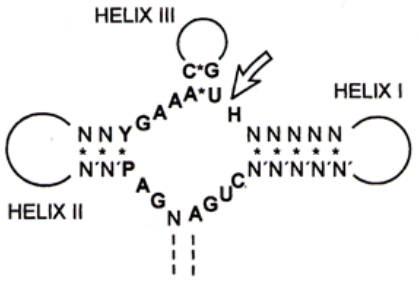


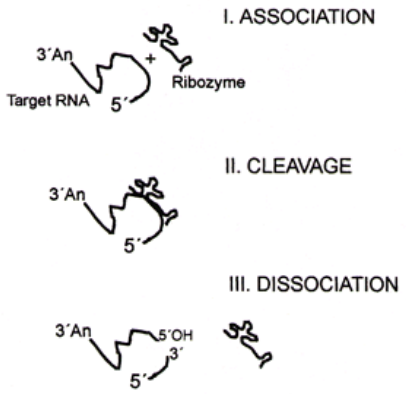
Structure the cells

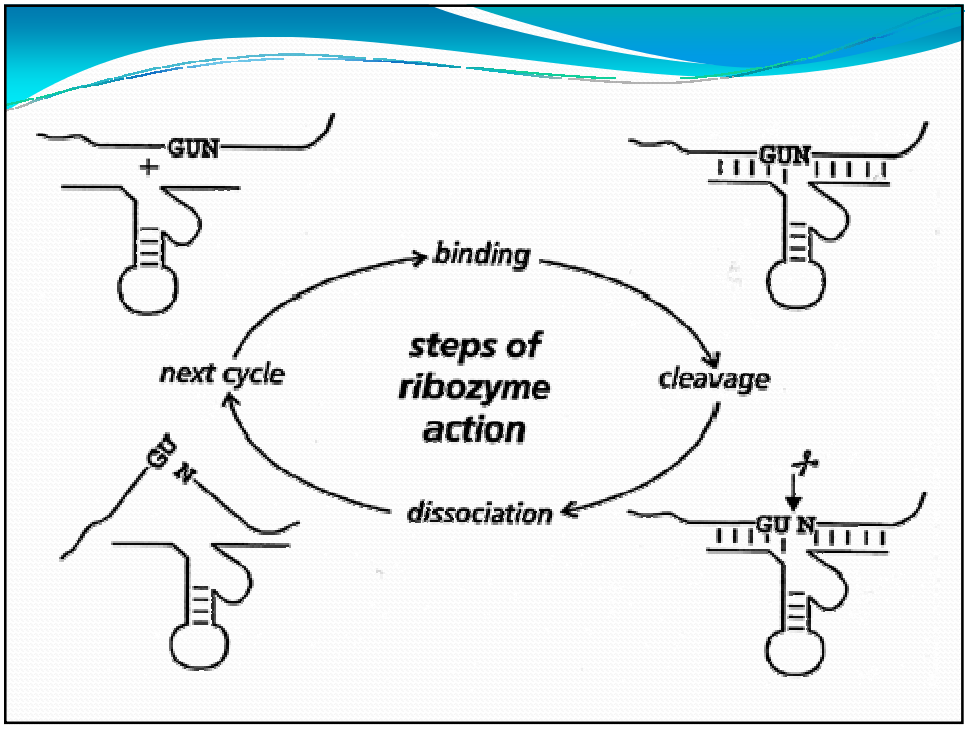
- http://www.youtube.com/watch?v=vCqQLoRaTNA
- http://www.youtube.com/watch?v=a6boqEbcJWI&feature=related
- http://www.youtube.com/watch?v=Us9TPtWK3C8

Discussion

- Where do these components come from?
- http://exploringorigins.org/







Next Lecture: Central Dogma

- DNA Replication Song…
- http://www.youtube.com/watch?v=dIZpb93NYlw

Reading Assignments

- Review: Macromolecules, Cellular Components and RNA World Hypothesis, Read http://exploringorigins.org/
- Preview: Central Dogma- Replication, Transcription and Translation. Structure of DNA, RNA and Protein
- The Lac Operon, Transcription factors.
- DNA wrapping, histone protein, DNA methylation, DNA acetylation
- What is mutation and what causes it? How does the cell try to fix this?
- http://www.sparknotes.com/biology/
- http://en.wikipedia.org/wiki/DNA_methylation