


**Chapter 9.**  
**Cellular Respiration**  
**Harvesting Chemical Energy**



AP Biology 2005-2006

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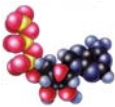
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What's the point?



**ATP**

**The Point is to Make ATP!**

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**Harvesting stored energy**

- **Energy is stored in organic molecules**
  - ♦ heterotrophs eat food (organic molecules)
    - digest organic molecules
      - ♦ serve as raw materials for building & fuels for energy
    - controlled release of energy
      - ♦ series of step-by-step enzyme-controlled reactions
  - ♦ "burning" fuels
    - carbohydrates, lipids, proteins, nucleic acids



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### Harvesting energy stored in glucose

- Glucose is the model
  - catabolism of glucose to produce ATP

**respiration**  
 glucose + oxygen → carbon dioxide + water + energy

$$C_6H_{12}O_6 + 6O_2 \rightarrow 6CO_2 + 6H_2O + ATP + \text{heat}$$

**combustion** = making heat energy by burning fuels in one step  
 fuel (carbohydrates) → CO<sub>2</sub> + H<sub>2</sub>O + heat

**respiration** = making ATP (& less heat) by burning fuels in many small steps  
 CO<sub>2</sub> + H<sub>2</sub>O + ATP (+ heat)

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### How do we harvest energy from fuels?

- Digest large molecules into smaller ones
  - break bonds & move electrons from one molecule to another
    - as electrons move they carry energy with them
    - that energy is stored in another bond, released as heat, or harvested to make ATP

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### How do we move electrons in biology?

- Moving electrons
  - in living systems, electrons do not move alone
    - electrons move as part of **H atom**

$$C_6H_{12}O_6 + 6O_2 \rightarrow 6CO_2 + 6H_2O + ATP$$


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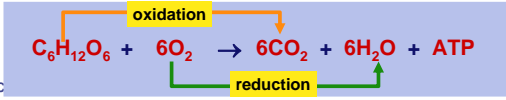
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### Coupling oxidation & reduction

- Redox reactions in respiration
  - release energy as breakdown molecules
    - break C-C bonds
    - strip off electrons from C-H bonds by removing H atoms
      - $C_6H_{12}O_6 \rightarrow CO_2$  = fuel has been oxidized
    - electrons attracted to more electronegative atoms
      - in biology, the most electronegative atom?  $\rightarrow O_2$
      - $O_2 \rightarrow H_2O$  = oxygen has been reduced
  - release energy to synthesize ATP




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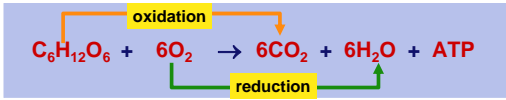
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### Oxidation & reduction

<ul style="list-style-type: none"> <li>Oxidation                             <ul style="list-style-type: none"> <li>adding O</li> <li>removing H</li> <li>loss of electrons</li> <li>releases energy</li> <li>exergonic</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>Reduction                             <ul style="list-style-type: none"> <li>removing O</li> <li>adding H</li> <li>gain of electrons</li> <li>stores energy</li> <li>endergonic</li> </ul> </li> </ul>
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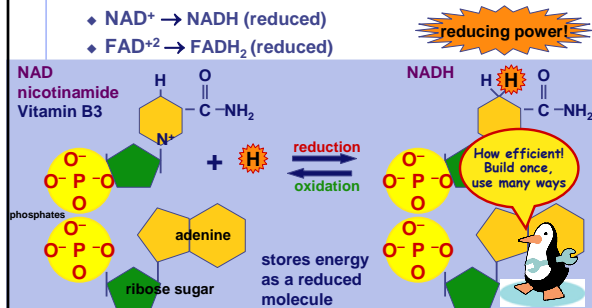
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### Moving electrons in respiration

- Electron carriers move electrons by shuttling H atoms around
  - $NAD^+ \rightarrow NADH$  (reduced)
  - $FAD^{+2} \rightarrow FADH_2$  (reduced)




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### Overview of cellular respiration

- 4 metabolic stages
  - Anaerobic respiration
    - 1. Glycolysis
      - respiration without O<sub>2</sub>
      - in cytosol
  - Aerobic respiration
    - respiration using O<sub>2</sub>
    - in mitochondria
    - 2. Pyruvate oxidation
    - 3. Kreb's cycle
    - 4. Electron transport chain



$C_6H_{12}O_6 + 6O_2 \rightarrow 6CO_2 + 6H_2O + ATP (+ heat)$

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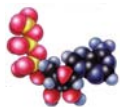
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### What's the point?



**The Point is to Make ATP!**

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### Chapter 9. Cellular Respiration

#### STAGE 1: Glycolysis



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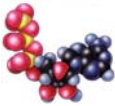
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What's the point?



**ATP**

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**Glycolysis**

- Breaking down glucose
  - "glyco - lysis" (splitting sugar)
    - glucose → → → → pyruvate  
6C 2x 3C
  - most ancient form of energy capture
    - starting point for all cellular respiration
  - inefficient
    - generate only 2 ATP for every 1 glucose
  - in cytosol
    - why does that make evolutionary sense?

MCC BP

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**Evolutionary perspective**

- Life on Earth first evolved without free oxygen (O<sub>2</sub>) in atmosphere
  - energy had to be captured from organic molecules in absence of O<sub>2</sub>
- Organisms that evolved glycolysis are ancestors of all modern life
  - all organisms still utilize glycolysis

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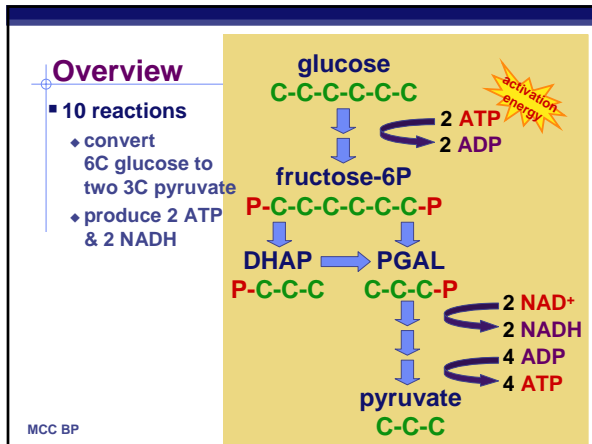
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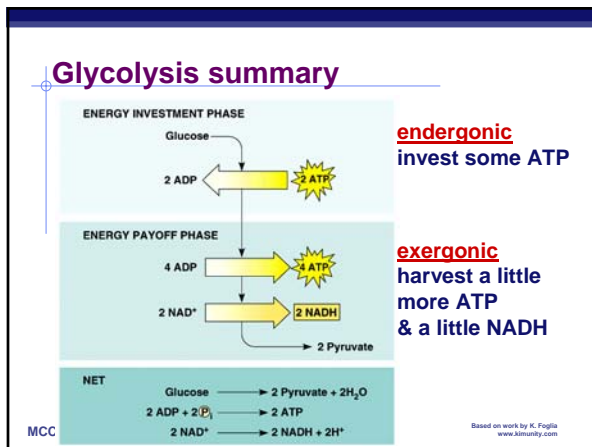
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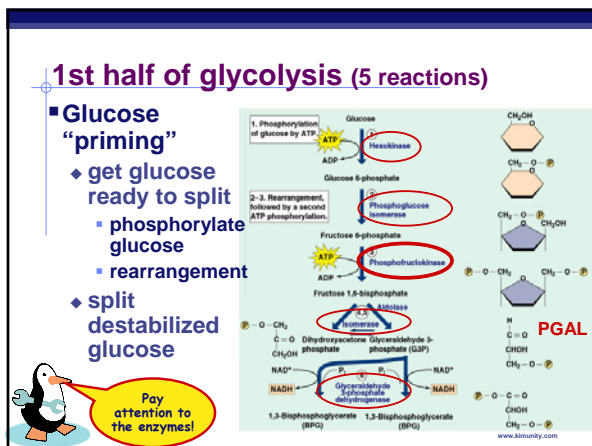
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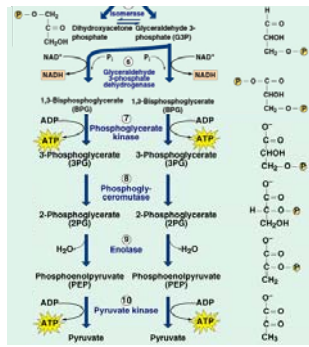
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**2nd half of glycolysis (5 reactions)**

- **Oxidation**
  - ◆ G3P donates H
  - ◆ NAD → NADH
- **ATP generation**
  - ◆ G3P → pyruvate
  - ◆ donates P
  - ◆ ADP → ATP




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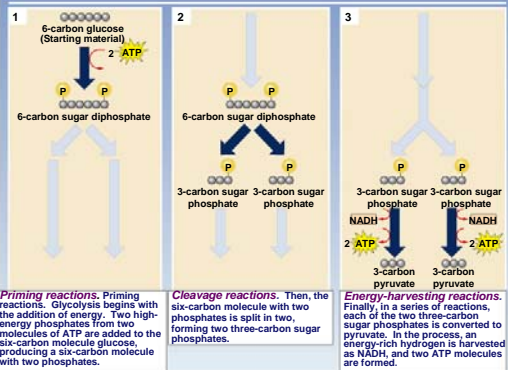
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**OVERVIEW OF GLYCOLYSIS**



**Priming reactions.** Glycolysis begins with the addition of energy. Two high-energy phosphates from two molecules of ATP are added to the six-carbon molecule glucose, producing a six-carbon molecule with two phosphates.

**Cleavage reactions.** Then, the six-carbon molecule with two phosphates is split in two, forming two three-carbon sugar phosphates.

**Energy-harvesting reactions.** Finally, in a series of reactions, each of the two three-carbon sugar phosphates is converted to pyruvate. In the process, an energy-rich hydrogen is harvested as NADH, and two ATP molecules are formed.

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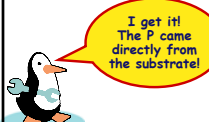
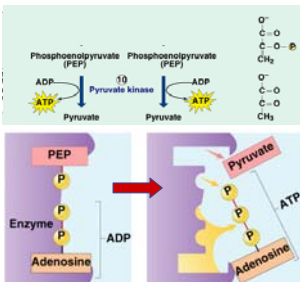
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**Substrate-level Phosphorylation**

- In the last step of glycolysis, where did the P come from to make ATP?

**P is transferred from PEP to ADP**

- kinase enzyme
- ADP → ATP




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### Energy accounting of glycolysis

$2 \text{ ATP} \rightarrow 2 \text{ ADP}$   
 $4 \text{ ADP} \rightarrow 4 \text{ ATP}$

$\text{glucose} \rightarrow \rightarrow \rightarrow \rightarrow \text{pyruvate}$   
 $6\text{C} \quad \quad \quad 2 \times 3\text{C}$

- Net gain = 2 ATP
  - some energy investment (2 ATP)
  - small energy return (4 ATP)
- 1 6C sugar  $\rightarrow$  2 3C sugars

All that work! And that's all I get?

MCC BP

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### Is that all there is?

- Not a lot of energy...
  - for 1 billion years+ this is how life on Earth survived
    - only harvest 3.5% of energy stored in glucose
    - slow growth, slow reproduction

Heck of a way to make a living!

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### We can't stop there....

- Glycolysis
 

$\text{glucose} + 2\text{ADP} + 2\text{P}_i + 2 \text{NAD}^+ \rightarrow 2 \text{ pyruvate} + 2\text{ATP} + 2\text{NADH}$

  - Going to run out of NAD<sup>+</sup>
  - How is NADH recycled to NAD<sup>+</sup>?
    - without regenerating NAD<sup>+</sup>, energy production would stop
    - another molecule must accept H from NADH

$\text{C}=\text{O} \text{ Dihydroxyacetone phosphate} \rightarrow \text{Glyceraldehyde 3-phosphate (G3P)}$   
 $\text{NAD}^+ \rightarrow \text{NADH} + \text{H}^+$   
 $\text{NADH} + \text{P}_i \rightarrow \text{NAD}^+ + \text{P}_i$   
 $\text{NADH} + \text{P}_i \rightarrow \text{NAD}^+ + \text{P}_i$   
 $\text{NADH} + \text{P}_i \rightarrow \text{NAD}^+ + \text{P}_i$   
 Glyceraldehyde 3-phosphate dehydrogenase  
 1,3-Bisphosphoglycerate (BPG) 1,3-Bisphosphoglycerate (BPG)

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### How is NADH recycled to NAD<sup>+</sup>?

- Another molecule must accept H from NADH
  - aerobic respiration
    - ethanol fermentation
    - lactic acid fermentation
  - aerobic respiration

Based on work by K. Foglia  
www.kimunity.com

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### Anaerobic ethanol fermentation

- Bacteria, yeast
 

$$\text{pyruvate} \rightarrow \text{ethanol} + \text{CO}_2$$

$3\text{C} \xrightarrow{\text{NADH}} 2\text{C} \quad 1\text{C}_2$

  - beer, wine, bread
  - at ~12% ethanol, kills yeast
- Animals, some fungi
 

$$\text{pyruvate} \rightarrow \text{lactic acid}$$

$3\text{C} \xrightarrow{\text{NADH}} 3\text{C}$

  - cheese, yogurt, anaerobic exercise (no O<sub>2</sub>)

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### Pyruvate is a branching point

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Based on work by K. Foglia  
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What's the point?



**ATP**

The Point is to Make ATP!

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Chapter 9.  
Cellular Respiration  
Oxidation of Pyruvate  
Krebs Cycle



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**Glycolysis is only the start**

- Glycolysis  
glucose  $\rightarrow \rightarrow \rightarrow \rightarrow$  pyruvate  
6C  $2 \times$  3C
- Pyruvate has more energy to yield
  - ◆ 3 more C to strip off (to oxidize)
  - ◆ if  $O_2$  is available, pyruvate enters mitochondria
  - ◆ enzymes of Krebs cycle complete oxidation of sugar to  $CO_2$

pyruvate  $\rightarrow \rightarrow \rightarrow \rightarrow$   $CO_2$   
3C 1C

MCC BP work by K. Foglia www.kmunity.com

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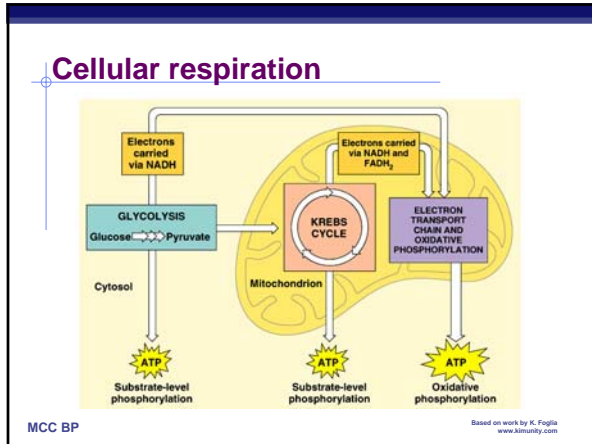
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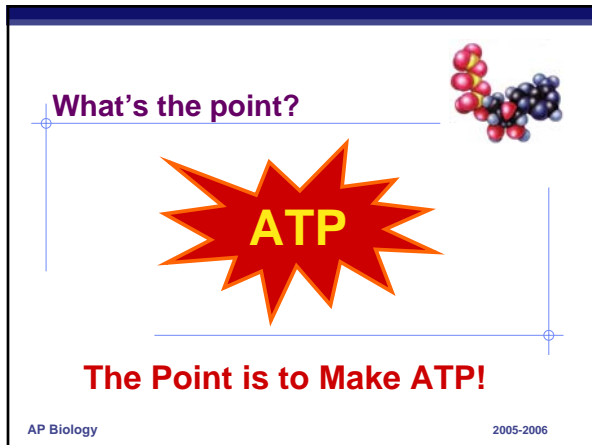
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### Oxidation of pyruvate

- Pyruvate enters mitochondria

$$2x \left[ \begin{array}{c} \text{pyruvate} \rightarrow \rightarrow \rightarrow \text{acetyl CoA} + \text{CO}_2 \\ \text{3C} \qquad \qquad \qquad \text{2C} \quad \text{1C} \\ \text{NAD} \rightarrow \text{NADH} \end{array} \right]$$

- 3 step oxidation process
- releases 1 CO<sub>2</sub> (count the carbons!)
- reduces NAD → NADH (stores energy)
- produces **acetyl CoA**

- Acetyl CoA enters Krebs cycle
- where does CO<sub>2</sub> go?

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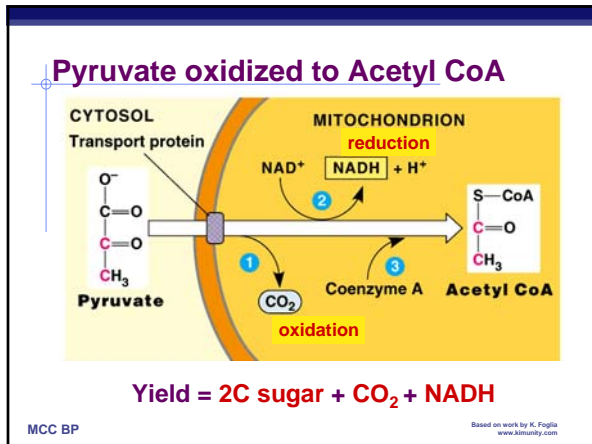
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### Krebs cycle

1937 | 1953

- aka Citric Acid Cycle
  - in mitochondrial matrix
  - 8 step pathway
    - each catalyzed by specific enzyme
    - step-wise catabolism of 6C citrate molecule
- Evolved later than glycolysis
  - does that make evolutionary sense?
    - bacteria → 3.5 billion years ago (glycolysis)
    - free O<sub>2</sub> → 2.7 billion years ago (photosynthesis)
    - eukaryotes → 1.5 billion years ago (aerobic respiration (organelles))

MCC BP Based on work by K. Foglia www.kimunity.com

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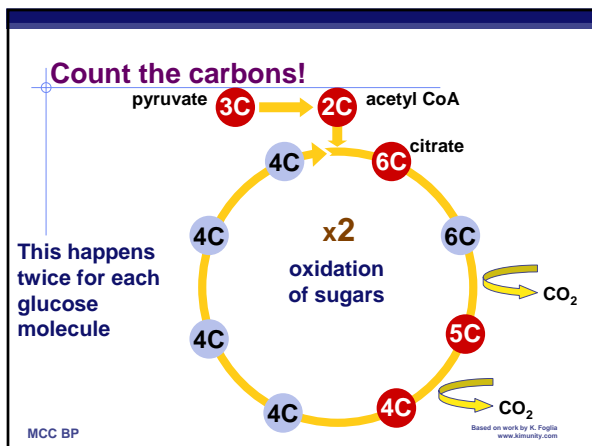
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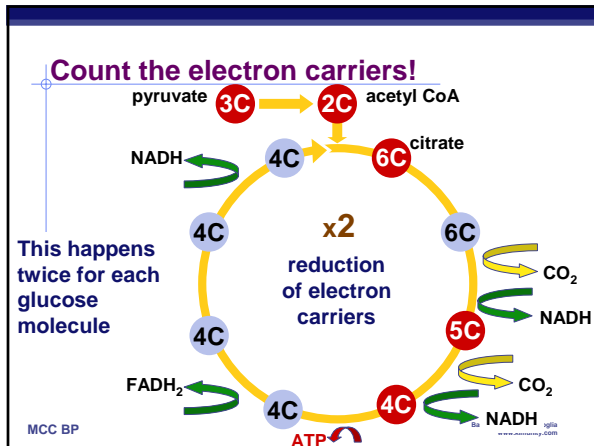
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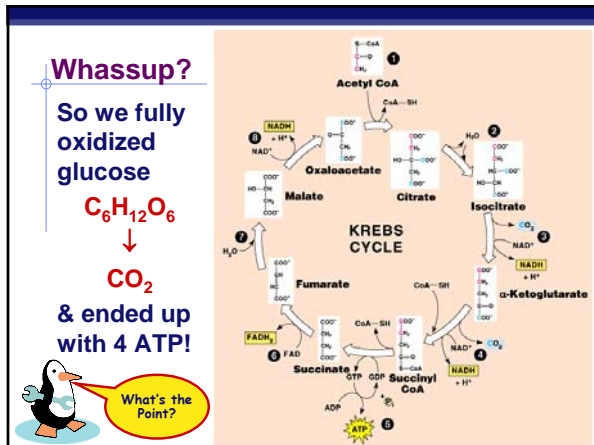
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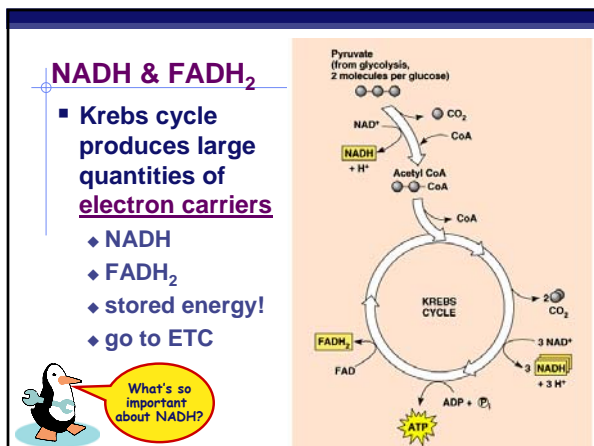
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**Chapter 9.**  
**Cellular Respiration**  
**Electron Transport Chain**



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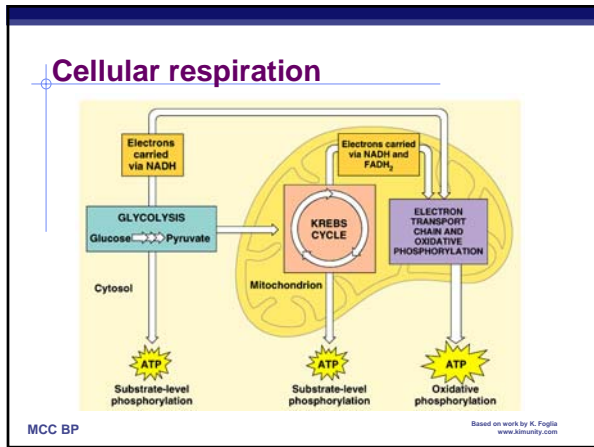
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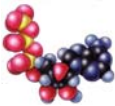
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**What's the point?**



**ATP**

**The Point is to Make ATP!**

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**ATP accounting so far...**

- Glycolysis → **2 ATP**
- Kreb's cycle → **2 ATP**
- Life takes a lot of energy to run, need to extract more energy than **4 ATP!**

**There's got to be a better way!**



Based on work by K. Foglia  
www.kimunity.com

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**There is a better way!**

- **Electron Transport Chain**
  - ◆ series of molecules built into inner mitochondrial membrane
    - mostly transport proteins
  - ◆ transport of electrons down ETC linked to ATP synthesis
  - ◆ yields **~34 ATP** from 1 glucose!
  - ◆ only in presence of O<sub>2</sub> (aerobic)



Based on work by K. Foglia  
www.kimunity.com

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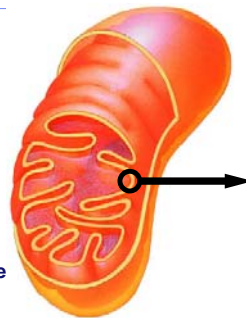
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**Mitochondria**

- **Double membrane**
  - ◆ outer membrane
  - ◆ inner membrane
    - highly folded cristae\*
    - fluid-filled space between membranes = intermembrane space
  - ◆ matrix
    - central fluid-filled space



**\* form fits function!**

Based on work by K. Foglia  
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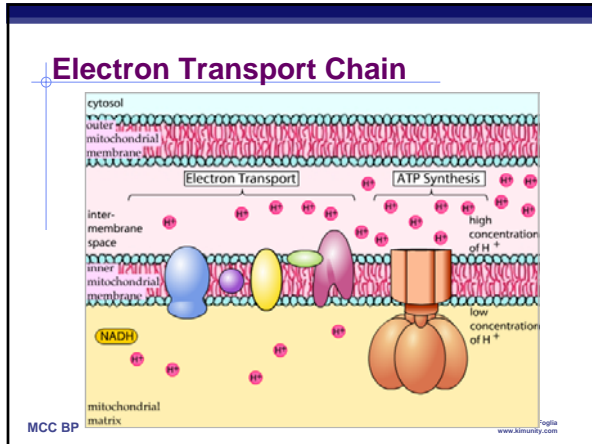
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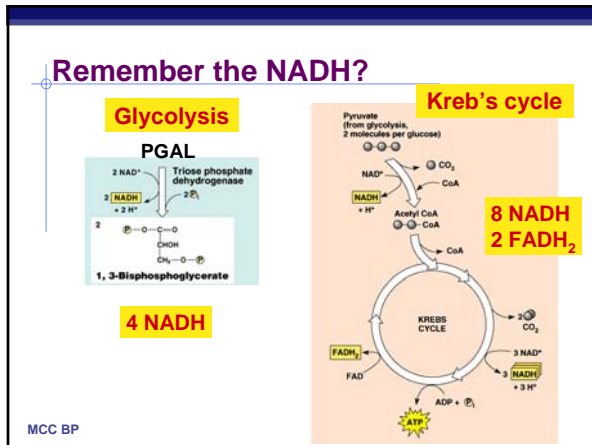
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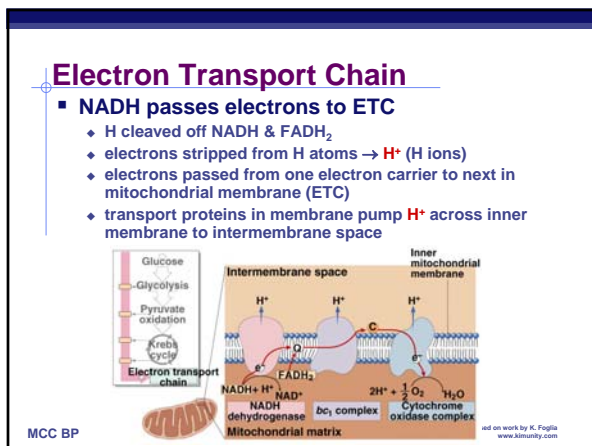
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### ATP synthesis

- Chemiosmosis couples ETC to ATP synthesis
  - build up of  $H^+$  gradient just so  $H^+$  could flow through ATP synthase enzyme to build ATP

So that's the point!

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### Peter Mitchell

1961 | 1978

- Proposed chemiosmotic hypothesis
  - revolutionary idea at the time

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### Cellular respiration

Maximum per glucose: About 38 ATP

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### Summary of cellular respiration

$C_6H_{12}O_6 + 6O_2 \rightarrow 6CO_2 + 6H_2O + \sim 36 \text{ ATP}$

- Where did the glucose come from?
- Where did the  $O_2$  come from?
- Where did the  $CO_2$  come from?
- Where did the  $H_2O$  come from?
- Where did the ATP come from?
- What else is produced that is not listed in this equation?
- Why do we breathe?

MCC BP Based on work by K. Foglia  
www.kimunity.com

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### Taking it beyond...

- What is the final electron acceptor in electron transport chain?  
 $O_2$
- So what happens if  $O_2$  unavailable?
  - ETC backs up
  - ATP production ceases
  - cells run out of energy
  - and you die!

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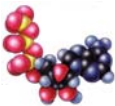
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### What's the point?



**The Point is to Make ATP!**

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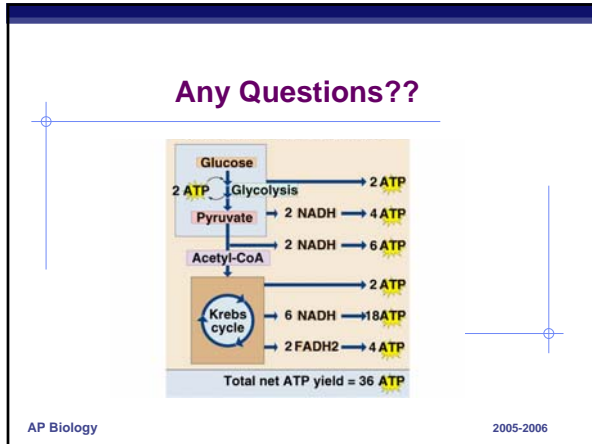
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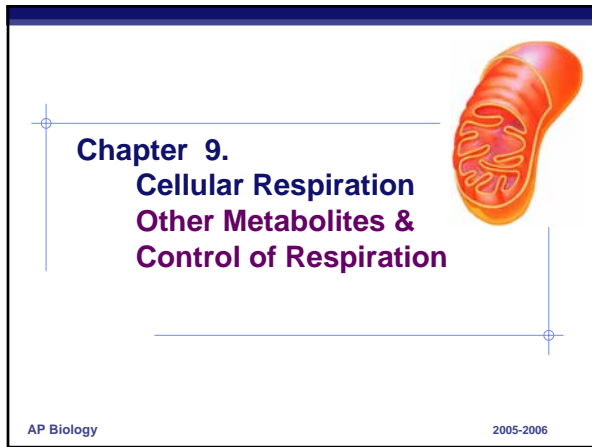
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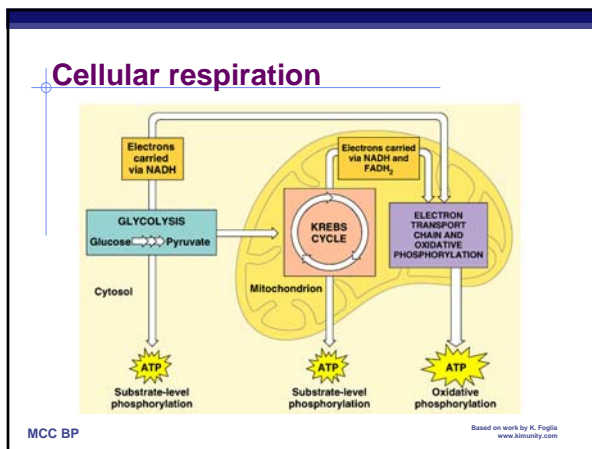
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### Beyond glucose: Other carbohydrates

- Glycolysis accepts a wide range of carbohydrates fuels
  - ♦ polysaccharides → → → glucose  
hydrolysis
    - ex. starch, glycogen
  - ♦ other 6C sugars → → → glucose  
modified
    - ex. galactose, fructose

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### Beyond glucose: Proteins

- Proteins → → → → amino acids  
hydrolysis

**waste** → amino group = waste product excreted as ammonia, urea, or uric acid

→ **glycolysis Krebs cycle** carbon skeleton = enters glycolysis or Krebs cycle at different stages

MI Based on work by K. Foglia www.kimunity.com

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### Beyond glucose: Fats

- Fats → → → → glycerol & fatty acids  
hydrolysis
- ♦ glycerol (3C) → → PGAL → → glycolysis
- ♦ fatty acids → 2C acetyl → acetyl → Krebs cycle  
groups coA cycle

**glycerol** → enters glycolysis as PGAL

→ **fatty acids** enter Krebs cycle as acetyl CoA

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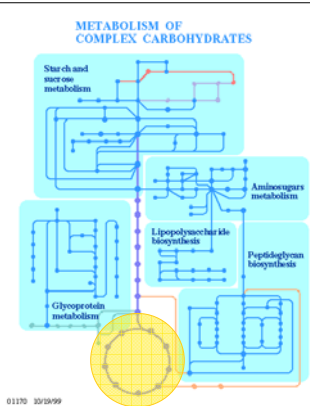
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### Carbohydrate Metabolism

- The many stops on the Carbohydrate Line

gluconeogenesis



METABOLISM OF COMPLEX CARBOHYDRATES

Starch and sucrose metabolism, Lipopolysaccharide biosynthesis, Glycoprotein metabolism, Amino sugar metabolism, Peptidoglycan biosynthesis

MCC BP 01170 10/10/99

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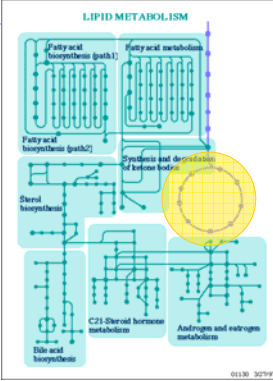
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### Lipid Metabolism

- The many stops on the Lipid Line



LIPID METABOLISM

Fatty acid biosynthesis (path 1), Fatty acid metabolism, Fatty acid biosynthesis (path 2), Synthesis and degradation of ketone bodies, Steroid biosynthesis, C21 Steroid hormone metabolism, Androgen and estrogen metabolism, Ether acid biosynthesis

MCC BP 01130 10/27/97

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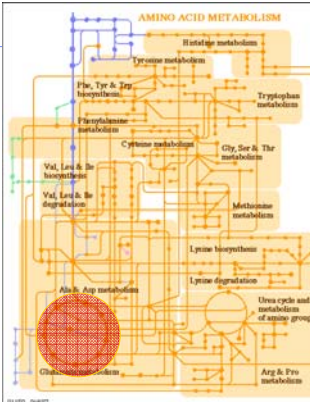
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### Amino Acid Metabolism

- The many stops on the AA Line



AMINO ACID METABOLISM

Histidine metabolism, Tyrosine metabolism, Phe, Tyr & Trp biosynthesis, Tryptophan metabolism, Phenylalanine metabolism, Cysteine metabolism, Gly, Ser & Thr metabolism, Val, Leu & Ile biosynthesis, Methionine metabolism, Val, Leu & Ile degradation, Lysine biosynthesis, Lysine degradation, Ala & Asp metabolism, Urea cycle and metabolism of amine groups, Glutamate metabolism, Arg & Pro metabolism

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### Nucleotide Metabolism

- The many stops on the GATC Line

The diagram illustrates the complex pathways of nucleotide metabolism. It is divided into three main sections: Nucleoside sugars metabolism (top left), Pyrimidine metabolism (top right), and Purine metabolism (bottom right). A central yellow circle represents the GATC line, with numerous red arrows indicating regulatory points where various metabolites can inhibit or stimulate different enzymes in the pathways.

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### Control of Respiration

#### Feedback Control

The diagram shows the metabolic pathway from Glucose to the Electron Transport Chain and Oxidative Phosphorylation. Key feedback control points are highlighted: Phosphofruktokinase is stimulated by AMP and inhibited by Fructose-1,6-bisphosphate. Citrate inhibits Phosphofruktokinase. Acetyl CoA inhibits the conversion of Pyruvate to Acetyl CoA. The diagram also shows the conversion of ATP to AMP and the entry of Acetyl CoA into the Krebs Cycle.

AP Biology

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### Feedback Inhibition

- Regulation & coordination of production
  - production is self-limiting
  - final product is inhibitor of earlier step
    - allosteric inhibitor of earlier enzyme
  - no unnecessary accumulation of product

The diagram shows a linear metabolic pathway: A → B → C → D → E → F → G. Each step is catalyzed by an enzyme (enzyme 1 to enzyme 6). A yellow arrow indicates that the final product, G, acts as an allosteric inhibitor of enzyme 1, providing feedback control to prevent overproduction.

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allosteric inhibitor of enzyme 1

work by K. Foglia  
www.kimunity.com

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### Respond to cell's needs

- Key points of control
  - phosphofructokinase
    - allosteric regulation of enzyme
      - "can't turn back" step before splitting glucose
    - AMP & ADP stimulate
    - ATP inhibits
    - citrate inhibits

**Why is this regulation important?**  
Balancing act: availability of raw materials vs. energy demands vs. synthesis

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### A Metabolic economy

- Basic principles of supply & demand regulate metabolic economy
  - balance the supply of raw materials with the products produced
  - these molecules become feedback regulators
    - they control enzymes at strategic points in glycolysis & Krebs cycle
      - AMP, ADP, ATP
        - regulation by final products & raw materials
      - levels of intermediates compounds in the pathways
        - regulation of earlier steps in pathways
      - levels of other biomolecules in body
        - regulates rate of siphoning off to synthesis pathways

MCC BP Based on work by K. Foglia www.kofoglia.com

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### It's a Balancing Act

- Balancing synthesis with availability of both energy & raw materials is essential for survival!
  - do it well & you survive longer
  - you survive longer & you have more offspring
  - you have more offspring & you get to "take over the world"

**Acetyl CoA is central to both energy production & synthesis make ATP or store it as fat**

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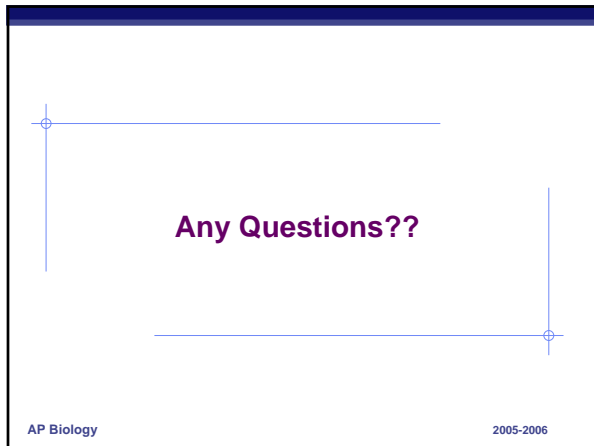
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