How Cells Make ATP: Energy-releasing Pathways

Lecture Outline

I. Aerobic respiration is a redox process
   A. Glucose contains energy that can be converted to ATP
   B. Process uses oxygen; called aerobic respiration
   C. Aerobic respiration is a redox process
      1. \( C_6H_{12}O_6 + 6 O_2 + 6 H_2O \rightarrow 6 CO_2 + 12 H_2O + \text{Energy} \)
      2. Water is both a reactant and a product
      3. Glucose is oxidized to form carbon dioxide
      4. Oxygen is reduced forming water
      5. The electrons produced are used to form ATP

II. Aerobic respiration has four stages
   A. Glycolysis
      1. Glucose is converted to 2 3-carbon molecules of pyruvate
      2. ATP and NADH are formed
      3. Occurs in the cytosol
   B. Formation of acetyl coenzyme A (acetyl CoA)
      1. Pyruvate is converted into acetyl CoA
      2. NADH is produced
      3. Carbon dioxide is a waste product
      4. Occurs in the mitochondrion
   C. The citric acid cycle
      1. Acetyl CoA combines with oxaloacetate forming citrate
      2. Citrate undergoes conversions, ultimately reforming oxaloacetate
      3. Carbon dioxide is a waste product
      4. ATP, NADH and FADH₂ are produced
   D. The electron transport system and chemiosmosis
      1. Electrons which originated in glucose are transferred via NADH and FADH₂ to a chain of electron acceptors
      2. Hydrogen ions are pumped across the inner mitochondrial membrane
      3. Via chemiosmosis, ATP is produced
   E. Reaction types
      1. Dehydrogenation
         a. Hydrogens are transferred to a coenzyme (NAD⁺ or FAD)
      2. Decarboxylations
         a. Carboxyl groups are removed from the substrate as carbon dioxide
      3. Preparation reactions
         a. Rearrangements of molecules in preparation for decarboxylations or dehydrogenations
   F. In glycolysis, glucose yields two pyruvates
      1. Glycolysis means "sugar splitting"
      2. One 6-carbon molecule is converted to two 3-carbon molecules
      3. Occurs in the cytosol
4. Occurs in aerobic or anaerobic conditions
5. A series of reactions; each catalyzed by a different enzyme
   a. The first phase of glycolysis requires an initial investment of ATP
      1). First steps of glycolysis
      2). Glucose $\rightarrow$ fructose-1,6-bisphosphate$\rightarrow$ 2 glyceraldehyde-3-phosphate (G3P)
      3). 2 ATP molecules are invested in this step
   b. The second phase of glycolysis yields NADH and ATP
      1). G3P is converted into 2 pyruvate molecules
      4). 4 molecules of ATP are produced (net yield 2)
      5). 2 molecules of NADH are produced

G. Pyruvate is converted to acetyl CoA
   1. A carboxyl group is removed from pyruvate (carbon dioxide is produced)
   2. NADH is produced
   3. The acetyl group joins with coenzyme A forming acetyl CoA
   4. Coenzyme A is made from pantothenic acid

H. The citric acid cycle oxidizes acetyl CoA
   1. Also known as TCA cycle or Krebs cycle
   2. Occurs in the mitochondrion
   3. 8 steps, all enzyme mediated
      a. Acetyl CoA combines with oxaloacetate$\rightarrow$ citrate and CoA
      b. Series of steps, ultimately reforming oxaloacetate
      c. 6 NADH and 2 FADH$_2$ are produced
      d. 2 ATP molecules are produced
   4. All of the energy of the glucose molecule is carried by NADH and FADH$_2$

I. The electron transport chain is coupled to ATP synthesis
   1. The electron transport chain transfers electrons from NADH and FADH$_2$ to oxygen
      a. Electrons $\rightarrow$ FMN$\rightarrow$ a series of cytochromes and CoQ
      b. Electrons lose energy as they pass through the chain
      c. Hydrogen ions (protons) are passed into the intermembrane space of the mitochondrion
      d. Electrons are finally passed to oxygen forming water
   2. The chemiosmotic model explains the coupling of ATP synthesis to electron transport
      a. A proton gradient is formed across the inner mitochondrial membrane
      b. In 1961, Peter Mitchell proposed the chemiosmotic model, and received the Nobel Prize in 1978
         1). A proton gradient is formed by the electron transport chain; protons are pumped into the intermembrane space of the mitochondrion
      c. Protons diffuse through the channels formed by the enzyme complex ATP synthase
      d. Movement of protons catalyzes production of ATP
III. Aerobic respiration of one glucose yields a maximum of 36 to 38 ATPs
   A. Glycolysis produces 2 ATP molecules
   B. 2 ATP molecules are produced in the citric acid cycle
   C. Remainder of ATP is produced in the electron transport system (32 or 34)
      1. Maximum yield of ATP from NADH is 3 per molecule
      2. NADHs from glycolysis may produce fewer ATPs due to the necessity of transport of NADH across the mitochondrial membrane
      3. Maximum yield of ATP from FADH₂ is 2
   D. Total ATP yield per molecule of glucose is 36-38
   E. Efficiency is about 40%; the remaining energy is disseminated as heat

IV. Nutrients other than glucose also provide energy
   A. Humans gain more energy from oxidation of fatty acids than glucose
      1. Lipids contain 9 kcal per gram
      2. Lipids are broken down and glycerol enters glycolysis; fatty acids are converted to acetyl CoA and enter the citric acid cycle
   B. Proteins are broken down to amino acids
      1. Amino acids are deaminated (the amino group is removed)
      2. Amino groups are converted to urea and excreted
      3. The remaining carbon chain enters at various points
      4. Proteins contain about 4 kcal per gram

V. Cells regulate aerobic respiration
   A. ATP synthesis continues until ADP stores are depleted
   B. Enzyme regulation is important
   C. An important control point is phosphofructokinase

VI. Anaerobic respiration and fermentation do not require oxygen
   A. Anaerobic respiration
      1. Various inorganic substances serve as the final electron acceptor
      2. Yields only the two ATP molecules from glycolysis
      3. Seen in some bacteria
   B. Alcohol fermentation and lactate fermentation are inefficient
      1. Alcoholic fermentation produces ethanol
         a. Pyruvate is converted to ethanol to regenerate NAD⁺
         b. Ethanol is a potentially toxic waste product
         c. Yeast carry out alcoholic fermentation when oxygen deprived
      2. Bacteria and some fungi carry out lactate fermentation
         a. Pyruvate is converted to lactate to regenerate NAD⁺
         b. Strenuous exercise in mammals results in lactate fermentation as well
      3. Yields only the two ATP molecules from glycolysis