Notes 11/20

Tuesday, November 20, 2007
9:04 AM

Notes 1120

Audio recording started: 9:04 AM Tuesday, November 20, 2007

Fermentation, Gluconeogenesis, and Pyruvate DH Complex Part I

Nov. 20, 2007

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1

Fermentation

- General term to describe a process that extracts energy (as ATP) without consuming oxygen nor changing the [NAD+] or [NADH]
- The H:C ratio of the reactants and products remains the same
- Carried out by wide variety of organisms

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2

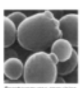
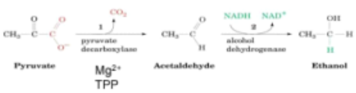


Figure 17-25

Alcohol Fermentation



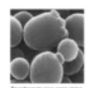


Figure 17-25

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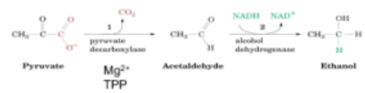

3

Alcohol Fermentation Balance Sheet

Glucose + 2ADP + 2 P_i -->
2 ethanol + 2CO_2 + 2ATP +2H_2O

Anaerobic respiration does not utilize the full energy potential of glucose

Aerobic respiration is best way to utilize full energy of glucose

Alcohol Fermentation Balance Sheet

Glucose + 2ADP + 2 P_i -->
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Anaerobic fermentation does not utilize the full energy potential of glucose

4

Figure 17-26

Thiamine pyrophosphate

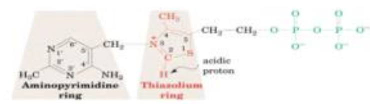
(TPP aka vitamin B1)

↖helps delocalize neg. charge

- Deficiency leads to beriberi
- Yeast needs this to catalyze reactions

Figure 17-26

Thiamine pyrophosphate



- Deficiency leads to beriberi

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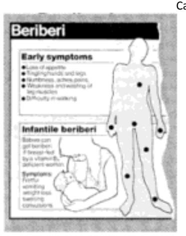
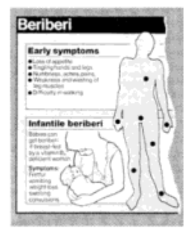


Caused by TPP deficiency from:

- Malnutrition
- Alcoholism



- Malnutrition
- Alcoholism

6

Liver Alcohol Dehydrogenase (LADH)

- Animals don't convert acetaladehyde to ethanol
- Animals convert ethanol to acetaldehyde using LADH
  Metabolizes ethanol in our livers
  Flora in our gut sometimes produces ethanol
- Too much ethanol can lead to veisalgia
  - Veisalgia - hangover

Liver Alcohol Dehydrogenase (LADH)

- Animals don't convert acetaldehyde to ethanol
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- Too much ethanol can lead to veisalgia

7

Veisalgia = hangover

- Norwegian *kveis* (uneasiness following debauchery) + Greek *algia* (pain)
- Symptoms: dehydration, fatigue, headache, nausea, diarrhea, weakness, anxiety, irritability
- NADH builds up and inhibits gluconeogenesis in the liver
- B_{12} deficiency

- Ethanol is dyeretic -> water loss ->decrease blood volume, decrease brain size (headache), irritates stomach (GI system)
- Each ethanol molecule uses 2 NADH molecules so NAD $^+$ is accumulated…. check this?
- Buildup of NAD^+ slows down gluconeogenisis
- Leads to hypoglycemia

Veisalgia = hangover

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8

Missing: picture of heart

Gluconeogenesis = "new sugar"

- Formation of glucose from pyruvate, lactate, glycerol, certain amino acids
- Occurs in all animals, plants, fungi, and microbes
- In mammals, mostly occurs in liver

Lactate is from anaerobic fermentation in mammals

Gluconeogenesis = "new sugar"

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9

Gluconeogenesis vs Glycolysis

- Gluconeogenisis utilizes glycolytic enzymes
- HK, PFK, PK are replaced by other enzymes
  - These enzymes catalyze reactions by high negative ΔG to enzymes that are more thermodynamically ideal
- Pyruvate --> Oxaloacetate --> PEP
  - Pyruvate: 3 C compound
  - Oxaloacetate: 4 C compound
  - PEP: 3 C compound
  - Enzymes:
    - Pyruvate Carboxylase
    - PEP carboxykinase (PEPCK)

Gluconeogenesis vs Glycolysis

- Gluconeogenesis utilizes glycolytic enzymes
- HK, PFK, PK are replaced
- Pyruvate-->Oxaloacetate-->PEP
  - Pyruvate carboxylase
  - PEP carboxykinase (PEPCK)

10

Figure 23-7

Different than glycolysis shown in red

Gluconeogenisis bottom to top

Different enzymes are generally used in gluconeogenisis when the reverse glycolysis step has high negative ΔG and therefore a high positive ΔG for gluconeogenisis

Having different enzymes for forward and reverse reaction allows them to be regulated independently

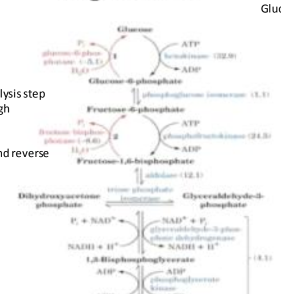
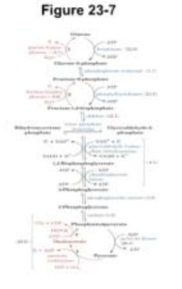


Figure 23-7



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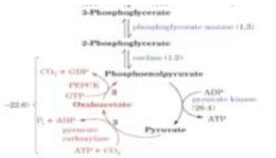

Last Fate of Pyruvate We'll Discuss: Aerobic Oxidation

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12

Aerobic Respiration

- Aerobic phase of catabolism is called respiration
- Cellular respiration: molecular process by which cells consume O_2 and produce CO_2
- 3 major stages

13

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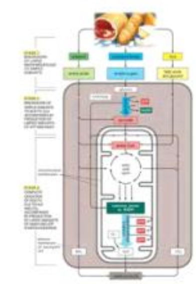
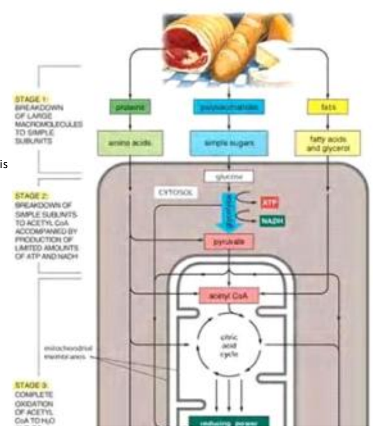
Oxidize pyruvate to H_2O and CO_2



14

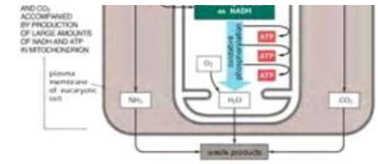
3 major stages of aerobic respiration

Source of pyruvate is not just from glycolysis



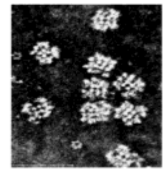
Oxidation of organic compounds to acetyl-coenzyme A is catalyzed by the Pyruvate Dehydrogenase Multienzyme Complex (PDC)

15



PDC

- Pyruvate + CoA + NAD^+ --> acetyl-CoA + CO_2 + NADH
- Bridges glycolysis (anaerobic metabolism) to TCA cycle (aerobic metabolism)
- mitochondria of eukaryotic cells, and cytosol of prokaryotic cells
- Cluster of 3 enzymes



16

Oxidation of organic compounds to acetyl-coenzyme A is catalyzed by the Pyruvate Dehydrogenase Multienzyme Complex (PDC)

PDC consists of 3 enzymes

- Pyruvate dehydrogenase (E_1)
  - TPP cofactor
- Dihydrolipoyl transacetylase (E_2)
  - Lipoamide cofactor, CoA coenzymes
- Dihydrolipoyl dehydrogenase (E_3)
  - FAD cofactor, NAD^+ coenzyme
- Eukaryotic PDC is complex!

17

PDC

- Pyruvate + CoA + NAD^+ --> acetyl-CoA + CO_2 + NADH

- Cluster of enzymes
- Bridges glycolysis (anaerobic metabolism) to TCA cycle (aerobic metabolism)
- mitochondria of eukaryotic cells, and cytosol of prokaryotic cells
- Catalyzes oxidative decarboxylation of pyruvate

Advantages of a multienzyme complex

- Diffusion of substrates is minimized between active sites
- Minimize side rxns
- Potential for coordinate control of activity

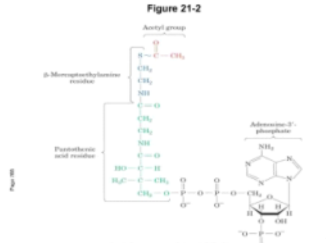
18

- Noncovalently associated cluster of enzymes
- Cluster of 3 enzymes (picture shows more than 3 since more than one cluster clumped together)

Mising Slide: PDC Consists of 3 enzymes

- Pyruvate dehydogenase (E_1)
  - TPP cofactor
- Dihydorlipoyl transacetylase (E_2)
  - Lipoamide cofactor, CoA coenzymes
- Dihydrolipoyl dehydrogenase (E_3)
  - FAD cofactor, NAD^+ coenzyme

Figure 21-2



19

Acetyl-CoA Formation Occurs in Five Rxns

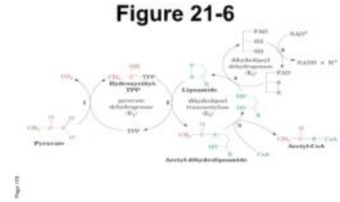
- E_1 catalyzes rxns 1 & 2
- E_2 catalyzes rxn 3
- E_3 catalyzes rxn 4 & 5

20

Missing Slide: Advantages of multienzyme complex

- Diffusion of substrates is minimized between active sites
- Minimize side reactions
- Potential for coordinate control of activity

Figure 21-6



Pyruvate + CoA + NAD^+ --> acetyl-CoA + CO_2 + NADH

21

Figure 21-2

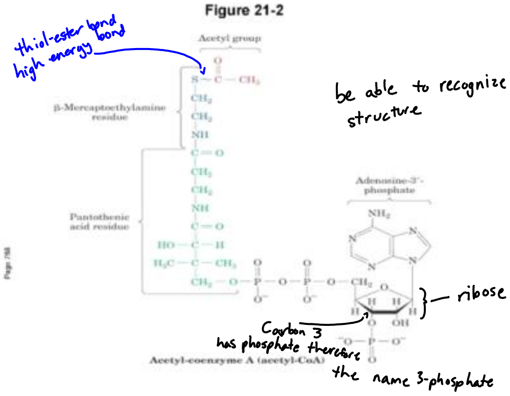


Table 21-1

Cofactor	Location	Function
Thiamine pyrophosphate (TPP)	Bound to E_1	Decarboxylates pyruvate, yielding a hydroxyethyl-TPP carbanion
Lipoic acid	Covalently linked to a Lys on E_2 (lipoamide)	Accepts the hydroxyethyl carbanion from TPP as an acetyl group
Coenzyme A (CoA)	Substrate for E_2	Accepts the acetyl group from acetyl-dihydrolipoamide
Flavin adenine dinucleotide (FAD)	Bound to E_3	Reduced by dihydrolipoamide
Nicotinamide adenine dinucleotide (NAD^+)	Substrate for E_3	Reduced by $FADH_2$

Page 771

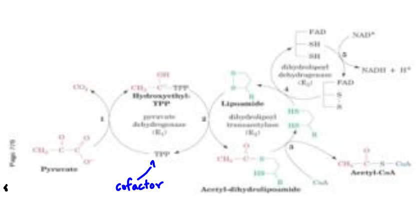
22

Missing Slide: Acetyl-CoA formation Ocurs in Five Reactions

- E_1 catalyzes reactions 1 & 2
- E_2 catalyzes reaction 3
- E_3 catalyzes reaction 4 & 5

Pyruvate (3 C compound) to acetyl-CoA (2 carbon compound)
CO_2 is byproduct
NADH is produced too (so NAD^+ is used in reaction)

Figure 21-6



Overall Reaction:
Pyruvate + CoA + NAD^+ --> acetyl-CoA + CO_2 + NADH

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Page 771

Did not cover from here on

Figure 21-7

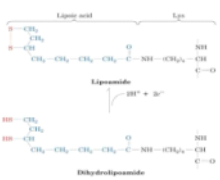

Figure 21-17a

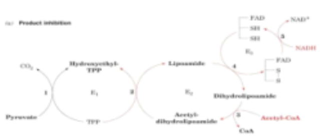

Figure 21-17b