Notes 11/30

Friday, November 30, 2007
9:59 AM

Notes 1130

Audio recording started: 10:02 AM Friday, November 30, 2007

Notes 1130

Audio recording started: 10:25 AM Friday, November 30, 2007

Glyoxylate Pathway, Electron Transport, and Oxidative Phosphorylation

Nov. 30, 2007

Announcements

- Quiz 6 next week
- Students in section 1D, Tuesday 1-2pm (Midge) will take the quiz with Rebecca in WGYH CS24 (Tues. Dec., 4th) . Ask Rebecca for directions to the room.
- Final (rooms will be announced later)
  - Lec. 1: Tues. Dec. 11, 3 PM to 6 PM
  - Lec. 2: Thurs. Dec. 13, 3 PM to 6 PM
  - 300 points
    - About 100 points on "older" material
    - About 200 points on material covered since midterm

Genius is 1% inspiration and 99% perspiration. Accordingly a genius is often merely a talented person who has done all of his or her homework.
--Thomas Edison

When you get into a tight place and everything goes against you, till it seems as though you could not hang on a minute longer, never give up then, for that is just the place and time that the tide will turn.
--Harriet Beecher Stowe

Success seems to be connected with action. Successful people keep moving. They make mistakes, but they don't quit.
---Conrad Hilton

The only question to ask yourself is, how much are you willing to sacrifice to achieve this success?
--Larry Flynt

What some students are doing to get high scores in this class

- Studying every day
- Attending office hours with questions
- Actively attending lecture (staying awake, writing notes, asking questions)
- Asking questions immediately after lecture
- Reading Voet & Voet for deeper understanding
- Practice drawing structures and mechanisms over and over and over and over…
- In summary, the successful students are active in their education

FINAL SLIDES:

Glyoxylate Pathway, Electron Transport, and Oxidative Phosphorylation

Nov. 30, 2007

1

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Overview

- Glyoxylate pathway
- Electron Transport and Oxidative Phosphorylation

Overview

- Clarification of previous topics
- Glyoxylate pathway
- Electron Transport and Oxidative Phosphorylation

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For clarification

Anaplerotic reactions
- Pyruvate carboxylase: liver, kidney
- PEP CK: heart, skeletal muscle
- PEP carboxylase: many types of cells of plants, yeast, bacteria
- Malic enzyme: widely distributed in eukaryotes and prokaryotes

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Missing slide: slide 8

Now the homolactic fermentation balance sheet makes sense

½ rxn of NAD^+

$NAD^+ + 2e^- + H^+ \longrightarrow NADH$

More clarification

Overall Balance Sheet of Glycolysis (from lecture notes)

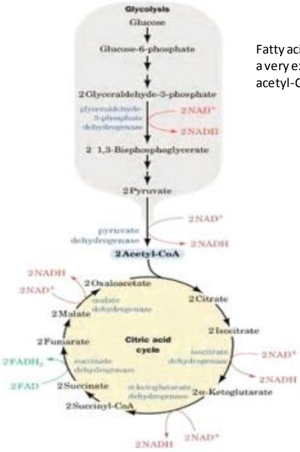
Glucose + $2NAD^+$ + 2ADP + $2P_i$ -->

2 pyruvate + + 2NADH + $2H^+$ + 2ATP + $2H_2O$

Voet & Voet

Glucose + $2NAD^+$ + 2ADP + $2P_i$ -->

Vertebrates cannot convert fatty acids to carbohydrates



Fatty acids are converted to acetyl-CoA. Pyruvate to Acetyl-CoA is a very exergonic reaction to the point it is not reversible from acetyl-CoA to pyruvate.

OAA can be converted into PEP, so why can't this be used for gluconeogenesis in vertebrates?

- OAA + GTP <--> PEP + CO_2 + GDP

# of carbons? I do not understand...

Glyoxylate Pathway

- Also called glyoxylate cycle

- Also called glyoxylate cycle, glyoxylate bypass, blyoxylate shunt
- Bypasses oxidative decarboxylation and thiol ester hydrolysis reactions of TCA cycle.
- Retains carbons to make OAA, but foregoes the production of NADH and GTP

2 pyruvate + + 2NADH + $4H^+$ + 2ATP + $2H_2O$

Either is correct. From now on, and to keep things simple, use the V&V version.

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Now the homolactic fermentation balance sheet makes sense

Glucose + 2ADP + $2P_i$ -->
2 lactate + 2ATP + $2H_2O$ + $2H^+$

Please don't agonize over balancing a water molecule or a proton. Know the intermediates, ATP, CO2, Pi, etc.

Know the redox rxns of NAD+ and FAD.

Please understand what the molecules are doing and why they are present.

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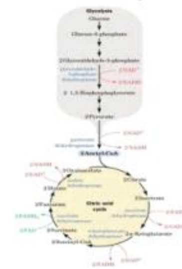
Vertebrates cannot convert fatty acids to carbohydrates



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OAA can be converted into PEP, so why can't this be used for gluconeogenesis in vertebrates?

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Glyoxylate Pathway

- Produces four-carbon compounds from acetate
- Seen in germinating seeds of plants, certain microbes that grow on acetate, but not in vertebrates
- Occurs in glyoxysomes of plants   Plants have own organelle called glyoxysomes (where glyoxylate occurs)
- Involves several TCA cycle enzymes and two others:
  - Isocitrate lyase
  - Malate synthase
- Coordinately regulated with TCA cycle
- Net formation of succinate, OAA, and other TCA cycle intermediates

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Glyoxylate pathway produces 4-carbon compounds from acetate

- Net conversion of acetate to oxaloacetate

- 2 Acetyl-CoA (2C cmpd) + 2NAD$^+$ + FAD --> OAA (4C cmpd) + 2CoA + 2NADH + FADH$_2$ + 2H$^+$

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Figure 23-10 The glyoxylate cycle.

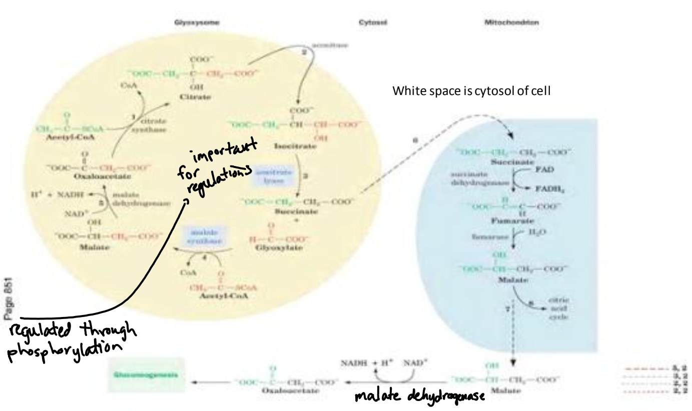

Figure 23-10 The glyoxylate cycle.

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Where can the glyoxylate pathway be found?


- Rumen microbes
- Germinating seeds
- *E. coli*
- *Mycobacterium tuberculosis*
- *Saccharomyces cerevisiae* yeast
- *Candida albicans*

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TCA and glyoxylate cycles are coordinately regulated

- Continuous interchange of intermediates between mitochondria, glyoxysomes, cytosol

TCA and glyoxylate cycles are coordinately regulated

- Continuous interchange of intermediates between mitochondria, glyoxysomes, cytosol in plants
- Isocitrate lyase is regulated by reversible phosphorylation

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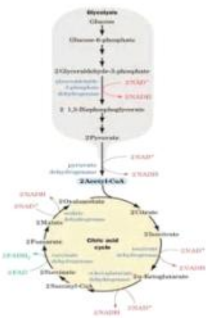
Electron Transport and Oxidative Phosphorylation

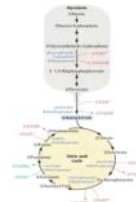


- Electrons are removed from glucose during its oxidation

combustion rxn

- $C_6H_{12}O_6 + 6O_2$--> $6CO_2 + 6H_2O$
- $\Delta G^{o\prime}$= -2823 kJ/mol

Electron Transport and Oxidative Phosphorylation



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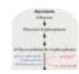
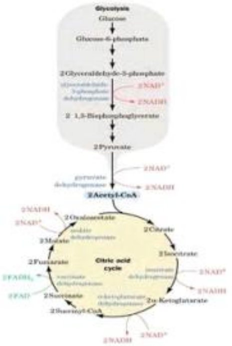
Electron Transport and Oxidative Phosphorylation



Glucose carbon atoms are oxidized

$C_6H_{12}O_6 + 6H_2O$ --> $6CO_2 + 24H^+ + 24e^-$

Electron Transport and Oxidative Phosphorylation



Glucose carbon atoms are oxidized

$C_6H_{12}O_6 + 6H_2O \dashrightarrow 6CO_2 + 24H^+ + 24e^-$

Molecular oxygen is reduced

$6O_2 + 24H^+ + 24e^- \dashrightarrow 12H_2O$

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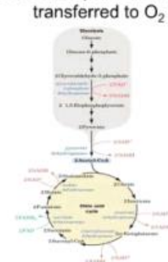
The 12 electron pairs are not directly transferred to O_2



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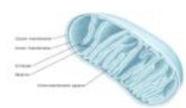
Electrons are passed into the electron-transport chain

- Reoxidation of NADH and $FADH_2$
- Over 10 redox centers are sequentially used
- Subsequently, protons are expelled from the mitochondria
- pH gradient forms between intermembrane space and matrix
- Energy stored in pH gradient is used to make ATP via oxidative phosphorylation



20

The 12 electron pairs are not directly transferred to O_2

10 pairs are found with NADH
2 pairs found with $FADH_2$

Ones in blue are involved in electron transfers

$4 \times 6 = 24e^-$
12 e^- pairs

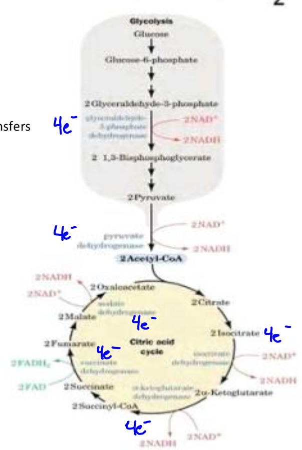
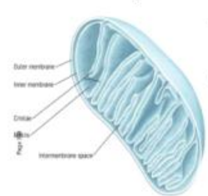


Figure 22-2b Mitochondria. (*b*) Cutaway diagram of a mitochondrion.



- Contains enzymes that mediate oxidative metabolism
- PDH, TCA cycle enzymes, enzymes catalyzing fatty acid oxidation, and players in electron transport & oxidative phosphorylation

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Cytoplasmic shuttle systems transport NADH electrons across the inner mitochondrial membrane

- Glycerophosphate shuttle in insects
- Malate-aspartate shuttle in mammals

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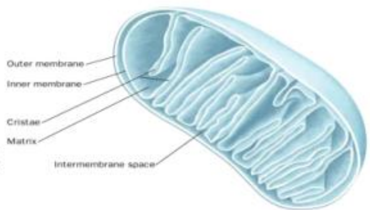
Figure 22-2b Mitochondria. (*b*) Cutaway diagram of a mitochondrion.



Outer membrane is relatively permeable and has things called porins that allow small size things to pass through.

Inner membrane is much more selective
- CO_2, O_2, and H_2O can go across inter-membrane space without carrier

Missing Slide: Cytoplasmic shuttle symstems transport NADH electrons across the inner mitochonrial membrane
- Glycerophosphate shuttle in insects
- Malate-aspartate shuttle in mammals

Figure 22-7 The malate–aspartate shuttle.