Notes 11/16

Friday, November 16, 2007
10:10 AM

Glycolysis

Nov. 16, 2007

1

Announcements

- Glycolysis and TCA handouts available
- Midterms are available
  - Regrades
  - Key
  - Feedback
- No class, discussion, office hours Thurs. and Fri. next week
- No quiz next week

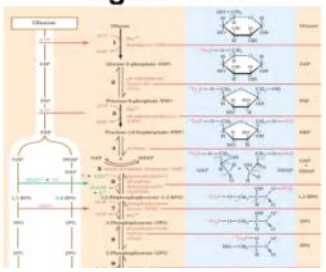
2

Overview

- Glycolysis
  - Pick up where we left off
  - Fates of pyruvate
  - Closer look at each step
  - Regulation and control

3

Figure 17-3



FINAL NOTES

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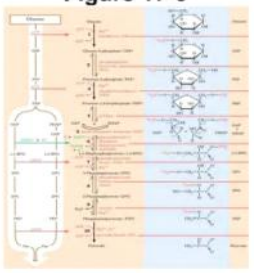

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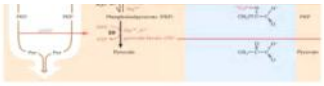

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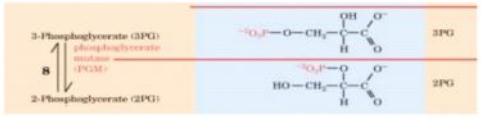
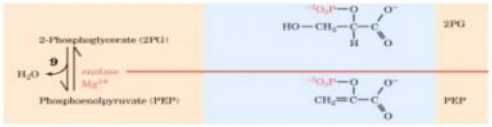


- Mutase because shifts functional group on same molecule
- Energy difference between 3PG and 2PG is small
- 2 step reaction (1 intermediate is 2,3-bisphosphoglycerate (BPG) which increases hemoglobin affinity for oxygen

5

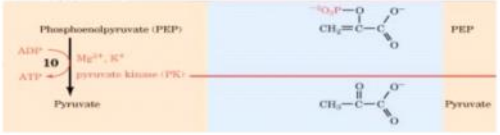
Figure 17-3



- Dehydration reaction of 2PG into PEP
- Enolase (makes enol pyruvate) needs Mg^{2+}

6

Figure 17-3



- Transfer of phosphoryl group
- Kinase - transfers phosphoryl grop from ATP
- Enzyme pyruvate kinase is named for reverse reaction... don't get confused over name
- -31.5kJ/mol nearly irreversible spontaneous reaction
- Energy required to make ATP on STP is 3.5kJ/mol

7

Figure 17-3

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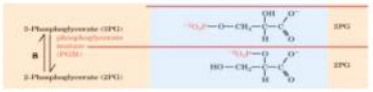

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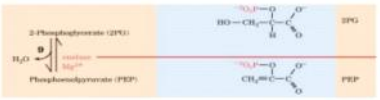

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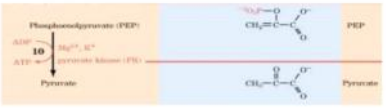
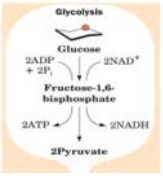


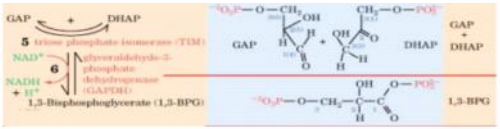
7

Overall Chemical Strategy of Glycolysis



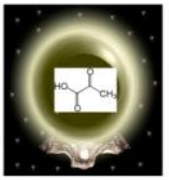
- Add phosphoryl groups to glucose
- Convert phosphorylated intermediates into cmpds w/ high energy
- Couple high energy cmpd hydrolysis with ATP synthesis

8



8

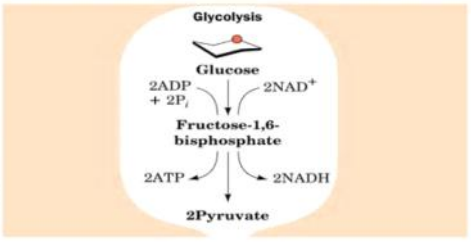
Fates of Pyruvate



- 3 Catabolic Routes
  - Aerobic oxidation
  - Lactic acid fermentation
  - Ethanol fermentation
- Many anabolic routes

9

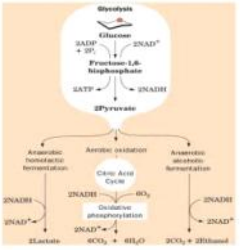
Figure 17-1



- Add phosphoryl groups to glucose
- Convert phosphorylate dintermediates into compounds with high energy
- Couple high energy compound hydrolysis with ATP synthesis

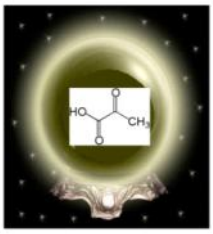
9

Figure 17-1
NAD+ must be recycled



10

Fates of Pyruvate



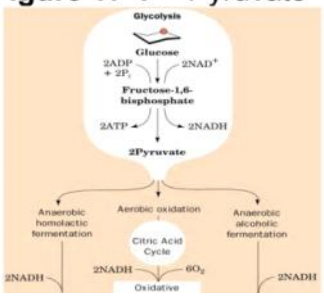
- 3 Catabolic Routes
  - Aerobic oxidation
  - Lactic acid fermentation
  - Ethanol fermentation
- Many anabolic Routes

10

Now for a Deeper Understanding of the Preparatory Phase of Glycolysis

11

Figure 17-1 Pyruvate

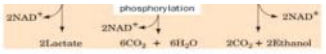


- When pyruvate goes through reactions it helps recycle NAD^+
- Pyruvate can undergo anarobic homolactic fermintation
  - Pyruvate becomes 2 lactates
- Yeast cells in absence of oxygen will undergo anarobic alcohol fermentation
  - Pyruvate becomes CO_2 and ethanol
- Cytric cycle, TCA, and Crebs cycle all mean same thing:
  - Pyruvate to CO_2 and H_2O

12

Step 1: Hexokinase

- Phosphorylation of glucose
- Rxn:
- Glucose + ATP --> G6P + ADP + H^+



11

Now for a Deeper Understanding of the Preparatory Phase of Glycolysis

12

Step 1: Hexokinase

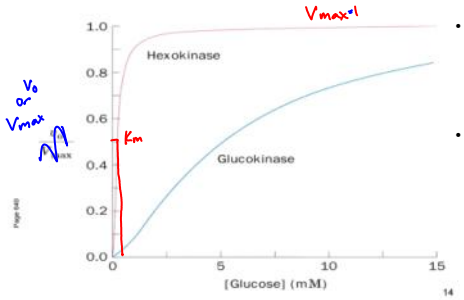
- Phosphorylation of glucose
- Rxn:
- Glucose + ATP --> G6P + ADP + H^+

- Coupled reaction
- When [ATP] is very high it acts as a competitive inhibitor
- Most kinases use proximity effects for reaction (including hexokinase)
- Conformational change

13

Figure 18-23

Glucokinase and hexokinase are isozymes. They catalyze same reaction but are not the same



14

- Hexokinase:
  - All cells
  - Obeys M-M kinetics (hyperbolic)
  - K_m<0.1mM
  - G6P inhibits it
- Glucokinase
  - Liver cells
  - Displays sigmoidal kinetics
  - $K_{0.5}$<5mM
  - Not inhibited by G6P
  - Monomeric so sigmoidal kinetics is puzzling
  - Phosphorylates glucose and makes glycogen

Step 2: Phosphoglucose Isomerase

- Isomerization of G6P

Hexokinase and Glucokinase are Isozymes

- Hexokinase
  - All cells
  - obeys M-M kinetics (hyperbolic)
  - K_m < 0.1 mM
  - G6P inhibits it
- Glucokinase
  - Liver cells
  - Displays sigmoidal kinetics
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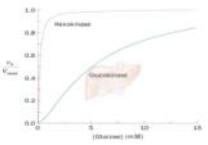

12

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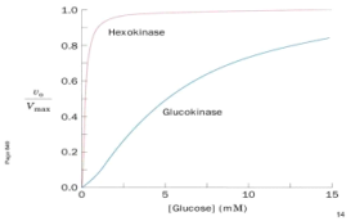


14

Step 2: Phosphoglucose Isomerase

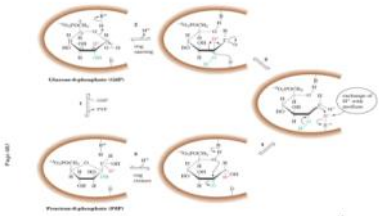
- Isomerization of G6P
- Rxn

Mg^{2+}

- G6P <--> F6P

15

Figure 17-6



16

- Rxn

Mg^{2+}

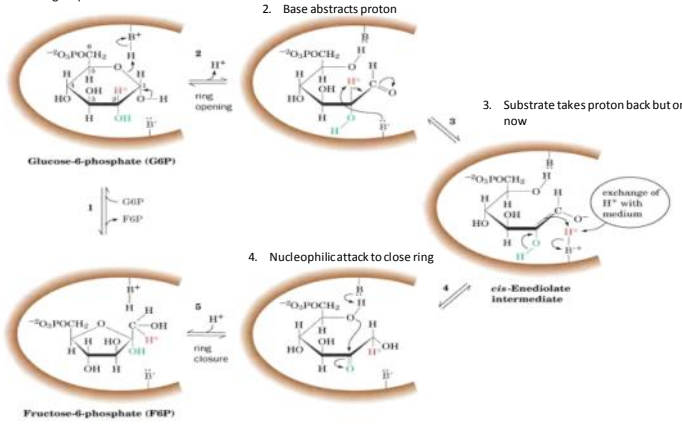
- G6P <--> F6P

- Converts aldose glucose-6-phosphate to ketose fructose-6-phosphate
- G6P and F6P is generally in ring structure so enzyme must open rings
- Acid base

15

Figure 17-6

1. Ring is opened
2. Base abstracts proton
3. Substrate takes proton back but on carbon 1 now
4. Nucleophilic attack to close ring
5. Product released from active site and enzyme regenerates



Page 587

16

Step 3: Phosphofructokinase (PFK)

- Phosphorylation of F6P
- Rxn

Mg^{2+}

- F6P + ATP --> F1,6P + ADP + H^+

- Functinos far from equilibrium
- Catalyzes RDS
- Homotetramer
  - Has 4 subunits and each subunit is identical
  - Has 2 states: R<-->T

17

Regulation of PFK

Positive Effectors	Negative Effectors	Other regulatory mechanisms
AMP or ADP	ATP	F6P availability
P_i, NH_4^+	Citrate	
F2,6P (except in plants and bacteria)	H^+	

18

Effectors of PFK in Heart Muscle
- Inhibitors
  - ATP
  - Citrate
  - PEP (phosphyl enol pyruvate)-2nd to last enzyme in glycolysis
- Deinhibitors (not same as activator) reverses the effect of inhibition.
- Deinhibitors reverse the effect of inhibitory concentrations of ATP
  - ADP, AMP
  - F1,6P,F2,6P,F6P
- F6P is homotropic allosteric effector

Step 3: Phosphofructokinase

- Phosphorylation of F6P
- Rxn:

Mg^{2+}

F6P + ATP --> F1,6P + ADP + H^+

- Functions far from equilibrium
- Catalyzes RDS
- Homotetramer
- R <--> T

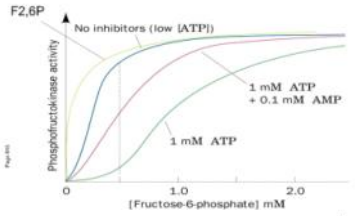
17

Effectors of PFK in Heart Muscle

- Inhibitors
  - –ATP
  - –Citrate
  - –PEP
- Deinhibitors reverse the effect of inhibitory concentrations of ATP
  - –ADP, AMP
  - –F1,6P, F2,6P, F6P

18

Figure 17-33 modified



19

Figure 18-24

Role of F2,6P in regulation of PFK

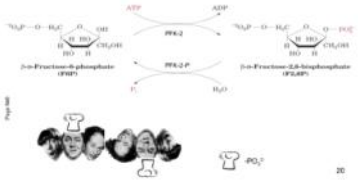


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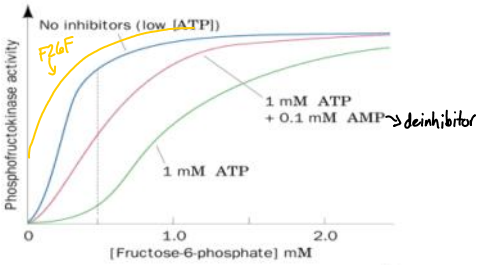
Figure 17-33



19

Figure 18-24

Role of F2,6P in regulation of PFK

(not intermediate)

PFK-2 has 2 forms
- Phosphorylated and dephosphorylated

PFK-2 is different from PFK

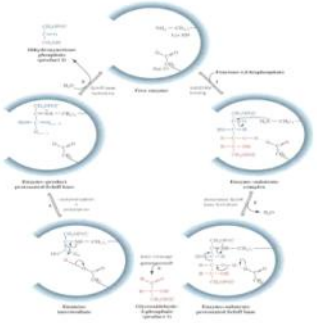
20

Step 4: Aldolase

- Cleavage of Fructose 1,6-bisphosphate into trioses
- Rxn
- F1,6P <--> dihydroxyacetone phosphate + glyceraldehyde 3-phosphate

21

Figure 17-9



22

Step 5: Triose phosphate isomerase

- Isomerization of dihydroxyacetone phosphate to glyceraldehyde 3-phosphate
- Rxn
- DHAP <--> G3P

23

Score card for the preparatory phase of glycolysis

- Glucose + 2 ATP --> 2 G3P + 2 ADP + 2 H^+

24