Chem 352 - Lecture 8
Carbohydrate Metabolism
Part II: Gluconeogenesis, Pentose Phosphate Pathway & Glycogen Metabolism

1

Review

Questions:

A. What is the net reaction equation for glycolysis?

2-1

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B. What is the metabolic purpose for glycolysis?

2-2

Review

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A. What is the net reaction equation for glycolysis?

B. What is the metabolic purpose for glycolysis?

C. Under anaerobic conditions, what are the options for reoxidizing the reduced NADH + H^+?

2-3

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  - Glycolysis is a catabolic pathway that coverts glucose to pyruvate.
  - The pathway also produces a net of 2 ATP's from ADP and P_i, plus it reduces 2 NAD^+ to NADH + H^+.

$$\text{Glucose} + 2\,NAD^+ + 2\,ADP + 2\,P_i \longrightarrow 2\,\text{Pyruvate} + 2\,NADH + H^+ + 2\,ATP + 2\,H_2O$$

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3-1

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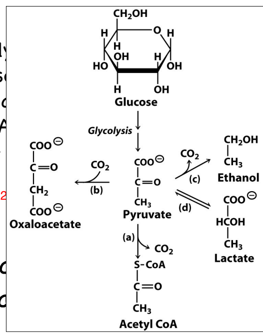

3-2

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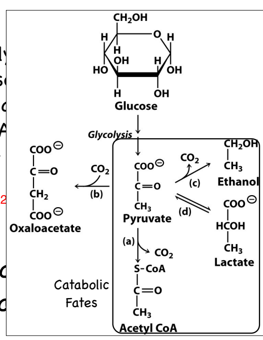

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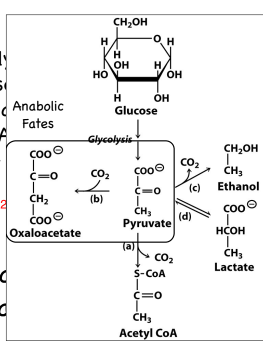

3-4

3-5

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4-1

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- Next we will look at an anabolic pathway that is used to synthesize glucose from smaller molecules.
  - We will also look at the various fates for glucose.
    - Release into the bloodstream
    - Conversion to pentoses along with the production of reduced NADPH + H^+ for biosynthetic pathways
    - Storage as glycogen or starch

4-2

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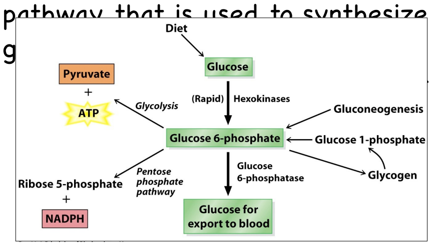

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- These various pathways have competing purposes and therefore must be regulated.
  - Catabolism versus Anabolism
  - Regulation of the flow of material is crucial in order to prevent "futile cycling"

5-1

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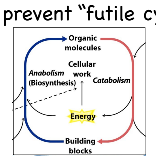

5-2

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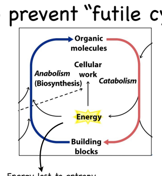

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Gluconeogenesis

- Gluconeogenesis means "new glucose"
  - Many, but not all of the reactions used in glycolysis are also used in gluconeogenesis.

6-1

6-2

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Table 11.1 The reactions and enzymes of glycolysis

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3. Fructose 6-phosphate + ATP ⟶ Fructose 1,6-*bis*phosphate + ADP + $H^{\oplus}$	Phosphofructokinase-1
4. Fructose 1,6-*bis*phosphate ⇌ Dihydroxyacetone phosphate + Glyceraldehyde 3-phosphate	Aldolase
5. Dihydroxyacetone phosphate ⇌ Glyceraldehyde 3-phosphate	Triose phosphate isomerase
6. Glyceraldehyde 3-phosphate + $NAD^{\oplus}$ + P_i ⇌ 1,3-*Bis*phosphoglycerate + NADH + $H^{\oplus}$	Glyceraldehyde 3-phosphate dehydrogenase
7. 1,3-*Bis*phosphoglycerate + ADP ⇌ 3-Phosphoglycerate + ATP	Phosphoglycerate kinase
8. 3-Phosphoglycerate ⇌ 2-Phosphoglycerate	Phosphoglycerate mutase
9. 2-Phosphoglycerate ⇌ Phosphoenolpyruvate + H_2O	Enolase
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6-3

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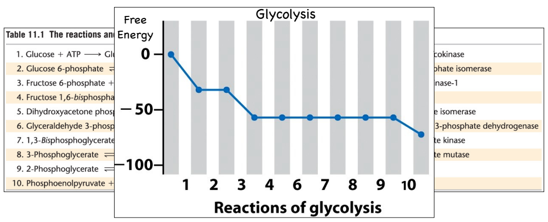

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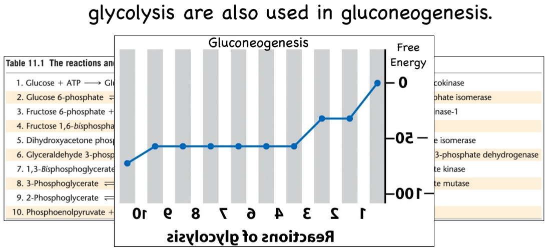

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Gluconeogenesis

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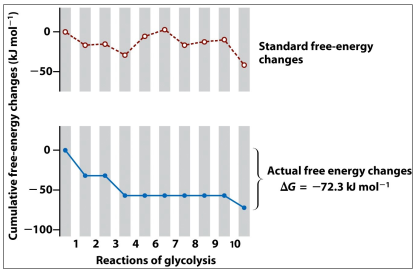

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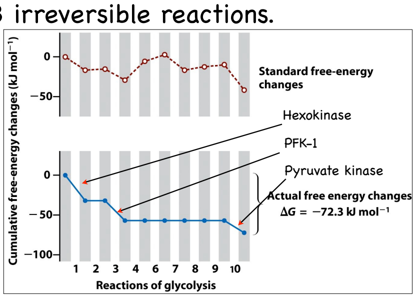

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Gluconeogenesis

- Glycolysis contains 7 reversible and 3 irreversible reactions.
  - Alternative pathways must be found for the 3 irreversible reactions

Change in free energy for each step of glycolysis[7]

Step	Reaction	$\Delta G^{\circ\prime}$ / (kJ/mol)	ΔG / (kJ/mol)
1	glucose + ATP^{4-} → glucose-6-phosphate^{2-} + ADP^{3-} + H^+	-16.7	-34
2	glucose-6-phosphate^{2-} → fructose-6-phosphate^{2-}	1.67	-2.9
3	fructose-6-phosphate^{2-} + ATP^{4-} → fructose-1,6-bisphosphate^{4-} + ADP^{3-} + H^+	-14.2	-19
4	fructose-1,6-bisphosphate^{4-} → dihydroxyacetone phosphate^{2-} + glyceraldehyde-3-phosphate^{2-}	23.9	-0.23
5	dihydroxyacetone phosphate^{2-} → glyceraldehyde-3-phosphate^{2-}	7.56	2.4
6	glyceraldehyde-3-phosphate^{2-} + P_i^{2-} + NAD^+ → 1,3-bisphosphoglycerate^{4-} + NADH + H^+	6.30	-1.29
7	1,3-bisphosphoglycerate^{4-} + ADP^{3-} → 3-phosphoglycerate^{3-} + ATP^{4-}	-18.9	0.09
8	3-phosphoglycerate^{3-} → 2-phosphoglycerate^{3-}	4.4	0.83
9	2-phosphoglycerate^{3-} → phosphoenolpyruvate^{3-} + H_2O	1.8	1.1
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9-1

Glucone

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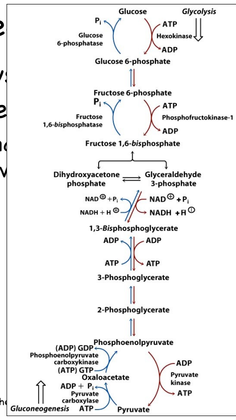

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Glucone

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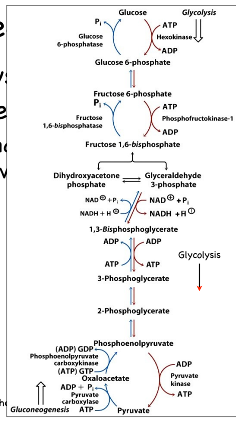

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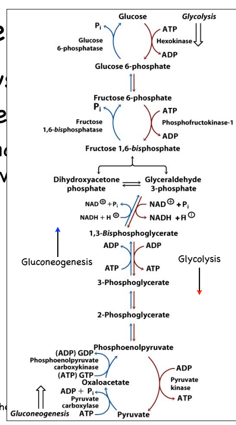

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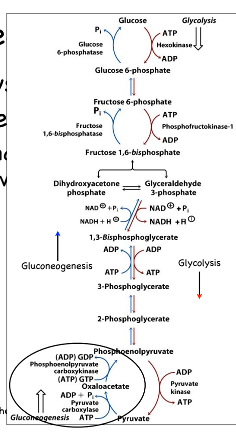

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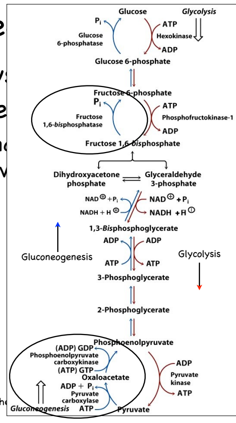
9-6

Glucone



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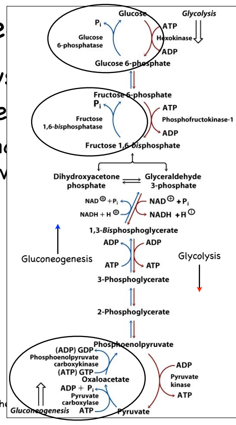

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10

Gluconeogenesis

- •Starting at pyruvate
  - The pyruvate kinase reaction is replaced with two reactions
    - Pyruvate carboxylase
    - Phosphoenolpyruvate carboxykinase

11-1

Gluconeogenesis

- •Pyruvate carboxylase

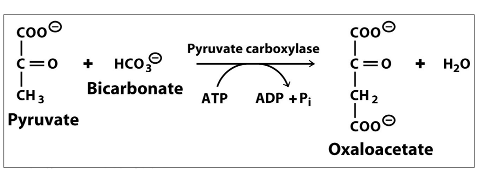

TABLE 7.2 Major coenzymes

Coenzyme	Vitamin source	Major metabolic roles	Mechanistic role
Adenosine triphosphate (ATP)	—	Transfer of phosphoryl or nucleotidyl groups	Cosubstrate
S-Adenosylmethionine	—	Transfer of methyl groups	Cosubstrate
Uridine diphosphate glucose	—	Transfer of glycosyl groups	Cosubstrate
Nicotinamide adenine dinucleotide ($NAD^{\oplus}$) and nicotinamide adenine dinucleotide phosphate ($NADP^{\oplus}$)	Niacin	Oxidation-reduction reactions involving two-electron transfers	Cosubstrate
Flavin mononucleotide (FMN) and flavin adenine dinucleotide (FAD)	Riboflavin (B_2)	Oxidation-reduction reactions involving one- and two-electron transfers	Prosthetic group
Coenzyme A (CoA)	Pantothenate (B_3)	Transfer of acyl groups	Cosubstrate
Thiamine pyrophosphate (TPP)	Thiamine (B_1)	Transfer of two-carbon fragments containing a carbonyl group	Prosthetic group
Pyridoxal phosphate (PLP)	Pyridoxine (B_6)	Transfer of groups to and from amino acids	Prosthetic group
Biotin	Biotin	ATP-dependent carboxylation of substrates or carboxyl-group transfer between substrates	Prosthetic group
Tetrahydrofolate	Folate	Transfer of one-carbon substituents, especially formyl and hydroxymethyl groups; provides the methyl group for thymine in DNA	Cosubstrate
Adenosylcobalamin	Cobalamin (B_{12})	Intramolecular rearrangements	Prosthetic group
Methylcobalamin	Cobalamin (B_{12})	Transfer of methyl groups	Prosthetic group
Lipoamide	—	Oxidation of a hydroxyalkyl group from TPP and subsequent transfer as an acyl group	Prosthetic group
Retinal	Vitamin A	Vision	Prosthetic group
Vitamin K	Vitamin K	Carboxylation of some glutamate residues	Prosthetic group
Ubiquinone (Q)	—	Lipid-soluble electron carrier	Cosubstrate

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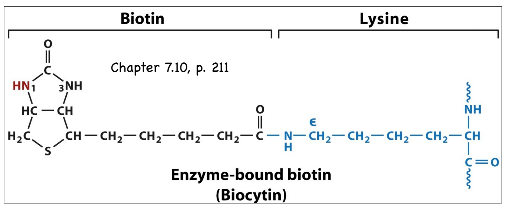
Gluconeogenesis

- Pyruvate carboxylase



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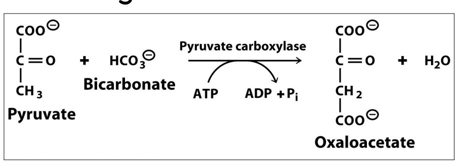
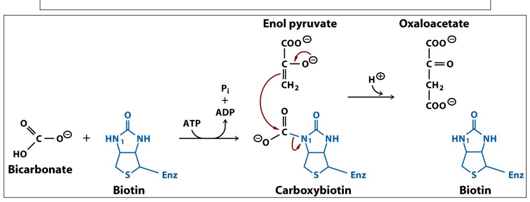
Gluconeogenesis





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Gluconeogenesis

- Pyruvate carboxylase
  - The oxaloacetate that is produced in this reaction is a citric acid cycle intermediate.
    - This reaction is also used to increase the quantity of citric acid cycle intermediates
  - Pyruvate carboxylase is stimulated by high Acetyl-CoA levels.
    - High Acetyl-CoA levels signal a need for citric acid cycle intermedates.

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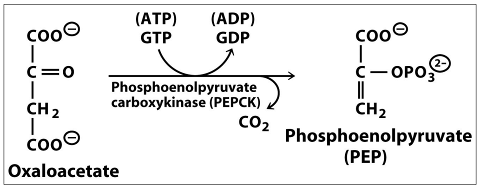
Gluconeogenesis

- Phosphoenolpyruvate carboxykinase
  - This is a decarboxylation reaction.
    - Decarboxylations have a high negative free energy change (ΔG << 0)



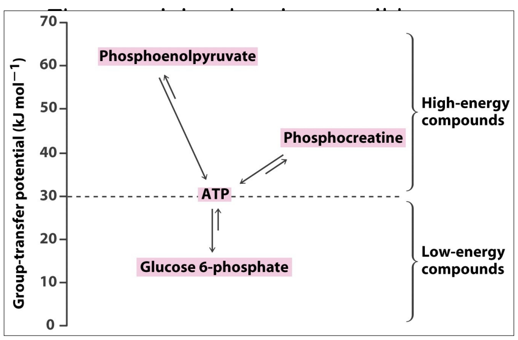
14-1

Gluconeogenesis

- The remaining two irreversible reactions from glycolysis which must be circumvented are the two kinase reactions near the beginning of the glycolytic pathway
  - Both are bypassed using phosphatase reactions, which hydrolyze phosphate esters.

14-2

Gluconeogenesis



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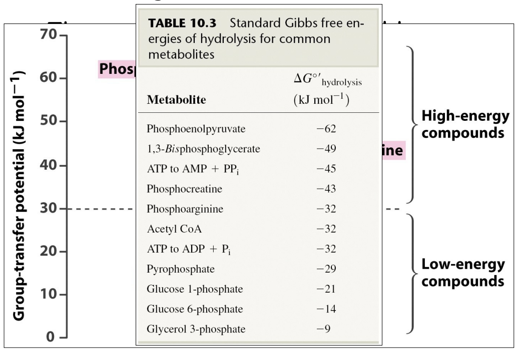

TABLE 10.3 Standard Gibbs free energies of hydrolysis for common metabolites

Metabolite	$\Delta G^{\circ\prime}_{\text{hydrolysis}}$ (kJ mol^{-1})
Phosphoenolpyruvate	−62
1,3-*Bis*phosphoglycerate	−49
ATP to AMP + PP_i	−45
Phosphocreatine	−43
Phosphoarginine	−32
Acetyl CoA	−32
ATP to ADP + P_i	−32
Pyrophosphate	−29
Glucose 1-phosphate	−21
Glucose 6-phosphate	−14
Glycerol 3-phosphate	−9

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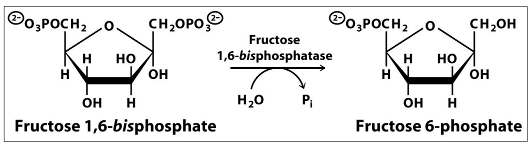
14-4

Gluconeogenesis

- Fructose 1,6-bisphosphatase



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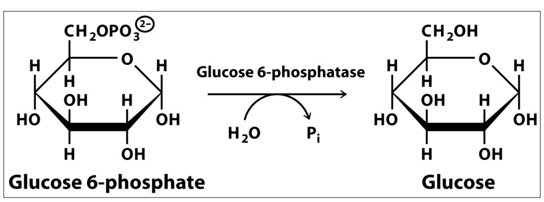
Gluconeogenesis

- Glucose 6-phosphatase



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Gluconeogenesis

- Glucose

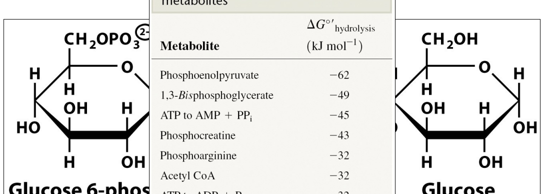


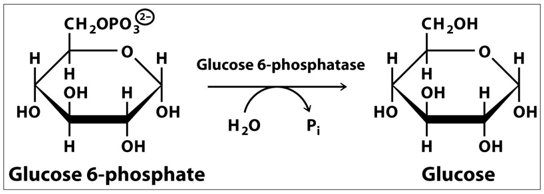
TABLE 10.3 Standard Gibbs free energies of hydrolysis for common metabolites

Metabolite	$\Delta G^{\circ\prime}_{hydrolysis}$ (kJ mol^{-1})
Phosphoenolpyruvate	−62
1,3-*Bis*phosphoglycerate	−49
ATP to AMP + PP_i	−45
Phosphocreatine	−43
Phosphoarginine	−32
Acetyl CoA	−32
ATP to ADP + P_i	−32
Pyrophosphate	−29
Glucose 1-phosphate	−21
Glucose 6-phosphate	−14
Glycerol 3-phosphate	−9

16-2

Gluconeogenesis

- Glucose 6-phosphatase



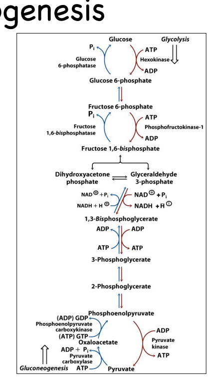
16-3

Gluconeogenesis

- Glucose 6-phosphatase
  - Only the liver, the kidneys and small intestine are capable of carrying out this reaction, for the purpose of increasing the blood glucose levels

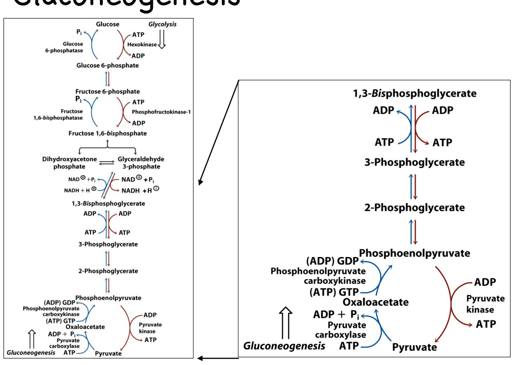
17

Gluconeogenesis



18

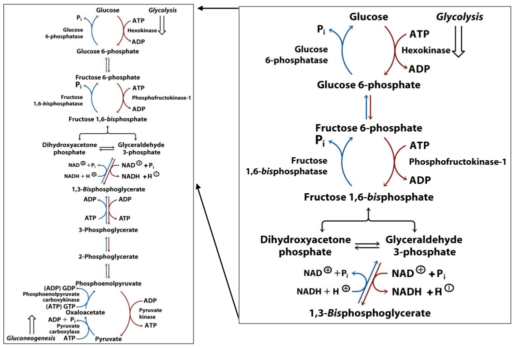
Gluconeogenesis



19

20

Gluconeogenesis



21

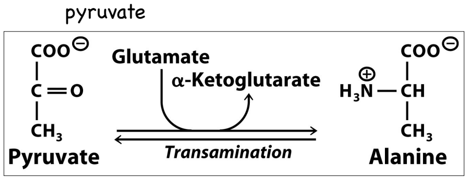
Gluconeogenesis

- Other molecules can serve as starting material for gluconeogenesis.
  - Amino Acids
    - Transamination of aspartic acid produces oxaloacetate

22

Gluconeogenesis

- Other molecules can serve as starting material for gluconeogenesis.
  - Amino Acids
    - Transamination of alanine produces pyruvate

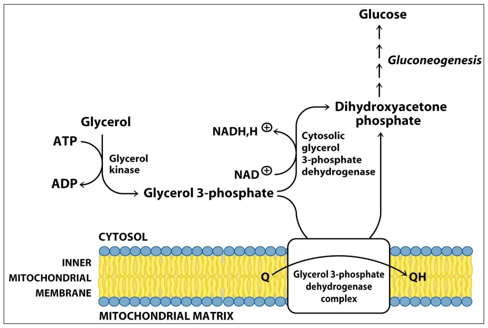


23-1

Gluconeogenesis

- Other molecules can serve as starting material for gluconeogenesis
  - Fats are broken down to produce Acetyl-CoA and glycerol.
    - Glycerol can be converted to dihydroxyacetone phosphate
    - Acetyl-CoA in some bacteria, plants an fungi (but not humans) can convert acetyl-CoA into oxaloacetate

Gluconeogenesis



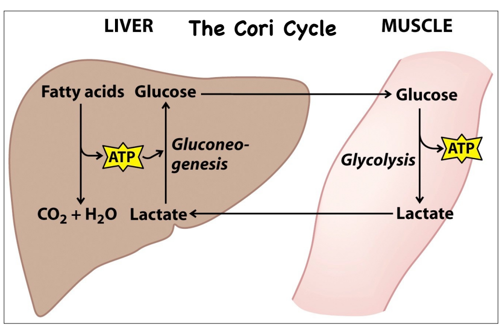
23-2

Gluconeogenesis

- Other molecules can serve as starting material for gluconeogenesis
  - Fats are broken down to produce Acetyl-CoA and glycerol.
    - Glycerol can be converted to dihydroxyacetone phosphate
    - Acetyl-CoA in some bacteria, plants an fungi (but not humans) can convert acetyl-CoA into oxaloacetate

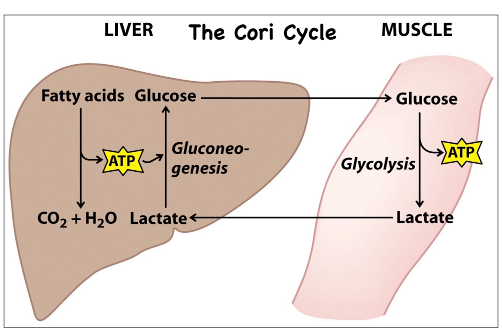
23-3

Gluconeogenesis



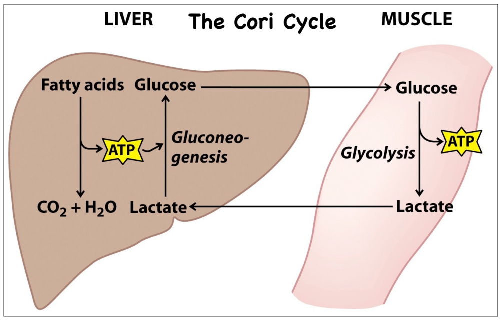
24-1

Gluconeogenesis



24-2

Gluconeogenesis



24-3

Gluconeogenesis

•Regulation of Gluconeogenesis

Glycolysis

Glucose + 2 NAD^+ + 2 ADP + 2 P_i ⟶

2 Pyruvate + 2 NADH + H^+ + 2 ATP + 2 H_2O

Gluconeogenesis

2 Pyruvate + 2 NADH + H^+ + 6 ATP + 6 H_2O

⟶

Glucose + 2 NAD^+ + 6 ADP + 6 P_i

Net Reaction

4 ATP + 4 H_2O ⟶ 4 ADP + 4 P_i

25-1

Gluconeo

•Regulati ... esis

Glycolysis

Glucose + 2 NAD^+

2 ATP + 2 H_2O

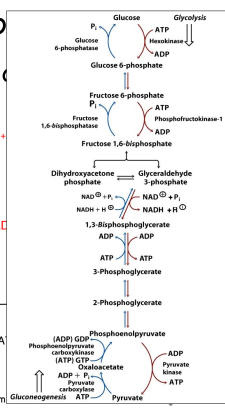
Gluconeogenesis

2 Pyruvate + 2 NAD

+ 6 P_i

Net Reaction

4 A ... 4 P_i



25-2

Gluconeogenesis

•Regulation of Gluconeogenesis

Glycolysis

Glucose + 2 NAD^+ + 2 ADP + 2 P_i ⟶

2 Pyruvate + 2 NADH + H^+ + 2 ATP + 2 H_2O

Gluconeogenesis

2 Pyruvate + 2 NADH + H^+ + 6 ATP + 6 H_2O

⟶

Glucose + 2 NAD^+ + 6 ADP + 6 P_i

Net Reaction

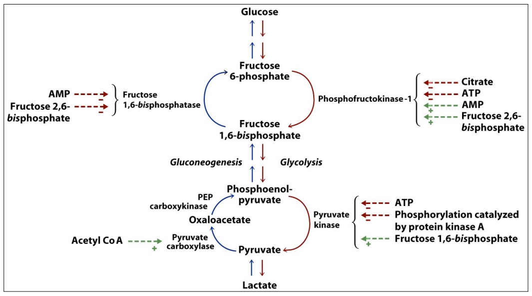
4 ATP + 4 H_2O ⟶ 4 ADP + 4 P_i

25-3

26-1

Gluconeogenesis

- Regulation of Gluconeogenesis



26-2

Gluconeogenesis

- Regulation of Gluconeogenesis

Clicker Question:

Fructose 2,6-bisphosphate coordinately regulates glycolysis and gluconeogenesis. The buildup of this this metabolite is signals which of the following states?

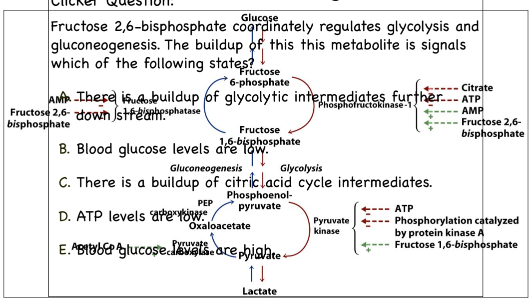
A. There is a buildup of glycolytic intermediates further down stream.

B. Blood glucose levels are low.

C. There is a buildup of citric acid cycle intermediates.

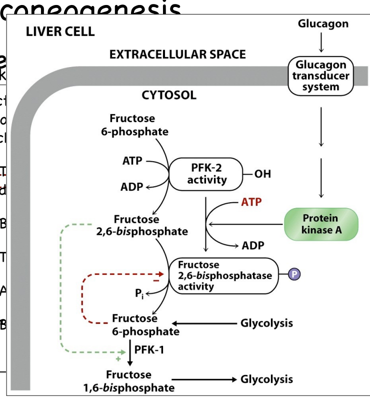
D. ATP levels are low.

E. Blood glucose levels are high.



26-3

Gluconeogenesis



26-4

Gluconeogenesis

- Regulation of Gluconeogenesis

Clicker Question:

Fructose 2,6-bisphosphate coordinately regulates glycolysis and gluconeogenesis. The buildup of this this metabolite is signals which of the following states?

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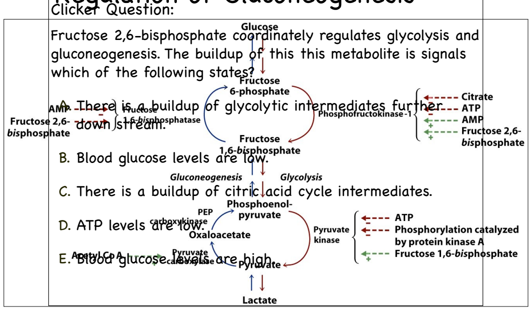
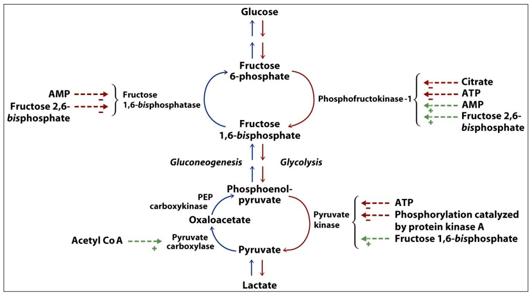


26-5

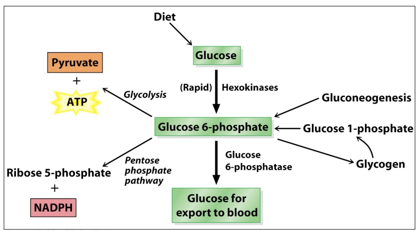
Gluconeogenesis

- Regulation of Gluconeogenesis



27

Fates for Glucose 6-Phosphate



28-1

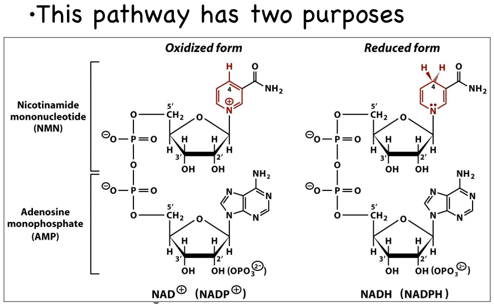
Pentose Phosphate Pathway

- This pathway has two purposes
  - **Produce pentoses** for nucleotide biosynthesis
  - **Produce reducing power**, in the form of reduced NADPH + H^+, for biosynthetic reactions.
- There are two stages to this pathway
  - **Oxidative**, which produces the pentose and the reduced NADPH + H^+.
  - **Non-oxidative**, which converts the pentoses back into glycolytic intermediates.

28-2

Pentose Phosphate Pathway

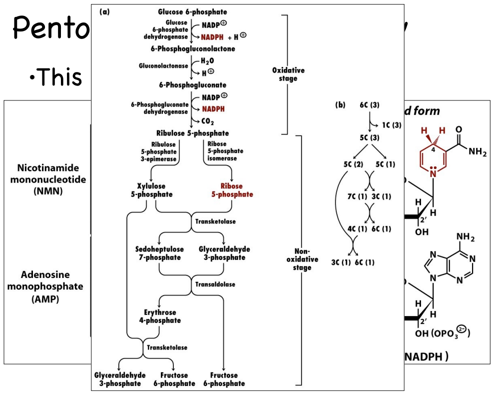
- This pathway has two purposes



28-3

Pento

•This



28-4

Pentose Phosphate Pathway

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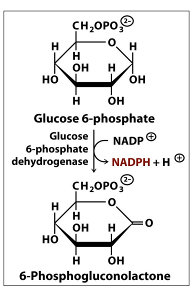
- There are two stages to this pathway
  - **Oxidative**, which produces the pentose and the reduced NADPH + H^+.
  - **Non-oxidative**, which converts the pentoses back into glycolytic intermediates.

29-1

Pentose Phosphate Pathway

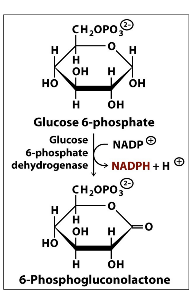
- Oxidative Stage:

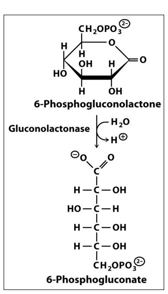


29-2

Pentose Phosphate Pathway

- Oxidative Stage:

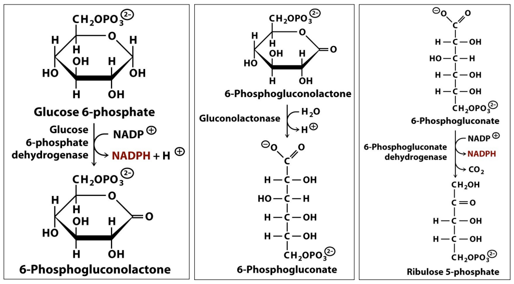




29-3

Pentose Phosphate Pathway

•Oxidative Stage:



30

Pentose Phosphate Pathway

•Oxidative Stage:

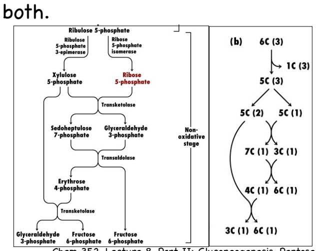
- This is the only stage that is used if the cell requires **both** pentoses and biosynthetic reducing power.
  - Such is the cases when cells are rapidly growing and dividing.

31-1

Pentose Phosphate Pathway

•Nonoxidative Stage:

- This stage is used when the cell requires **only** pentoses **or** reducing power, but not both.

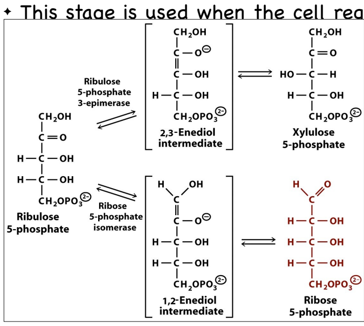


31-2

Pentose Phosphate Pathway

•Nonoxidative Stage:

- This stage is used when the cell requires ... t not



Pentose Phosphate Pathway

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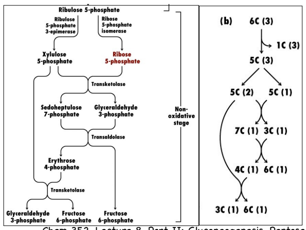
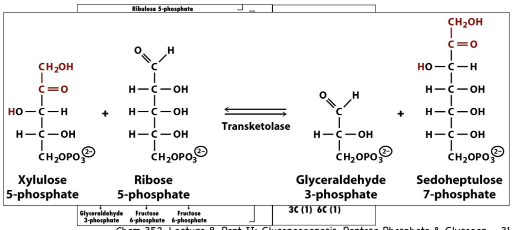


31-3

Pentose Phosphate Pathway

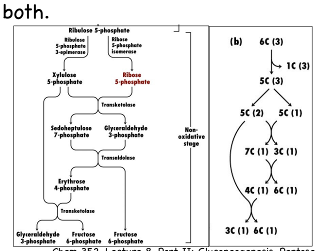
- Nonoxidative Stage:
  - This stage is used when the cell requires **only** pentoses **or** reducing power, but not both.



31-4

Pentose Phosphate Pathway

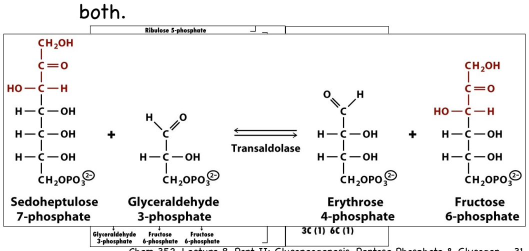
- Nonoxidative Stage:
  - This stage is used when the cell requires **only** pentoses **or** reducing power, but not both.



31-5

Pentose Phosphate Pathway

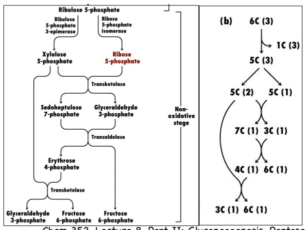
- Nonoxidative Stage:
  - This stage is used when the cell requires **only** pentoses **or** reducing power, but not both.



31-6

Pentose Phosphate Pathway

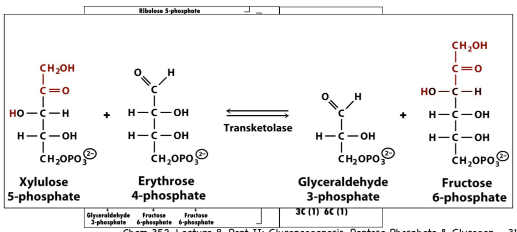
- Nonoxidative Stage:
  - This stage is used when the cell requires **only** pentoses **or** reducing power, but not both.



31-7

Pentose Phosphate Pathway

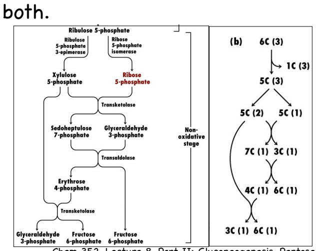
- Nonoxidative Stage:
  - This stage is used when the cell requires **only** pentoses **or** reducing power, but not both.



31-8

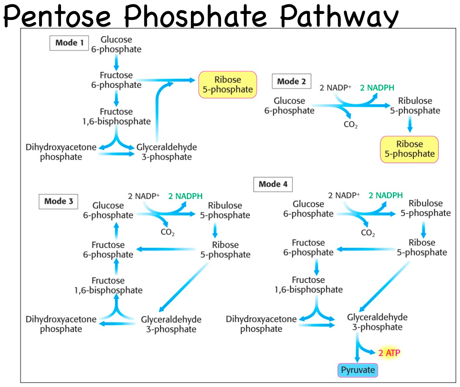
Pentose Phosphate Pathway

- Nonoxidative Stage:
  - This stage is used when the cell requires **only** pentoses **or** reducing power, but not both.



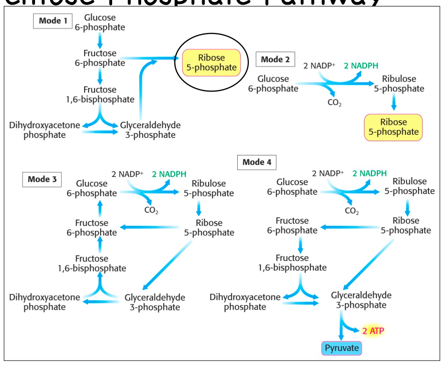
31-9

Pentose Phosphate Pathway



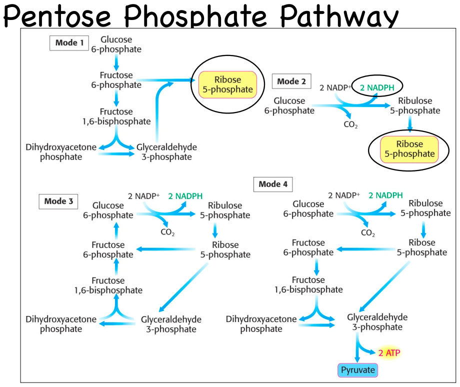
32-1

Pentose Phosphate Pathway



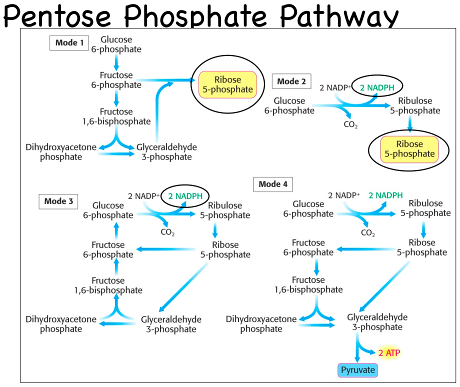
32-2

Pentose Phosphate Pathway



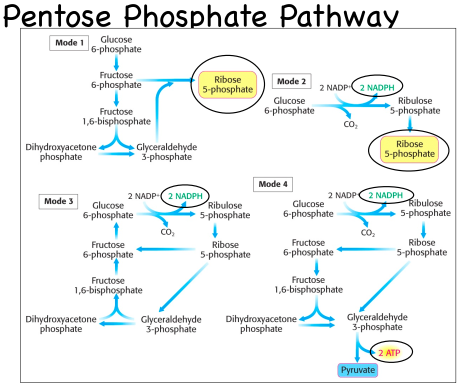
32-3

Pentose Phosphate Pathway



32-4

Pentose Phosphate Pathway



32-5

Pentose Phosphate Pathway

32-6

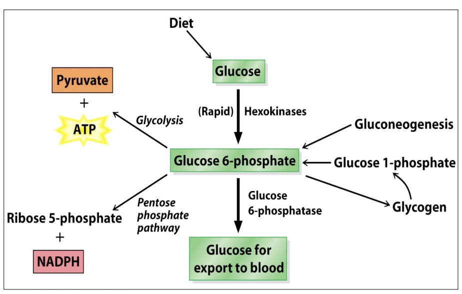
Chem 352 - Lecture 8
Carbohydrate Metabolism
Part II: Gluconeogenesis, Pentose Phosphate Pathway & Glycogen Metabolism
9. April, 2014

Question for the Day: How is the storage of glucose as glycogen in the liver tied to the blood glucose levels?

33

Glycogen Metabolism

Glycogen is a storage form of glucose.

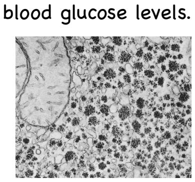


34-1

Glycogen Metabolism

Glycogen is a storage form of glucose.

- It is stored in muscles as a readily available energy resource for future activity.
- It is stored in the liver as a resource for regulating blood glucose levels.



34-2

35-1

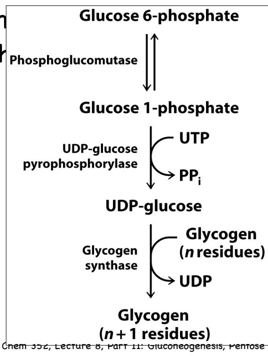
Glycogen Metabolism

Glycogen is synthesized from glucose 6-phosphate.

35-2

Glycogen Metabolism

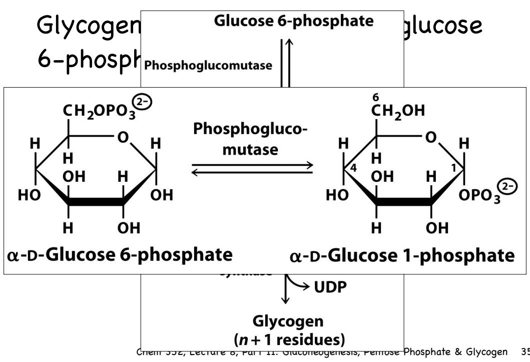
Glycogen ... glucose
6-phosph...



35-3

Glycogen Metabolism

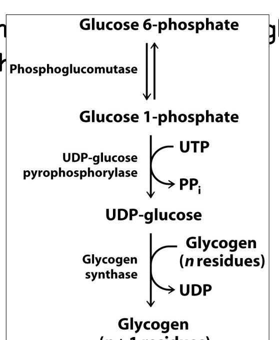
Glycogen ... glucose
6-phosph...



35-4

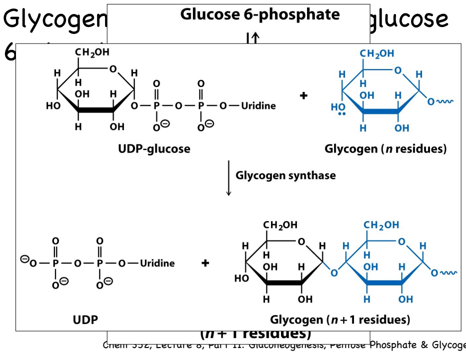
Glycogen Metabolism

Glycogen ... glucose
6-phosph...



Glycogen Metabolism

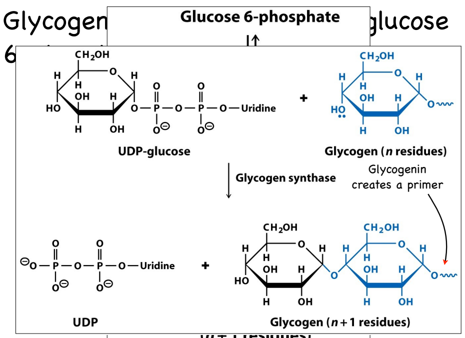
Glycogen glucose
6



35-5

Glycogen Metabolism

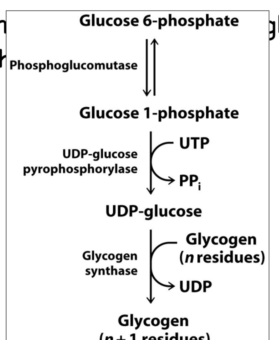
Glycogen glucose
6



35-6

Glycogen Metabolism

Glycogen glucose
6-phosph



35-7

Glycogen Metabolism

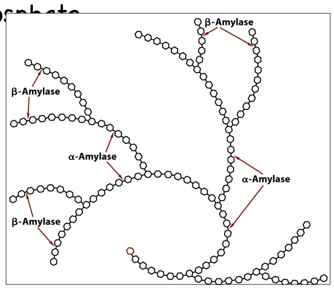
Glycogen is synthesized from glucose 6-phosphate.

35-8

35-9

Glycogen Metabolism

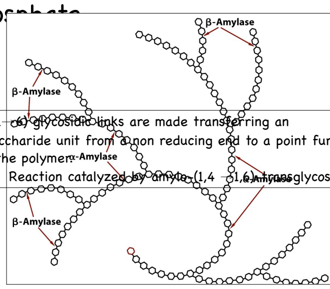
Glycogen is synthesized from glucose 6-phosphate



35-10

Glycogen Metabolism

Glycogen is synthesized from glucose 6-phosphate



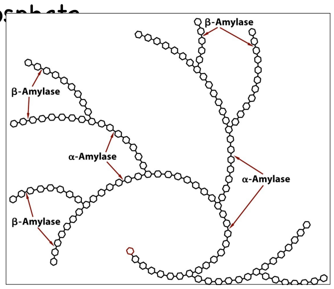
The α(1→6) glycosidic links are made transferring an oligosaccharide unit from a non reducing end to a point further in along the polymer.

- Reaction catalyzed by amylo-(1,4 → 1,6)-transglycosylase.

35-11

Glycogen Metabolism

Glycogen is synthesized from glucose 6-phosphate



36-1

Glycogen Metabolism

Glycogen degradation is catalyzed with phosphorylases instead of hydrolases

- This leaves the glucose units that are removed with a phosphate attached.

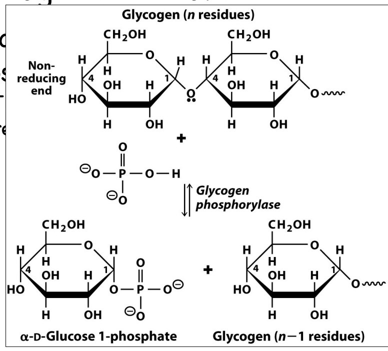
36-2

Glycogen Metabolism

Glyc ith

phos s

- T
  re



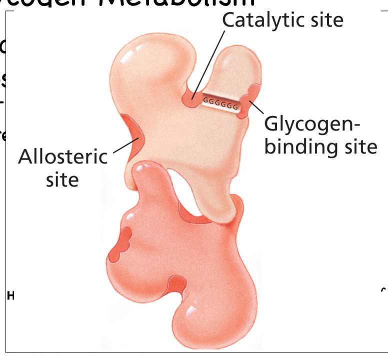
36-3

Glycogen Metabolism

Glyc ith

phos s

- T
  re



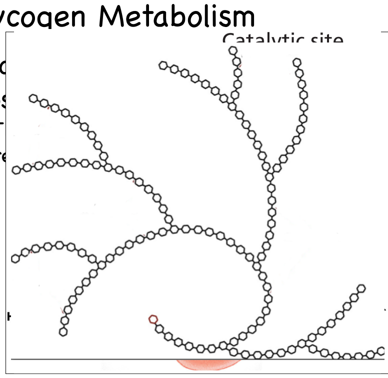
36-4

Glycogen Metabolism

Glyc ith

phos s

- T
  re



36-5

Glycogen Metabolism

Glyc ith

phos s

- T
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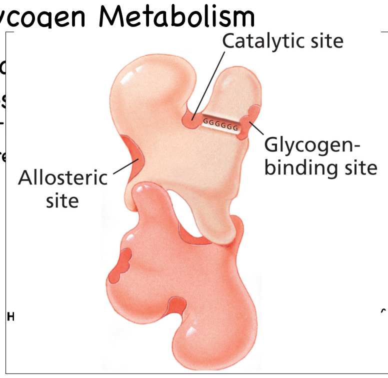
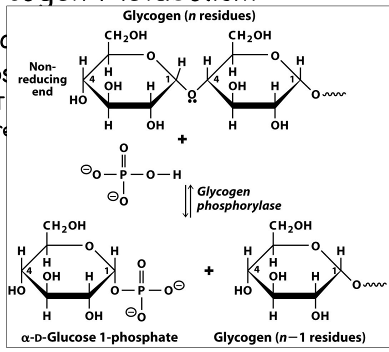


36-6

Glycogen Metabolism

Glyc … vith
phos … s
- T…
  re…



36-7

Glycogen Metabolism

Glycogen degradation is catalyzed with phosphorylases instead of hydrolases

- This leaves the glucose units that are removed with a phosphate attached.

37-1

Glycogen Metabolism

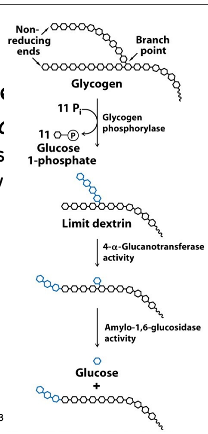
Glycogen degradation is catalyzed with phosphorylases instead of hydrolases

- This leaves the glucose units that are removed with a phosphate attached.

37-2

Glycogen …

Glycogen de… …lyzed with
phosphoryl… …drolases
- This leaves … …t are
  removed w… …ed.



38-1

Glycogen Metabolism

- Regulation of glycogen synthesis and degradation are coordinated.
  - As we saw with glycolysis and gluconeogenesis, this is done to prevent substrate (futile) cycling.
- Insulin, glucagon and epinephrine (adrenaline) are the hormones that regulate glycogen metabolism.

38-2

Glycogen Metabolism

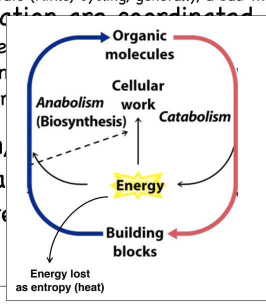
Question:
Why is substrate (futile) cycling, generally, a bad thing?

- Regulation of glycogen synthesis and degradation are coordinated.
  - As we saw with glycolysis and gluconeogenesis, this is done to prevent substrate (futile) cycling.
- Insulin, glucagon and epinephrine (adrenaline) are the hormones that regulate glycogen metabolism.

38-3

Glycogen Metabolism

Question:
Why is substrate (futile) cycling, generally, a bad thing?



38-4

Glycogen Metabolism

- Regulation of glycogen synthesis and degradation are coordinated.
  - As we saw with glycolysis and gluconeogenesis, this is done to prevent substrate (futile) cycling.
- Insulin, glucagon and epinephrine (adrenaline) are the hormones that regulate glycogen metabolism.

Regulation of Glycogen Metabolism

Glycogen metabolism is strictly regulated.

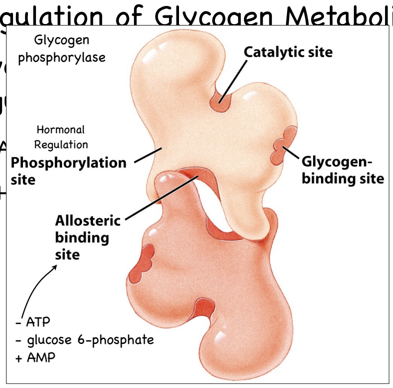
- Allosterically
- Hormonally

39-1

Regulation of Glycogen Metabolism

Gly
reg

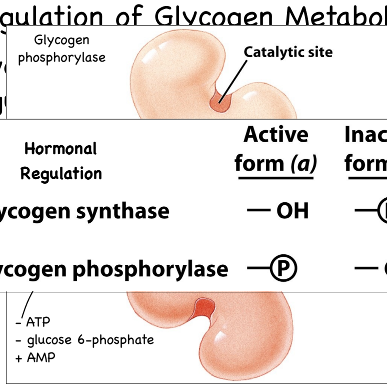
- A
- H



39-2

Regulation of Glycogen Metabolism

Gly
reg



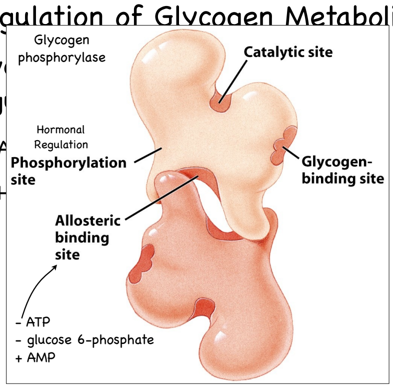
Hormonal Regulation	Active form *(a)*	Inactive form *(b)*
Glycogen synthase	— OH	—Ⓟ
Glycogen phosphorylase	—Ⓟ	— OH

39-3

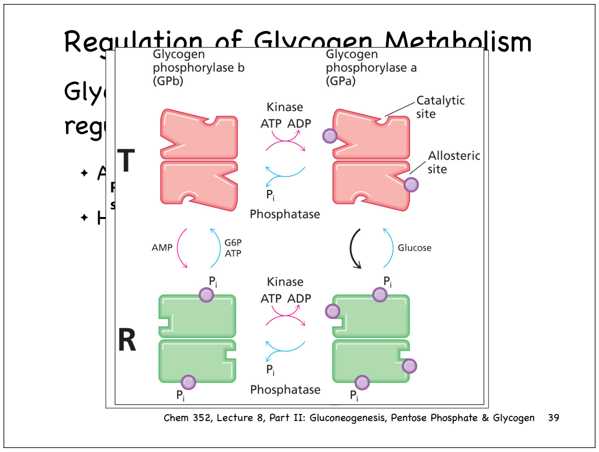
Regulation of Glycogen Metabolism

Gly
reg

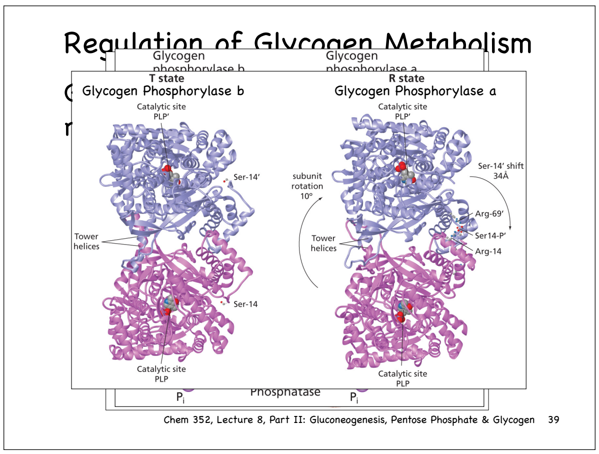
- A
- H



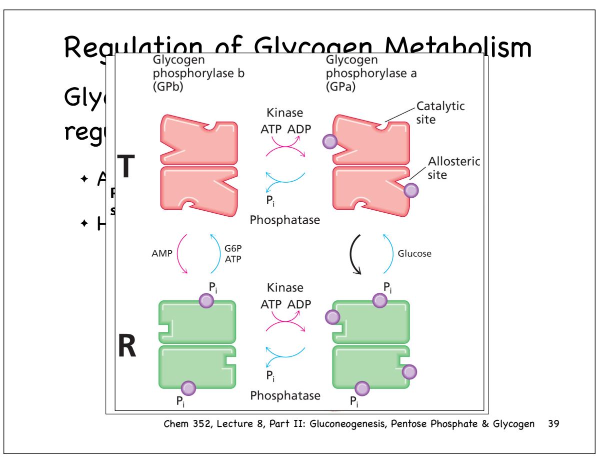
39-4



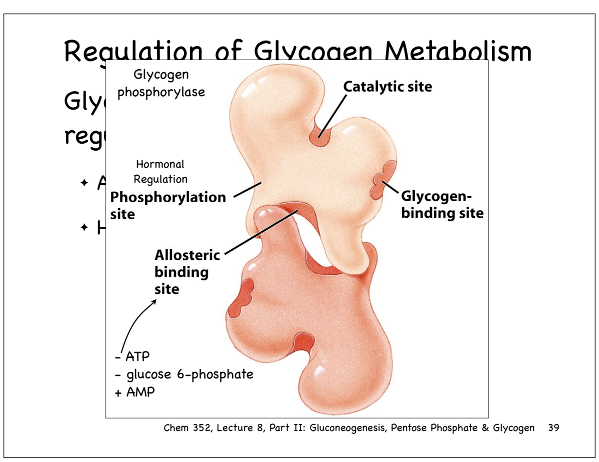
39-5



39-6



39-7



39-8

Regulation of Glycogen Metabolism

Glycogen metabolism is strictly regulated.

- Allosterically
- Hormonally

39-9

Glycogen Metabolism

Insulin

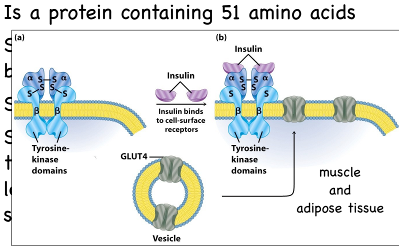
- Is a protein containing 51 amino acids
- Secreted by the pancreas in response to high blood glucose levels
- Stimulates the uptake of glucose by tissues
- Stimulates glycogen synthesis in the liver through a signal transduction pathway that leads to dephosphorylation of glycogen synthetase and glycogen phosphorylase

40-1

Glycogen Metabolism

Insulin

- Is a protein containing 51 amino acids
- S ... high
  b
- S ... es
- S
  t ... at
  l
  s



40-2

Glycogen Metabolism

Insulin

- Is a protein containing 51 amino acids
- Secreted by the pancreas in response to high blood glucose levels
- Stimulates the uptake of glucose by tissues
- Stimulates glycogen synthesis in the liver through a signal transduction pathway that leads to dephosphorylation of glycogen synthetase and glycogen phosphorylase

40-3

40-4

Glycogen Metabolism

Insulin

- Is a protein containing 51 amino acids
- Secreted by the pancreas in response to high

	Active form *(a)*	Inactive form *(b)*
Glycogen synthase	— OH	—Ⓟ
Glycogen phosphorylase	—Ⓟ	— OH

40-5

Glycogen Metabolism

Insulin

- Is a protein containing 51 amino acids
- Secreted by the pancreas in response to high blood glucose levels
- Stimulates the uptake of glucose by tissues
- Stimulates glycogen synthesis in the liver through a signal transduction pathway that leads to dephosphorylation of glycogen synthetase and glycogen phosphorylase

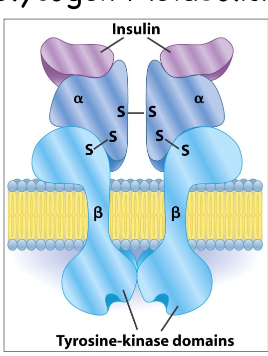
41-1

Glycogen Metabolism

•Insulin binds to a tyrosine kinase type receptor. (Chapter 9.12, Section D)

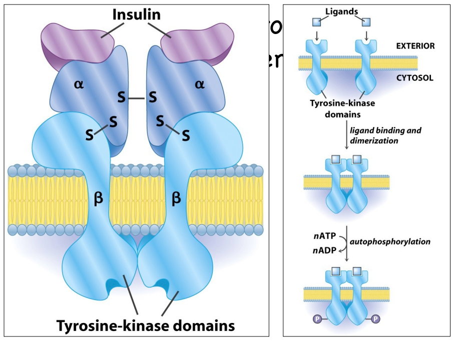
41-2

Glycogen Metabolism



osine kinase
r 9.12, Section

Glycogen Metabolism



41-3

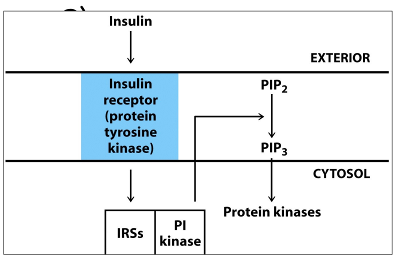
Glycogen Metabolism

- Insulin binds to a tyrosine kinase type receptor. (Chapter 9.12, Section D)

41-4

Glycogen Metabolism

- Insulin binds to a tyrosine kinase type receptor. (Chapter 9.12, Section



IRS = Insulin receptor substrate
PI = phosphotidylinositide kinase
PIP_2 = phosphotidyl inositol 4,5-bisphosphate
PIP_3 = phosphotidyl inositol 3,4,5-trisphosphate

42

Glycogen Metabolism

- Glucagon
  - Is a peptide hormone containing 29 amino acids
  - Secreted by the α cells in the pancreas in response to low blood glucose levels
  - Stimulates glycogen degradation in the liver through a signal transduction pathway that leads to phosphorylation of glycogen synthetase and glycogen phosphorylase

43-1

43-2

Glycogen Metabolism

- Glucagon
  - Is a peptide hormone containing 29 amino acids
  - Secreted by the α cells in the pancreas in

	Active form *(a)*	Inactive form *(b)*
Glycogen synthase	— OH	—Ⓟ
Glycogen phosphorylase	—Ⓟ	— OH

43-3

Glycogen Metabolism

- Glucagon
  - Is a peptide hormone containing 29 amino acids
  - Secreted by the α cells in the pancreas in response to low blood glucose levels
  - Stimulates glycogen degradation in the liver through a signal transduction pathway that leads to phosphorylation of glycogen synthetase and glycogen phosphorylase

44-1

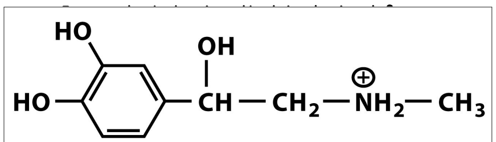
Glycogen Metabolism

- Epinephrine
  - Is a catacholamine that is derived from tyrosine.
  - Released by the adrenal glands by a neural signal that is triggered by the "Fight-or-Flight" response.
  - Stimulates the breakdown of glycogen
  - Binds to adrenergic receptors in the muscle (β) and the liver (α_1).
    - Signal transduction pathway leads to activation of protein kinase A (β) and C (α_1).

44-2

Glycogen Metabolism

- Epinephrine



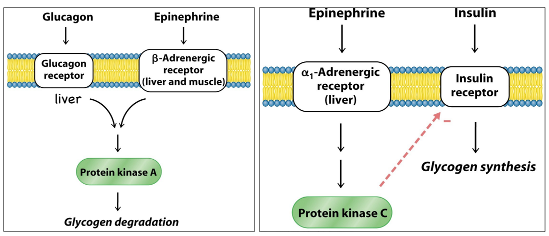
Epinephrine (Adrenaline)

Glycogen Metabolism

- Epinephrine
  - Is a catacholamine that is derived from tyrosine.
  - Released by the adrenal glands by a neural signal that is triggered by the "Fight-or-Flight" response.
  - Stimulates the breakdown of glycogen
  - Binds to adrenergic receptors in the muscle (β) and the liver (α_1).
    - Signal transduction pathway leads to activation of protein kinase A (β) and C (α_1).

44-3

Glycogen Metabolism

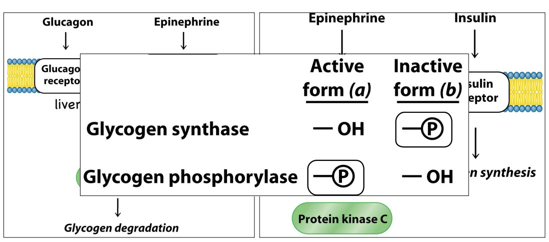


Both activate glycogen degradation by phosphorylating Glycogen synthase (inactive) and Glycogen phosphorylase (active)

Both inhibit the action of insulin by phosphorylating the insulin receptor

45-1

Glycogen Metabolism



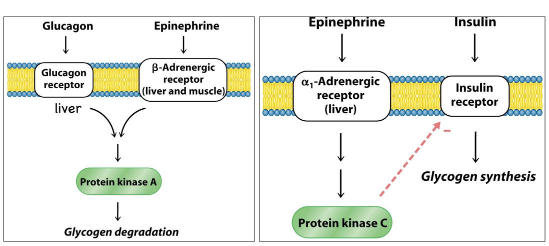
	Active form (a)	Inactive form (b)
Glycogen synthase	— OH	—Ⓟ
Glycogen phosphorylase	—Ⓟ	— OH

Both activate glycogen degradation by phosphorylating Glycogen synthase (inactive) and Glycogen phosphorylase (active)

Both inhibit the action of insulin by phosphorylating the insulin receptor

45-2

Glycogen Metabolism

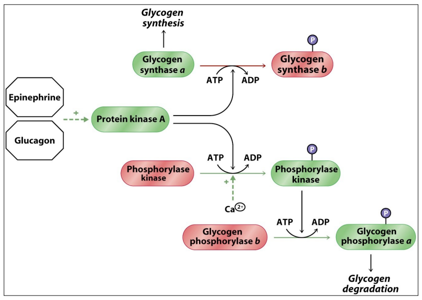


Both activate glycogen degradation by phosphorylating Glycogen synthase (inactive) and Glycogen phosphorylase (active)

Both inhibit the action of insulin by phosphorylating the insulin receptor

45-3

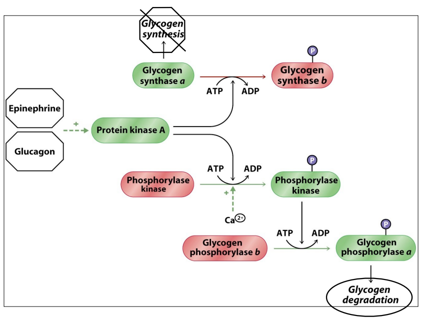
Glycogen Metabolism



Chem 352, Lecture 8, Part II: Gluconeogenesis, Pentose Phosphate & Glycogen

46-1

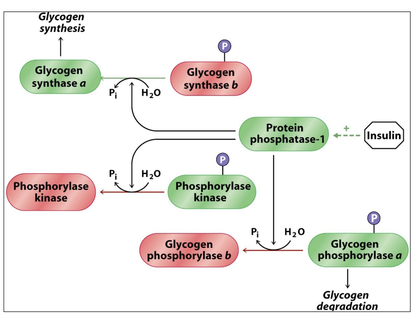
Glycogen Metabolism



Chem 352, Lecture 8, Part II: Gluconeogenesis, Pentose Phosphate & Glycogen

46-2

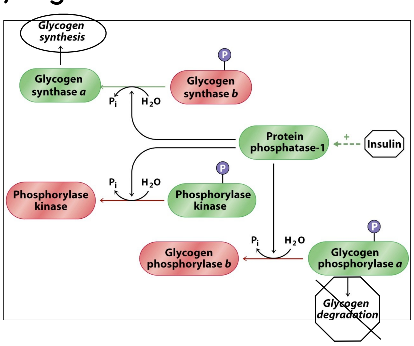
Glycogen Metabolism



Chem 352, Lecture 8, Part II: Gluconeogenesis, Pentose Phosphate & Glycogen

47-1

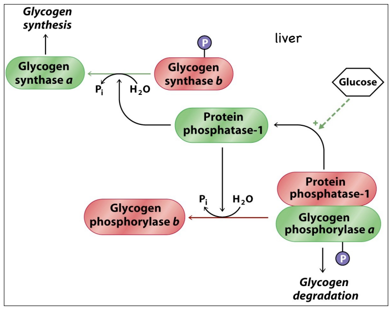
Glycogen Metabolism



Chem 352, Lecture 8, Part II: Gluconeogenesis, Pentose Phosphate & Glycogen

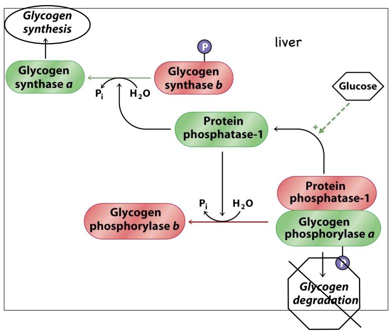
47-2

Glycogen Metabolism



48-1

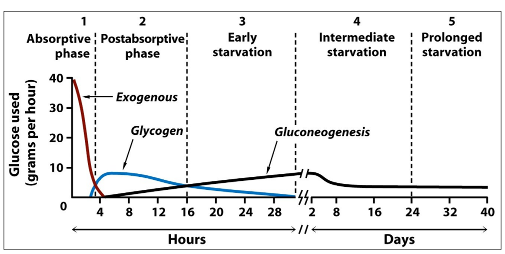
Glycogen Metabolism



48-2

Glycogen Metabolism

- Time since last meal
  - 40 days in the desert after eating a sugary dessert.



49

Carbohydrate Metabolism

Question:

Tumor cells often lack an extensive capillary network and must function under conditions of limited oxygen supply. Explain why these cancer cells take up far more glucose than other tissues and may overproduce some of the glycolytic enzymes?

50

Carbohydrate Metabolism

Question:

Rapid glycolysis during strenuous exercise provides the ATP needed for muscle contraction.

A. Since the lactate dehydrogenase reaction does not produce any ATP, would glycolysis be more efficient if pyruvate rather than lactate were the end product?

B. What is the fate of the lactate that is produced in the muscles during strenuous exercise?

51-1

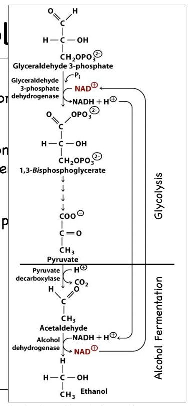
Carbohydrate Metabol

Question:

Rapid glycolysis during strenuous exercise pr
needed for muscle contraction.

A. Since the lactate dehydrogenase reaction
any ATP, would glycolysis be more efficie
than lactate were the end product?

B. What is the fate of the lactate that is p
muscles during strenuous exercise?



51-2

Carbohydrate Metabolism

Question:

Rapid glycolysis during strenuous exercise provides the ATP needed for muscle contraction.

A. Since the lactate dehydrogenase reaction does not produce any ATP, would glycolysis be more efficient if pyruvate rather than lactate were the end product?

B. What is the fate of the lactate that is produced in the muscles during strenuous exercise?

51-3

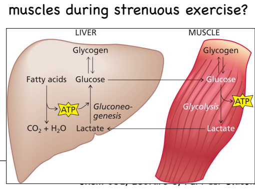
Carbohydrate Metabolism

Question:

Rapid glycolysis during strenuous exercise provides the ATP needed for muscle contraction.

A. Since the lactate dehydrogenase reaction does not produce any ATP, would glycolysis be more efficient if pyruvate rather than lactate were the end product?

B. What is the fate of the lactate that is produced in the muscles during strenuous exercise?



51-4

Carbohydrate Metabolism

52-1

Question:

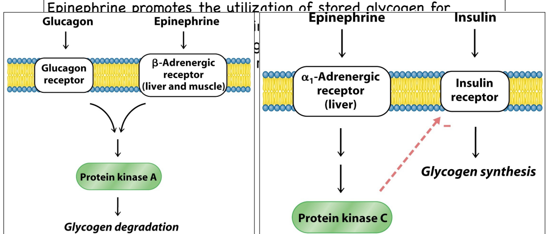
Epinephrine promotes the utilization of stored glycogen for glycolysis and ATP production in muscles. How does epinephrine promote the use of liver glycogen stores for the generating the energy needed by contracting muscles?

Carbohydrate Metabolism

52-2

Question:

Epinephrine promotes the utilization of stored glycogen for



Carbohydrate Metabolism

52-3

Question:

Epinephrine promotes the utilization of stored glycogen for glycolysis and ATP production in muscles. How does epinephrine promote the use of liver glycogen stores for the generating the energy needed by contracting muscles?

Carbohydrate Metabolism

53-1

Question:

The polypeptide hormone glucagon is released from the pancreas in response to low blood glucose levels. In liver cells, glucagon plays a major role in regulating the rates of the opposing glycolysis and gluconeogenesis pathways by influencing the concentrations of fructose 2,6-bisphosphate.

A. If glucagon causes a decrease in the concentrations of fructose 2,6-bisphosphate, how does this result in an increase in blood glucose levels?

53-2

Carbohydrate Metabolism

Question:

The polypeptide hormone glucagon is released from the pancreas in response to low blood glucose levels. In liver cells, glucagon plays a major role in regulating the rates of the opposing glycolysis and gluconeogenesis pathways by influencing the concentrations of fructose 2,6-bisphosphate.

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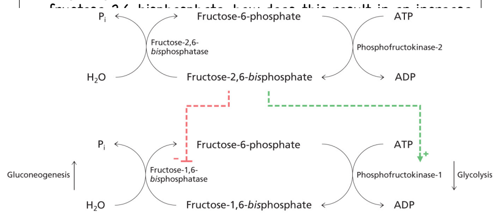


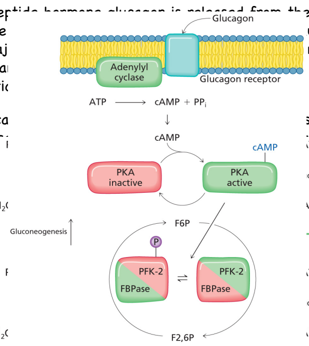
53-3

Carbohydrate Metabolism

Question:

The polypep... pancreas in response ... ucagon plays a maj... ng glycolysis a... the concentratio...

A. If gluca... s of



53-4

Carbohydrate Metabolism

Question:

The polypeptide hormone glucagon is released from the pancreas in response to low blood glucose levels. In liver cells, glucagon plays a major role in regulating the rates of the opposing glycolysis and gluconeogenesis pathways by influencing the concentrations of fructose 2,6-bisphosphate.

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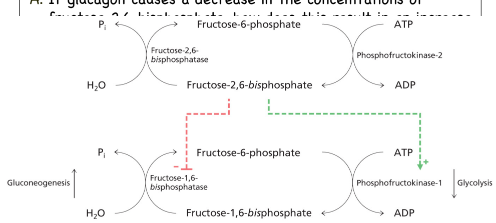

53-5

Carbohydrate Metabolism

Question:

The polypeptide hormone glucagon is released from the pancreas in response to low blood glucose levels. In liver cells, glucagon plays a major role in regulating the rates of the opposing glycolysis and gluconeogenesis pathways by influencing the concentrations of fructose 2,6-bisphosphate.

A. If glucagon causes a decrease in the concentrations of fructose 2,6-bisphosphate, how does this result in an increase in blood glucose levels?

Carbohydrate Metabolism

Question:

The pentose phosphate pathway and the glycolytic pathway are interdependent, since they have in common several metabolites whose concentrations affect the rates of enzymes in both pathways.

A. Which metabolites are common to both pathways?

54

Next Up

- Lecture 8 - Carbohydrate Metabolism
  - Part III: Citric Acid Cycle (Chapter 13)

55