Chem 352 - Lecture 8
Carbohydrate Metabolism
Part III: Citric Acid Cycle

1

Introduction

The citric acid cycle has both catabolic and anabolic functions.

- **Catabolic** - Oxidizes the 2-carbon acetyl group to CO_2 and produces reduced nucleotides ($NADH + H^+$ and $FADH_2$)
- **Anabolic** - The citric acid cycle intermediates serve as starting material for the biosynthesis of amino acids, heme groups, glucose, et al.

2

Introduction

The citric acid cycle was discovered by Hans Kreb's and colleagues in 1937.

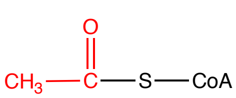
- Citric acid cycle is also called the Kreb's Cycle and the TCA (tricarboxylic acid) Cycle.

Hans Krebs (1900-1981)
Nobel Prize in Physiology and Medicine, 1953

3

Acetyl CoA

•The entry point of carbon into the citric acid cycle is acetyl CoA



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4-2

Acetyl CoA

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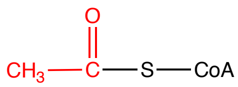
•Questions:

Acetyl CoA contains a thioester group. What can you say about the thermodynamics for the hydrolysis of thioester groups?



4-3

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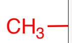

TABLE 10.3 Standard Gibbs free energies of hydrolysis for common metabolites

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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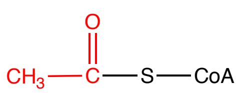

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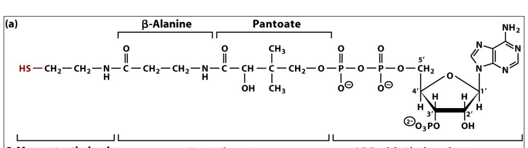

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4-6

Acetyl CoA

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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
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4-7

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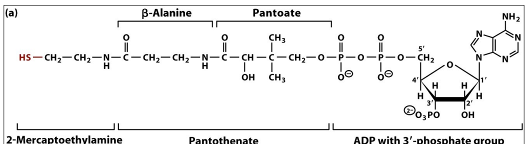

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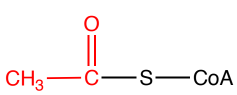


5

Acetyl CoA

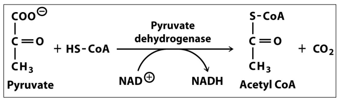
- The entry point of carbon into the citric acid cycle is acetyl CoA

- Acetyl CoA is produced from
  - The oxidative decarboxylation of pyruvate from the glycolysis pathway.
  - The degradation of fatty acids

6

Conversion of Pyruvate to Acetyl CoA

- Pyruvate dehydrogenase is a large enzyme complex that converts pyruvate to acetyl-CoA and CO_2.



- This is the catabolic entry point into the citric acid cycle of carbon coming from glycolysis.

7

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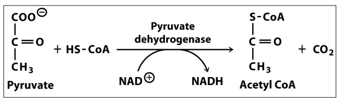
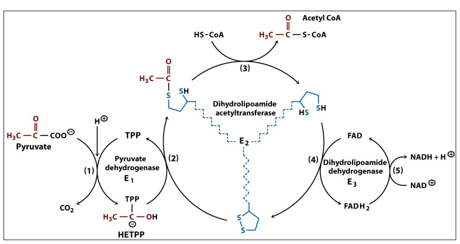


- Three different subunits catalyze five sub-reactions to to carry out this overall reaction.

8-1

Conversion of Pyruvate to Acetyl CoA

- Pyruvate Dehydrogenase



8-2

Conversion of Pyruvate to Acetyl CoA

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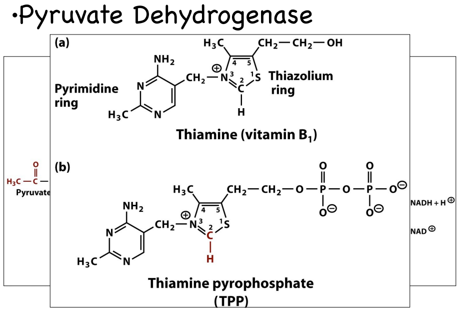

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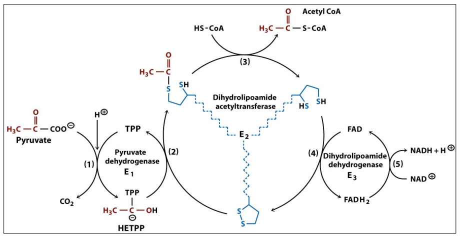

8-3

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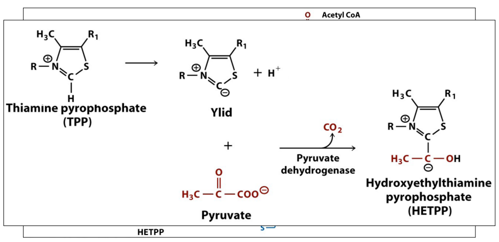

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Conver… l CoA

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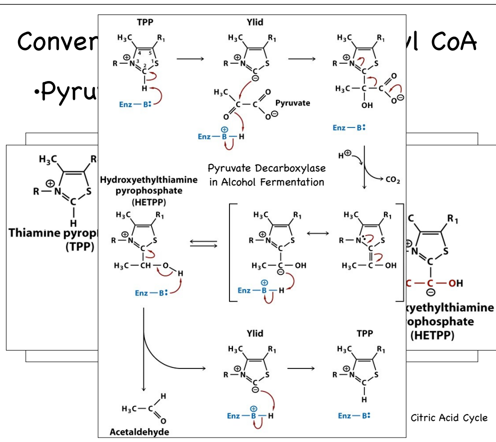

8-5

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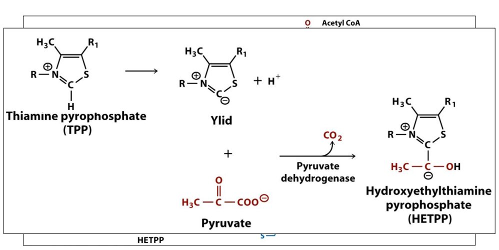
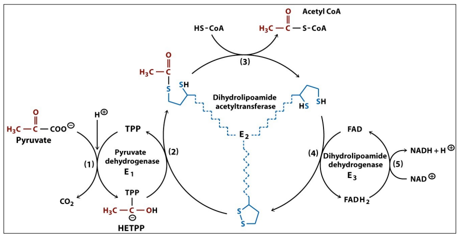


8-6

Conversion of Pyruvate to Acetyl CoA

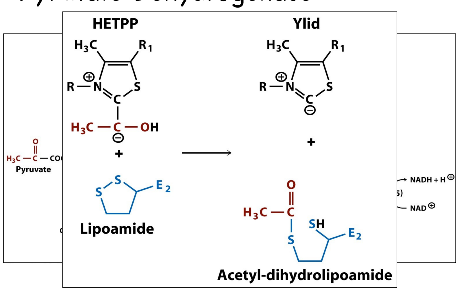
- Pyruvate Dehydrogenase



8-7

Conversion of Pyruvate to Acetyl CoA

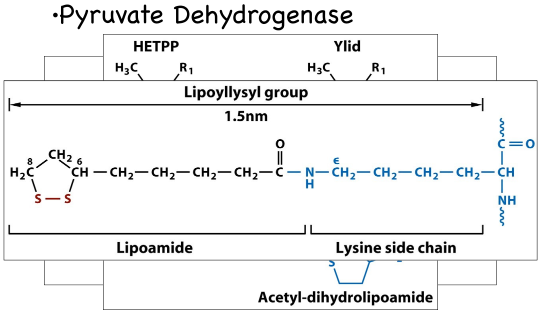
- Pyruvate Dehydrogenase



8-8

Conversion of Pyruvate to Acetyl CoA

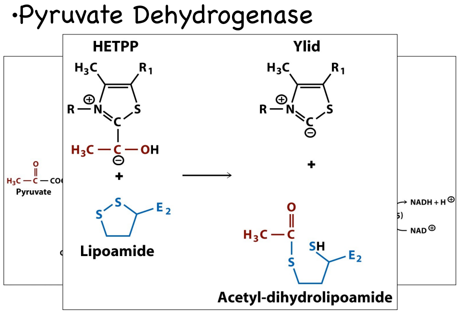
- Pyruvate Dehydrogenase



8-9

Conversion of Pyruvate to Acetyl CoA

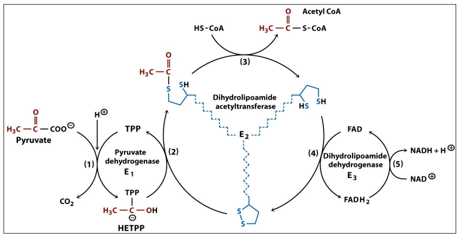
- Pyruvate Dehydrogenase



8-10

Conversion of Pyruvate to Acetyl CoA

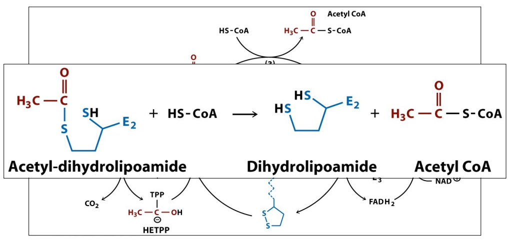
- Pyruvate Dehydrogenase



8-11

Conversion of Pyruvate to Acetyl CoA

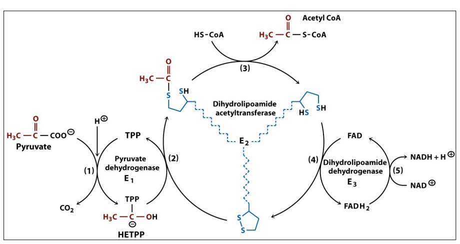
- Pyruvate Dehydrogenase



8-12

Conversion of Pyruvate to Acetyl CoA

- Pyruvate Dehydrogenase



8-13

Conversion of Pyruvate to Acetyl CoA

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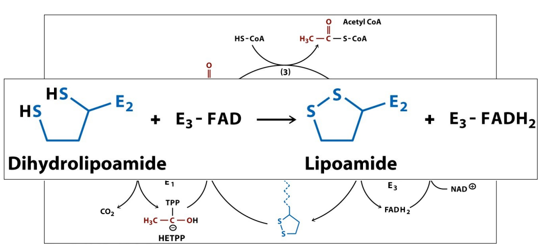

8-14

Conversion of Pyruvate to Acetyl CoA

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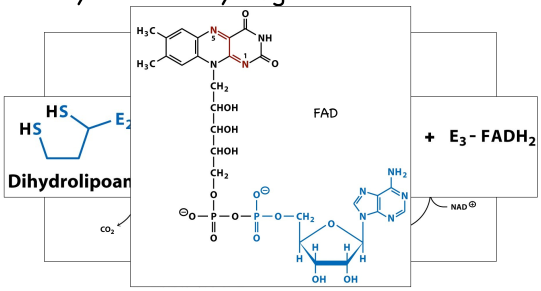

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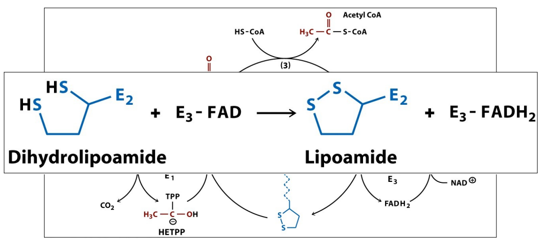
8-15

Conversion of Pyruvate to Acetyl CoA

- Pyruvate Dehydrogenase



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8-16

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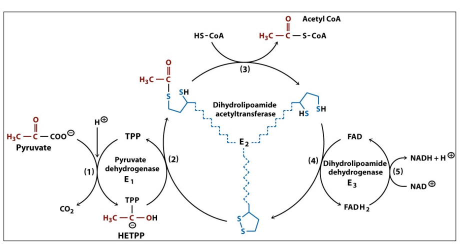

Chem 352, Lecture 8, Part III: Citric Acid Cycle

8-17

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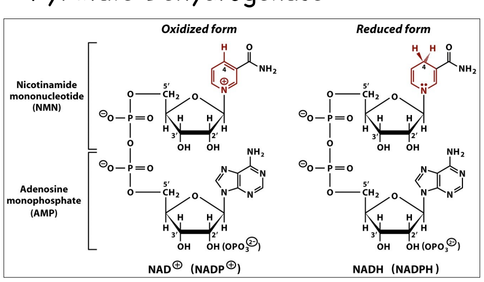

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8-19

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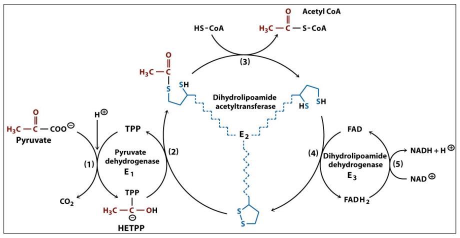

9-1

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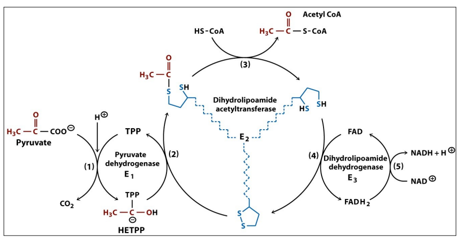

9-2

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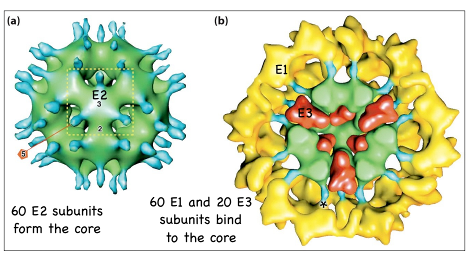

9-3

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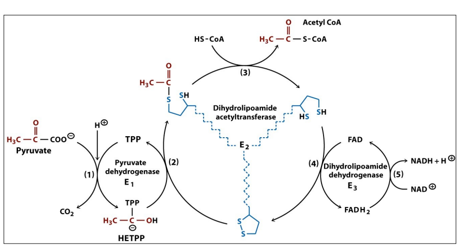

10-1

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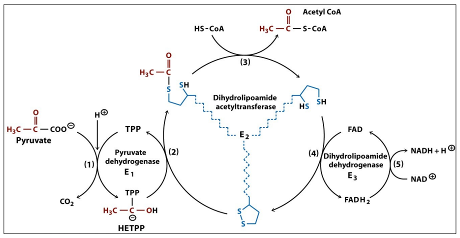

10-2

Conversion of Pyruvate to Acetyl CoA

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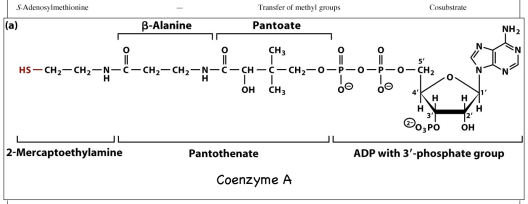

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10-5

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Conversion of Pyruvate to Acetyl CoA

10-6

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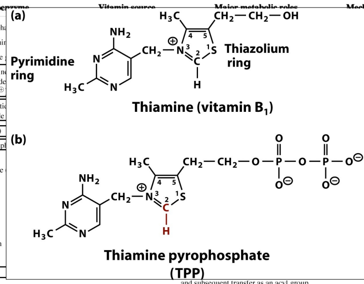

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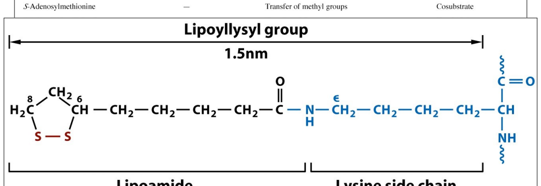
10-8

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



Coenzyme	Vitamin source	Major metabolic roles	Mechanistic role
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

Conversion of Pyruvate to Acetyl CoA

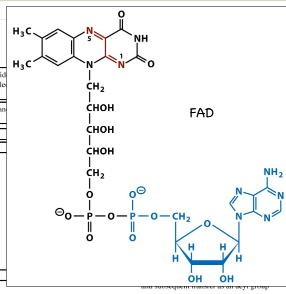
TABLE 7.2 Major coenzymes

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

10-9

Conversion of Pyruvate to Acetyl CoA

TABLE 7.2 Major coenzymes



Coenzyme	Vitamin source	Major metabolic roles	Mechanistic role
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Vitamin K	Vitamin K	Carboxylation of some glutamate residues	Prosthetic group
Ubiquinone (Q)	—	Lipid-soluble electron carrier	Cosubstrate

10-10

Conversion of Pyruvate to Acetyl CoA

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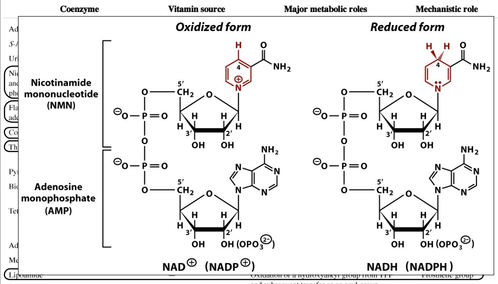
10-11

Conversion of Pyruvate to Acetyl CoA

TABLE 7.2 Major coenzymes



Coenzyme	Vitamin source	Major metabolic roles	Mechanistic role
		and subsequent transfer as an acyl group	
Retinal	Vitamin A	Vision	Prosthetic group
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Ubiquinone (Q)	—	Lipid-soluble electron carrier	Cosubstrate

10-12

Conversion of Pyruvate to Acetyl CoA

10-13

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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
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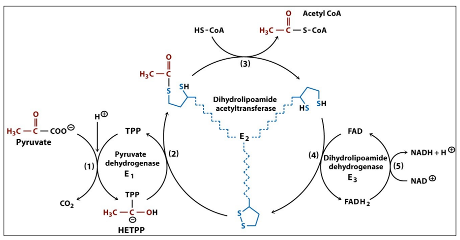
Lipoamide	—	Oxidation of a hydroxyalkyl group from TPP and subsequent transfer as an acyl group	Prosthetic group
Retinal	Vitamin A	Vision	Prosthetic group
Vitamin K	Vitamin K	Carboxylation of some glutamate residues	Prosthetic group
Ubiquinone (Q)	—	Lipid-soluble electron carrier	Cosubstrate

Conversion of Pyruvate to Acetyl CoA

10-14

- Pyruvate Dehydrogenase



The Citric Acid Cycle

11-1

- Catabolic Mode

TABLE 13.1 The enzymatic reactions of the citric acid cycle.

Reaction	Enzyme
1. Acetyl CoA + Oxaloacetate + H_2O ⟶ Citrate + HS-CoA + $H^{\oplus}$	Citrate synthase
2. Citrate ⇌ Isocitrate	Aconitase (Aconitate hydratase)
3. Isocitrate + $NAD^{\oplus}$ ⟶ α-Ketoglutarate + NADH + CO_2	Isocitrate dehydrogenase
4. α-Ketoglutarate + HS-CoA + $NAD^{\oplus}$ ⟶ Succinyl CoA + NADH + CO_2	α-Ketoglutarate dehydrogenase complex
5. Succinyl CoA + GDP (or ADP) + P_i ⇌ Succinate + GTP(or ATP) + HS-CoA	Succinyl-CoA synthetase
6. Succinate + Q ⇌ Fumarate + QH_2	Succinate dehydrogenase complex
7. Fumarate + H_2O ⇌ L-Malate	Fumarase (Fumarate hydratase)
8. L-Malate + $NAD^{\oplus}$ ⇌ Oxaloacetate + NADH + $H^{\oplus}$	Malate dehydrogenase
Net equation:	
Acetyl CoA + 3 $NAD^{\oplus}$ + Q + GDP (or ADP) + P_i + 2 H_2O ⟶ HS-CoA + 3 NADH + QH_2 + GTP (or ATP) + 2 CO_2 + 2 $H^{\oplus}$	

The Ci

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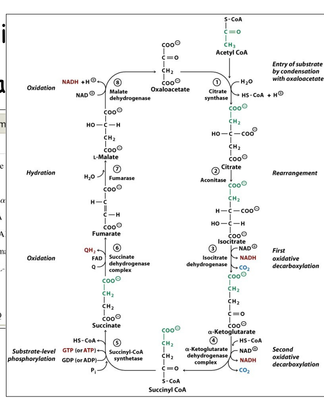
- Cata

TABLE 13.1 The enzym

Reaction	
1. Acetyl CoA + Oxaloacetate	thase
2. Citrate ⇌ Isocitrate	(Aconitate hydratase)
3. Isocitrate + $NAD^{\oplus}$ ⟶ α	ehydrogenase
4. α-Ketoglutarate + HS-CoA	arate dehydrogenase complex
5. Succinyl CoA + GDP (or A	oA synthetase
6. Succinate + Q ⇌ Fum	ehydrogenase complex
7. Fumarate + H_2O ⇌ L-	Fumarate hydratase)
8. L-Malate + $NAD^{\oplus}$ ⇌	ydrogenase
Net equation:	
Acetyl CoA + 3 $NAD^{\oplus}$ + Q	2 CO_2 + 2 $H^{\oplus}$



The Citric Acid Cycle

- Catabolic Mode

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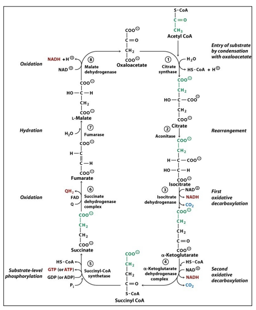
4. α-Ketoglutarate + HS-CoA + $NAD^{\oplus}$ ⟶ Succinyl CoA + NADH + CO_2	α-Ketoglutarate dehydrogenase complex
5. Succinyl CoA + GDP (or ADP) + P_i ⇌ Succinate + GTP(or ATP) + HS-CoA	Succinyl-CoA synthetase
6. Succinate + Q ⇌ Fumarate + QH_2	Succinate dehydrogenase complex
7. Fumarate + H_2O ⇌ L-Malate	Fumarase (Fumarate hydratase)
8. L-Malate + $NAD^{\oplus}$ ⇌ Oxaloacetate + NADH + $H^{\oplus}$	Malate dehydrogenase
Net equation:	
Acetyl CoA + 3 $NAD^{\oplus}$ + Q + GDP (or ADP) + P_i + 2 H_2O ⟶ HS-CoA + 3 NADH + QH_2 + GTP (or ATP) + 2 CO_2 + 2 $H^{\oplus}$	

11-3

The Citric Acid Cycle

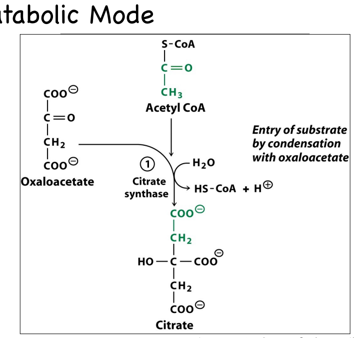
- Catabolic Mode



12-1

The Citric Acid Cycle

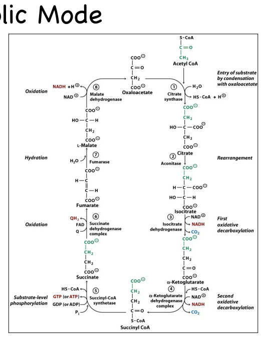
- Catabolic Mode



12-2

The Citric Acid Cycle

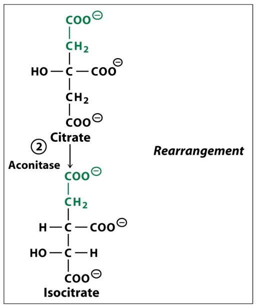
- Catabolic Mode



12-3

The Citric Acid Cycle

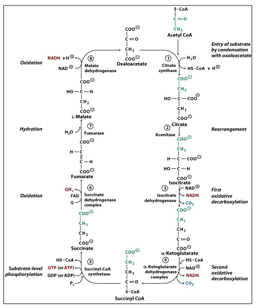
- Catabolic Mode



12-4

The Citric Acid Cycle

- Catabolic Mode



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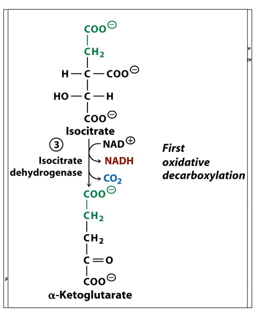
The Citric Acid Cycle

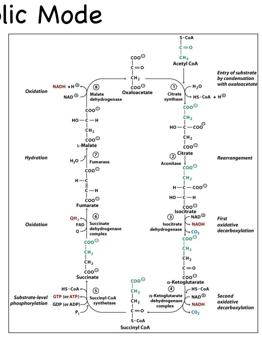
- Catabolic Mode



12-6

The Citric Acid Cycle

- Catabolic Mode



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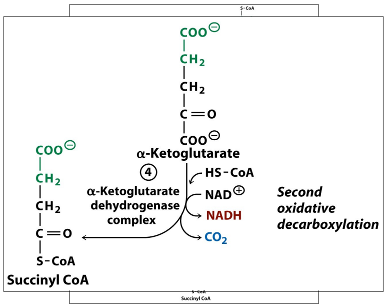
12-8

The Citric Acid Cycle

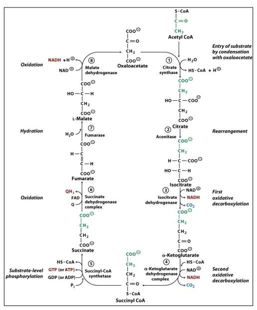
- Catabolic Mode



12-9

The Citric Acid Cycle

- Catabolic Mode



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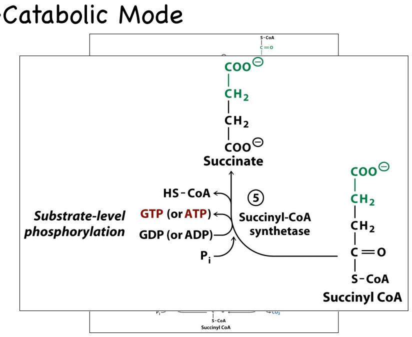
The Citric Acid Cycle

- Catabolic Mode



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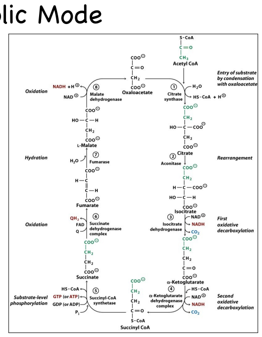
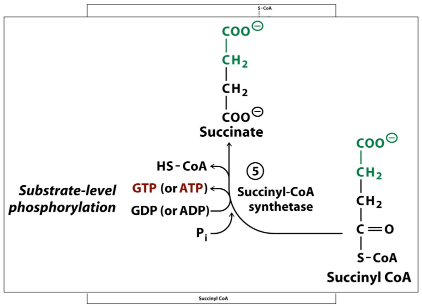
The Citric Acid Cycle

- Catabolic Mode



The Citric Acid Cycle

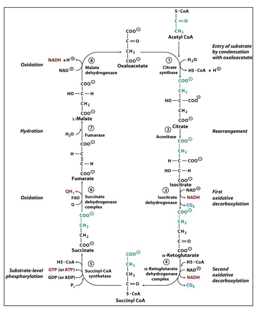
- Catabolic Mode



12-12

The Citric Acid Cycle

- Catabolic Mode



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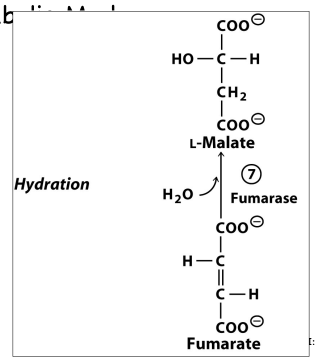
The Citric Acid Cycle

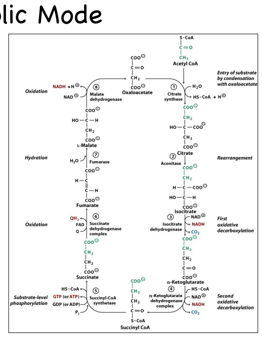
- Catab



12-14

The Citric Acid Cycle

- Catabolic Mode

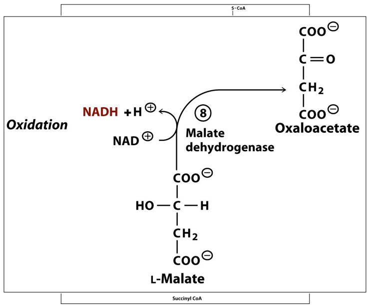


12-15

12-16

The Citric Acid Cycle

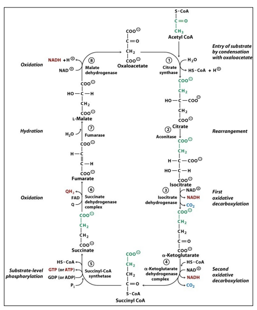
- Catabolic Mode



12-17

The Citric Acid Cycle

- Catabolic Mode



12-18

The Citric Acid Cycle

- Catabolic Mode

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Reaction	Enzyme
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2. Citrate ⇌ Isocitrate	Aconitase (Aconitate hydratase)
3. Isocitrate + $NAD^{\oplus}$ ⟶ α-Ketoglutarate + NADH + CO_2	Isocitrate dehydrogenase
4. α-Ketoglutarate + HS-CoA + $NAD^{\oplus}$ ⟶ Succinyl CoA + NADH + CO_2	α-Ketoglutarate dehydrogenase complex
5. Succinyl CoA + GDP (or ADP) + P_i ⇌ Succinate + GTP(or ATP) + HS-CoA	Succinyl-CoA synthetase
6. Succinate + Q ⇌ Fumarate + QH_2	Succinate dehydrogenase complex
7. Fumarate + H_2O ⇌ L-Malate	Fumarase (Fumarate hydratase)
8. L-Malate + $NAD^{\oplus}$ ⇌ Oxaloacetate + NADH + $H^{\oplus}$	Malate dehydrogenase

Net equation:

Acetyl CoA + 3 $NAD^{\oplus}$ + Q + GDP (or ADP) + P_i + 2 H_2O ⟶ HS-CoA + 3 NADH + QH_2 + GTP (or ATP) + 2 CO_2 + 2 $H^{\oplus}$

13

Chem 352 - Lecture 8
Carbohydrate Metabolism
Part III: Citric Acid Cycle
14. April, 2014

Question for the Day: One of the observations that led Hans Krebs to discover the citric acid cycle, was that dicarboxylic acids, such as fumarate and succinate, had a catalytic effect on the oxidation of glucose to CO_2 and H_2O by muscle tissue. Explain this observation.

The Citric Acid Cycle

- What you should know about each reaction in the citric acid cycle
  - The structures and names of each intermediates
  - The structures and names of the subtrates and products.
  - The names of the enzymes.
  - One interesting aspect each reaction in the cycle.

14-1

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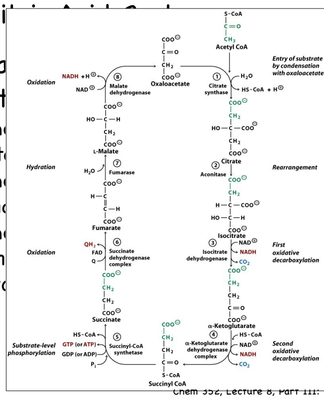


14-2

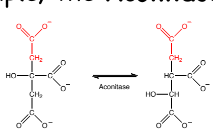
The Citric Acid Cycle

- What you should know about each reaction in the citric acid cycle
  - The structures and names of each intermediates
  - The structures and names of the subtrates and products.
  - The names of the enzymes.
  - One interesting aspect each reaction in the cycle.

14-3

The Citric Acid Cycle

- For example, the **Aconitase** reaction



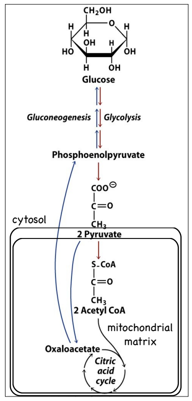
Citrate Isocitrate

  - Class: Isomerase
  - Interesting features of the reaction:
    - The -OH is moved towards the carbon that came from the oxaloacetate used in the citrate synthase reaction.
    - Of the 4 possible stereoisomers of isocitrate, only one is produced (2R,3S)

15

The Citric Acid Cycle

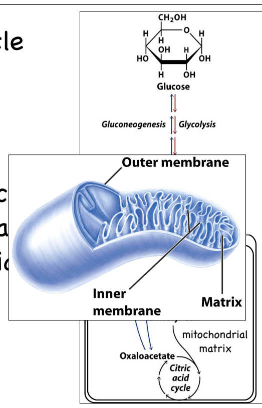
- In mammals, the pyruvate dehydrogenase reaction and the citric acid cycle take place in the mitochondrial matrix.



16-1

The Citric Acid Cycle

- In mammals, the pyruvate dehydrogenase reaction and the c acid cycle take pla in the mitochondri matrix.



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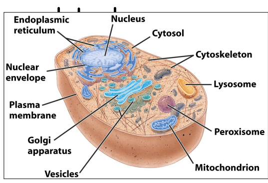
The Citric Acid Cycle

- In mammals, the pyruvate



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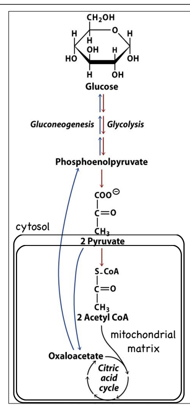

16-3

The Citric Acid Cycle

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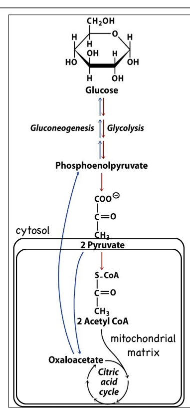
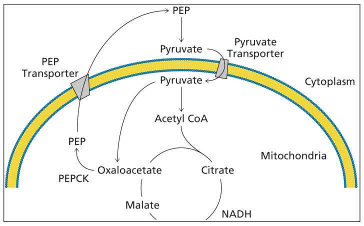


16-4

The Citric Acid Cycle

- Transporters are used to move pyruvate through the inner mitochondrial membrane and into the matrix.



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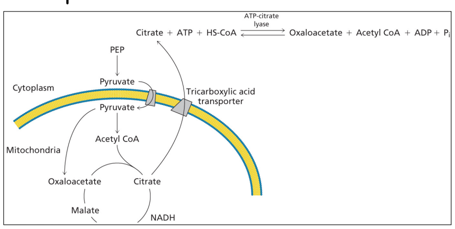
The Citric Acid Cycle

- When Acetyl CoA is require in the cytoplasm for fatty acid synthesis, it is transported out as citrate.



18

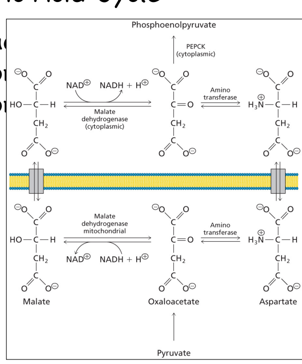
The Citric Acid Cycle

- For gluconeogenesis, and alternative to transporting PEP out of the matrix is to transport oxaloacetate out as malate.

19-1

The Citric Acid Cycle

- For gluc ve to transpo k is to transpo te.



19-2

19-3

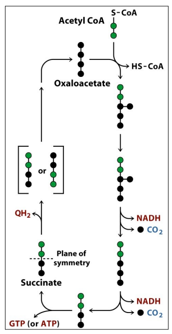
The Citric Acid Cycle

- For gluconeogenesis, and alternative to transporting PEP out of the matrix is to transport oxaloacetate out as malate.

20

The Citric Acid Cycle

- Catabolic Mode
  - None of CO_2 released in the first round comes directly from the acetyl group.

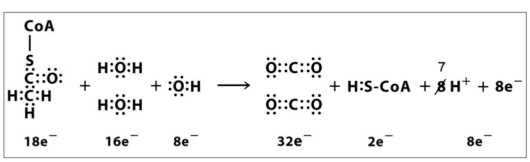


21-1

The Citric Acid Cycle

- Where do the electrons come from?

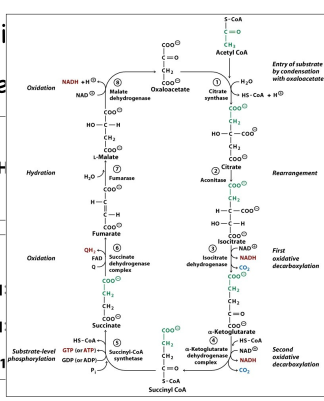
$$CH_3\text{-}C(=O)\text{-}S\text{-}CoA + 2\,H_2O + OH^{\ominus} \longrightarrow 2\,CO_2 + HS\text{-}CoA + 7\,H^{\oplus} + 8e^{\ominus}$$



21-2

The Ci

- Whe … from?



The Citric Acid Cycle

•Where do the electrons come from?

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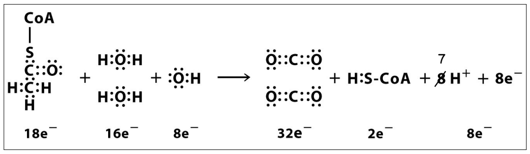


21-3

The Citric Acid Cycle

•Substrate level phosphorylation.

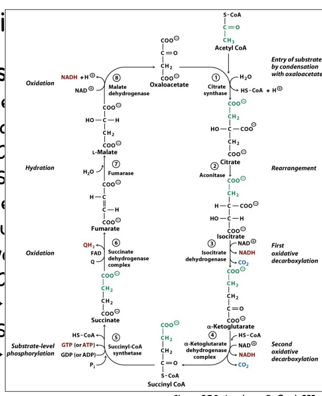
- ✦ There are two reactions that involve the hydrolysis of a “high energy” thioester bond.
  - ‣ Citrate synthase
  - ‣ Succinyl-CoA synthetase
- ✦ The high negative free energy (≈ -31 kJ/mol) is used for two different purposes in these two reactions.
  - ‣ Citrate synthase
    - ✦ Drives cycle in the clockwise direction.
  - ‣ Succinyl-CoA synthetase
    - ✦ Coupled to the synthesis of GTP (ATP)

22-1

The Ci

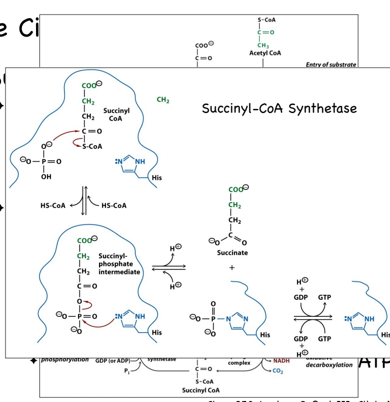
•Subs

✦ The ... the
hyd ... r bond.
✦ The ... kJ/mol)
is u ... these
tw ... ction.
... ATP)



22-2

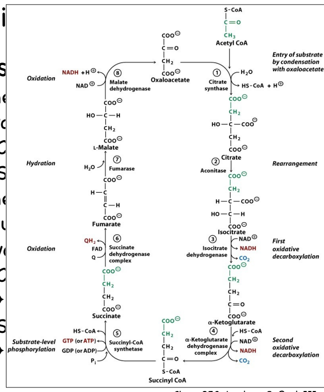
The Ci



22-3

22-4

The Ci



•Subs
- The ... the hy... r bond.
  - C
  - S
- The ... kJ/mol) is u... these tw...
  - C
    - ... ction.
  - S
    - ... ATP)

22-5

The Citric Acid Cycle

•Substrate level phosphorylation.
- There are two reactions that involve the hydrolysis of a "high energy" thioester bond.
  - Citrate synthase
  - Succinyl-CoA synthetase
- The high negative free energy (≈ -31 kJ/mol) is used for two different purposes in these two reactions.
  - Citrate synthase
    - Drives cycle in the clockwise direction.
  - Succinyl-CoA synthetase
    - Coupled to the synthesis of GTP (ATP)

23-1

The Citric Acid Cycle

•Reduced nucleotides are used in oxidative phosphorylation to make ATP.

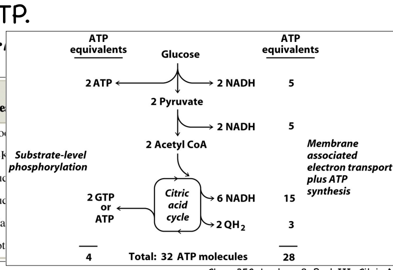
•ATP's produced per Acetyl-CoA

Reaction	Energy-yielding product	ATP equivalents
Isocitrate dehydrogenase	NADH	2.5
α-Ketoglutarate dehydrogenase complex	NADH	2.5
Succinyl-CoA synthetase	GTP or ATP	1.0
Succinate dehydrogenase complex	QH_2	1.5
Malate dehydrogenase	NADH	2.5
Total		10.0

23-2

The Citric Acid Cycle

•Reduced nucleotides are used in oxidative phosphorylation to make ATP.



23-3

The Citric Acid Cycle

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Succinyl-CoA synthetase	GTP or ATP	1.0
Succinate dehydrogenase complex	QH_2	1.5
Malate dehydrogenase	NADH	2.5
Total		10.0

24

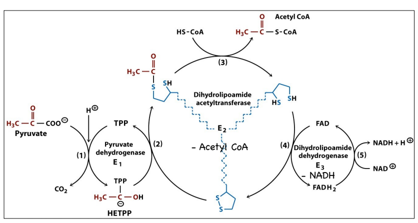
Regulation of the The Citric Acid Cycle

- Like glycolysis and gluconeogenesis, the citric acid cycle is closely regulated to meet the catabolic and anabolic needs of the cell and the organism.

25-1

Regulation of the The Citric Acid Cycle

- The flow of Acetyl-CoA into the cycle is regulated by the pyruvate dehydrogenase complex



25-2

Regulation of the The Citric Acid Cycle

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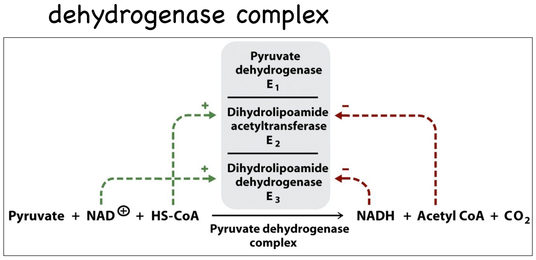

Regulation of the The Citric Acid Cycle

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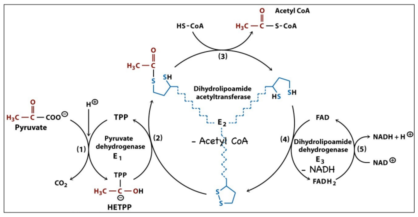
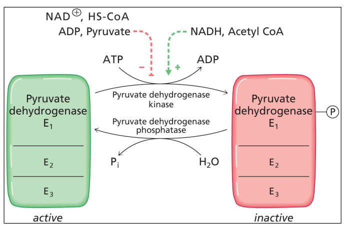


25-3

Regulation of the The Citric Acid Cycle

- Mammalian pyruvate dehydrogenase is also covalently regulated



26

Regulation of the The Citric Acid Cycle

- Three reactions in the citric acid cycle are also allosterically regulated
  - Citrate synthase
    - + α-Ketoglutarate (bacteria)
    - - NADH (bacteria)

27

Regulation of the The Citric Acid Cycle

- Three reactions in the citric acid cycle are allosterically regulated
  - Isocitrate dehydrogenase
    - + Ca^{2+} (mammals)
    - + ADP (mammals)
    - - NADH (mammals)

28-1

Regulation of the The Citric Acid Cycle

- Three reactions in the citric acid cycle are allosterically regulated
  - Isocitrate dehydrogenase
    - + Ca^{2+} (mammals)
    - + ADP (mammals)
    - - NADH (mammals)

Ca^{2+} is a secondary messenger, whose levels are hormonally controlled in the mitochondria

28-2

Regulation of the The Citric Acid Cycle

- Three reactions in the citric acid cycle are allosterically regulated
  - α-Ketoglutarate dehydrogenase
    - Unlike pyruvate dehydrogenase, it is not regulated by phosphorylation
    - + Ca^{2+} (Bind to E_1 and lower K_M)
    - - Succinyl-CoA
    - - NADH

29

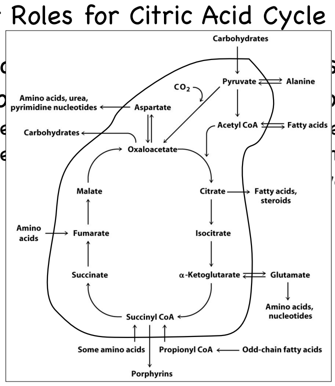
Other Roles for Citric Acid Cycle

- Besides serving as intermediates in the oxidation of acetyl groups to CO_2,
  - the citric acid cycle intermediates are also the starting and ending points for a number of other anabolic and catabolic pathways.

30-1

Other Roles for Citric Acid Cycle

- Besi... in the o... CO_2,
  - the ... also the ... number of ...ays.



30-2

Other Roles for Citric Acid Cycle

- Besides serving as intermediates in the oxidation of acetyl groups to CO_2,
  - the citric acid cycle intermediates are also the starting and ending points for a number of other anabolic and catabolic pathways.

30-3

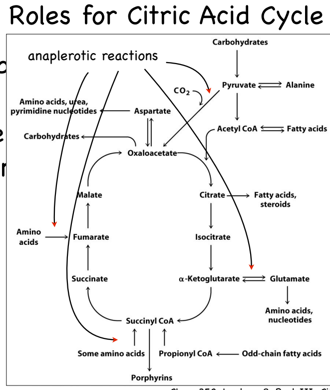
Other Roles for Citric Acid Cycle

- Anaplerotic reactions ("filling up") feed material into the citric acid cycle as citric acid cycle intermediates.

31-1

Other Roles for Citric Acid Cycle

- Anap… feed… cycle… interm…



31-2

Other Roles for Citric Acid Cycle

- Anaplerotic reactions ("filling up") feed material into the citric acid cycle as citric acid cycle intermediates.

31-3

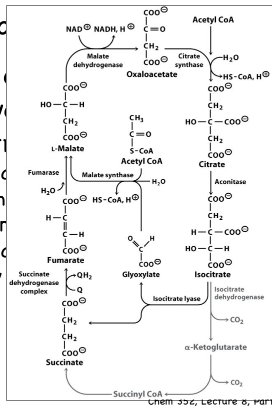
The Glyoxylate Pathway (Shunt)

- Many organisms are able to bypass the two decarboxylation reactions in the citric acid cycle.
  - This allows Acetyl-CoA to be used to build up the levels of the citric acid cycle intermediates.
  - This allows Acetyl-CoA that is derived from fatty acids to be used for glucose synthesis.

32-1

The Glyo

- Many bypass the tw tions in the cit
  - This d to build up th cle interm
  - This rived from fatty synthesis.



32-2

The Glyoxylate Pathway (Shunt)

- Many organisms are able to bypass the two decarboxylation reactions in the citric acid cycle.
  - This allows Acetyl-CoA to be used to build up the levels of the citric acid cycle intermediates.
  - This allows Acetyl-CoA that is derived from fatty acids to be used for glucose synthesis.

32-3

The Glyoxylate Pathway (Shunt)

- The glycoxylate shunt is turned on by phosphorylating isocitrate dehydrogenase
- Isocitrate, oxaloacetate, pyruvate, 3-phosphoglycerate, PEP promote dephosphorylation
  - Turning off the glyoxylate shunt.

33-1

The Glyo)

•The gl ned on
by phos
dehydr

•Isocitr vate, 3-
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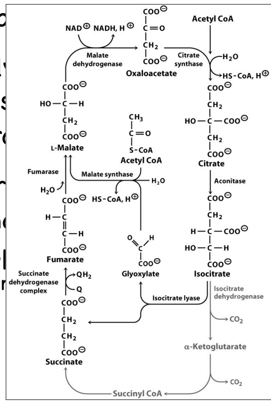
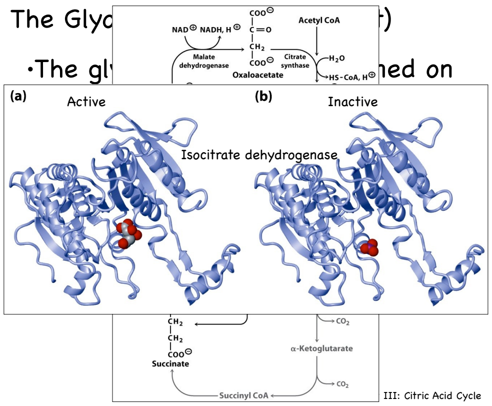


33-2

The Glyo)

•The gl ned on



33-3

The Glyo)

•The gl ned on
by phos
dehydr

•Isocitr vate, 3-
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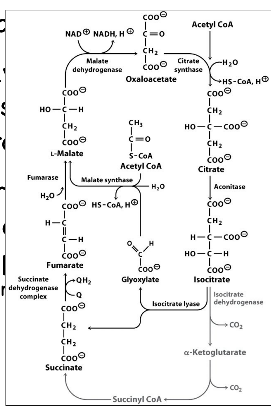


33-4

The Glyoxylate Pathway (Shunt)

•The glycoxylate shunt is turned on by phosphorylating isocitrate dehydrogenase

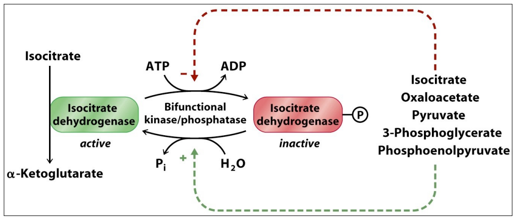
•Isocitrate, oxaloacetate, pyruvate, 3-phosphoglycerate, PEP promote dephosphorylation

✦ Turning off the glyoxylate shunt.

33-5

The Glyoxylate Pathway (Shunt)

- The glycoxylate shunt is turned on



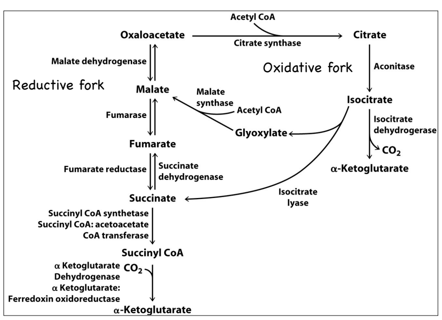
33-6

The Glyoxylate Pathway (Shunt)

- The glycoxylate shunt is turned on by phosphorylating isocitrate dehydrogenase
- Isocitrate, oxaloacetate, pyruvate, 3-phosphoglycerate, PEP promote dephosphorylation
  - Turning off the glyoxylate shunt.

33-7

Evolution of the Citric Acid Cycle



34

Next Up

- Lecture 8 - Carbohydrate Metabolism
  - Part IV: Electron Transport and ATP Synthesis (Moran et al., Chapter 14)

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