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

Introduction

The citric acid cycle has both catabolic and anabolic functions.

- Catabolic Oxidizes the 2-carbon acetyl group to CO₂ and produces reduced nucleotides (NADH + H⁺ and FADH₂)
- Anabolic The citric acid cycle intermediates serve as starting material for the biosynthesis of amino acids, heme groups, glucose, et al.

Chem 352, Lecture 8, Part III: Citric Acid Cycle 2

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.



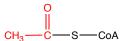
Hans Krebs (1900–1981) Nobel Prize in Physiology and Medicine, 1953

Chem 352, Lecture 8, Part III: Citric Acid Cycle 3

3

Acetyl CoA

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

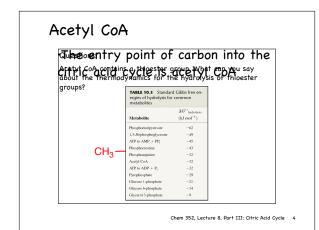


Chem 352, Lecture 8, Part III: Citric Acid Cycle 4

Acetyl CoA Theoentry point of carbon into the critical concentring of the star space what copy a say about the mer modynamics for the hydrodysis of filoester groups? CH3—C—S—COA

Chem 352, Lecture 8, Part III: Citric Acid Cycle 4

4-2



4-3

Acetyl CoA
•The entry point of carbon into the citric acid cycle is acetyl CoA
O CH ₃
Chem 352, Lecture 8, Part III: Citric Acid Cycle 4

4-4

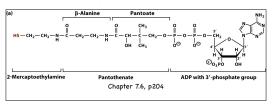
-The entry point of carbon into the citric acid cycle is acetyl CoA

(a) β-Alanine Pantoate
HS-CH₂-CH₂-CH₂-CH₃-CH₃-CH₃-CH₄-CH₂-CH₂-CH₂-CH₂-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-CH₃-

Acetyl CoA

Acetyl CoA

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



Chem 352, Lecture 8, Part III: Citric Acid Cycle 4

4-7

Acetyl CoA

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

Chem 352, Lecture 8, Part III: Citric Acid Cycle 4

4-8

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

5

,, ...,,,,,,

Chem 352, Lecture 8, Part III: Citric Acid Cycle 5

•Pyruvate dehydrogenase is a large enzyme complex that converts pyruvate to acetyl-CoA and CO₂.

coo [©] c=o + HS-CoA	dehvdr	ivate ogenase	S-CoA C=0	+ co,
CH ₂	NAD⊕	NADH	´ CH₃ Acetyl CoA	-

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

Chem 352, Lecture 8, Part III: Citric Acid Cycle 6

1	•	٦	۰	
٠	۰	٦	١	
١		,		

Conversion of Pyruvate to Acetyl CoA

•Pyruvate dehydrogenase is a large enzyme complex that converts pyruvate to acetyl-CoA and CO₂.

$$\begin{array}{c|c} \mathsf{COO}^{\bigodot} & \mathsf{Pyruvate} \\ | & \mathsf{C} = \mathsf{O} \\ | & \mathsf{C} + \mathsf{D} \\ | & \mathsf{CH}_3 \\ \mathsf{Pyruvate} & \mathsf{NAD}^{\bigodot} & \mathsf{NADH} & \mathsf{Acetyl CoA} \\ \end{array}$$

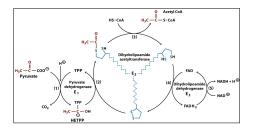
 Three different subunits catalyze five subreactions to to carry out this overall reaction.

Chem 352, Lecture 8, Part III: Citric Acid Cycle 7

7

0

Conversion of Pyruvate to Acetyl CoA •Pyruvate Dehydrogenase

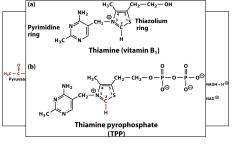


Chem 352, Lecture 8, Part III: Citric Acid Cycle

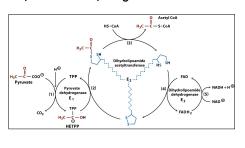
8-1

Conversion of Pyruvate to Acetyl CoA

·Pyruvate Dehydrogenase



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



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

8-4

8-3

Conversion of Pyruvate to Acetyl CoA

•Pyruvate Dehydrogenase

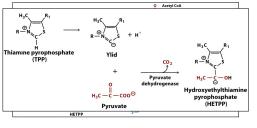
Chem 352, Lecture 8, Part III: Citric Acid Cycle

8-5

	TPP Ylid
Conver	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$
•Pyru	H ₂ C - C - Pyruvate OH OO
H₃C ,R	Enz—B;
R-N _C S	Hydroxyethylthiamine pyrophosphate (HETPP)
 H Thiamine pyropi (TPP)	"-"\c\c\c\c\c\c\c\c\c\c\c\c\c\c\c\c\c\c\
	H ₂ C-CH-O _H E _{RX} = B-1 H ₃ C-C-OH H ₃ C-C-OH C-OH
	yethylthiamine ophosphate (HETPP)
	$\begin{array}{cccccccccccccccccccccccccccccccccccc$
	H ₃ C-C Enz-B Enz-B Citric Acid Cycle Acetaldehyde

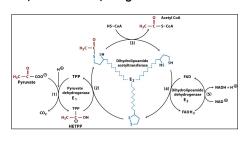
Conversion of Pyruvate to Acetyl CoA

•Pyruvate Dehydrogenase



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

Conversion of Pyruvate to Acetyl CoA •Pyruvate Dehydrogenase

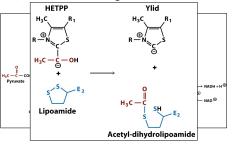


Chem 352, Lecture 8, Part III: Citric Acid Cycle

8-7

Conversion of Pyruvate to Acetyl CoA

·Pyruvate Dehydrogenase

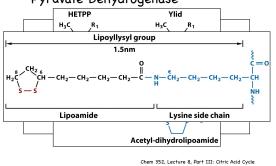


Chem 352, Lecture 8, Part III: Citric Acid Cycle

8-8

Conversion of Pyruvate to Acetyl CoA

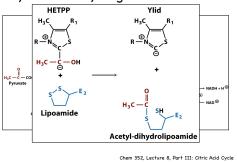
·Pyruvate Dehydrogenase



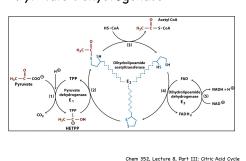
8-9

Conversion of Pyruvate to Acetyl CoA

·Pyruvate Dehydrogenase

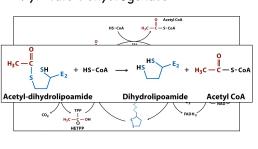


Conversion of Pyruvate to Acetyl CoA ·Pyruvate Dehydrogenase



8-11

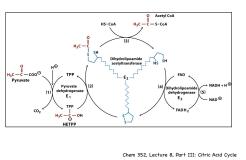
Conversion of Pyruvate to Acetyl CoA ·Pyruvate Dehydrogenase



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

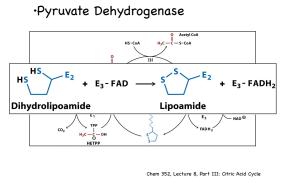
8-12

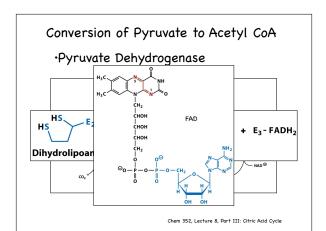
Conversion of Pyruvate to Acetyl CoA ·Pyruvate Dehydrogenase



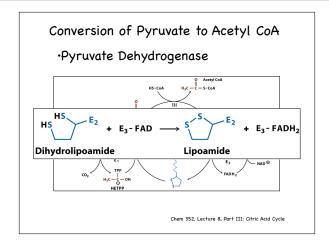
8-13

Conversion of Pyruvate to Acetyl CoA ·Pyruvate Dehydrogenase









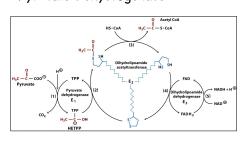
8-16

·Pyruvate Dehyd	rogenase O Acetyl CoA
H ₃ C - C O O O Pyruvate (2) H ₃ C - C - C O O O Pyruvate (2) H ₃ C - C - C O O O O O O O O O O O O O O O	CoA H ₁ C = C = 5-CoA Dihydrolipoamide Actyltranifenses E = 1

8-17

	Oxidized form	Reduced form
L	VH2 ONH2 VH2 ON OH OH OH OHO NADO (NADO () NADO () NA	O P P O H H H H H H H H H H H H H H H H

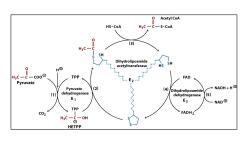
Conversion of Pyruvate to Acetyl CoA •Pyruvate Dehydrogenase



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

8-19

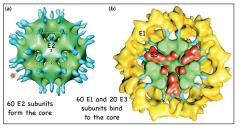
Conversion of Pyruvate to Acetyl CoA •Pyruvate Dehydrogenase



Chem 352, Lecture 8, Part III: Citric Acid Cycle 9

9-1

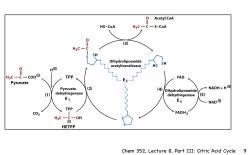
Conversion of Pyruvate to Acetyl	CoA
·Pyruvate Dehydrogenase	



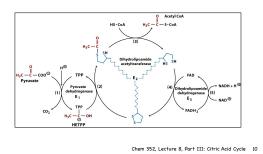
Chem 352, Lecture 8, Part III: Citric Acid Cycle 9

9-2

Conversion of Pyruvate to Acetyl CoA •Pyruvate Dehydrogenase



Conversion of Pyruvate to Acetyl CoA •Pyruvate Dehydrogenase



10-1

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 [⊕]) and nicotinamide adenine dinucleotide phosphate (NADP [⊕])	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	
Lipcamide	-	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	

10-2

Conversion	of Pyruvate	to Acetyl	CoA

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 [⊕]) and nicotinamide adenine dinucleotide phosphate (NADP [⊕])	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
Lipcumide	_	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

10-3

Conversion of Pyruvate to Acetyl CoA

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
)(3-Alanine	Pantoate	
	11	CH ₁ O O	N_
Ĭ	Ĭ	1.2	5'
HS-CH ₂ -CH ₂ -N-C-	CH ₂ —CH ₂ —N—C—C	CH — C — CH2—O—P—O—P—O—	CH ₂ O N
		bh ch₃ ò⊝ ò⊝ ,	1 1
		G-	3' 2'
			O₃PO OH
-Mercaptoethylamine	Pantothen	ate ADP with 3'	phosphate gro
			, ,
	Coen	zyme A	
Adenosylcobalamin	Coen	Intramolecular rearrangements	Prosthetic group
Adenosylcobalamin Methylcobalamin		<u>'</u>	Prosthetic group Prosthetic group
	Cobalamin (B ₁₂)	Intramolecular rearrangements Transfer of methyl groups Oxidation of a hydroxyalkyl group from TPP	0 1
Methylcobalamin	Cobalamin (B ₁₂)	Intramolecular rearrangements Transfer of methyl groups	Prosthetic group
Methylcobalamin	Cobalamin (B ₁₂)	Intramolecular rearrangements Transfer of methyl groups Oxidation of a hydroxyalkyl group from TPP	Prosthetic group
Methylcobalamin Lipcamide	Cobalamin (B ₁₂) Cobalamin (B ₁₂) -	Intramolecular rearrangements Transfer of methyl groups Oxidation of a hydroxyalkyl group from TPP and subsequent transfer as an acyl group	Prosthetic group Prosthetic group

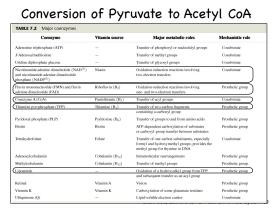
Conversion of Pyruvate to Acetyl CoA

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 [⊕]) and nicotinamide adenine dinucleotide phosphate (NADP [⊕])	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
Lipcamide	_	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 (O)	_	Lipid-soluble electron carrier	Cosubstrate

10-5

		ruvate to Acet	•
TABLE 7.2 Major coenzyn	nes		
Coc. (a)	Vitamin course	Major motobolic roles	Manistic role
Adenosine triphospha		H₃C CH₂—CH₂—OH	abstrate
S-Adenosylmethionia	NH ₂	⊕ /4 5\	ubstrate
	\CH	12-N3 2 Is Thiazolium	distrate
Pyrimi	dine 🏋 🦷	°Ç´ ring	ubstrate
and nicotinamide ade	H,C N	i i	atomate.
phosphate (NADP®	,		
Flavin mononucleotic	Thia	amine (vitamin B ₁)	thetic group
			ibstrate
(Thiamine pyrophospi		0 0	thetic group
Thiamine pyrophospi			
Pyridoxal phosphate	н₃с	сн₂—сн₂—о—Ё—о—Ё	thetic group
Biotin	NH ₂		O thetic group
	CH₂⊕N	3 2 1S	
Tetrahydrofolate	N Y C.12	%دِّ	abstrate
	.人丿	7	
Adenosylcobalamin	. N		thetic group
Methylcobalamin	Thiamin	ie pyrophosphate	thetic group
Lincamide		(TPP)	thetic group
		and subsequent transfer as an acyl group	manu group
Retinal	Vitamin A	Vision	Prosthetic group
Vitamin K	Vitamin K	Carboxylation of some glutamate residues	Prosthetic group
Ubiquinone (O)		Lipid-soluble electron carrier	Cosubstrate

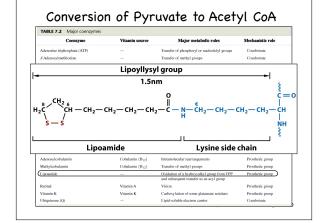
10-6



10-7

_b	

1

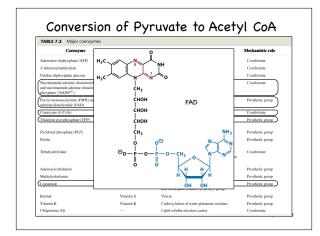


10-8	

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
Lipcamide	-	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



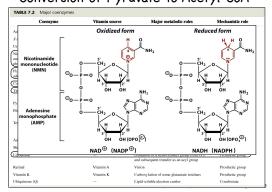
10-10

Conversion of Pyruvate to Acetyl CoA

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
Adenosylcobulamin	Cobalamin (B ₁₂)	Intramolecular rearrangements	Prosthetic group
Methylcobalamin	Cobalamin (B ₁₂)	Transfer of methyl groups	Prosthetic group
Lipcamide	-	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

10-11

Conversion of Pyruvate to Acetyl CoA

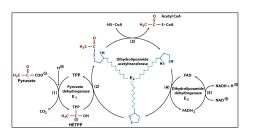


Conversion of Pyruvate to Acetyl CoA

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
Lipcomide	_	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

10-13

Conversion of Pyruvate to Acetyl CoA •Pyruvate Dehydrogenase



10-14

Chem 352, Lecture 8, Part III: Citric Acid Cycle 10

Chem 352, Lecture 8, Part III: Citric Acid Cycle 11

The Citric Acid Cycle •Catabolic Mode

Reaction	Enzyme
 Acetyl CoA + Oxaloacetate + H₂O → Citrate + HS-CoA + H[⊕] 	Citrate synthase
2. Citrate === Isocitrate	Aconitase (Aconitate hydratase)
3. Isocitrate + NAD $^{\oplus}$ $\longrightarrow \alpha$ -Ketoglutarate + NADH + CO ₂	Isocitrate dehydrogenase
4. α-Ketoglutarate + HS-CoA + NAD⊕ → Succinyl CoA + NADH + CO ₂	α-Ketoglutarate dehydrogenase comple
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. Furnarate + H ₂ O ⇒ L-Malate	Fumarase (Fumarate hydratase)
8. L-Malate + NAD⊕ ⇒ Oxaloacetate + NADH + H⊕	Malate dehydrogenase
Net equation:	
Acetyl CoA + 3 NAD \oplus + Q + GDP (or ADP) + P _i + 2 H ₂ O \longrightarrow HS-CoA + 3 NADH + QH	2 + GTP (or ATP) + 2 CO ₂ + 2 H [⊕]
Acetyl CoA + 3 NAD $^{\odot}$ + Q + GDP (or ADP) + P _i + 2 H ₂ O \longrightarrow HS-CoA + 3 NADH + QH	2 + GTP (or ATP) + 2 CO ₂ + 2 H [⊕]

11-1

11-2

TABLE 13.1 The enzym Rection 1. Acryl CoA + Obuloaceter 2. Cinner | Societate | NAD | Double | National | Nat

The Citric Acid Cycle

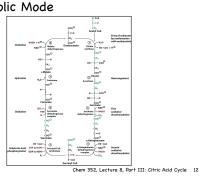
·Catabolic Mode

Reaction	Enzyme
1. Acetyl CoA + Oxaloacetate + $H_2O \longrightarrow Citrate + HS-CoA + H^{\oplus}$	Citrate synthase
2. Citrate === Isocitrate	Aconitase (Aconitate hydratase)
 Isocitrate + NAD[⊕] → α-Ketoglutarate + NADH + CO₂ 	Isocitrate dehydrogenase
 α-Ketoglutarate + HS-CoA + NAD⊕ → Succinyl CoA + NADH + CO₂ 	α-Ketoglutarate dehydrogenase comple:
5. Succinyl CoA + GDP (or ADP) + P _i = Succinate + GTP(or ATP) + HS-CoA	Succinyl-CoA synthetase
6. Succinate + Q	Succinate dehydrogenase complex
7. Fumarate + H ₂ O === L-Malate	Fumarase (Fumarate hydratase)
8. L-Malate + NAD⊕ ⇒ Oxaloacetate + NADH + H⊕	Malate dehydrogenase
Net equation:	
$Acetyl \; CoA \; + \; 3 \; NAD^{\scriptsize\textcircled{\tiny\dag}} \; + \; Q \; + \; GDP \left(or \; ADP \right) \; + \; P_i \; + \; 2 \; H_2O \; \longrightarrow \; HS \cdot CoA \; + \; 3 \; NADH \; + \; QH_2O \; \longrightarrow \; HS \cdot CoA \; + \; 3 \; NADH \; + \; QH_2O \; \longrightarrow \; HS \cdot CoA \; + \; 3 \; NADH \; + \; QH_2O \; \longrightarrow \; HS \cdot CoA \; + \; 3 \; NADH \; + \; QH_2O \; \longrightarrow \; HS \cdot CoA \; + \; 3 \; NADH \; + \; QH_2O \; \longrightarrow \; HS \cdot CoA \; + \; 3 \; NADH \; + \; QH_2O \; \longrightarrow \; HS \cdot CoA \; + \; 3 \; NADH \; + \; QH_2O \; \longrightarrow \; HS \cdot CoA \; + \; 3 \; NADH \; + \; QH_2O \; \longrightarrow \; HS \cdot CoA \; + \; 3 \; NADH \; + \; QH_2O \; \longrightarrow \; HS \cdot CoA \; + \; 3 \; NADH \; + \; QH_2O \; \longrightarrow \; HS \cdot CoA \; + \; 3 \; NADH \; + \; QH_2O \; \longrightarrow \; HS \cdot CoA \; + \; 3 \; NADH \; + \; QH_2O \; \longrightarrow \; HS \cdot CoA \; + \; 3 \; NADH \; + \; QH_2O \; \longrightarrow \; HS \cdot CoA \; + \; 3 \; NADH \; + \; QH_2O \; \longrightarrow \; HS \cdot CoA \; + \; 3 \; NADH \; + \; QH_2O \; \longrightarrow \; HS \cdot CoA \; + \; 3 \; NADH \; + \; QH_2O \; \longrightarrow \; HS \cdot CoA \; + \; 3 \; NADH \; + \; QH_2O \; \longrightarrow \; HS \cdot CoA \; + \; 3 \; NADH \; + \; QH_2O \; \longrightarrow \; HS \cdot CoA \; + \; 3 \; NADH \; + \; QH_2O \; \longrightarrow \; HS \cdot CoA \; + \; 3 \; NADH \; + \; QH_2O \; \longrightarrow \; HS \cdot CoA \; + \; 3 \; NADH \; + \; QH_2O \; \longrightarrow \; HS \cdot CoA \; + \; 3 \; NADH \; + \; QH_2O \; \longrightarrow \; HS \cdot CoA \; + \; 3 \; NADH \; + \; QH_2O \; \longrightarrow \; HS \cdot CoA \; + \; 3 \; NADH \; + \; QH_2O \; \longrightarrow \; $	2 + GTP (or ATP) + 2 CO ₂ + 2 H [⊕]

11-3

The	Citric	Acid	Cycle
1110		, ,,,,,	0,010

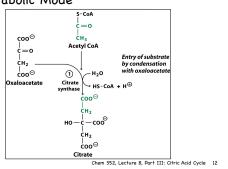
·Catabolic Mode



12-1

The	Citric	Acid	Cycle
-----	--------	------	-------

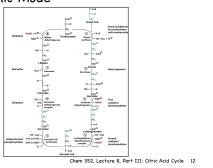
·Catabolic Mode



12-2

The Citric Acid Cycle

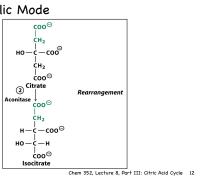
·Catabolic Mode



2-3			



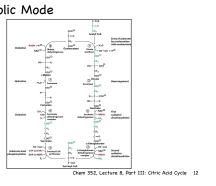
·Catabolic Mode



12-4

The	Citric	Acid	Cycle
1110		, ,,,,,	0,010

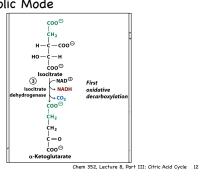
·Catabolic Mode



12-5

The	Citric	Acid	Cycle
-----	--------	------	-------

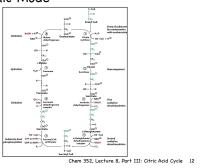
·Catabolic Mode

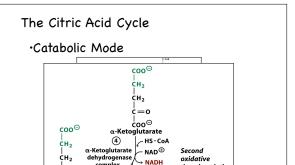


12-6

The Citric Acid Cycle

·Catabolic Mode



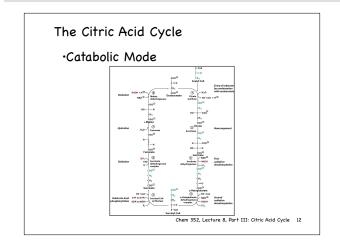


→ CO₂

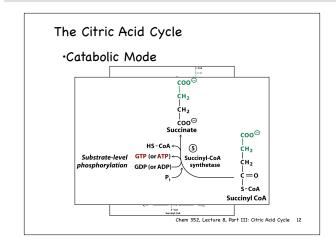
Chem 352, Lecture 8, Part III: Citric Acid Cycle 12

Succinyl CoA

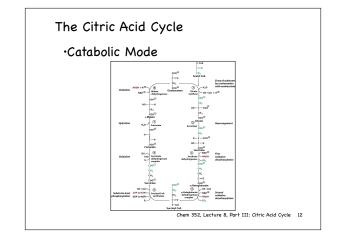




12-9



12-10



Catabolic Mode

*Catabolic Mode

COO

CH2

CH2

CH2

COO

Succinate

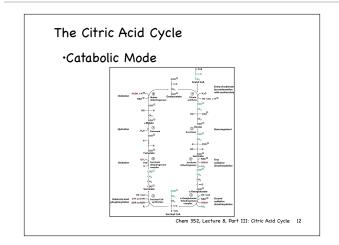
Substrate-level phosphorylation

GTP (or ATP)

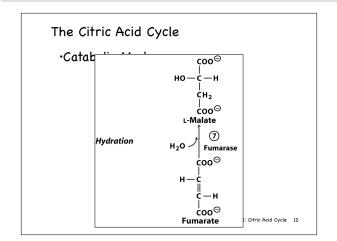
Supplement of the cool of the cool

Chem 352, Lecture 8, Part III: Citric Acid Cycle 12

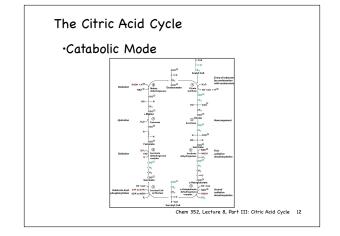




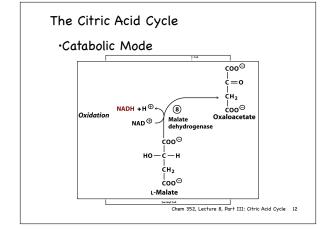








<u> </u>			





The Citri	: A	cid Cyc	cle			
•Catabol	ic N	Node				
	Oxidation	NAZON + N ⁻¹⁰ - O O Malene O O O O O O O O O O O O O O O O O O	COO®	S-Call CH, Acetyl Call Obsete HS-Call	detry of substrate by condensation with ounlescender • H [®]	
	Mydration	HO C H COO Mater HO Personne COO H COO H COO FOR		MO-C-COO® ON: COO® ON: COO® ON: COO® ON: COO® ON: Accelerate COO® ON: H- CCOO®	Acutangement	
	Oxidation	Fumerate Off Sociality Sociality Construction Construction Off Sociality Sociality Construction Construction Off Sociality Sociality Construction Off Sociality Constructi	6el	HO — C — III (000 III III	First existetive decorbusylation	
	Substrate-level pheaphorylasion	,		S. Ketoghtarate © S. Ketoghtarate © S. Ketoghtarate Magnification	Second oxidetive decarbusylation	

·Catabo	olic Mode	
	S-CA	Second whates
TABLE 13.1 The enzymatic re	eactions of the citric acid cycle.	
Reaction		Enzyme
1. Acetyl CoA + Oxaloacetate + H ₂ C	O → Citrate + HS-CoA + H [⊕]	Citrate synthase
2. Citrate === Isocitrate		Aconitase (Aconitate hydratase)
3. Isocitrate $+$ NAD $^{\oplus}$ $\longrightarrow \alpha$ -Ketog	lutarate + NADH + CO ₂	Isocitrate dehydrogenase
4. α-Ketoglutarate + HS-CoA + NAI	O [⊕] → Succinyl CoA + NADH + CO ₂	α-Ketoglutarate dehydrogenase comple
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 ₂ O === L-Malate		Fumarase (Fumarate hydratase)
8. L-Malate + NAD⊕ ← Oxalos	icetate + NADH + H⊕	Malate dehydrogenase
Net equation:	$P \text{ (or ADP)} + P_1 + 2 \text{ H-O} \longrightarrow \text{HS-CoA} + 3 \text{ NADH} + \text{OH-}$	± GTP (∞ ATP) ± 2 CO, ± 2 H [⊕]

12-18	3		

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.

13	

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.

Chem 352, Lecture 8, Part III: Citric Acid Cycle 14

1	4.	-1
	т.	- 1

The Ci[S-CoA C=0		
				CH ₃		
·Wha react			ċ=o i cH₂		Entry of substrate by condensation	ach
VVIIG	Oxidation	NADH +H®+ (8) Malete	COO ① Oxaloacetate Citra	H ₂ O	with axaloacetate	acii
react		NAD [©] Malete dehydrogensse	syntha	HS-COA	+ H ₀	
		но-с-н		CH ₂		
+ The		COD®	NO.	CH2		
int		L-Malate	@1	coo [©] Citrate		
+ The	Hydration	H ₂ O Furnarase	Aconitas	. cooo	Rearrangement	otrates
		н-с		CH ₂		7114166
and		соо [©]		-c-coo [©]		
+ The		Fumarate	_ Is	COO®		
4.05	Oxidation	QH, - Succinate dehydrogenase	(3) Isocitra dehydrogena	NAD [©] NADH	First axidative	ı in the
+ On		o 1 complex coo⊝	detydrogena	C00 [©]	decarboxylation	i in the
cyd		ÇH,		CH ₂ CH ₂		
		ćн ₂ coo⊕		C=0		
		Succinate	coo [©] g-Ker	coo [©] toglutarate		
		HS-CoA - 3	CH ₂ (1)	HS-CoA	Second	
	Substrate-level phosphorylation	GDP (or ADP) Succinyl-CoA synthetase	CH ₂ dehydrogena complex	NADH	axidative decarboxylation	
		P)	C=0	CO2	accaromynanian	

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

Chem 352, Lecture 8, Part III: Citric Acid Cycle	14	

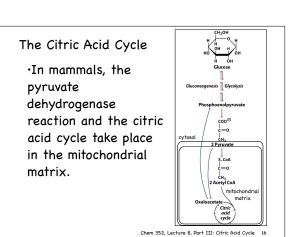
The	Citric	Acid	Cycle
1110		/ 101G	0,000

·For example, the Aconitase reaction

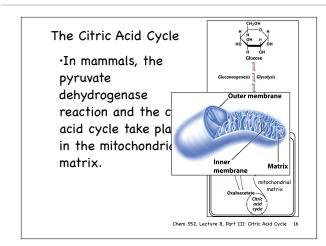
- + Class: Isomerase
- + Interesting features of the reaction:
- \cdot The -OH is moved towards the carbon that came from the oxaloacetate used in the citrate synthase reaction.
- Of the 4 possible stereoisomers of isocitrate, only one is produced (2R,3S)

Chem 352, Lecture 8, Part III: Citric Acid Cycle 15

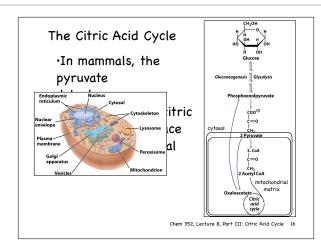
15







16-2

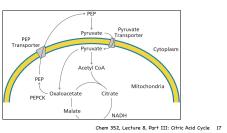


The Citric Acid Cycle	CH ₂ OH H H OH
•In mammals, the pyruvate dehydrogenase reaction and the citric acid cycle take place in the mitochondrial matrix.	Glucose Glucose Glucose Glucose Glucoses Glucoses Glucoses COO® C

6-4	

The	Citric	Acid	$C \setminus$	/cl	6
1116		noiu	\sim	· • •	٠, ۲

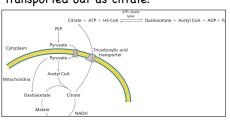
•Transporters are used to move pyruvate through the inner mitochondrial membrane and into the matrix.



17

The Citric Acid Cycle

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



Chem 352, Lecture 8, Part III: Citric Acid Cycle 18

18

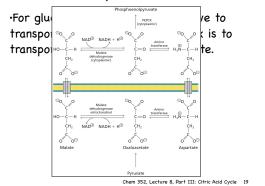
The Citric Acid Cycle

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

Chem 352, Lecture 8, Part III: Citric Acid Cycle 19

19-1

The Citric Acid Cycle



The Citric Acid Cycle

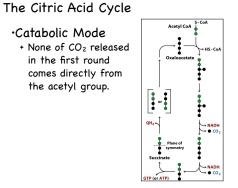
·For gluconeogenesis, and alternative to transporting PEP out of the matrix is to transport oxaloacetate out as malate.

Chem 352, Lecture 8, Part III: Citric Acid Cycle 19

19-3

·Catabolic Mode

+ None of CO2 released in the first round comes directly from the acetyl group.



Chem 352, Lecture 8, Part III: Citric Acid Cycle 20

20

The Citric Acid Cycle

·Where do the electrons come from?

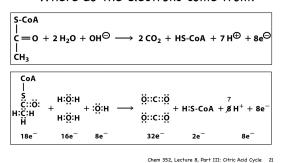
Chem 352, Lecture 8, Part III: Citric Acid Cycle 21

21-1

The C	i		coo [©]	S-CoA C=0 CH ₃ Acetyl CoA	Entry of substrate	
·Whe	2 Oxidation	NADH +H® - (8) Malate debydrogenase	coo⊖ Oxaloacetate	Citrate H5-CoA	by condensation with axaloacetate	from?
S-CoA C=O + 21 CH ₃	Hydration	Ho Coo	Ac	HO—C—COO® CH2 COO® Gitrate contase COO® CH2 H—C—COO®	Rearrangement	'H [⊕] + 8e [©]
CoA S C::O: +		Funnarate QH J FAID Sociaste dehydragenase coogle CH J CH J COOG	ls debydri	CH2 CH2 CH2	First oxidative decarboxylation	7 % H ⁺ + 8e ⁻
18e ⁻	Substrate-level phosphorylation	Succinate HS-CoA GTP (or ATP) Succity/-CoA Synthetase Pi	COO® CH2 CH2 dehyde com S-CoA uccinyl CoA	ogenase /	Second oxidative decarboxylation	8e ⁻

The Citric Acid Cycle

·Where do the electrons come from?



21-3

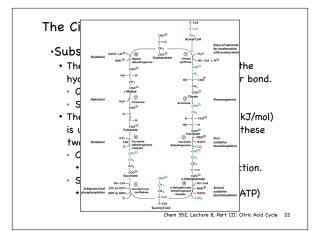
The Citric Acid Cycle

·Substrate level phosphorylation.

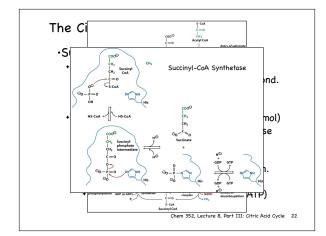
- There are two reactions that involve the hydrolysis of a "high energy" thioester bond.
- · Citrate synthase
- · Succinyl-CoA synthetase
- * The high negative free energy (\approx -31 kJ/mol) is used for two different purposes in these two reactions.
 - · Citrate synthase
 - + Drives cycle in the clockwise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

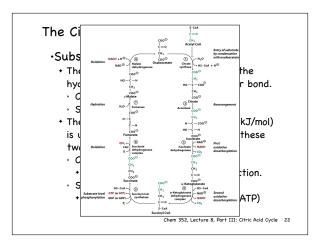
Chem 352, Lecture 8, Part III: Citric Acid Cycle 22

22-1



22-2





22-4

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 (\approx -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)

Chem 352, Lecture 8, Part III: Citric Acid Cycle 22

22-5

23-1

The Citric Acid Cycle

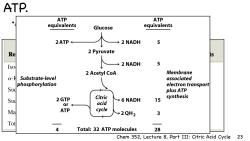
- •Reduced nucleotides are used in oxidative phosphorylation to make ATP.
- ·ATP's produced per Acetyl-CoA

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

Chem 352, Lecture 8, Part III: Citric Acid Cycle 23

The Citric Acid Cycle

•Reduced nucleotides are used in oxidative phosphorylation to make



The	Citric	Acid	CVC	ءا
11111		TCIU	CYC	ιe

•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

Chem 352, Lecture 8, Part III: Citric Acid Cycle 23

വാ	2
∠ى	-0
_	_

Ren	ulation	of	the	The	Citric	Acid	Cycle
neu	Jularion	O1	1116	1116		TCIU	Cycle

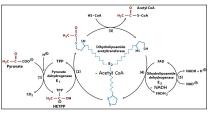
·Like glycolysis and gluconeogenesis, the citric acid cycle is closely regulated to meet the catabolic and anabolic needs of the cell and the organism.

Chem 352, Lecture 8, Part III: Citric Acid Cycle 24

24

Regulation of the The Citric Acid Cycle

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

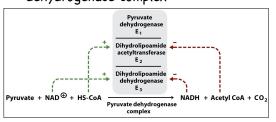


Chem 352, Lecture 8, Part III: Citric Acid Cycle

25-1

Regulation of the The Citric Acid Cycle

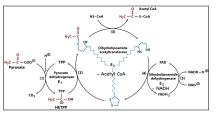
•The flow of Acetyl-CoA into the cycle is regulated by the pyruvate dehydrogenase complex



Chem 352, Lecture 8, Part III: Citric Acid Cycle 25

Regulation of the The Citric Acid Cycle

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

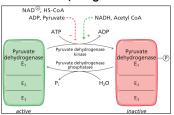


Chem 352, Lecture 8, Part III: Citric Acid Cycle 25

25-3	3
------	---

Regulation of the The Citric Acid Cycle

·Mammalian pyruvate dehydrogenase is also covalently regulated



Chem 352, Lecture 8, Part III: Citric Acid Cycle 26

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)

Chem 352, Lecture 8, Part III: Citric Acid Cycle 27

27

Regulation of the The Citric Acid Cycle

·Three reactions in the citric acid cycle are allosterically regulated

- Isocitrate dehydrogenase
- + Ca²⁺ (mammals)
- + ADP (mammals)
- NADH (mammals)

28-1

Chem 352, Lecture 8, Part III: Citric Acid Cycle 28

28-2 Regulation of the The Citric Acid Cycle ·Three reactions in the citric acid cycle are allosterically regulated + Isocitrate dehydrogenase + Ca²⁺ (mammals) + ADP (mammals) Ca²⁺ is a secondary messenger, whose levels are hormonally - NADH (mammals) controlled in the mitochondria Chem 352, Lecture 8, Part III: Citric Acid Cycle 28 29 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 \rightarrow + Ca²⁺ (Bind to E₁ and lower K_M) - Succinyl-CoA - NADH Chem 352, Lecture 8, Part III: Citric Acid Cycle 29 30-1 Other Roles for Citric Acid Cycle ·Besides serving as intermediates in the oxidation of acetyl groups to CO2, + the citric acid cycle intermediates are also the starting and ending points for a number of other anabolic and catabolic pathways. Chem 352, Lecture 8, Part III: Citric Acid Cycle 30 30-2 Other Roles for Citric Acid Cycle ·Besid in CO₂, the a + the also the ıumber of ays.

Chem 352, Lecture 8, Part III: Citric Acid Cycle 30

Other Roles for Citric Acid Cycle

- ·Besides serving as intermediates in the oxidation of acetyl groups to CO₂,
 - the citric acid cycle intermediates are also the starting and ending points for a number of other anabolic and catabolic pathways.

Chem 352, Lecture 8, Part III: Citric Acid Cycle 30

30-3

Other Roles for Citric Acid Cycle

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

Chem 352, Lecture 8, Part III: Citric Acid Cycle 31

31-1

Other Roles for Citric Acid Cycle

Anap

feed

Cycle

Anap

Amino acids, yea, private Alanine

Cycle

Carbohydrates

Apartate

Copy | Private Alanine

Aceyl Coh

Fatty acids, steroids

Amino acids, yea, private

Carbohydrates

Alanine

Fatty acids, steroids

Amino acids, yea, private

Carbohydrates

Alanine

Fatty acids, steroids

Amino acids, yea, private

Carbohydrates

Alanine

Fatty acids, steroids

31-2

Other Roles for Citric Acid Cycle

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

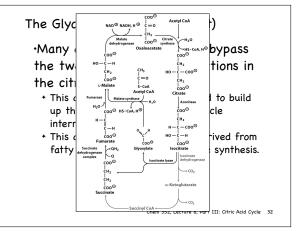
Chem 352, Lecture 8, Part III: Citric Acid Cycle 31

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.

Chem 352, Lecture 8, Part III: Citric Acid Cycle 32





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.

Chem 352, Lecture 8, Part III: Citric Acid Cycle 32

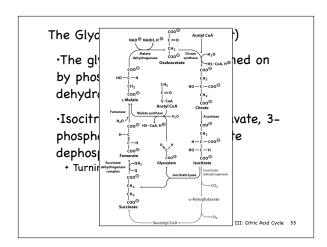
32-3

The Glyoxylate Pathway (Shunt)

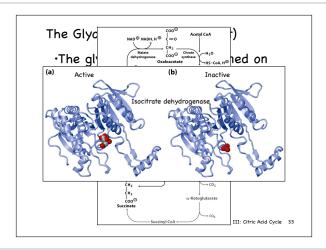
- ·The glycoxylate shunt is turned on by phosphorylating isocitrate dehydrogenase
- ·Isocitrate, oxaloacetate, pyruvate, 3phosphoglycerate, PEP promote dephosphorylation
- + Turning off the glyoxylate shunt.

33-1

Chem 352, Lecture 8, Part III: Citric Acid Cycle 33



33-2



33-3

The Glyd	COO® NAD® NADH, H® C=0 Acetyl CoA
·The gl	Malate COO® Clirate H10 CH12 COO® Symthate COO® Symthate COO® COO® COO® COO® COO® COO® COO®
by phos	но-с-н сн₂
dehydro	$ \begin{array}{cccc} CH_2 & CH_3 & HO - C - COO^{\odot} \\ COO^{\odot} & C = O & CH_2 \\ I-Malate & -CoO & COO^{\odot} \\ & & Acetyl CoA & Citrate \\ \end{array} $
·Isocitr	H ₃ O (Malate symthase) H ₃ O (Aconitase Vare, 3-
phospho	H-C CH2 H-C-cooΘ
dephosi	COO
+ Turnir	Succinate Oils Glycoylate Inocitrate In
	Succinyl CoA — III: Citric Acid Cycle 33

33-4

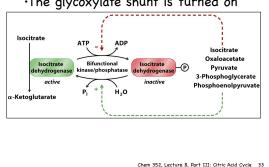
The Glyoxylate Pathway (Shunt)

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

Chem 352, Lecture 8, Part III: Citric Acid Cycle 33

The Glyoxylate Pathway (Shunt)

·The glycoxylate shunt is turned on



33-6

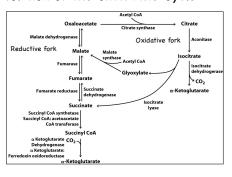
The Glyoxylate Pathway (Shunt)

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

Chem 352, Lecture 8, Part III: Citric Acid Cycle 33

33-7

Evolution of the Citric Acid Cycle



Chem 352, Lecture 8, Part III: Citric Acid Cycle 34

34

Next Up

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

35

Chem 352, Lecture 8, Part III: Citric Acid Cycle 35