

TRICARBOXYLIC ACID CYCLE:

rvsd 11/5/93, 11/7/94, 11/6/95, 11/13/96, 9 Nov 01, 18 Nov 02, 10 Nov 03, 24 Oct 07, 29Oct08
p. 344-, BHK 5th: 405-415, 6th: 255-265, 7th: 258-

ELUCIDATED BY KREBS, got Nobel prize in 1953.

Pyruvate enters mitochondrial matrix where:

Oxidation to Acetyl CoA: pyruvate dehydrogenase: pyruvate is **alpha keto acid** (keto draws e⁻ away)

a: **decarboxylation** (requires TPP) *yields energy which drives the reaction*

b: **oxidizes substrate**, producing NADH at #2 C (-7.5 kcal).

c: **activates two carbon acetyl fragment** by attaching to CoASH

CoA: adenine-3-PO₄, 5- pyroPO₄-pantothenic acid-NHCH₂CH₂SH (a thiol) (p. 256)

Forms *thioester*, a high energy bond, capable of donating to substrate (oxaloacetate)

TCA cycle: (p. 261)

step	process	product
1	acetylation: Acetyl CoA transfers acetyl group to oxaloacetate (C-4) <i>via CH₃ end</i>	citrate
2	dehydration, rehydration: citrate (tertiary alcohol) isomerized to isocitrate, with oxidizable secondary alcohol	isocitrate
3	oxidation, decarboxylation: 2° hydroxyl isocitrate oxidized , making NADH , creates unstable molecule, decarboxylates (drives rxn) yielding α-ketoglutarate. (first decarboxylation)	α-ketoglutarate
4	oxidation, decarboxylation, form thioester: α-ketoglutarate is similar to pyruvate: an α-keto acid, similar to formation of acetyl CoA: oxidation, makes NADH, decarboxylation (makes CO ₂) and CoA thioester high energy bond (succinyl CoA).	succinyl CoA
5	thioester split, phosphorylation of GDP: Thioester bond used to PO₄ylate GDP , release succinate and CoASH. GTP PO ₄ ylates ADP (only direct ATP in cycle)	succinate
6	oxidation: Succinate α,β carbons dehydrogenated, forming FADH₂ (not enough energy to form NADH) and fumarate	fumarate
7	hydration: fumarate is hydrated to form malate	malate
8	oxidation: malate (a secondary alcohol) is oxidized to form oxaloacetate, producing NADH .	oxaloacetate

FAT CATABOLISM: BETA OXIDATION, FEEDS INTO TCA (p. not in text???):

beta oxidation: (Steps 2-4 = TCA 6-8, succinate to oxaloacetate) occurs in mitochondria

Reaction	Details	Product
1. Activation:	FA +CoASH condensed using ATP to AMP + PPi	CoA-S-FA
2. Dehydrogenation:	α, β carbons dehydrogenated, make	FADH ₂
3. Hydration:	water added to double bond, making	β OH CoA-S-FA
4. Oxidation:	NAD used to oxidize β OH to	carbonyl
5. Thioester creation:	acetyl CoA splits off, new CoASH attached (Mnemonic: DHOT)	acetyl CoA

PROTEIN CATABOLISM:

first deamination or transamination to α keto acid

3 of 20 AA give deaminated products feeding into TCA, rest need further changes

TCA CYCLE IS AMPHIBOLIC

It can either 'burn' glucose, etc, or its intermediates can be used for synthesis:

succinyl CoA is used to synthesize amino acids and heme

citrate to acetyl CoA (reverse reaction from usual), used for fatty acid synthesis

Replenishment of intermediates possible by carboxylation of glycolytic intermediates.