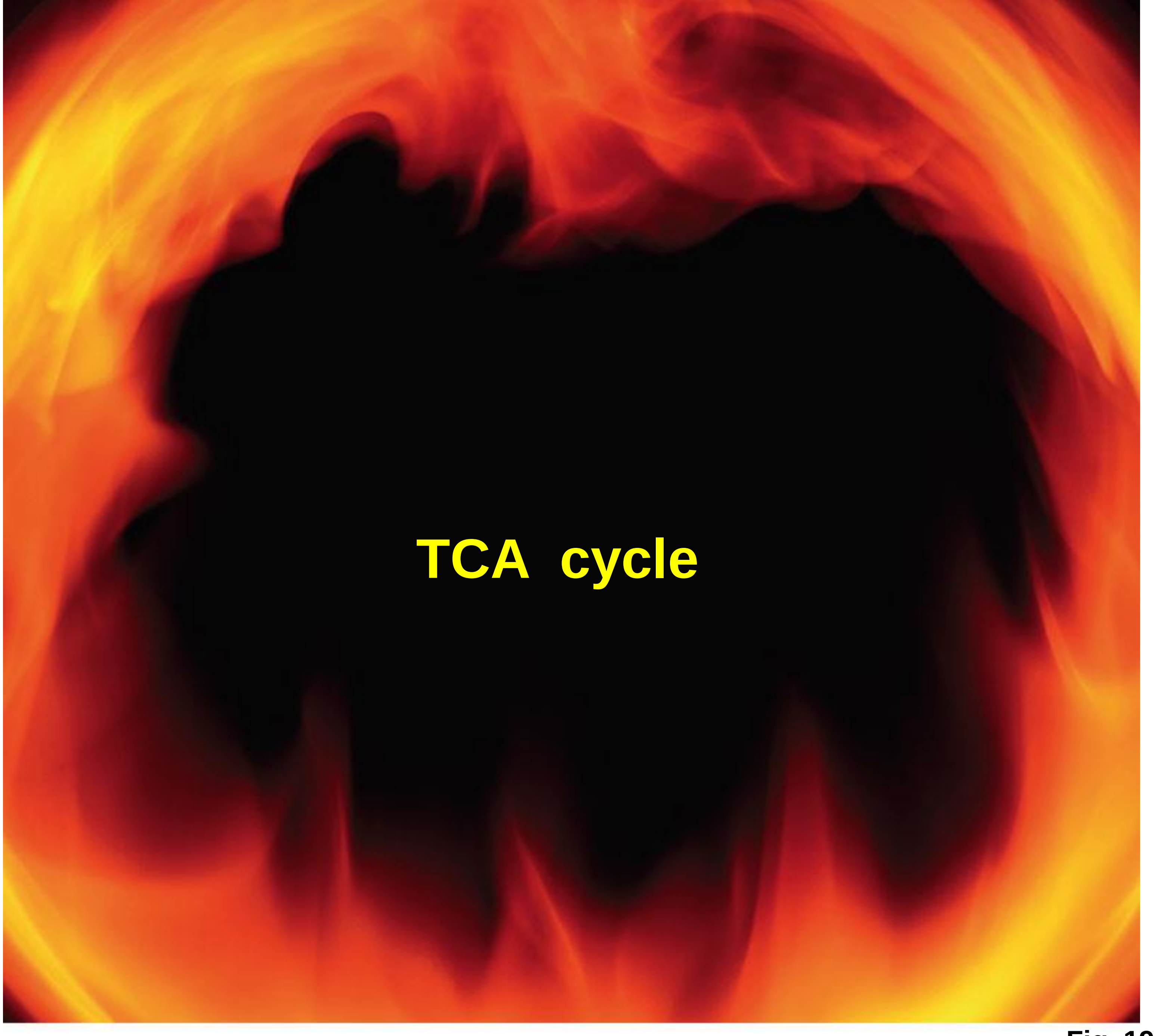
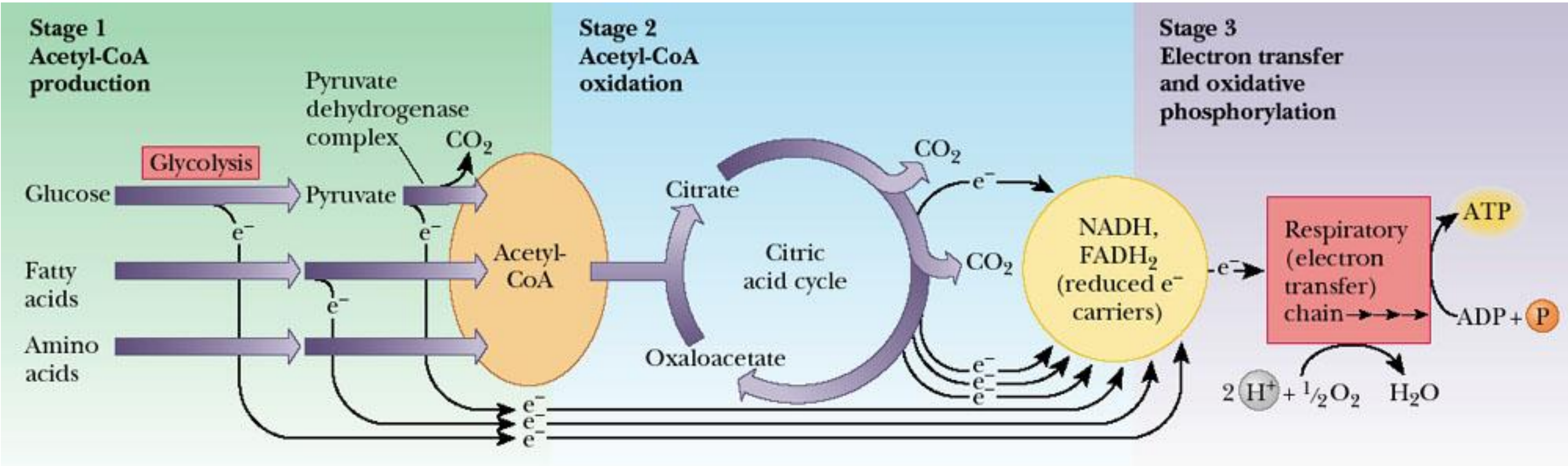


Fig. 19-CO, p.511

TCA cycle
(Tricarboxylic acid cycle)

- **Kreb's cycle**
- **Citric acid cycle**
- 구연산회로

TCA cycle과 산화적 인산화의 관계



① **Series of oxidation -----> NADH, $FADH_2$ 생성**
(완전한 산화)

② 호기적 조건 필요
Glucose + 6 O_2 ------> 6 CO2 + 6 H_2O

③ 전자전달계로 연결되어 **ATP** 생성

Fig. 19-1, p.512

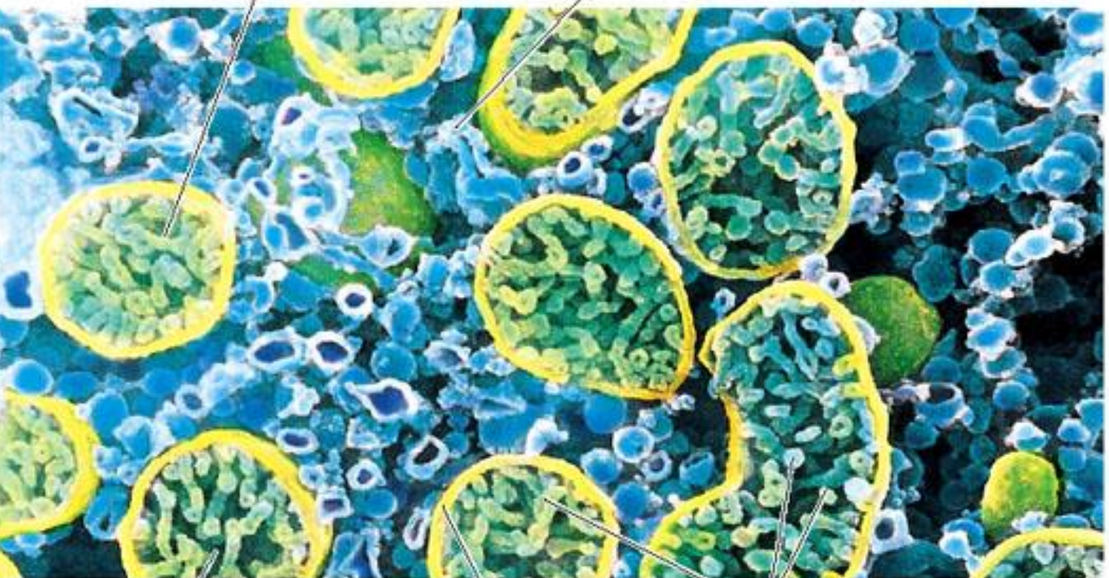
TCA cycle의 역할

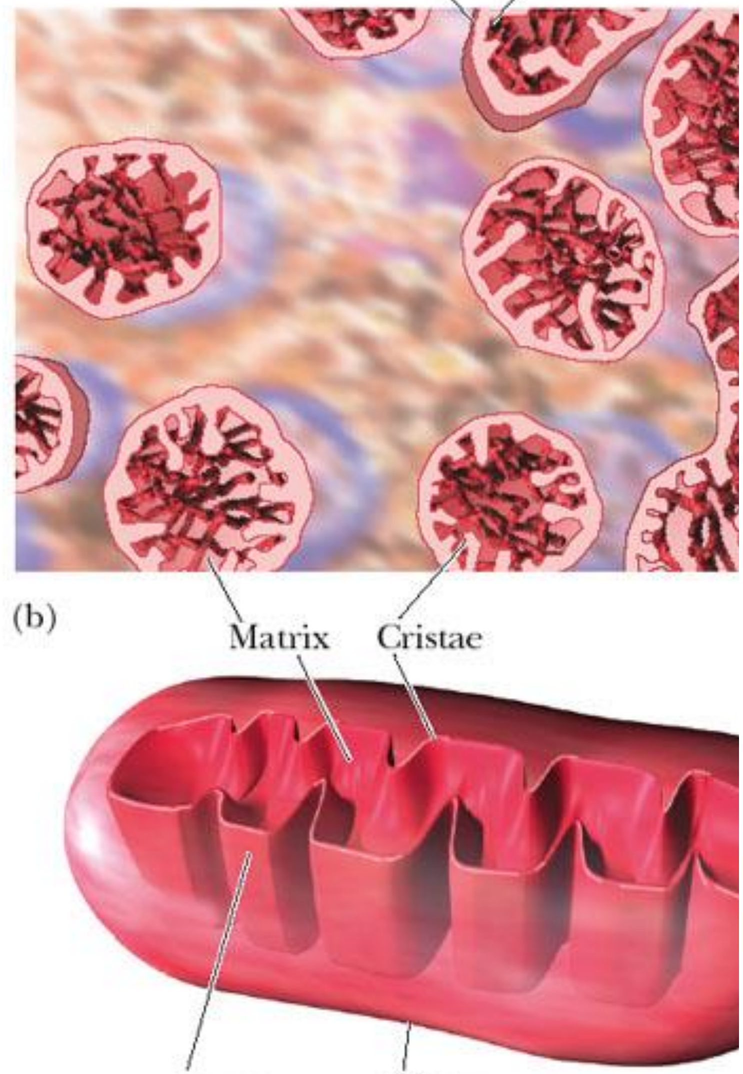
① Series of oxidation -----> NADH, $FADH_2$ 생성
(완전한 산화)
② 호기적 조건 필요
Glucose + 6 O_2 ------> 6 CO_2 + 6 H_2O
③ 전자전달계로 연결되어 ATP 생성

④ 생합성에 필요한 중간물질 공급
예) **ketoglutarate <-----> glutamic acid**
oxaloacetate <-----> aspartic acid
succinyl CoA <------> protophorphyrin

⑤ **absolutely necessary for survival**

⑥ 회로가 계속되기 위해서는 중간물질들이 계속적으로 보충되어야 한다 (예: **oxaloacetate** 등)





TCA가 일어나는 장소:
미토콘드리아의 기질 (matrix)

Fig. 19-2, p.513

미토콘드리아 구조

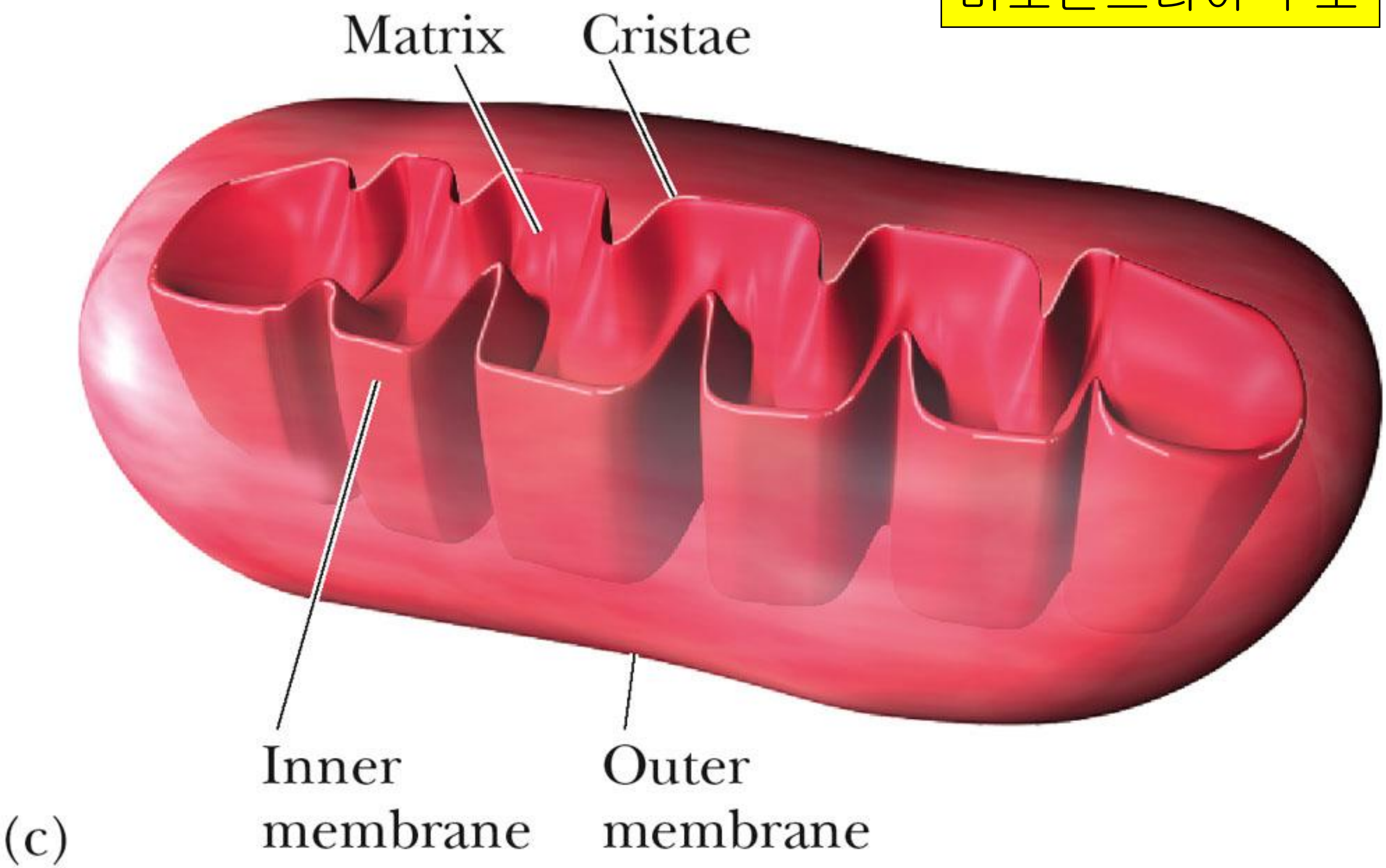


Fig. 19-2c, p.513

TCA의 여러 반응

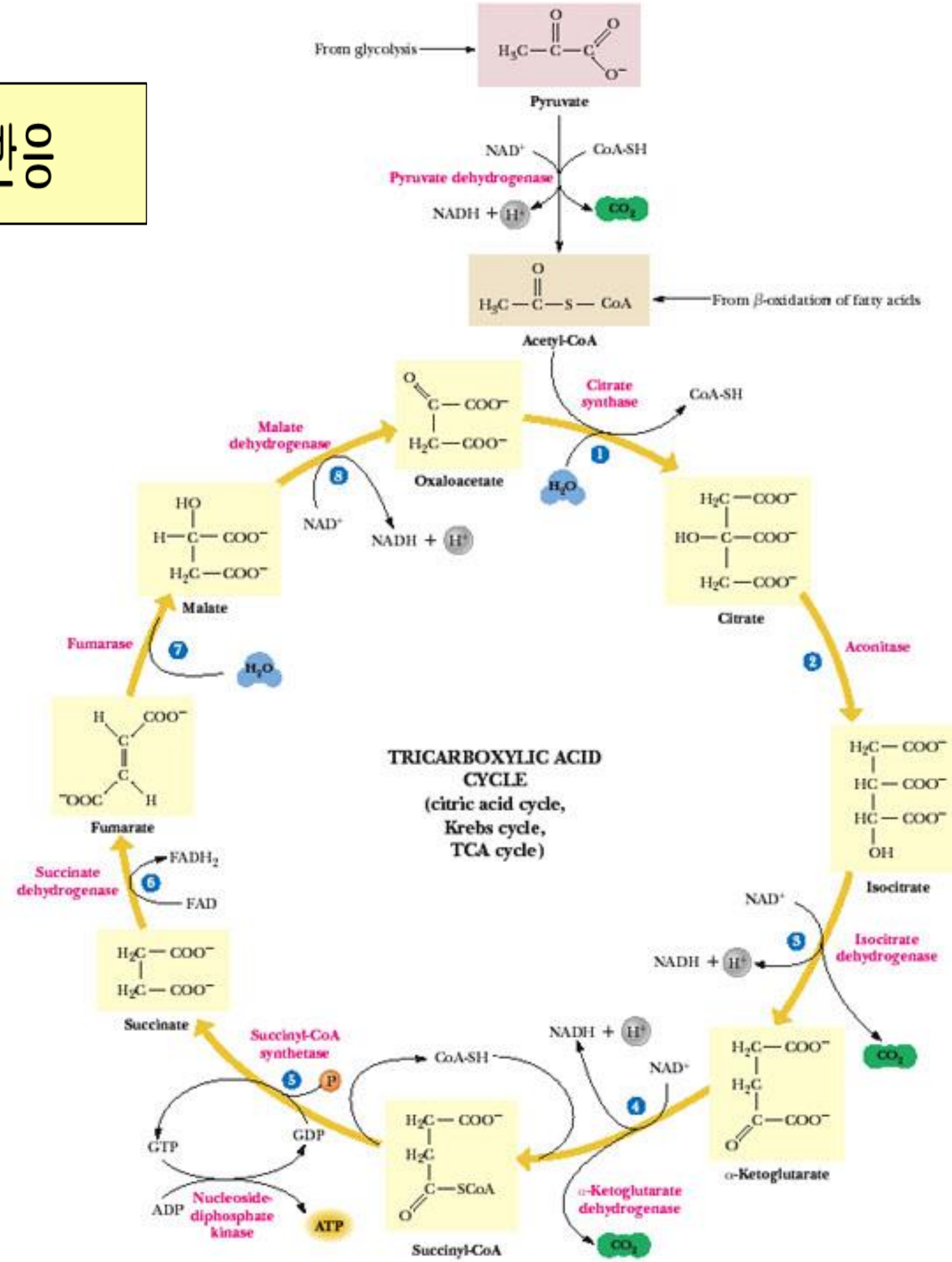


Fig. 19-3, p.514

TCA회로의 반응

1. **Acetyl CoA의 생성**

Pyruvate + NAD+ + CoA -----> Acetyl CoA + CO_2 + NADH + H^+

관련효소: **Pyruvate dehydrogenase complexes**

- Pyruvate dehydrogenase (TPP)
- Dihydrolipoyl transacylase (lipoamide)
- Dihydrolipoyl dehydrogenase (FAD)

Acetyl CoA의 생성

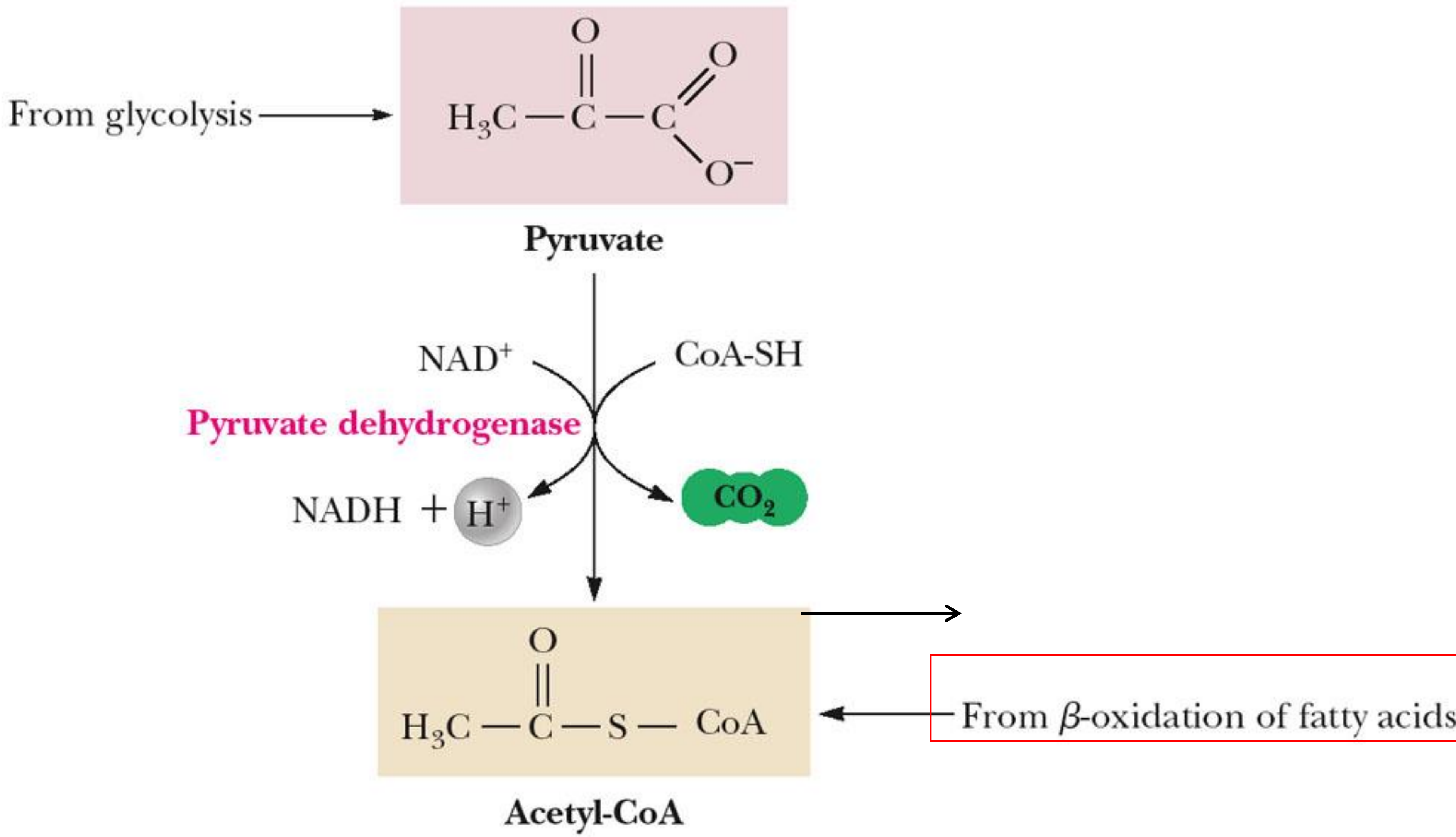
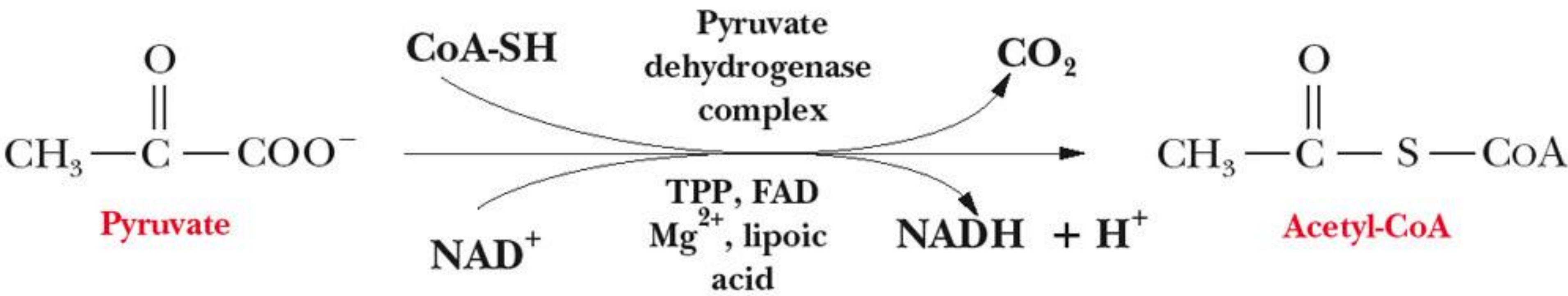


Fig. 19-3a, p.514

Acetyl CoA의 생성



Acetyl CoA의 생성

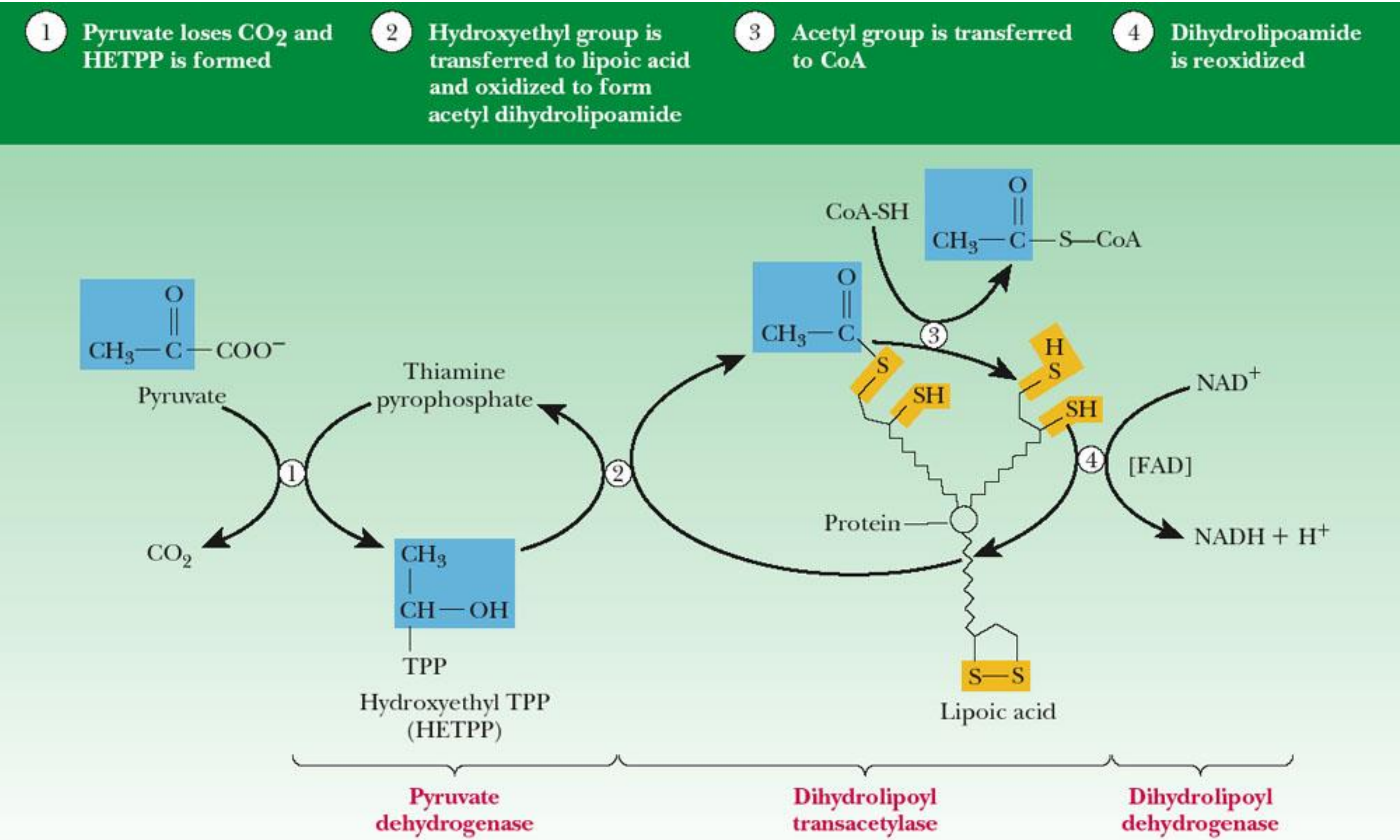


Fig. 19-4, p.516

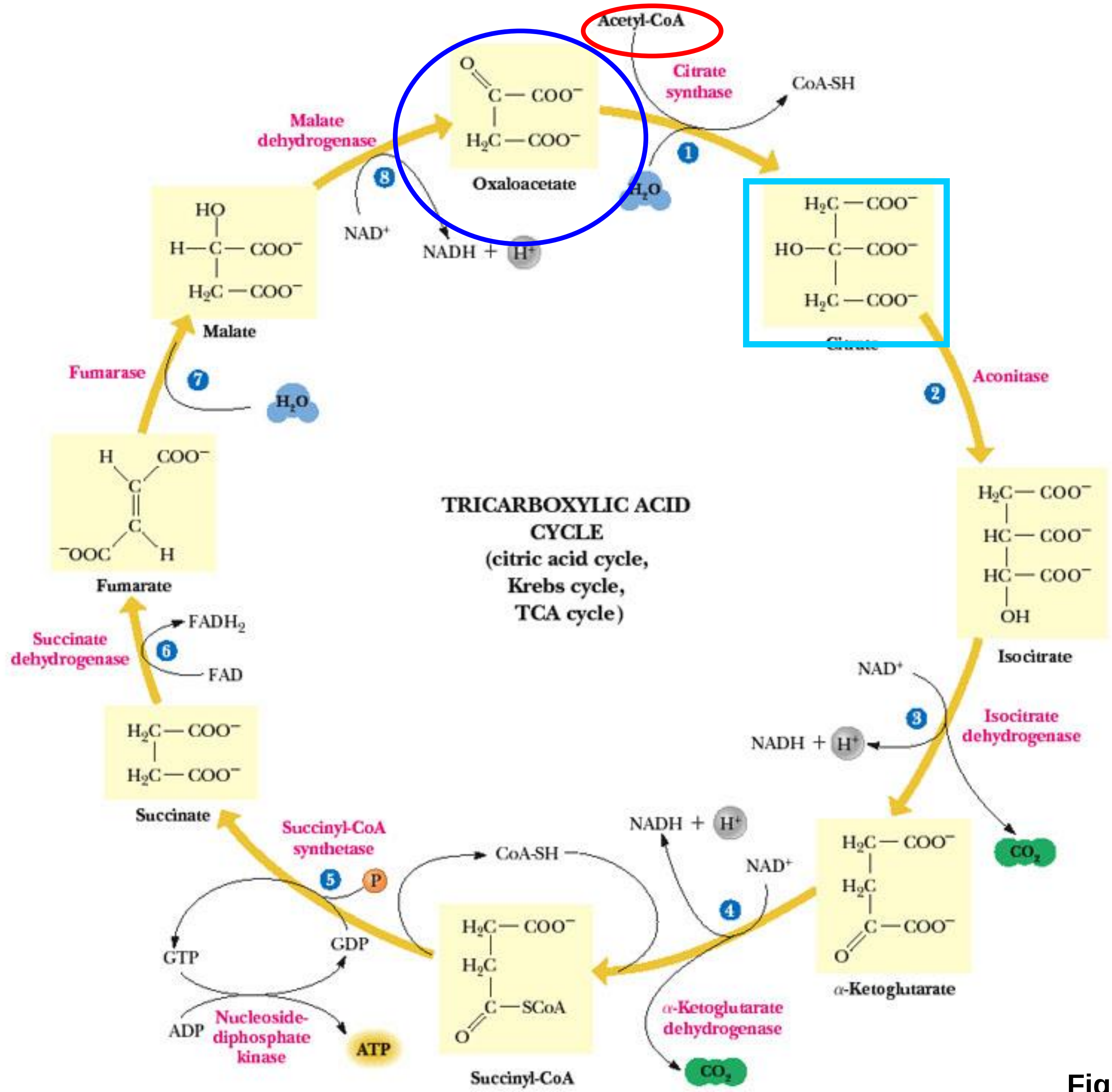


Fig. 19-3b, p.514

Oxaloacetate의 생성

① Pyruvate + HCO_3^- + ATP -----> Oxaloacetate + ADP + Pi

② Biotin is cofactor

③ activated by acetyl CoA

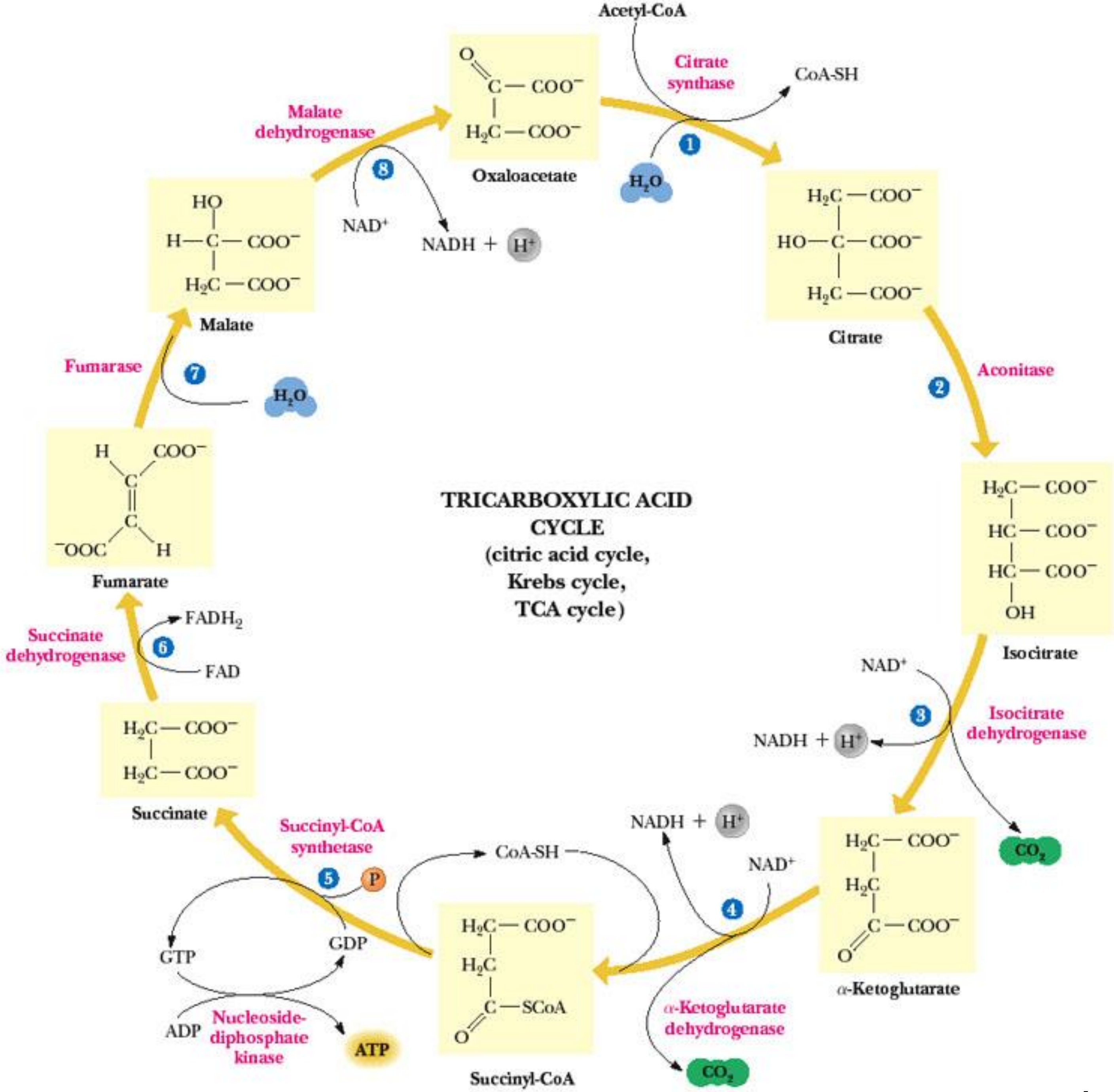


Fig. 19-3b, p.514

TCA회로의 반응

Table 19.1

The Reactions of the Citric Acid Cycle

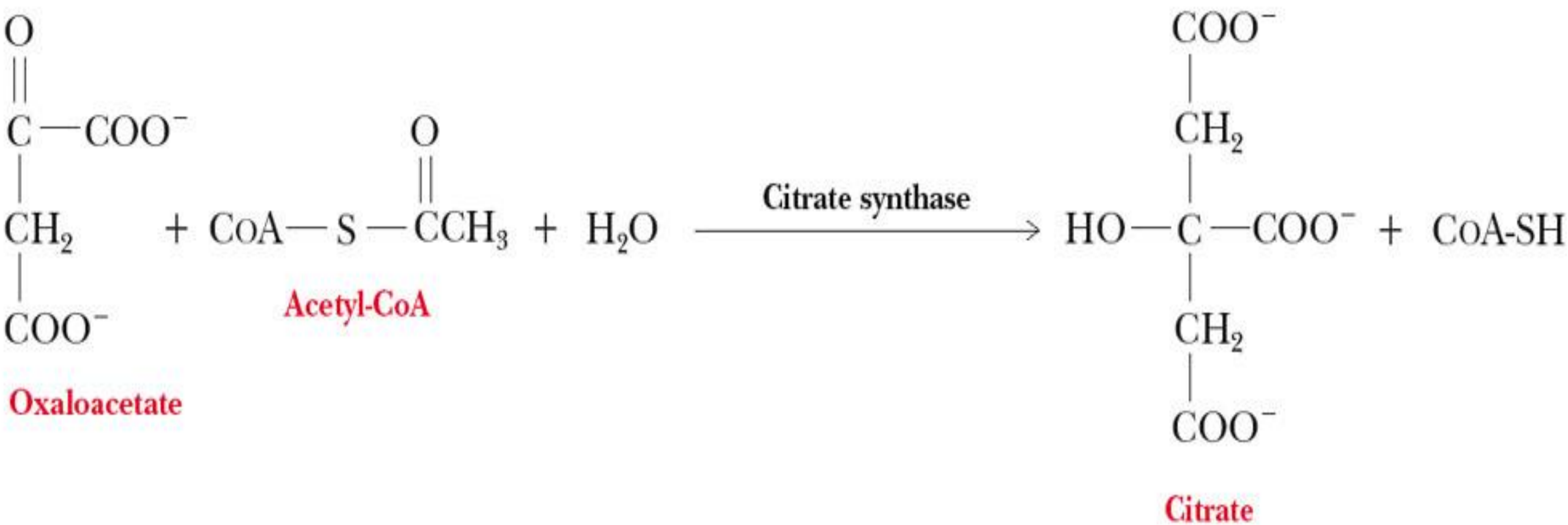
Step	Reaction	Reaction
1	Acetyl-CoA + Oxaloacetate + $H_2O \rightarrow$ Citrate + CoA-SH	Citrate synthase
2	Citrate $\rightarrow$ Isocitrate	Aconitase
3	Isocitrate + $NAD^+ \rightarrow$ α-Ketoglutarate + NADH + CO_2 + H^+	Isocitrate dehydrogenase
4	α-Ketoglutarate + NAD^+ + CoA-SH $\rightarrow$ Succinyl-CoA + NADH + CO_2 + H^+	α-Ketoglutarate dehydrogenase
5	Succinyl-CoA + GDP + $P_i \rightarrow$ Succinate + GTP + CoA-SH	Succinyl-CoA synthetase
6	Succinate + FAD $\rightarrow$ Fumarate + $FADH_2$	Succinate dehydrogenase
7	Fumarate + $H_2O \rightarrow$ L-Malate	Fumarase
8	L-Malate + $NAD^+ \rightarrow$ Oxaloacetate + NADH + H^+	Malate dehydrogenase

Table 19-1, p.518

TCA회로의 반응

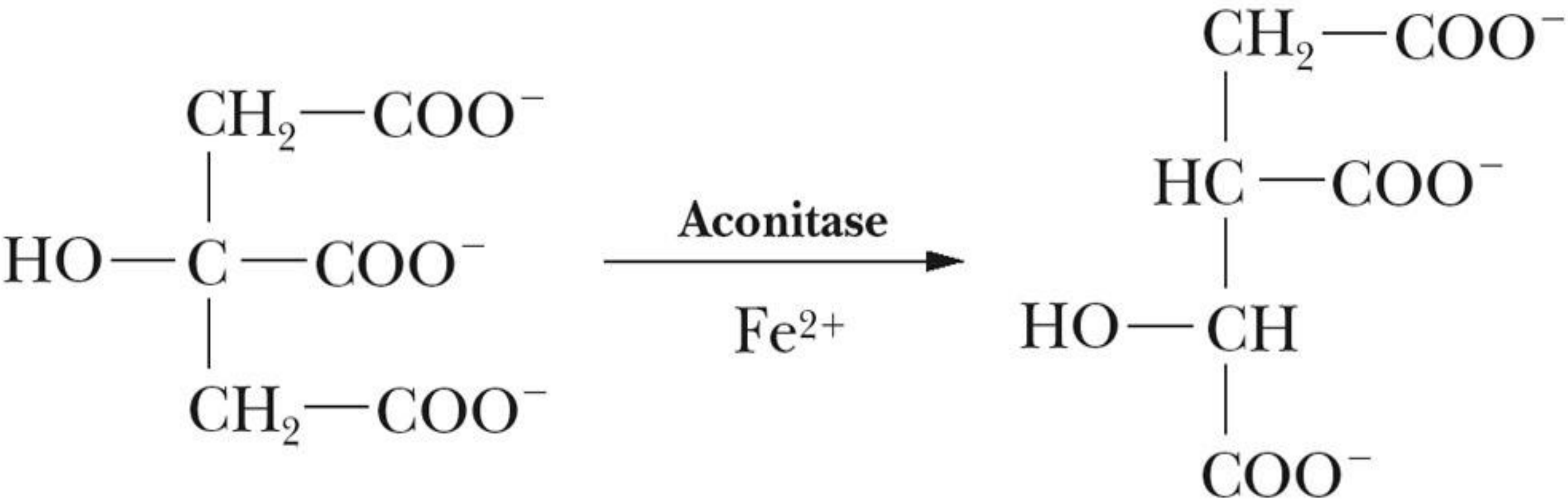
The condensation of acetyl-CoA and oxaloacetate
to form citrate

Overall reaction



p.518

TCA회로의 반응



Citrate

Isocitrate

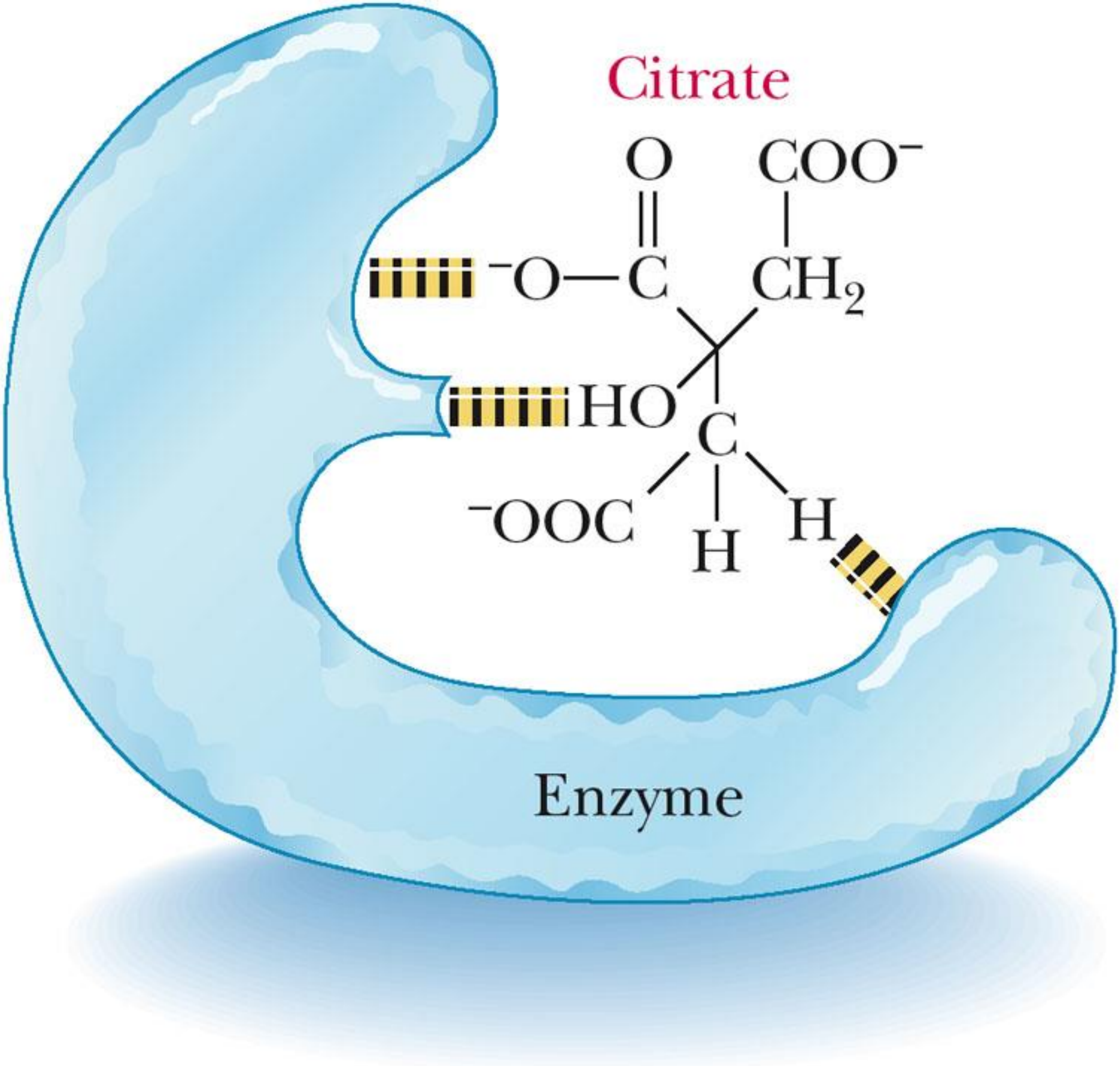


Fig. 19-6, p.519

TCA회로의 반응

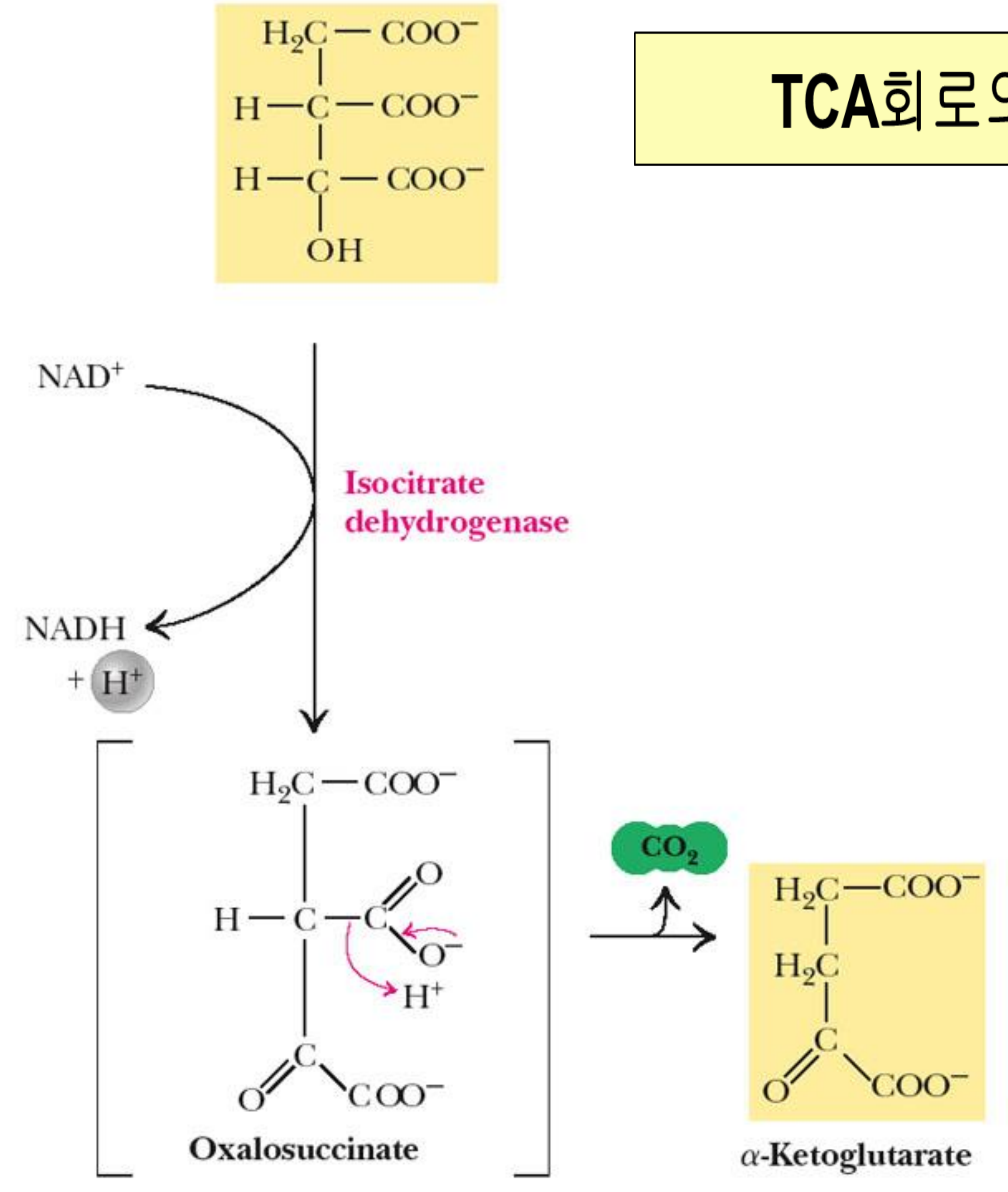
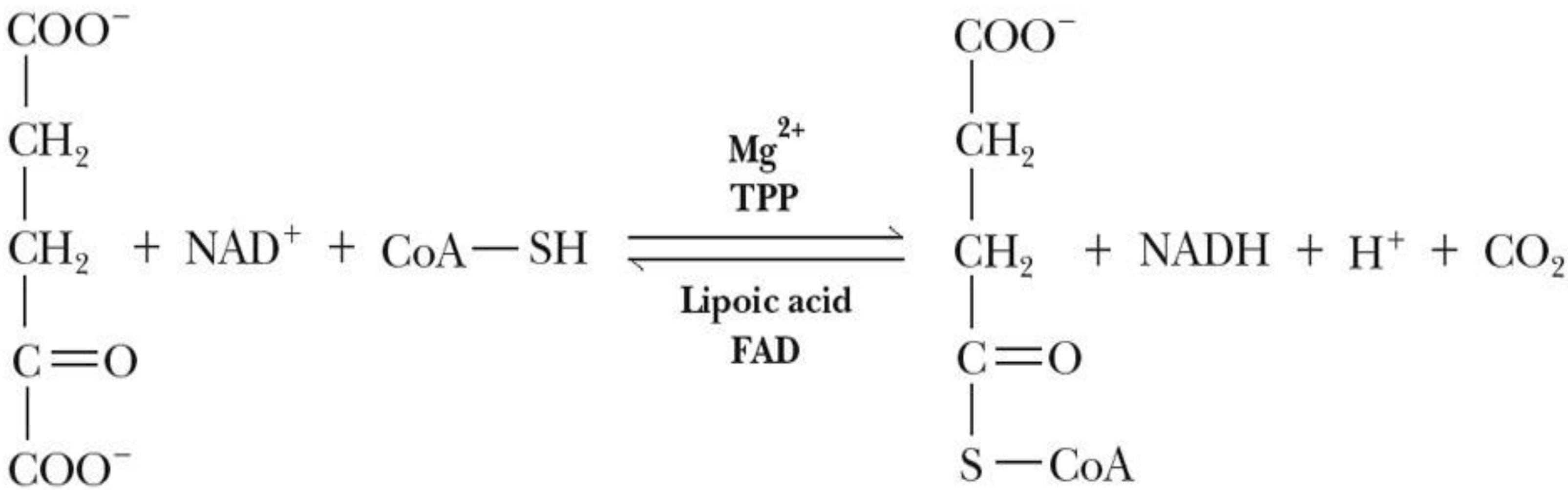


Fig. 19-7, p.521

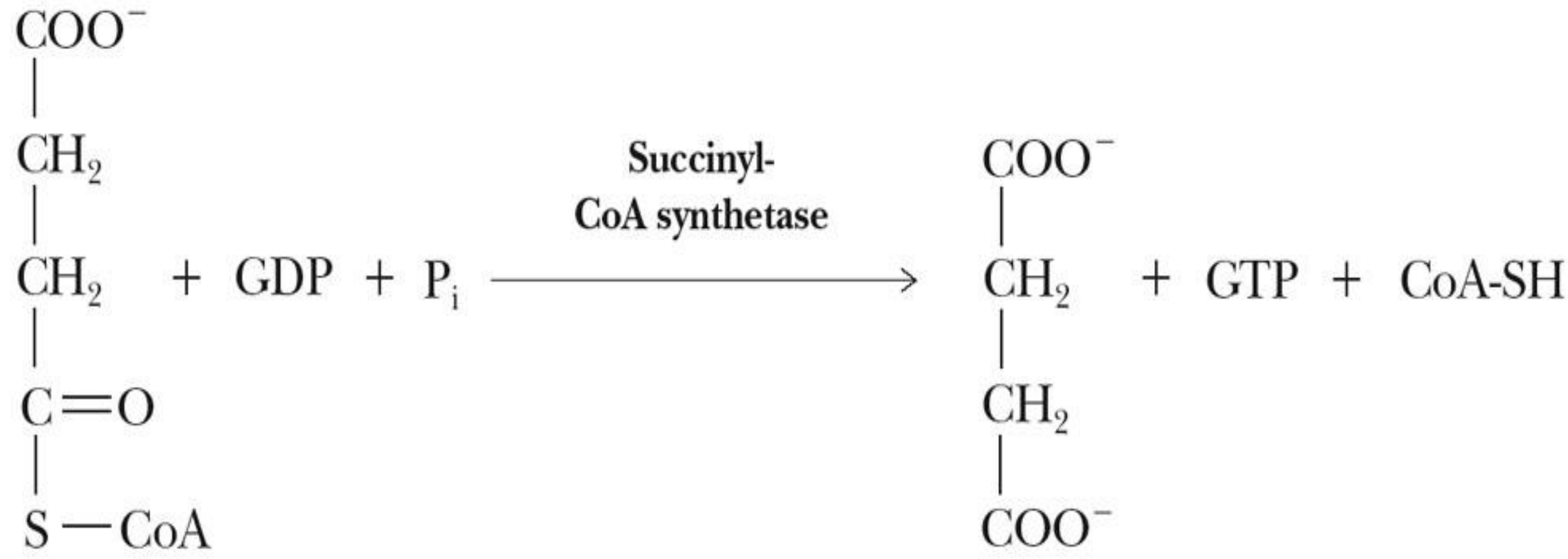
TCA회로의 반응



α-Ketoglutarate

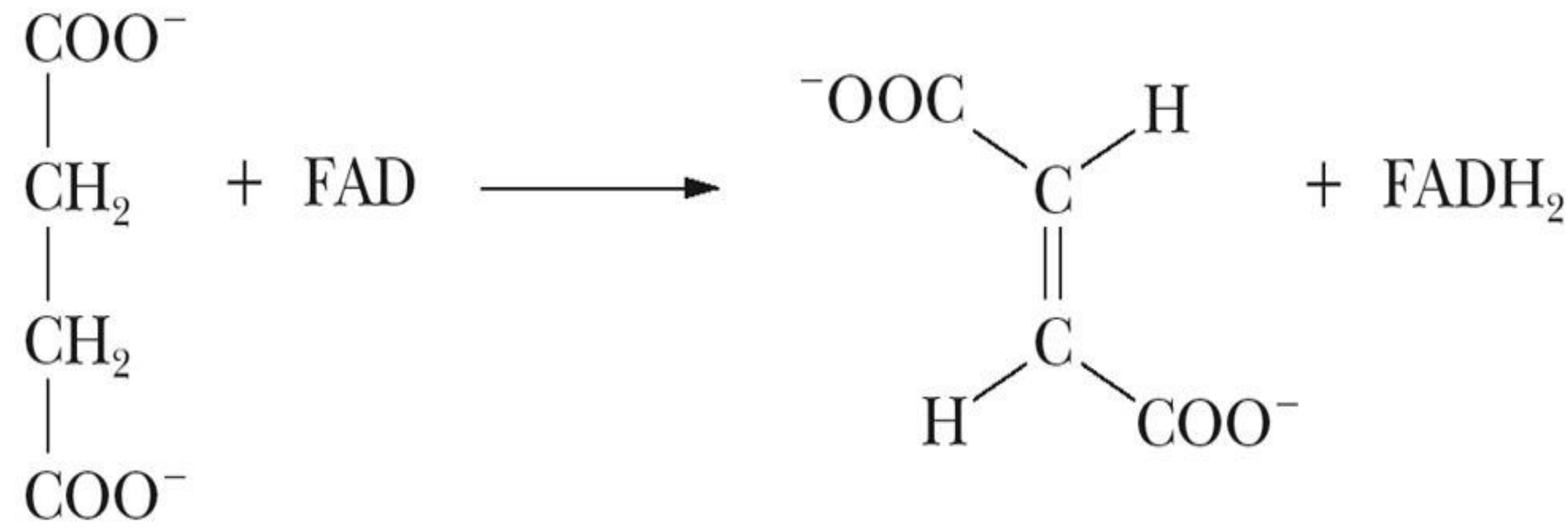
Succinyl-CoA

TCA회로의 반응



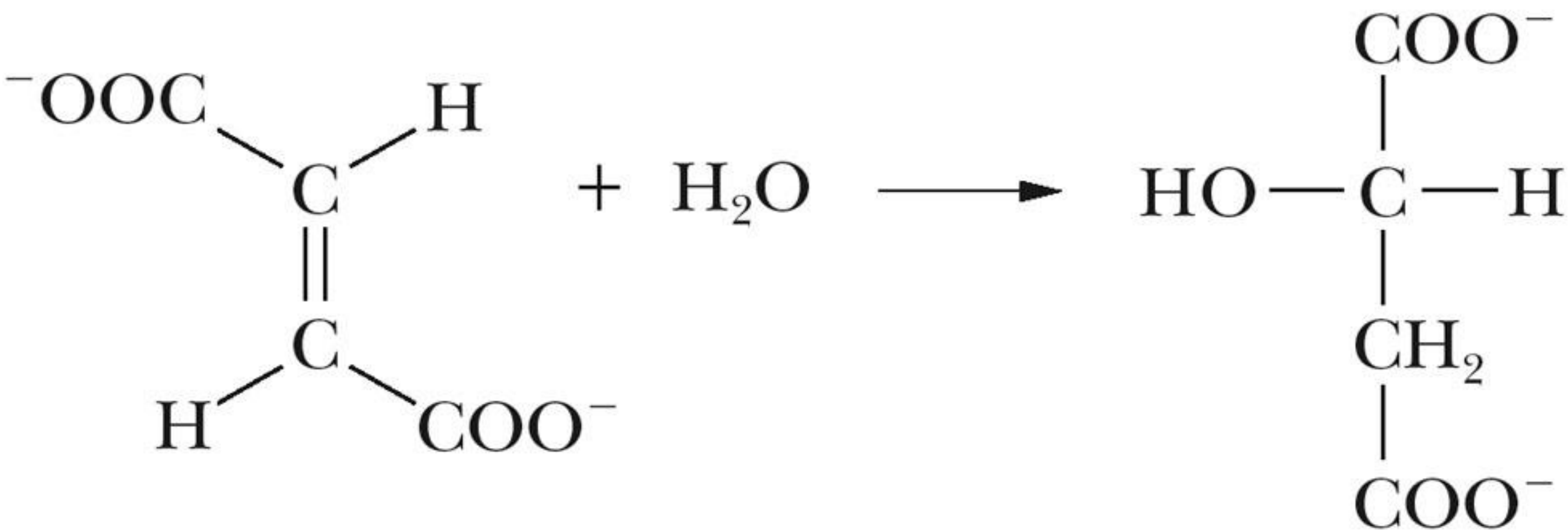
Succinyl-CoA　　　　Succinate

TCA회로의 반응



Succinate Fumarate

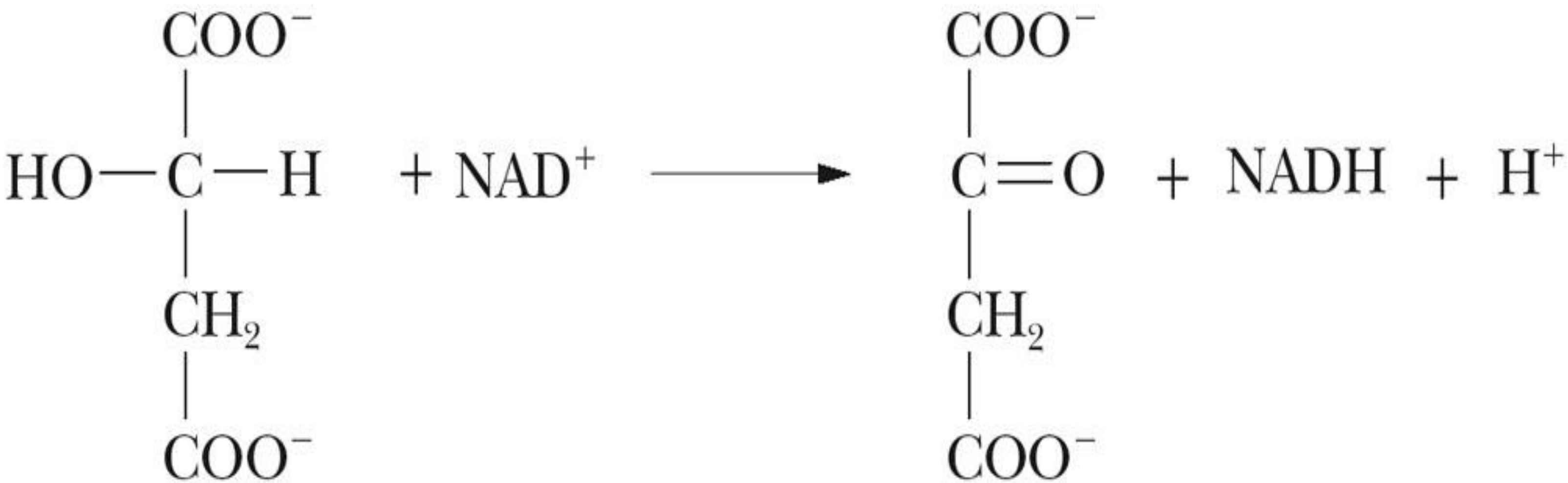
TCA회로의 반응



Fumarate

L-Malate

TCA회로의 반응



L-Malate Oxaloacetate

TCA회로의 자유에너지 변화

Table 19.2

The Energetics of Conversion of Pyruvate to CO_2

Step	Reaction	$\Delta G^{\circ\prime}$ kJ mol^{-1}	$\Delta G^{\circ\prime}$ kcal mol^{-1}
	Pyruvate + CoA-SH + NAD^+ → Acetyl-CoA + NADH + CO_2	−33.4	−8.0
1	Acetyl-CoA + Oxaloacetate + H_2O → Citrate + CoA-SH + H^+	−32.2	−7.7
2	Citrate → Isocitrate	+6.3	+1.5
3	Isocitrate + NAD^+ → α-Ketoglutarate + NADH + CO_2 + H^+	−7.1	−1.7
4	α-Ketoglutarate + NAD^+ + CoA-SH → Succinyl-CoA + NADH + CO_2 + H	−33.4	−8.0
5	Succinyl-CoA + GDP + P_i → Succinate + GTP + CoA-SH	−3.3	−0.8
6	Succinate + FAD → Fumarate + $FADH_2$	~0	~0
7	Fumarate + H_2O → L-Malate	−3.8	−0.9
8	L-Malate + NAD^+ → Oxaloacetate + NADH + H^+	+29.2	+7.0
Overall:	Pyruvate + 4 NAD^+ + FAD + GDP + P_i + 2 H_2O → CO_2 + 4 NADH + $FADH_2$ + GTP + 4 H^+	−77.7	−18.6

Table 19-2, p.526

TCA 요약 1

- **acetyl CoA**는 **oxaloacetate**와 결합하여 **citrate**로 된다.
- 회로가 한번 끝나면 **OAA**는 재생되고 탄소 **2**개는 **CO_2**의 형태로 떠난다 .

- 포도당 한 분자는 **TCA**에서 **30 ATP** 생성
- 산소는 **TCA** 회로에 직접 참여하는 것이 아니라 **NADH**나 **$FADH_2$**를 **NAD+**와 **FAD+**로 재생하게 함으로써 **TCA**를 지속되게 한다.

- **acetyl CoA**는 지방산 합성에 이용되기도 한다
- **acetyl CoA**는 **glucose** 합성에 이용될 수 없다 **(**동물에서**)**

TCA 요약 2

NADH 생성효소:

- **pyruvate dehydrogenase complex**
- **Isocitrate dehydrogenase**
- **ketoglutarate dehydrogenase complex**
- **malate dehydrogenase**

GTP 생성효소: Succinyl CoA synthetase

$FADH_2$ 생성효소: Succinate dehydrogenase

TCA의 에너지 수득율

① Acetyl CoA + 3 NAD+ + FAD+ + GDP + Pi + 2 H_2O
----> 2 CO_2 + 3 NADH + $FADH_2$ + GTP + 3 H^+ + CoA

② Pyruvate + 4 NAD+ + FAD + GDP + Pi + 2 H_2O
-----> 3 CO_2 + 4 NADH + $FADH_2$ + GTP + 4 H^+ + CoA

TCA회로의 조절

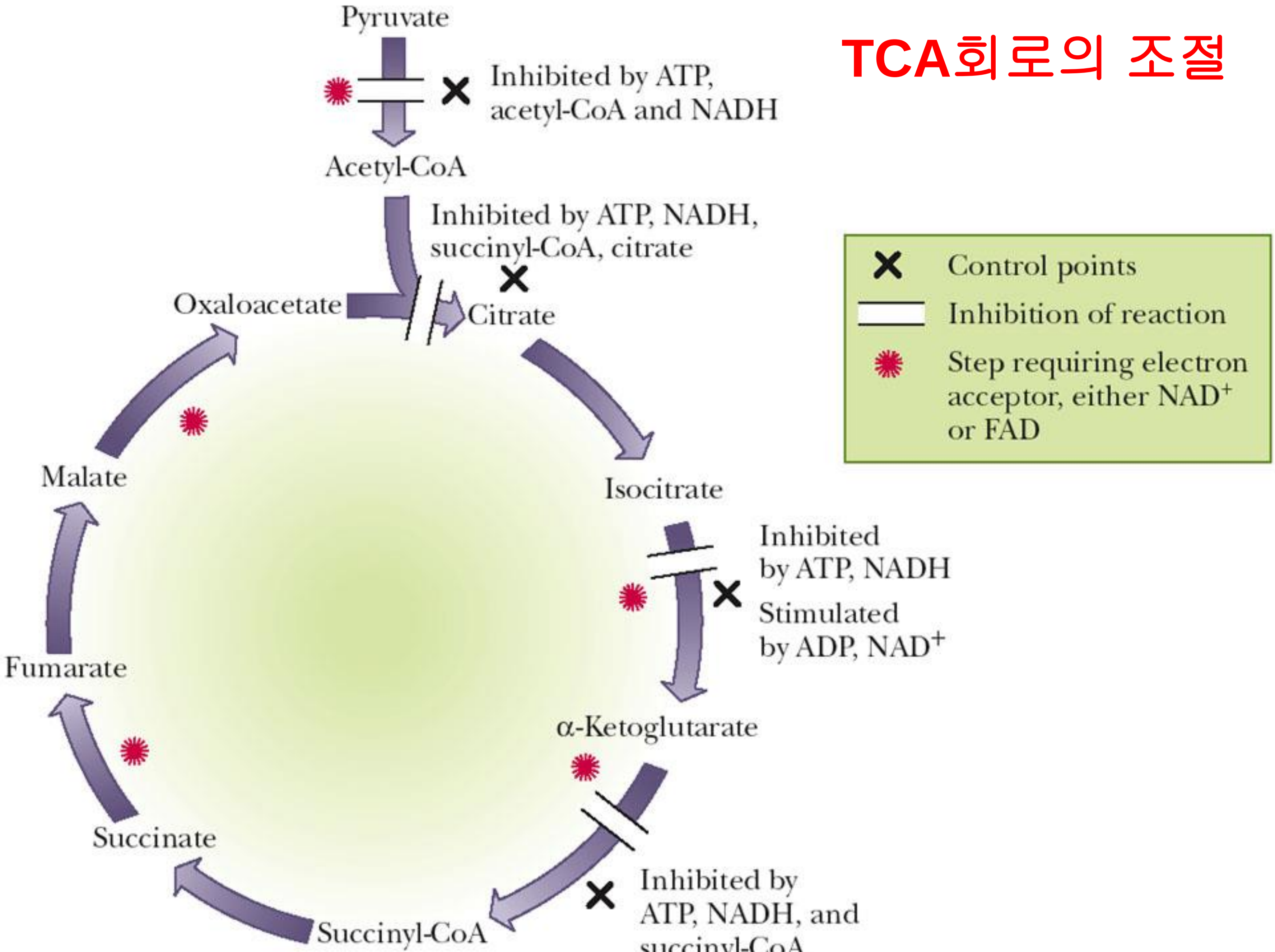


Fig. 19-8, p.526

Pyruvate DH 복합체의 조절

① 생성물 방해 .... **acetyl CoA, NADH**

② 에너지 부하 .... **inhibited by GTP**

activated by AMP

③ 가역적 인산화에 의한 조절

TCA회로의 조절

① citrate synthase

ATP

Succinyl CoA

② Isocitrate dehydrogenase

ADP

NADH, products

③ Ketoglutarate dehydrogenase

products (NADH, succinyl CoA)

ATP

Long chain fatty acid

TCA 회로의 방해제

① **malonate**
(succinate와 구조적으로 유사)

② **fluoroacetate**
(FCH_2COOH)

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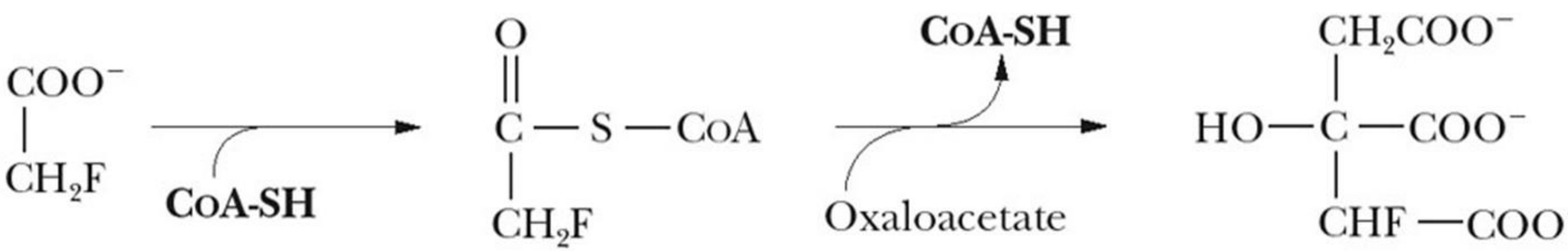


Fluoroacetate Fluoroacetyl-CoA Fluorocitrate

Table 19.3

Relationship between the Metabolic State of a Cell and the ATP/ADP and NADH/NAD^+ Ratios

Cells in a resting metabolic state

Need and use comparatively little energy

High ATP, low ADP levels imply high ATP/ADP ratio

High NADH, low NAD^+ levels imply high NADH/NAD^+ ratio

Cells in a highly active metabolic state

Need and use more energy than resting cells

Low ATP, high ADP levels imply low ATP/ADP ratio

Low NADH, high NAD^+ levels imply low NADH/NAD^+ ratio

Table 19-3, p.527

Glyoxylate cycle

- 식물체와 박테리아에서 일어난다
- 식물과 박테리아가 **acetate**를 영양분으로 살수 있게 한다

- 지질을 분해하여 당질로 합성
- **glyoxysome**에서 일어난다
- **TCA**와 연계하여 일어난다.

Glyoxylate cycle

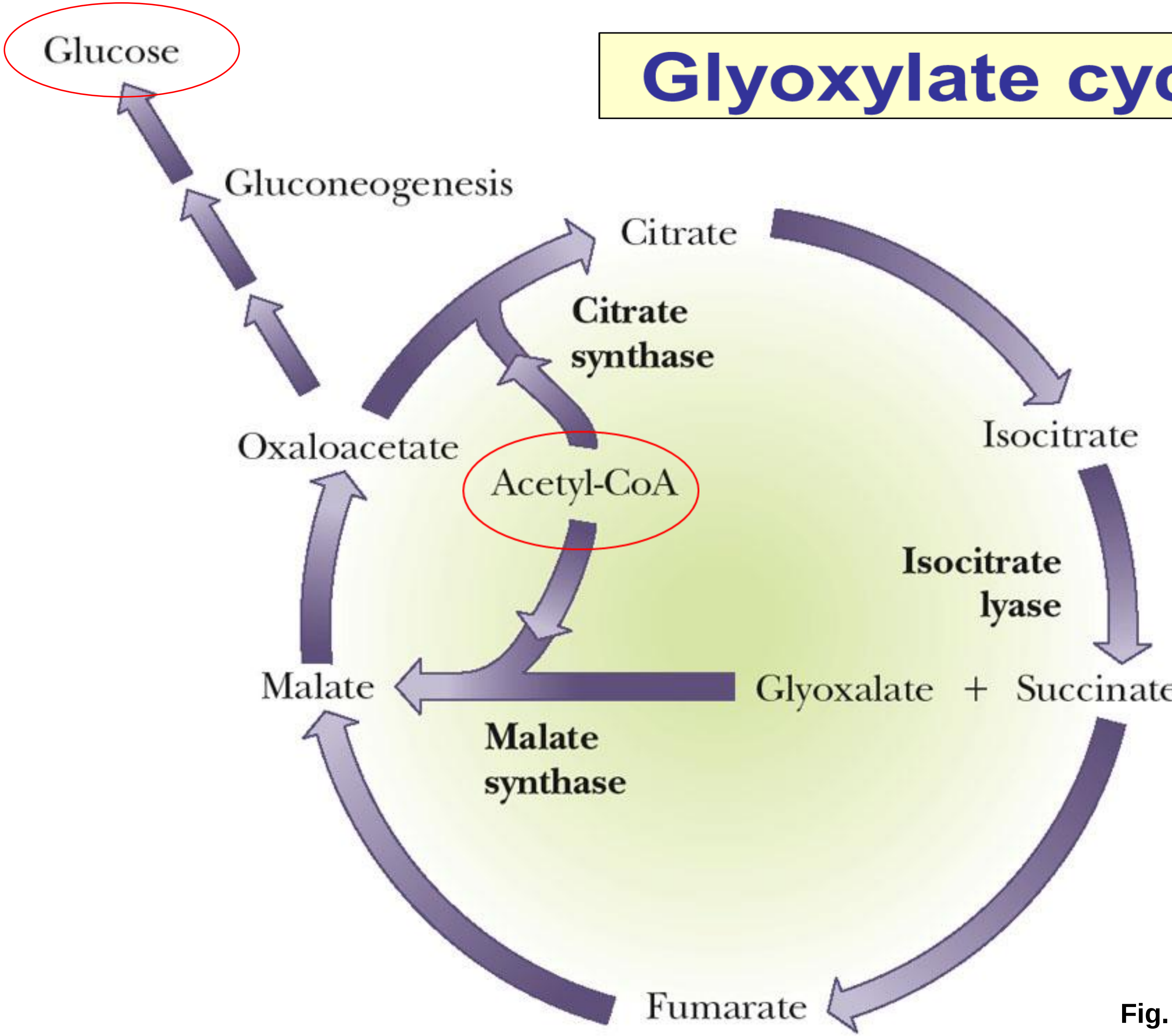


Fig. 19-9, p.529

TCA 회로의 중요성

① 이화 작용에서의 역할

- 효과적인 에너지 생산 체계

② 동화작용에서의 역할

-지질대사

-아미노산 대사

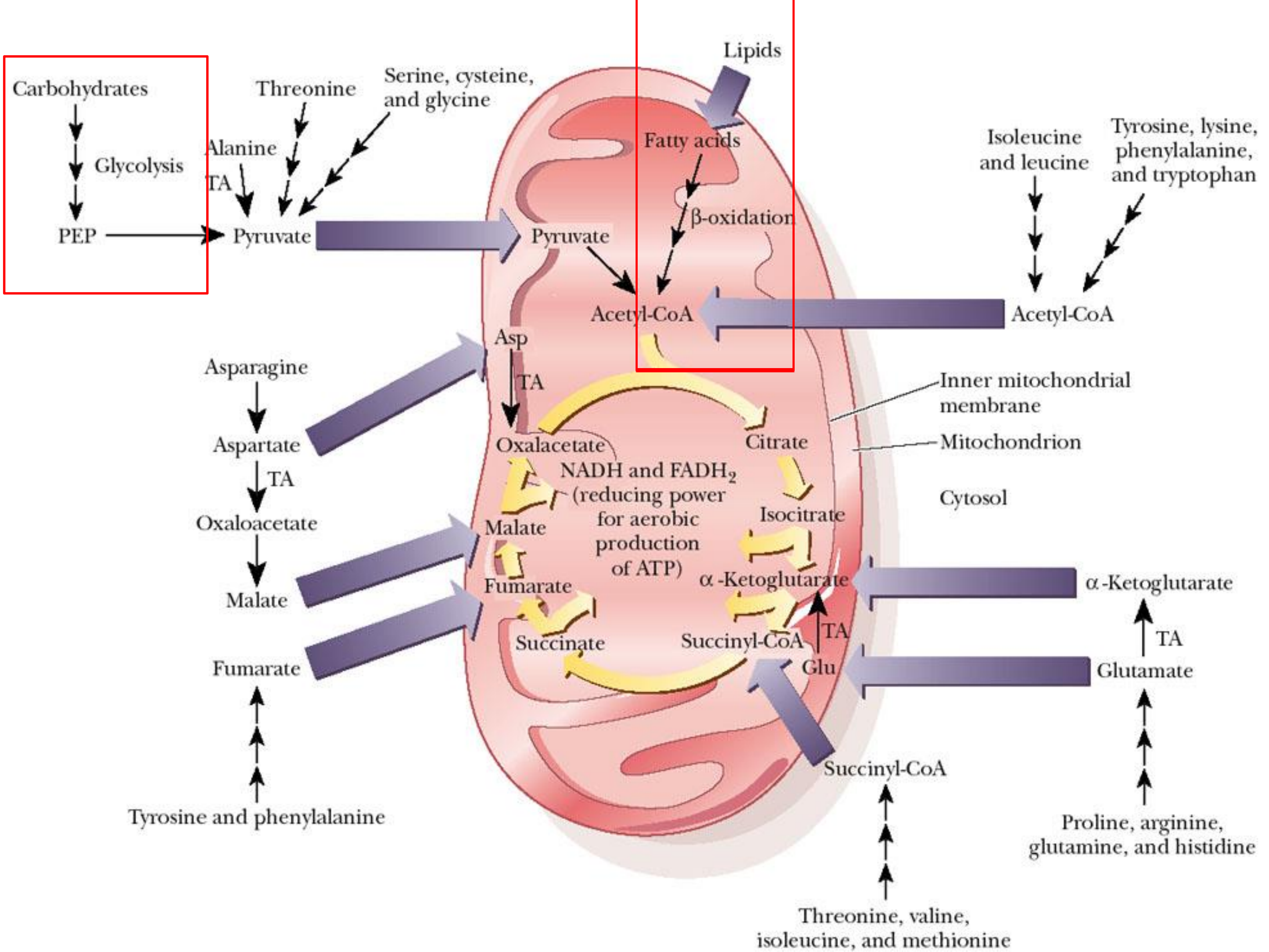


Fig. 19-10, p.530

당질은 지방산과 아미노산으로 전환된다

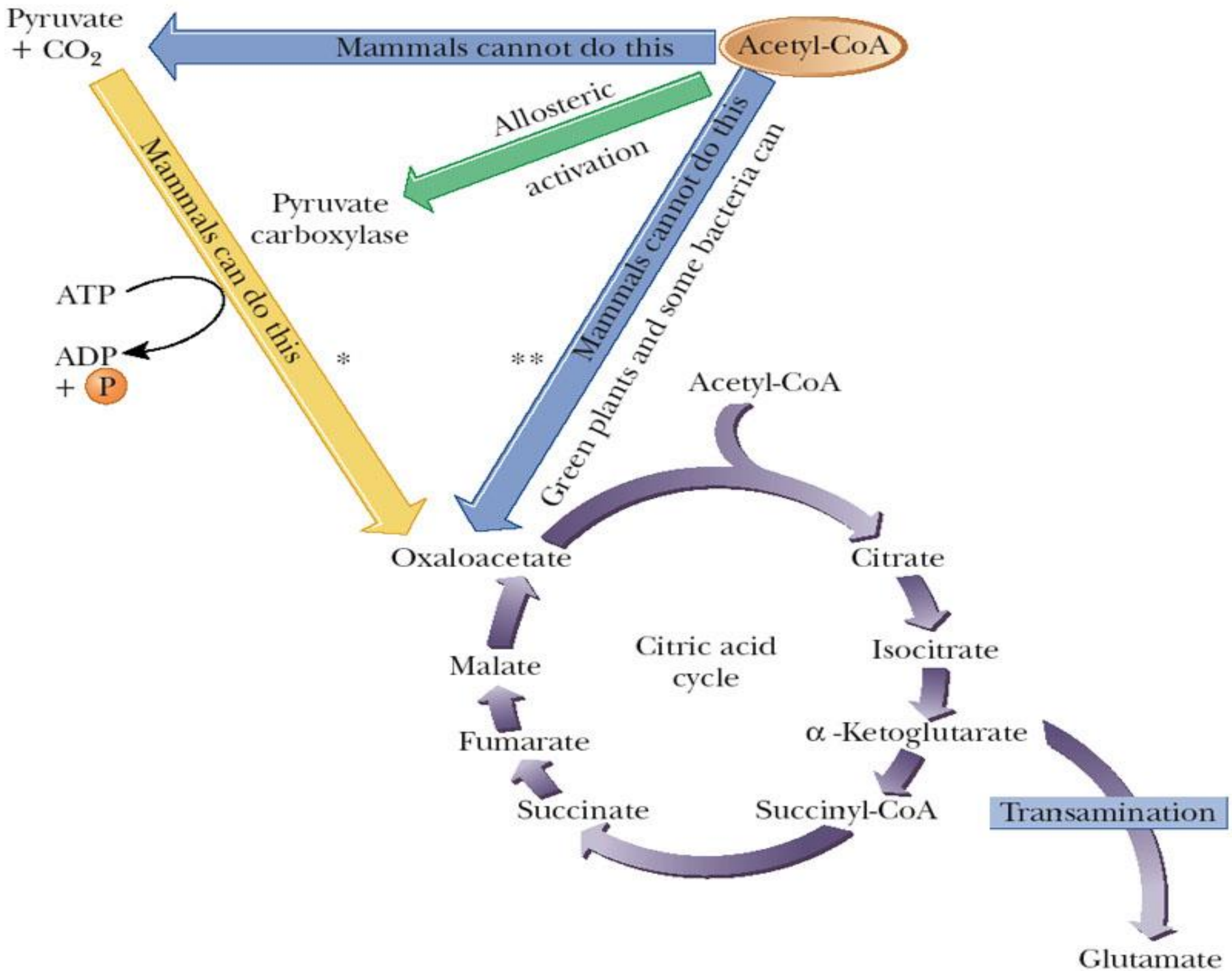


Fig. 19-11, p.531

당신생

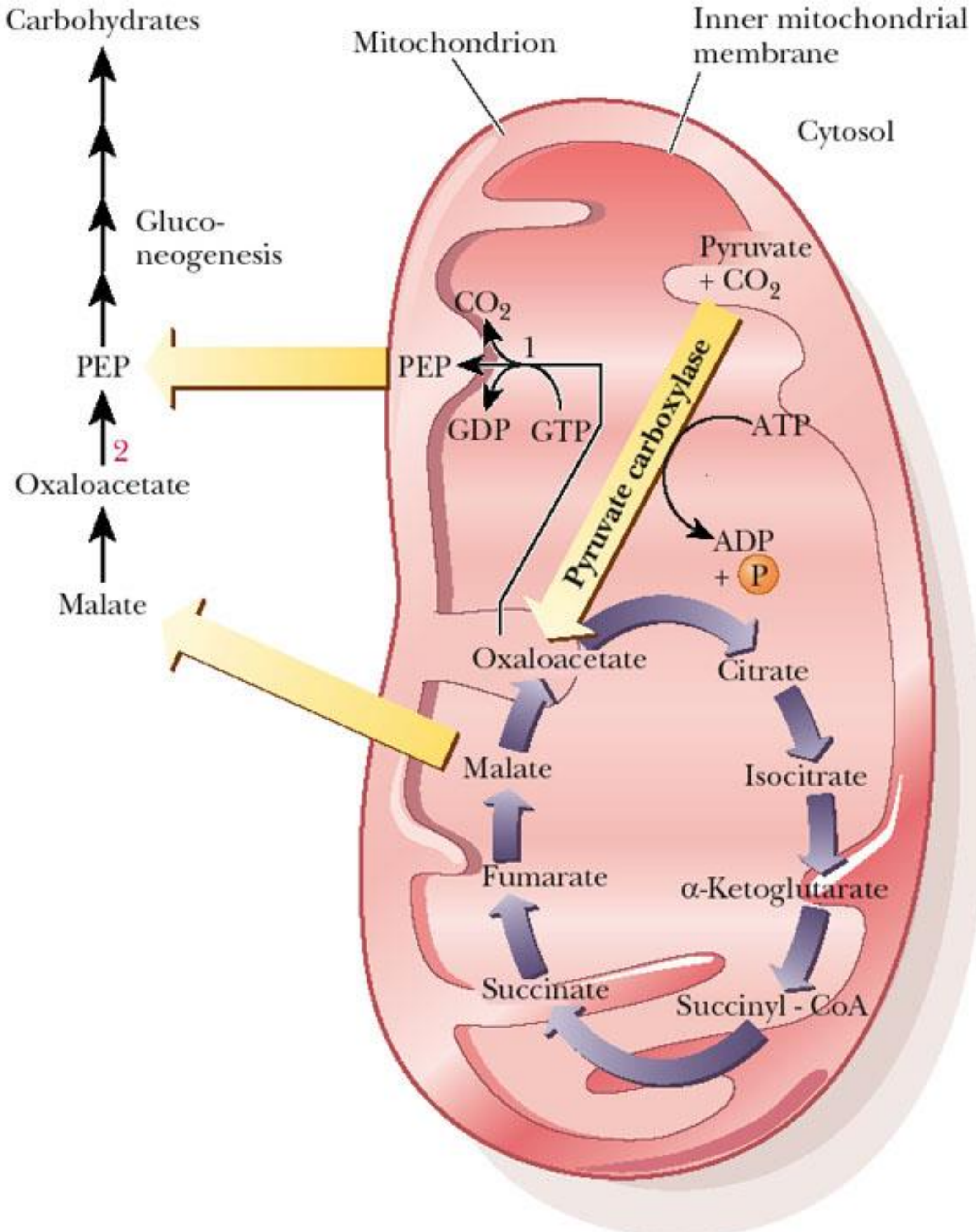


Fig. 19-12, p.533

미토콘드리아 내막의 특성

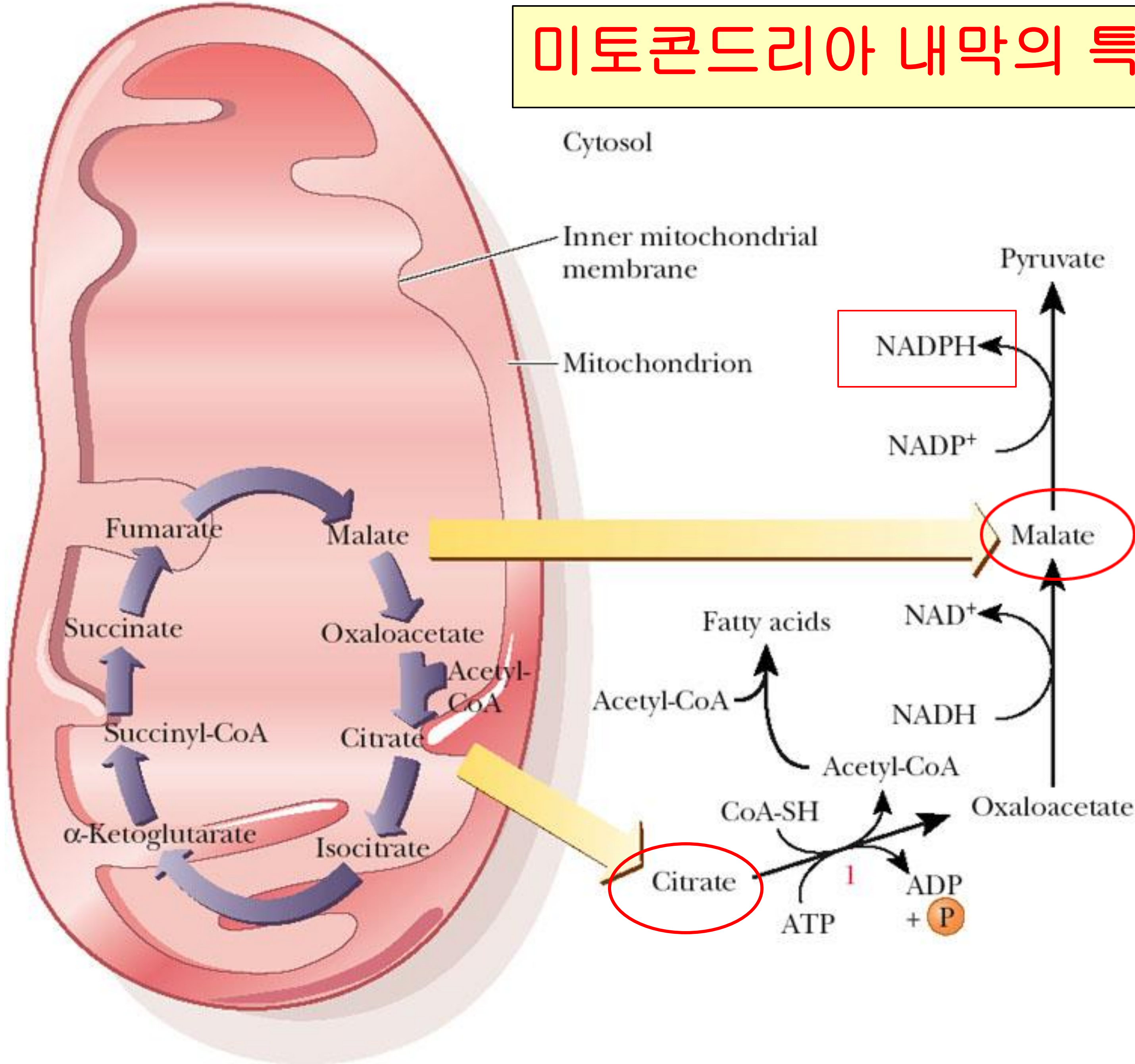


Fig. 19-13, p.533

NADPH의 생성

$$^{-}OOC-CH_2-\overset{\overset{\displaystyle O}{\|}}{C}-COO^{-} + NADH + H^{+} \xrightarrow{\text{Malate dehydrogenase}} {}^{-}OOC-CH_2-\overset{\overset{\displaystyle OH}{|}}{CH}-COO^{-} + NAD^{+}$$

Oxaloacetate → Malate

$$^{-}OOC-CH_2-\overset{\overset{\displaystyle OH}{|}}{CH}-COO^{-} + NADP^{+} \xrightarrow{\text{Malic enzyme}} CH_3-\overset{\overset{\displaystyle O}{\|}}{C}-COO^{-} + CO_2 + NADPH + H^{+}$$

Malate → Pyruvate

Fig. 19-14, p.534

TCA 회로의 중요성 및 역할 요약

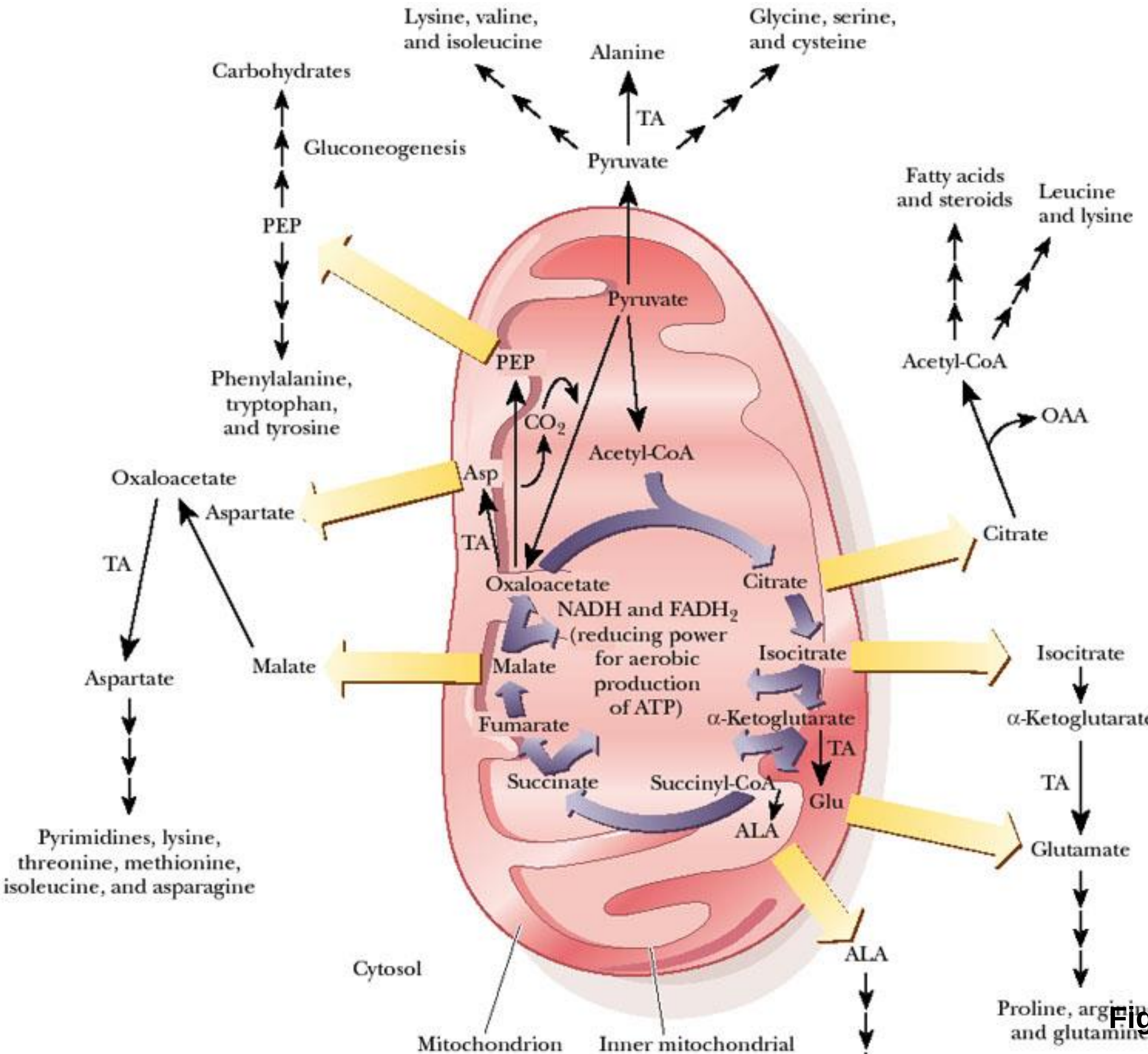
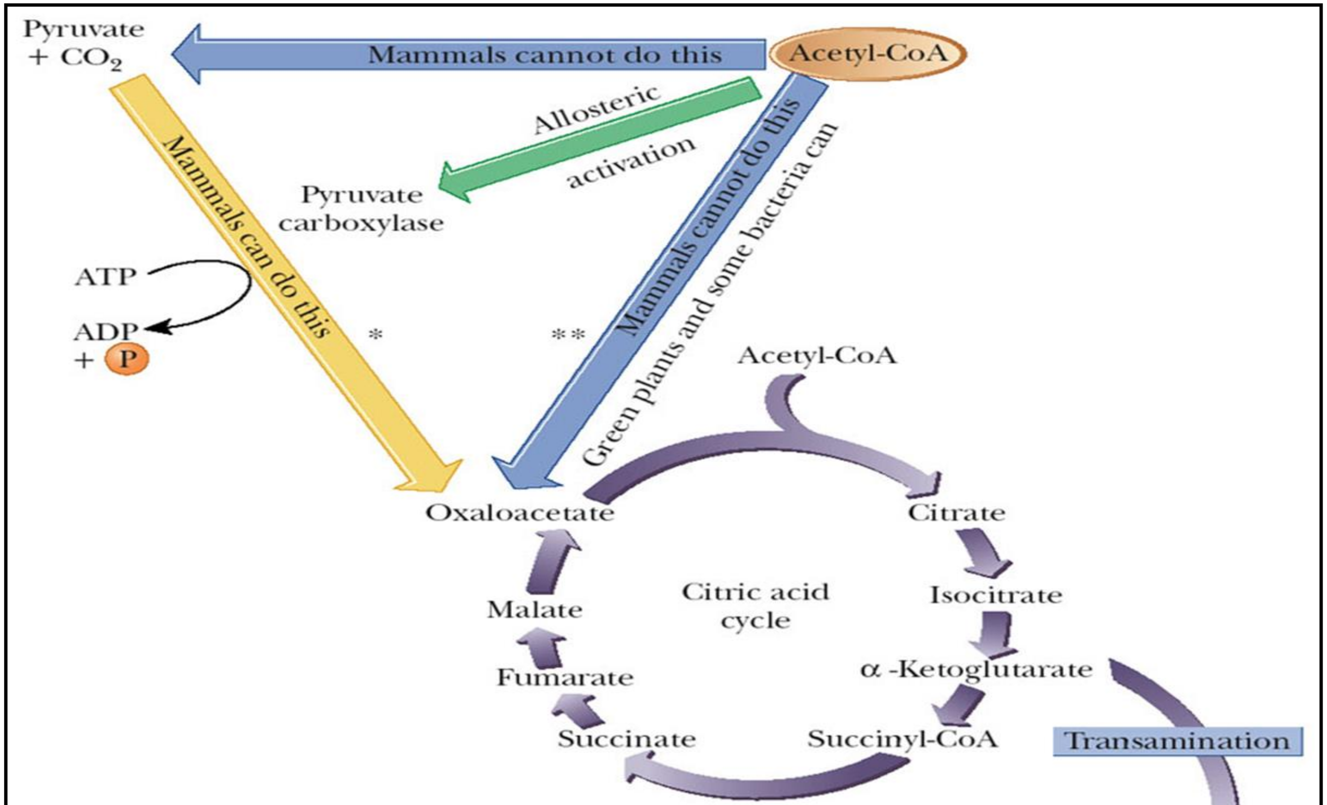


Fig. 19-15, p.535

Why is it hard to lose weight?

- All roads lead to fat
- Fat cannot back to carbohydrates



TCA회로는 에너지대사의 핵심이다.

그러므로 열심히 공부할 필요가 있다.

숙제 (572-573쪽)

- 문제 5번
- 문제 8번
- 문제 32-35번
- 문제 36번
- 문제 40번
- 문제 45-47번
- 문제 51번