# ATP AND METABOLISM-II
# The Mitochondria &
# The Krebs Cycle & ETC/S

## Learning Objectives:

- ❖ Describe the structure , conformational states and reproduction of mitochondria. Compare between inner & outer membranes structure of the mitochondria.

- ❖ Describe BRIEFLY the Krebs cycle and list its products.
- ❖ Describe BRIEFLY the electron transport system/chain and list its product.
- ❖ Describe the breakdown of ATP production per one glucose usage (the total ATP accounting).

## ATP Production:

❖ Glucose breakdown & ATP production (cellular respiration) shown in the equation in the previous lecture, is complex process and involves three main pathways:

***Last Lecture***

***We are here Today!***

1. **Glycolysis**, ***occurs in the cell cytoplasm***.

2. **The Krebs cycle**, ***occurs in the mitochondria***.
3. **The electron transport chain & oxidative phosphrylation*, also occurs in the mitochondria.***

❖ So, the cellular respiration occurs in tow sites within the cell, ***the cytoplasm (glycolysis)*** and ***the mitochondria (The Krebs cycle & ETC).***

❖ The three pathways will produce a total of **36 ATP molecules** *(2 from glycolysis, 2 from Krebs cycle, and 32 from ETS)* **from one glucose**.

# Lets Understand First, What are "The Mitochondria"

***The sites of the reactions of today's lecture!***

## The Mitochondria:

- ❖ The powerhouse of the cell, ***where most ATP production occurs***.
- ❖ 0.5 - 1.0 µm diameter, and about 7 µm long, but variable in size and shape.
- ❖ Each cell may contain 100, or several thousand, depending on metabolic activity.
- ❖ They are smaller in cells which contain more, because rapidly dividing.
- ❖ **Mitochondria Reproduction:**
  - ➢ They contain a *double strand of circular DNA which codes for some of their protein.*
  - ➢ They also contain ribosomes, *they do transcription and translation like a cell*.
  - ➢ They import some of their proteins, i.e. *they are genetically only semi-autonomous.*
  - ➢ Sperms do not bring mitochondria into the egg, so *we inherit mitochondrial DNA from our mothers only.*

# The Mitochondria - *Anatomy:*

- They consist of an ***inner and an outer membrane,*** with ***fluid-filled intermembrane space.***

- Differences between the two membranes:

| **Outer Membrane** | **Inner Membrane** |
|---|---|
| Thinner | Thicker |
| Smooth, no spheres | Spheres (enzyme complexes) are inside |
| No cristae or other folds | Folds called **cristae** increase the surface area. Cristae vary in number, size and shape, depending on tissue type. |
| Freely permeable to all substances of MW less than 5000 | Freely permeable to substances of MW less than 100 or 150. Selectively permeable (need transport proteins) to substances MW >100-150. |
| Less protein, mainly phospholipid. Contains cholesterol | More protein, because many enzymes embedded in the membrane. |

## The Mitochondria:

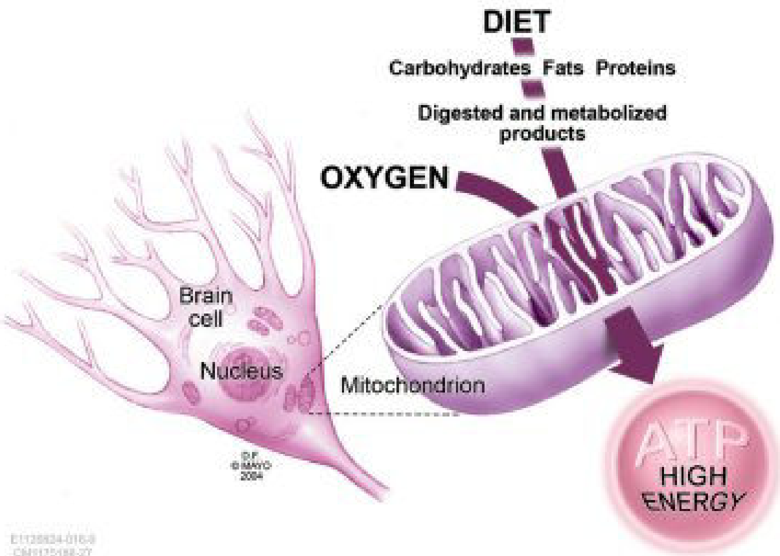
❖ Mitochondria exist in two conformational states:

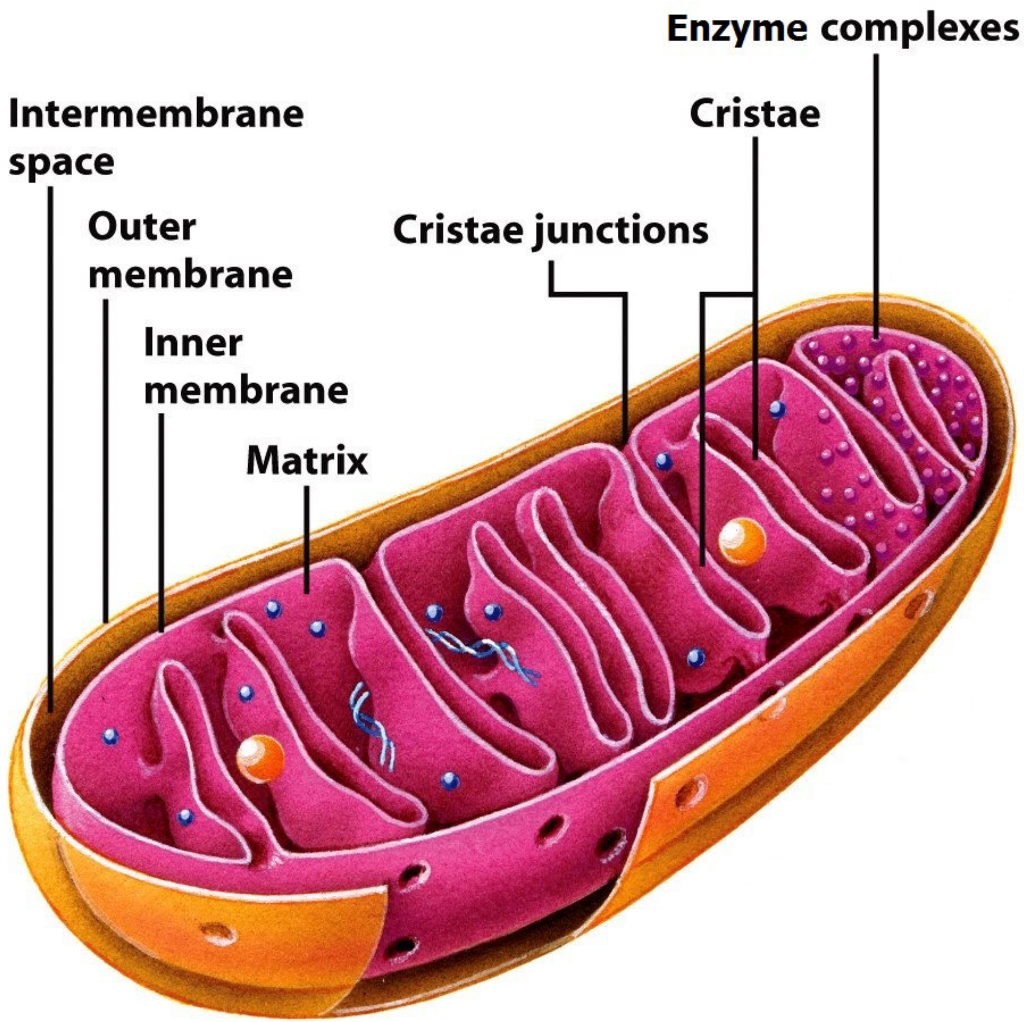
1. **Orthodox conformational state**: Typical of inactive mitochondria, when there is an abundance of ATP.

2. **Condensed conformational state**: If ADP begins to predominate over ATP, it binds to translocase on the inner membrane and that triggers a change to the physiologically more active "condensed" conformational state. The intermembrane space is greatly enlarged, and the cristae become closer together. ***This is part of a process designed to accelerate ATP production.***

❖ *Inner membrane spheres are found on the inner side of the inner membrane, and they contain the enzymes and coenzymes involved in ATP production.* When biochemical pathways are membrane-bound, this may increase their efficiency.

# The Mitochondria:

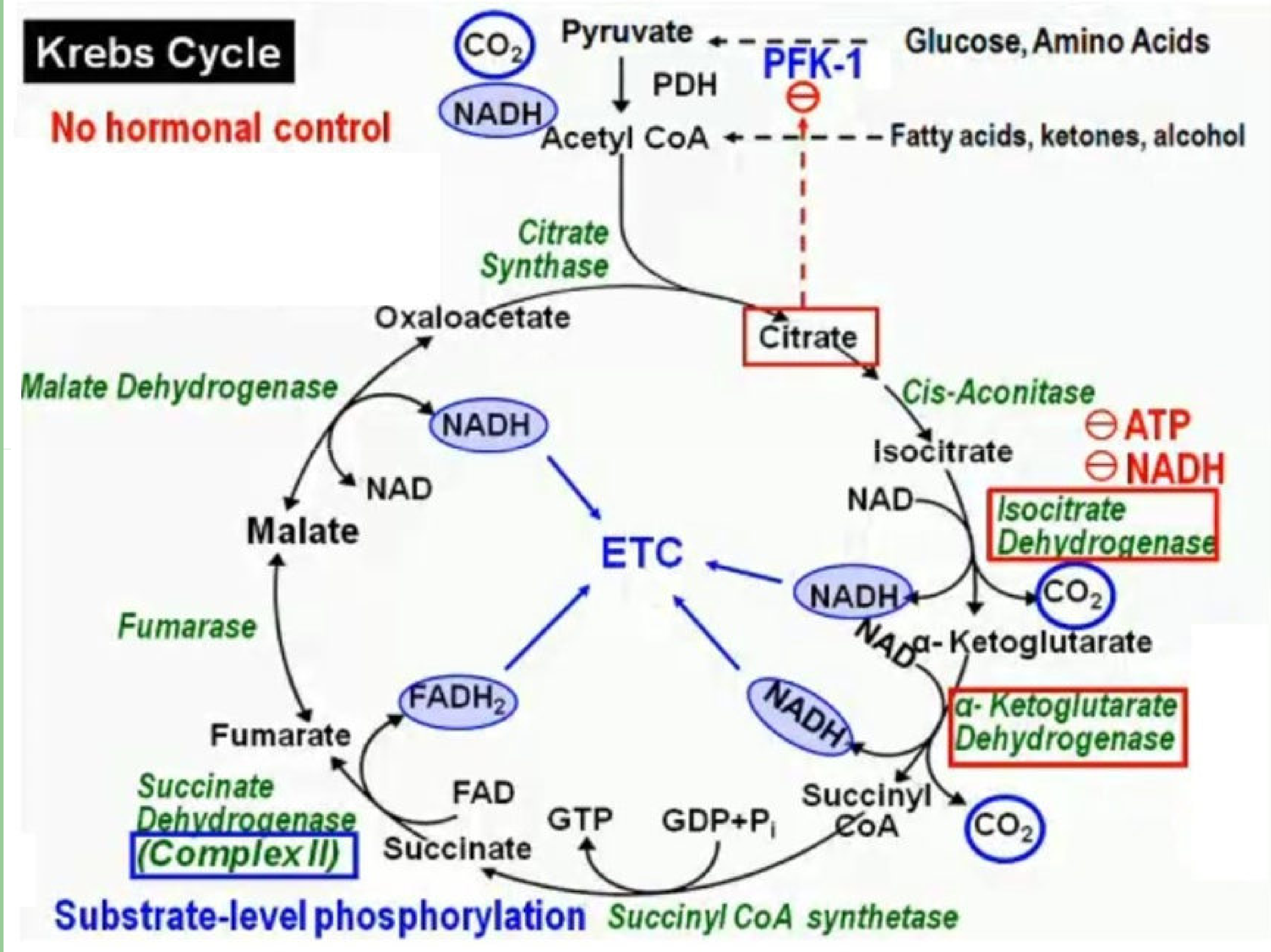


## The Krebs Cycle at A Glance:

- **KREBS CYCLE aka CITRIC ACID CYCLE aka TCA CYCLE**:
  - ***Oxaloacetate***, the final product from the previous turn of the cycle, picks up the ***acetyl group*** from ***acetyl coenzyme A***, to form ***citrate***.
  - ***Citrate*** undergoes a series of conversions, to make ***oxaloacetate***.
  - 1 step is a ***substrate level phosphorylation*** which ***makes GTP and then ATP***.
  - 3 steps are ***oxidation reactions*** involving $NAD^+$ reduction to $NADH + H^+$.
  - 1 step is an ***oxidation reaction*** involving reduction of FAD to $FADH_2$.
  - 2 steps involve ***$CO_2$ production***. ***(4 $CO_2$ molecules per glucose molecule).***
  - ***Note that on the basis of per glucose molecule, all the above figures are doubled.***

## The Krebs Cycle in Details:



## The Krebs Cycle (Simplified Version):

- **Reaction 1**: Oxaloacetate, which is the final product of a previous "turn" of the cycle, reacts with acetyl CoA to form citrate. Coenzyme A is released and able to be recycled.

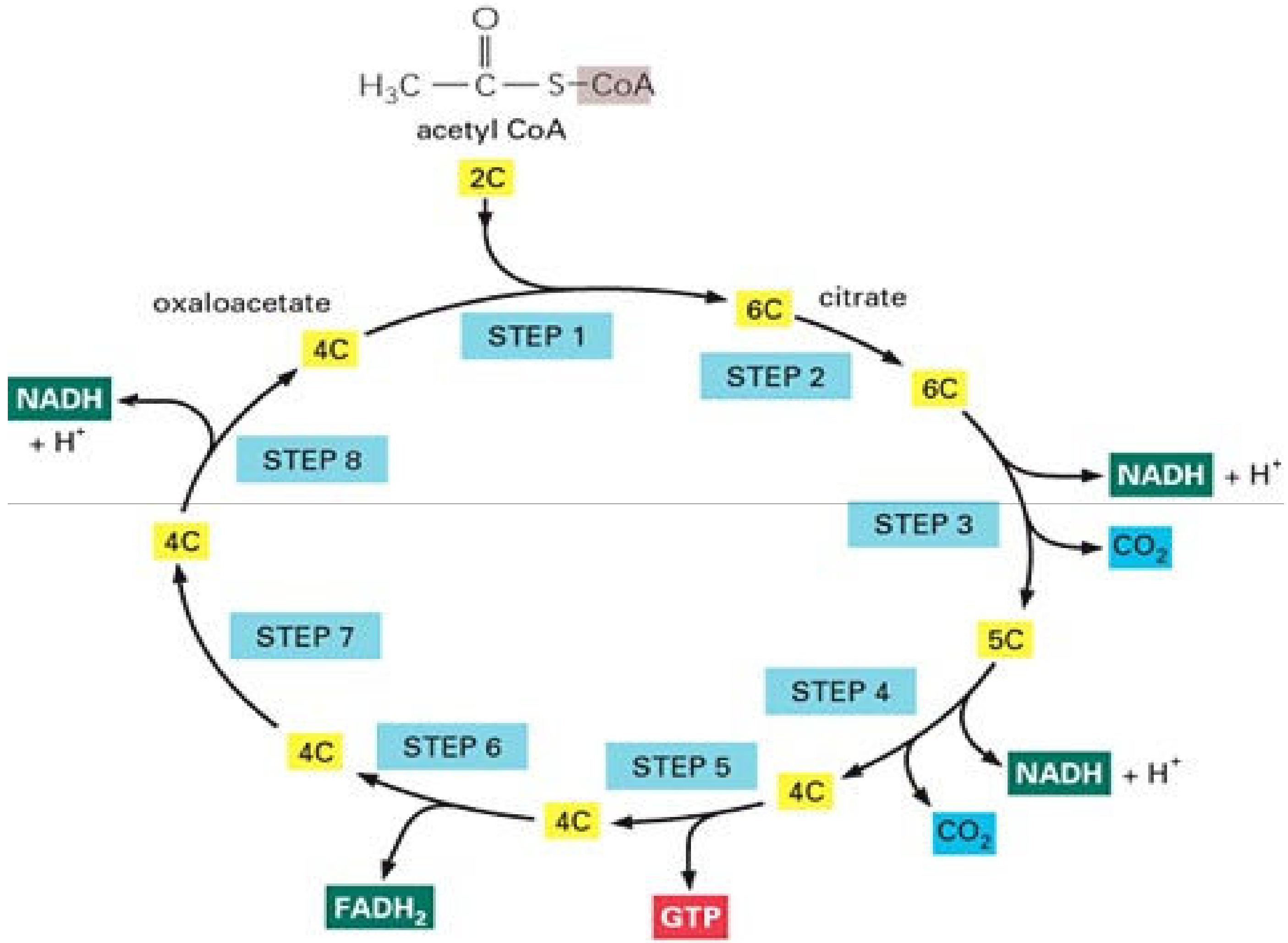
- **Reactions 3-4**: $CO_2$ is given off, 1 molecule from each of these 2 reactions. These are oxidative decarboxylation reactions. NAD is reduced to NADH + H in each of these 2 reactions.

- **Reaction 5:** This is **substrate-level phosphorylation** in which GDP is phosphorylated to GTP. After that, the GTP can phosphorylate ADP to make ATP. So this is considered to be a substrate-level phosphorylation reaction to make A TP.

- **Reaction 6:** This is an oxidation step. The redox potential of this step is not great enough to use NAD as the electron acceptor. Therefore FAD is reduced to FADH2 instead, because it has a lower redox potential.

- **Reaction 8:** This is the final step of the Krebs cycle, taking us back to oxaloacetate. This is an oxidation step, in which NAD is used as electron acceptor.

# The Krebs Cycle (Simplified Version):




**NET: 3 NADH, 1 ATP, 1 $FADH_2$, & 2 $CO_2$**

**(Double the above figures per one glucose molecule)**

## Krebs Cycle Summary:

- ***It requires Oxygen (Aerobic).***

- Cyclical series of reactions that give off $CO_2$ and produce one ATP per cycle

- ***Turns twice per glucose molecule. Produces 2 ATP molecules***.

- ***ATP is produced by substrate level phosphorylation.***

- ***Takes place in matrix of mitochondria.***

- Each turn of the Krebs Cycle also produces ***3 NADH,1 FADH$_2$, and 2 CO$_2$ . (Double these figures per one glucose molecule).***

# Electron Transport System/Chain (ETS/ETC) at A Glance:

- **NADH & $FADH_2$** can be used to power ATP production. ***How much NADH & $FADH_2$ do we have?***
  - **NADH:** 2 from glycolysis, 2 from pyruvate ⇨ acetyl CoA, 6 from Krebs cycle **= 10 total.**
  - **$FADH_2$** : 2 $FADH_2$ from Krebs cycle **= 2 total.**

- Electrons from NADH are passed along a chain of electron acceptors in turn.. ***Each electron acceptor has a lower "redox potential" than the one before it in the chain***

- ***Wherever the redox potential is much lower than that of the previous electron acceptor, there is enough energy left over to power the production of 1 A TP molecule.***

- ETS components, in order, are NAD ⇨ *FMN ⇨ CoQ ⇨ *cytochrome ⇨ *oxygen.

- * ***shows the 3 points at which 1 ATP is made by oxidative phosphorylation.***

- From the stepwise oxidation of each of 10 NADH which are made from all the above reactions, 3 ATP (total 30) can be made (2 ATP are used to transfer NADH of stage 2 glycolysis to the mitochondria, so remaining 28 ATP). Also the 2 ATP per one $FADH_2$ (4 ATP). Total from ETS is (28+4)= **32 ATP**

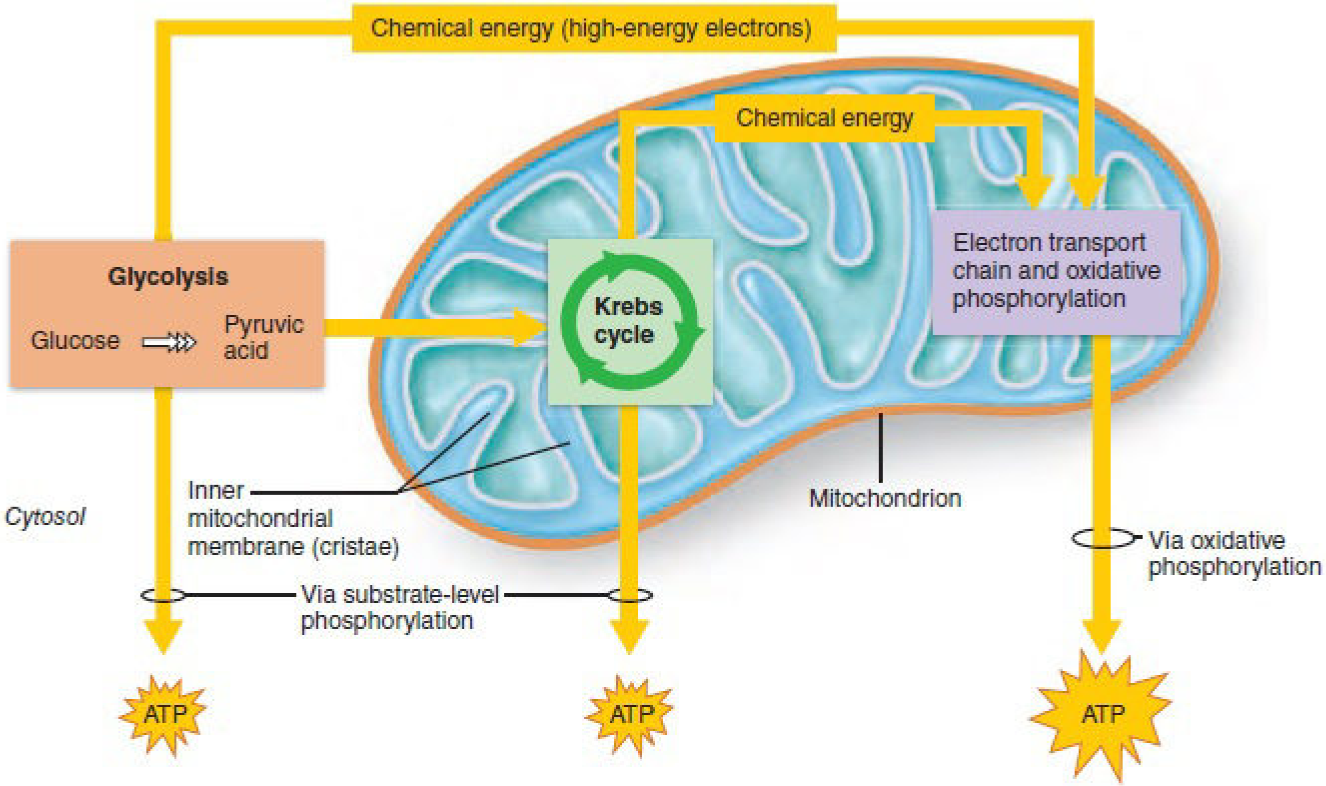
# Electron Transport Chain Summary:

- 32 ATP Produced.
- ATP is produced by Oxidative Phosphorylation.
- $H_2O$ Produced.
- Occurs Across Inner Mitochondrial membrane.
- Uses coenzymes $NAD^+$ and $FAD^+$ to accept electrons from glucose.

## ATP ACCOUNTING (Grand Total):

**Grand total ATP: 2 from glycolysis, 2 from Krebs cycle, 32 from ECT= 36 ATP**

# ATP Production:




① Glycolysis, in the cytosol, breaks down each glucose molecule into two molecules of pyruvic acid.

② The pyruvic acid then enters the mitochondrial matrix, where the Krebs cycle decomposes it to $CO_2$. During glycolysis and the Krebs cycle, substrate-level phosphorylation forms small amounts of ATP.

③ Energy-rich electrons picked up by coenzymes are transferred to the electron transport chain, built into the cristae membrane. The electron transport chain carries out oxidative phosphorylation, which accounts for most of the ATP generated by cellular respiration.

***During cellular respiration, ATP is formed in the cytosol and in the mitochondria.***