

## The Krebs cycle completes the energy-yielding oxidation of organic molecules:

### A CLOSER LOOK

- More than 75% of the original energy in glucose is still present in two molecules of pyruvate.
- If oxygen is present, pyruvate enters the mitochondrion where enzymes of the Krebs cycle complete the oxidation (loss of electrons) of the pyruvate to carbon dioxide.
- As pyruvate enters the mitochondrion, a multienzyme complex modifies pyruvate to **acetyl CoA** which then enters the Krebs cycle in the matrix.  
***THIS IS CONSIDERED THE JUNCTION BETWEEN GLYCOLYSIS AND THE KREBS CYCLE OR THE PRE KREBS CYCLE!!***
  - A carboxyl group is removed as  $\text{CO}_2$ . The  $\text{CO}_2$  will diffuse out of the cell.
  - A pair of electrons is transferred from the remaining two-carbon fragment to  $\text{NAD}^+$  to form  $\text{NADH}$ .
  - The oxidized fragment, acetate, combines with coenzyme A to form acetyl CoA (a 2 carbon product).
- The Krebs cycle is named after Hans Krebs who was largely responsible for clearly explaining its pathways in the 1930's.
  - This cycle ***begins*** when acetate (2C) from acetyl CoA combines with oxaloacetate (4C) to form citrate.
  - Ultimately, the oxaloacetate is recycled and the acetate is broken down to  $\text{CO}_2$ .
- Each turn of the Krebs cycle produces **one ATP** by substrate-level phosphorylation, **three NADH**, and **one FADH<sub>2</sub>** (another electron carrier) from each molecule of acetyl CoA.
- The Krebs cycle consists of eight steps (*see page 165 in text*).
- The conversion of pyruvate and the Krebs cycle produces large quantities of electron carriers.

## The inner mitochondrial membrane couples electron transport to ATP synthesis:

### A CLOSER LOOK

- Only **4** of the 38 ATP ultimately produced by respiration of glucose come from substrate-level phosphorylation (*NOT from the electron transport chain*).
- The vast majority of the ATP comes from the **energy** in the **electrons** carried by **NADH (and FADH<sub>2</sub>)**.
- The energy in these electrons is used in the electron transport chain to power ATP synthesis (to build ATP).
- **Thousands of copies** of the electron transport chain are found in the extensive surface of the cristae, the inner membrane of the mitochondrion.
  - Most components of the chain are proteins embedded in the membrane that are bound with prosthetic groups (non-protein components) that can alternate between reduced and oxidized states as they accept and donate electrons.
- Electrons drop in free energy as they pass down the electron transport chain.
- Electrons carried by NADH are transferred to the first molecule in the electron transport chain, flavoprotein.
  - The electrons continue along the chain which includes several **cytochrome** proteins (pg. 166) and one lipid carrier.
- The electrons carried by FADH<sub>2</sub> have lower free energy and are added to a later point in the chain.
- Electrons from NADH or FADH<sub>2</sub> ultimately pass to oxygen.
  - For every two electron carriers (four electrons), one O<sub>2</sub> molecule is reduced to two molecules of water.
- The electron transport chain generates **no ATP directly**.
- Its function is to break the large free energy drop from food to oxygen into a series of smaller steps that release energy in manageable amounts.
- The **movement** of electrons along the electron transport chain **does** contribute to chemiosmosis and ATP synthesis.
- Chemiosmosis – an energy coupling mechanism that uses energy stored in the form of a hydrogen ion gradient across a membrane to drive cellular work, such as the synthesis of ATP. Most ATP synthesis in cells occurs by chemiosmosis.

- A protein complex, **ATP synthase**, located in the cristae actually makes ATP from ADP and  $P_i$ . (*what kind of protein is ATP synthase??*)
- ATP synthase uses the energy of an existing proton (ion) gradient to power ATP synthesis - - that is, the power source for the ATP synthase is a difference in concentration of  $H^+$  on opposite sides of the inner mitochondrial membrane
  - This proton gradient develops between the intermembrane space and the matrix.
- The proton gradient is produced by the movement of electrons along the electron transport chain.
- Several chain molecules can use the exergonic flow of electrons to pump  $H^+$  from the matrix to the intermembrane space.
  - This concentration of  $H^+$  is the **proton-motive force**.
- The ATP synthase molecules are the only places along the membrane that will allow  $H^+$  to diffuse back to the matrix.
- This exergonic flow of  $H^+$  is used by ATP synthase to generate ATP.
- This coupling of the redox reactions of the electron transport chain to ATP synthesis is called **chemiosmosis**.
- The mechanism of ATP generation by ATP synthase is still an area of active investigation.
  - As hydrogen ions flow down their gradient, they cause the cylinder portion and attached rod of ATP synthase to rotate.
  - The spinning rod causes a conformational change in the knob region, activating catalytic sites where ADP and inorganic phosphate combine to make ATP.

- Chemiosmosis is an energy-coupling mechanism that uses energy stored in the form of an  $H^+$  gradient across a membrane to drive cellular work.
  - In the mitochondrion, chemiosmosis generates ATP.
  - Chemiosmosis in chloroplasts also generates ATP, but light drives the electron flow down an electron transport chain and  $H^+$  gradient formation.
  - Prokaryotes generate  $H^+$  gradients across their plasma membrane.
    - They can use this proton-motive force not only to generate ATP but also to pump nutrients and waste products across the membrane and to rotate their flagella.

## Cellular respiration generates many ATP molecules for each sugar molecule it oxidizes: A *REVIEW*

- During respiration, most energy flows from glucose → NADH → electron transport chain → proton-motive force → ATP.
- The 6 carbons in the glucose molecule are oxidized to six CO<sub>2</sub> molecules.
- Some ATP is produced by substrate-level phosphorylation during glycolysis and the Krebs cycle, but most comes from oxidative phosphorylation.
- Each NADH from the Krebs cycle and the conversion of pyruvate contributes enough energy to generate a maximum of 3 ATP (rounding up).
  - The NADH from glycolysis may also yield 3 ATP.
- Each FADH<sub>2</sub> from the Krebs cycle can be used to generate about 2 ATP.
- In some eukaryotic cells, NADH produced in the cytosol by glycolysis may be worth only 2 ATP.
  - The electrons must be shuttled to the mitochondrion.
  - In some shuttle systems, the electrons are passed to NAD<sup>+</sup>, in others the electrons are passed to FAD.
- Assuming the most energy-efficient shuttle of NADH from glycolysis, a maximum yield of 34 ATP is produced by oxidative phosphorylation.
- This plus the 4 ATP from substrate-level phosphorylation gives a maximum number of 38 ATP.
  - This maximum figure does not consider other uses of the proton-motive force.
- How efficient is respiration in generating ATP?
  - Complete oxidation of glucose releases 686 kcal per mole.
  - Formation of each ATP requires at least 7.3 kcal/mole.
  - Efficiency of respiration is:
 
$$\frac{7.3 \text{ kcal/mole} \times 38 \text{ ATP per glucose}}{686 \text{ kcal/mole glucose}}$$
  - The other ~ 60% is lost as heat.
- Cellular respiration is remarkably efficient in energy conversion.
- Compare that to the efficiency of a car engine, which is about 25%....we are pretty efficient machines!!!