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QUESTION
Describe the mechanism in aerobic respiration

ANSWER

Aerobic respiration requires oxygen (O_2) in order to create ATP. Although carbohydrates, fats, and proteins are consumed as reactants, it is the preferred method of pyruvate breakdown in glycolysis and requires that pyruvate enter the mitochondria in order to be fully oxidized by the Krebs cycle. The products of this process are carbon dioxide and water, but the energy transferred is used to break bonds in ADP as the third phosphate group is added to form ATP (adenosine triphosphate), by substrate-level phosphorylation, NADH and $FADH_2$
Simplified reaction: $C_6H_{12}O_6\ (s) + 6\ O_2\ (g) \rightarrow 6\ CO_2\ (g) + 6\ H_2O\ (l) + \text{heat}$
$\Delta G = -2880$ kJ per mol of $C_6H_{12}O_6$
The negative ΔG indicates that the reaction can occur spontaneously.
The potential of NADH and $FADH_2$ is converted to more ATP through an electron transport chain with oxygen and protons (hydrogen) as the "terminal electron acceptors".Most of the ATP produced by aerobic cellular respiration is made by oxidative phosphorylation. The energy of O_2 released is used to create a chemiosmotic potential by pumping protons across a membrane. This potential is then used to drive ATP synthase and produce ATP from ADP and a phosphate group. Biology textbooks often state that 38 ATP molecules can be made per oxidized glucose molecule during cellular respiration (2 from glycolysis, 2 from the Krebs cycle, and about 34 from the electron transport system). However, this maximum yield is never quite reached because of losses due to leaky membranes as well as the cost of moving pyruvate and ADP into the mitochondrial matrix, and current estimates range around 29 to 30 ATP per glucose.

Aerobic metabolism is up to 15 times more efficient than anaerobic metabolism (which yields 2 molecules ATP per 1 molecule glucose) because the double bond in O_2 is of higher energy than other double bonds or pairs of single bonds in other common molecules in the biosphere.However, some anaerobic organisms, such as methanogens are able to continue with anaerobic respiration, yielding more ATP by using other inorganic molecules (not oxygen) of high energy as final electron acceptors in the electron transport chain. They share the initial pathway of glycolysis but aerobic metabolism continues with the Krebs cycle and oxidative phosphorylation. The post-glycolytic reactions take place in the mitochondria in eukaryotic cells, and in the cytoplasm in prokaryotic cells.

Glycolysis

Out of the cytoplasm it goes into the Krebs cycle with the acetyl CoA. It then mixes with CO_2 and makes 2 ATP, NADH, and FADH. From there the NADH and FADH go into the NADH reductase, which produces the enzyme. The NADH pulls the enzyme's electrons to send through the electron transport chain. The electron transport chain pulls H^+ ions through the chain. From the electron transport chain, the released hydrogen ions make ADP for an end result of 32 ATP. O_2 provides most of the energy for the process and combines with protons and the electrons to make water. Lastly, ATP leaves through the ATP channel and out of the mitochondria.

Glycolysis is a metabolic pathway that takes place in the cytosol of cells in all living organisms. Glycolysis can be literally translated as "sugar splitting"[5], which functions with or without the presence of oxygen. In humans, aerobic conditions produce pyruvate and anaerobic conditions produce lactate. In aerobic conditions, the process converts one molecule of glucose into two molecules of pyruvate (pyruvic acid), generating energy in the form of two net molecules of ATP. Four molecules of ATP per glucose are actually produced, however, two are consumed as part of the preparatory phase. The initial phosphorylation of glucose is required to increase the reactivity (decrease its stability) in order for the molecule to be cleaved into two pyruvate molecules by the enzyme aldolase. During the pay-off phase of glycolysis, four phosphate groups are transferred to ADP by substrate-level phosphorylation to make four ATP, and two NADH are produced when the pyruvate is oxidized. The overall reaction can be expressed this way:

$$\text{Glucose} + 2\ NAD^+ + 2\ P_i + 2\ ADP \rightarrow 2\ \text{pyruvate} + 2\ H^+ + 2\ NADH + 2\ ATP + 2\ H^+ + 2\ H_2O + \text{energy}$$

Starting with glucose, 1 ATP is used to donate a phosphate to glucose to produce glucose 6-phosphate. Glycogen can be converted into glucose 6-phosphate as well with the help of glycogen phosphorylase. During energy metabolism, glucose 6-phosphate becomes fructose 6-phosphate. An additional ATP is used to phosphorylate fructose 6-phosphate into fructose 1,6-bisphosphate by the help of phosphofructokinase. Fructose 1,6-biphosphate then splits into two phosphorylated molecules with three carbon chains which later degrades into pyruvate.

Oxidative decarboxylation of pyruvate

Main article: Pyruvate decarboxylation

Pyruvate is oxidized to acetyl-CoA and CO_2 by the pyruvate dehydrogenase complex (PDC). The PDC contains multiple copies of three enzymes and is located in the mitochondria of eukaryotic cells and in the cytosol of prokaryotes. In the conversion of pyruvate to acetyl-CoA, one molecule of NADH and one molecule of CO_2 is formed.

Krebs Cycle:

The cycle was discovered by Hans Krebs (1937, 1940, Nobel Prize 1953). It occurs inside mitochondria. The cycle is also named as citric acid cycle or tricarboxylic acid (TCA) cycle after the initial product. Krebs cycle is stepwise oxidative and cyclic degradation of activated acetate derived from pyruvate.

Oxidation of Pyruvate to Acetyl-CoA:

Pyruvate enters mitochondria. It is decarboxylated oxidatively to produce CO2 and NADH. The product combines with sulphur containing coenzyme A to form acetyl CoA or activated acetate. The reaction occurs in the presence of an enzyme complex pyruvate dehydrogenase (made up of a decarboxylase, lipoic acid, TPP, transacetylase and Mg2+).Acetyl CoA functions as substrate entrant for Krebs cycle. The acceptor molecule of Krebs cycle is a 4-carbon compound oxaloacetate. Kerbs cycle involves two decarboxylations and four dehydrogenations. The various components of Krebs cycle are as follows.

1. Condensation:
Acetyl CoA (2-carbon compound) combines with oxalo-acetate (4-carbon compound) in the presence of condensing enzyme citrate synthetase to form a tricarboxylic 6-carbon compound called citric acid. It is the first product of Krebs cycle. CoA is liberated.
2. Dehydration:
Citrate undergoes reorganisation in the presence of aconitase forming cis aconitate releasing water.
3. Hydration:
Cis-aconitate is converted into isocitrate with the addition of water in the presence of iron containing enzyme aconitase.
4. Dehydrogenation:
Isocitrate is dehydrogenated to oxalosuccinate in the presence of enzyme isocitrate dehydrogenases and Mn2+. NADH2 (NADPH2) according to some workers) is produced.
5. Decarboxylation:
Oxalosuccinate is decarboxylated to form a-ketoglutarate through enzyme decarboxylase. Carbon dioxide is released.
6. Dehydrogenation and Decarboxylation:
α-Ketoglutarate is both dehydrogenated (with the help of NAD+) and decarboxylated by an enzyme complex a-ketoglutarate dehydrogenase. The enzyme complex contains TPP and lipoic acid. The product combines with CoA to form succinyl CoA.
7. Formation of ATP/GTP:
Succinyl CoA is acted upon by enzyme succinyl thiokinase to form succinate. The reaction releases sufficient energy to form ATP (in plants) or GTP (in animals).
8. Dehydrogenation:
Succinate undergoes dehydrogenation to form fumarate with the help of a dehydrogenase. FADH2 (reduced flavin adenine dinucleotide) is produced.
Succinate + FAD Succinate, → Dehydrogenase, Fumarate + FADH2
9. Hydration:
A molecule of water gets added to fumarate to form malate. The enzyme is called fumarase.
10. Dehyrogenation:
Malate is dehydrogenated or oxidised through the agency of malate dehydrogenase to produce oxaloacetate. Hydrogen is accepted by NADP+ NAD+
Oxaloacetate picks up another molecule of activated acetate to repeat the cycle.

A molecule of glucose yields two molecules of NADH2, 2ATP and two pyruvate while undergoing glycolysis. The two molecules of pyruvate are completely degraded in Krebs cycle to form two molecules of ATP, 8NADH2, and 2FADH2.
Glucose + 4ADP + 4H3PO4+10NAD+ + 2FAD -> 6CO2 + 4ATP + 10NADH + 10H+ +2FADH2

Terminal Oxidation:
It is the name of oxidation found in aerobic respiration that occurs towards the end of catabolic process and involves the passage of both electrons and protons of reduced coenzymes to oxygen.
Terminal oxidation consists of two processes-electron transport and oxidative phosphorylation.

1 Electron Transport Chain:
Inner mitochondrial membrane contains groups of electron and proton transporting enzymes. In each group the enzymes are arranged in a specific series called electron transport chain (ETC) or mitochondrial respiratory chain or electron transport system (ETS).
An electron transport chain or system is a series of coenzymes and cytochromes that take part in the passage of electrons from a chemical to its ultimate acceptor. The passage of electrons from one enzyme or cytochrome to the next is a downhill journey with a loss of energy at each step. At each step the electron carriers include flavins, iron sulphur complexes, quinones and cytochromes.
Most of them are prosthetic groups of proteins. Quinones are highly mobile electron carriers. Four enzymes are involved in electron transport—(i) NADH-Q reductase or NADH-dehydrogenase (ii) Succinate Q-reductase complex (iii) QH2-cytochrome c reductase complex (iv) Cytochrome c oxidase complex. NADH-Q reductase (or NADH- dehydrogenase) has two prosthetic groups, flavin mononucleotide (FMN) and iron sulphur (Fe-S) complexes. Both electrons and protons pass from NADH2 to FMN. The latter is reduced.

2. Oxidative phosphorylation
Oxidative phosphorylation is the synthesis of energy rich ATP molecules with the help of energy liberated during oxidation of reduced co-enzymes (NADH2, FADH2) produced in respiration. The enzyme required for this synthesis is called ATP synthetase.
It is located in F1 or head piece of F0-F1 or elementary particles present in the inner mitochondrial membrane. ATP-synthetase becomes active in ATP formation only where there is a proton gradient having higher concentration of H+ or protons on the F0 side as compared to F1 side.
Increased proton concentration is produced in the outer chamber or outer surface of inner mitochondrial membrane by the pushing of protons with the help of energy liberated, by passage of electrons from one carrier to another.
Transport of the electrons from nadh2 over ETC helps in pushing three pairs of protons to the outer chamber while two pairs of protons are sent outwardly during electron flow from fadh2 (as the latter donates its electrons further down to the ETC).

Higher proton concentration in the outer chamber causes the protons to pass inwardly into matrix or inner chamber through the inner membrane. The latter possesses special proton channels in the region of FQ (base) of the F0—F1 particles.

The flow of protons through the F0 channel induces F, particles to function as ATP-synthetase. The energy of the proton gradient is used in attaching a phosphate radicle to ADP by high energy bond. This produces ATP. Oxidation of one molecule of NADH2 produces 3 ATP molecules while a similar oxidation of FADH2 forms 2 ATP molecules.2 ATP molecules are produced during glycolysis and 2 ATP (GTP) molecules during double Krebs cycle. Glycolysis also forms 2NADH2. Its reducing power is transferred to mitochondria for ATP synthesis. For this a shuttle system operates at the inner mitochondrion membrane. (i) NADH2 —> NAD -> NADH2. (ii) NADH2 -> FAD -> FADH2.

The former operates in liver, heart and kidney cells. No energy is spent. The second method occurs in muscle and nerve cells. It lowers the energy level of 2NADH2 by 2ATP molecules. A total of 10 NADH2 and 2FADH2 molecules are formed in aerobic respiration.

They help in formation of 34 ATP molecules. The net gain from complete oxidation of a molecule of glucose in muscle and nerve cells is 36 ATP molecules (10 NADH2 = 30 ATP, 2 FADH2 = 4 ATP, four formed by substrate level phosphorylation in glycolysis and Krebs cycle and two consumed in transport of theNADH2 molecules into mitochondria).

In procaryotes, heart, liver, and kidneys, 38 ATP molecules are produced per glucose molecules oxidised. Passage of ATP molecules from inside of mitochondria to cytoplasm is through facilitated diffusion.Since, one ATP molecule stores 8.9 kcal/mole (7 kcal/mole according to early estimates) the total energy trapped per gm mole of glucose is 338.2 kcal (266 kcal) or an efficiency of 49.3% (38.8% according to older estimates). The rest of the energy is lost as heat.