Life 21 - Aerobic respiration – Raven & Johnson Chapter 9 (parts)

Objectives

1: Describe the overall action of the Krebs cycle in generating ATP, NADH and $FADH_2$ from acetyl-CoA

2: Understand the generation of ATP from NADH and $FADH_2$ by the electron transport chain

3: Explain why NADH produced by glycolysis and by the Krebs cycle, and $FADH_2$, differ in the number of ATP they produce

4: Compare the energy efficiency of aerobic respiration of glucose with that of glycolysis alone

The Krebs cycle (Fig. 9.13, and simplified form)

Carbon from carbohydrates, fats and proteins all ends up as the 2-C acetyl group of acetyl-CoA. This is oxidised to synthesise ATP

The oxidation occurs in a series of 9 reactions forming a cycle (compare the linear sequence of glycolysis)

Krebs cycle – Sir Hans Krebs (discoverer in the 1930s), or

Citric acid cycle – first molecule in the cycle is citric acid or citrate. Organic acids (citric) exist as anions (citrate) at pH 7 in the cell

The Krebs cycle occurs in the matrix (contents) of the mitochondria – "power plants" of the cell

Reaction (1) combines the 4-C oxaloacetate with the 2-C acetyl group to form the 6-C citrate and release coenzyme A

The whole cycle involves removal of 2 CO_2 to return to the 4-C oxaloacetate, in a series of oxidations

Reaction (4) is the first oxidation, with CO_2 removed and NAD^+ reduced to NADH. This gives the 5-C α ketoglutarate

Reaction (5) is the second oxidation, with another CO_2 removed and reduction of another NAD^+ to NADH

The molecule also combines with coenzyme A to give the 4-C succinyl-CoA, with a high-energy bond

This bond is broken in reaction (6) to form guanosine triphosphate (GTP) from guanosine diphosphate (GDP) and Pi. This is similar to ATP/ADP

The ~P is transferred to ATP in a substrate-level phosphorylation

Reaction (7) is the third oxidation, with flavin adenine dinucleotide (FAD) reduced to $FADH_2$

Similar to NAD^+/NADH, but has a smaller ΔG. This oxidation does not yield enough energy to reduce NAD^+

Reaction (9) is the fourth oxidation, NAD^+ is reduced to NADH, and oxaloacetate is restored

Oxaloacetate combines with acetyl-CoA to start another turn of the Krebs cycle

The net result of glycolysis and the Krebs cycle is that the 6-C glucose has been converted to six CO_2 (and water)

The Krebs cycle also generates 2 ATP from each glucose molecule by substrate-level phosphorylation, the same yield as glycolysis

More important, catabolism has harvested many electrons as reduced electron carriers. A total of 10 NADH and 2 $FADH_2$ from each glucose molecule

6 NADH and 2 $FADH_2$ from the Krebs cycle (2 turns per glucose)
2 NADH from glycolysis
2 NADH in formation of acetyl-CoA (2 molecules per glucose)

Energy is harvested from these carriers as electrons move along the electron transport chain

Energy moves with the electrons. The change in free energy at each stage depends on the change in position of the valency (bond) electron relative to the atomic nuclei

Carbon and hydrogen atoms have low electronegativity; their nuclei attract the electrons in a covalent bond weakly

An electron in a C-H bond is shared equally (on average a median position) between the two nuclei. This bond has high energy. Energy decreases as the bond electron moves closer to the nucleus

Oxygen atoms have high electronegativity and attract bond electrons strongly. An electron in a C-O or H-O bond is close to the oxygen; the bond has low energy

Electrons in NADH have high energy. If they were donated directly to oxygen, the energy released would be large and most would be lost as heat

Instead, they pass along the chain to carriers of increasing electronegativity. Energy is released in a series of small steps (Fig. 9.14)

Some of these steps are just large enough to synthesise ATP, so the loss of energy to heat is small

At the end the electrons are donated to oxygen, the final electron acceptor, where they combine with protons (H^+) to form water

The chain is a series of molecules (mostly proteins) embedded in the inner mitochondrial membranes of eukaryotes and the plasma membrane of prokaryotes

The surface area is increased by folding into cristae, especially in metabolically active tissues (Fig. 9.16)

The molecules are in geometrically ordered assemblies. A liver cell has 1000 mitochondria, each with 15000 assemblies

NADH and $FADH_2$ each have a pair of high-energy electrons, which move along the chain

1: NADH dehydrogenase + NADH $\Rightarrow$ pumps out H^+
2: Ubiquinone (coenzyme Q, carrier) + $FADH_2$
3: bc1 complex (cytochrome) $\Rightarrow$ pumps out H^+
4: cytochrome c (carrier)
5: cytochrome oxidase $\Rightarrow$ pumps out H^+
6: oxygen

Cytochromes have haem groups (with iron) similar to haemoglobin, red colour. Iron changes between Fe^{3+} and Fe^{2+} as electrons move along, in a series of redox changes. Fe^{3+} is the oxidised and Fe^{2+} is the reduced state (with electron)

Unlike haemoglobin which always has Fe^{2+}, and combines with molecular oxygen, rather than being chemically oxidised. Oxyhaemoglobin has molecular O_2, deoxyhaemoglobin does not; both have Fe^{2+}

Haemoglobin with Fe^{3+} (methaemoglobin) has been poisoned, non-functional

The last step, cytochrome oxidase, donates the electrons to oxygen. Cyanide inhibits this therefore is quickly lethal, stops aerobic respiration

Each pair of electrons from NADH that move along the chain pump 3 protons (H^+) from the matrix through the inner mitochondrial membrane

The proteins are excited by the electrons and change shape, moving H^+ through the membrane, in one direction only; out

The pair of electrons from $FADH_2$ enter the chain at step 2, bypassing the first pump, and so only move out 2 H^+

Pumping out H^+ leaves the matrix slightly negatively charged

H^+ tend to move back through the inner membrane, following both electrical (inside negative) and chemical concentration (inside low H^+) gradients

H^+ re-enter the matrix through protein channels in the inner membrane, as the membrane itself is relatively impermeable to ions (Fig. 9.17)

Channels are ATP synthase enzymes, form ATP in the matrix as the H^+ pass through. Moving subunit structures – smallest rotary engines in nature

The formation of ATP is thus driven by a diffusion process similar to osmosis, known as chemiosmosis …

Or oxidative phosphorylation, ATP synthesis by electron transport, not by phosphorylated chemical intermediates (substrate-level phosphorylation)

One ATP is generated by each proton pumped out of the matrix. (Fig. 9.19)
NADH $\Rightarrow$ 3 ATP and $FADH_2 \Rightarrow$ 2 ATP (from step 2)

But 2 of the NADH are produced by glycolysis in the cytoplasm, and these yield only 2 ATP each, as it costs energy to move them into the matrix

In theory, glycolysis and oxidation of glucose would give 36 ATP

But the membrane is slightly leaky to protons and some of them avoid the ATP synthase channels

Also some H^+ are used to transport pyruvate into the matrix to form acetyl-CoA. The actual yield is about 30 ATP per glucose molecule

Aerobic respiration is much more efficient than glycolysis alone

About 32% of the energy available from glucose is harvested as ATP, compared to 2% for glycolysis (and to a car engine at about 25%)

This efficiency puts a natural limit on the length of food chains, of 3 or 4 stages, as most of the energy is still lost as heat at each trophic level

Anaerobic respiration, using other inorganic molecules to accept electrons, does not use an electron transport chain

The process is inefficient, e.g. sulphate oxidation,
$SO_4 \Rightarrow H_2S$ in sulphur bacteria, gives 6 ATP per molecule of glucose, a yield more like fermentation