

Metabolic Biochemistry: Fuel Use in Cells, made Unnecessarily Complicated

- Acquisition of nutrients -

These circulate, being largely soluble; there are numerous transporter proteins mediating their uptake. Transport is usually active, and/or sodium-associated. Most amino acids are intracellularly derived, by de-novo synthesis or from lysis of old proteins. Using the AAs for fuel is a last-ditch measure, like selling your furniture for drug money.

CARBOHYDRATES
Pulled from the bloodstream, as glucose. Insulin increases this by acting on some of the GLUT transporters in fat and muscle tissues. Also you can get hold of glucose by lysis of intracellular glycogen, a starchy glucose chain which is the major form of long-term glucose storage.

LIPIDS
Travel the bloodstream as lipoproteins. The lipoproteins bind to LDL receptors on cells, and the cells endocytose the whole blob of lipoprotein. Free fatty acids can get across the membrane by passive diffusion, and apparently by uptake via the "Fatty Acid Binding Protein" (FABP), but that's still a bit controversial...

AA transporter

Glucose active transporter

FABP

Tg.

ANAEROBIC PATHWAY: GLYCOLYSIS

PRIMING PHASE
- Uses up 2 ATP to make glyceraldehyde-3-phosphate

DEGRADATION
The g-3-p is degraded into pyruvate, yielding 4 ATP and 2 NADH out of 2 NAD+

PYRUVATE

When UNDER ANAEROBIC CONDITIONS
Otherwise...

IF theres plenty of oxygen, the NAD+ is oxidised in the oxidative phosphorylation reaction, and pyruvate may proceed to the TCA cycle

- No oxygen required
- Happens in the cytoplasm
- Yields 6 to 8 moles of ATP
- Whats the goddamn point? Well; glycolysis yields ATP but requires no oxygen- PLUS it runs like 100 times faster than the TCA cycle. Exercising muscles use this pathway to produce some quick energy.

If there is no oxygen, the NAD get depleted quickly, and glycolysis stops. THUS, LDH converts NADH back to NAD+ so the cycle may continue.

LACTATE
Lactate Dehydrogenase (LDH)
...Wheres all that lactate going to go? Well; it diffuses back into the bloodstream and travels to highly oxygenated tissues so that it may return to being PYRUVATE.

Fatty acids must bind CoA to be of any to the fuel cycle

Triglycerides have to be broken down into 3 fatty acids and glycerol

Fatty Acyl CoA

Fatty Acyl CoA Synthase

CARNITINE Acyltransferase

β- Oxidation

Repetitive removal of 2 carbon atoms from the fatty acids each turn of the cycle. each turn of the beta-oxidation spiral produces one NADH, one FADH₂, and one acetyl-CoA. All reduced cofactors are used to produce heaps and heaps of ATP. Palmitate produces 129 ATPs

ACETYL-CoA FADH + NADH

amino acids fall into three categories:
glucogenic
ketogenic
both glucogenic and ketogenic.
All amino acids except lysine and leucine are at least partly glucogenic. **GLUCOGENIC** means they can be stripped of their amine group (turning into alpha-ketoacids) and sent into the TCA cycle. The amine group is essentially ammonia and needs to be eliminated via the UREA CYCLE. **KETOGENIC** means they can be made into fatty acids and stored in this way until they are required-when they are transformed into ketones and sent into the bloodstream.

3-carbon PYRUVATE
Coenzyme A

This is the Pyruvate Dehydrogenase Complex, which connects fatty acids, amino acids and glucose into the TCA cycle.

ACETYL-CoA

2 carbons; 1 lost to CO₂

NAD is recycled into the TCA

Once you got ATP, its no use to you hanging around the mitochondria, so it gets exchanged for ADP by the Adenine Nucleotide Translocase protein

4C Oxaloacetate

The TCA or "Kreb's" Cycle

6C Citrate

4C Malate

6 carbon citrate is broken down progressively back into the 4 carbon oxaloacetate. This releases some CO₂, some water and some hydrogen ions which are picked up by NAD and FAD, which turn into NADH and FADH. Its all about those hydrogen ions!

6C Isocitrate

4C Fumarate

4C Succinate

4C Succinil-CoA

5C α-Ketoglutarate

NADH and FADH

NAD and FAD

Complex IV marks the end of the electron's travels; it comes to rest with an oxygen atom, making up a molecule of water. This is used to pump another H+ ion out of the matrix

Here, complex III uses the travelling electron to lure a hydrogen atom out of a water molecule. Negative OH molecules begin to collect in the matrix.

ULTIMATELY: you get a whole lot of NAD and FAD carrying hydrogen ions.

COMPLEXES I and II:

Complex I strips hydrogen from the NADH and pumps them into the intermembrane space. Also takes an Electron (red arrow) and passes it along the transport chain. Complex II does this for FADH. Both complexes I and II contribute e- and H+ to Coenzyme Q

Intermembrane space: pH of 3; lots of H+

