Respiration:  
Oxidative metabolism of all metabolic fuels (carbohydrates, fats) via Acetyl CoA  
-- Mitochondrial reactions  
-- Require O₂ (or another e⁻ acceptor)  
-- We can metabolize carbohydrates anaerobically or aerobically  
-- We can only metabolize lipids aerobically  

**Stages:**  
1. PDH: P → AcCoA + NADH  
2. TCA: AcCoA → CO₂ + ATP/GTP + NADH + FADH₂  
3. Electron transport and oxidative phosphorylation → Oxidation of FADH₂ and NADH → Energy → ATP  

**2. TCA Cycle - Overview**  
-- receives Acetyl CoA from PDH  
Glycolysis FA Oxidation (later) via PDH → AcCoA (C2)  
OA (C4) oxaloacetate  
TCA (Krebs) Cycle (8 Steps)  
2 CO₂  
3 NADH @ 3 ATP/NADH  
1 FADH₂ @ 2 ATP/FADH₂  
1 GTP ~ 1 ATP  
12 ATP per C2 of AcCoA oxidized  

**The Chemistry**  
Citrate Synthase (CS) is stereospecific. AcCoA attacks from top (S₁) face only. More detail on this later.  

Oxaloacetate (OA)  
Citroyl CoA  

Claisen Reaction  

Citrate  

Note: The cycle is catalytic - 2 carbons go in; 2 carbons go out; the [intermediates] do not change - they are the "catalysts"  

**Introducing: The Mitochondrion**  
Outer membrane  
Inner Membrane  
Cytoplasm  
IMS (inner membrane space)  
Matrix  
Complexes:  
E₁ E₂ E₃  
FAD  FADH₂  
NAD  NADH  
ATP synthesis  
Harvesting of these e⁻  
Toxicity of AsO₃³⁻  
Lipoic acid  
Products  
a.) Acetyl CoA  
b.) NADH  

Basically, the pair of electrons move left to right across PDH (E₁ E₂ E₃) and reduce FAD → FADH₂. Then, in a redox-challenged last step, FADH₂ gives its electrons to NAD⁺ to yield NADH. The NADH is oxidized by the electron transfer chain (later.)
**Session 10**

**A**

- **From AcCoA**
  - **H$_2$C$\text{CO}_2^\theta$**
  - **H$_2$C$\text{CO}_2^\theta$**
  - **H$_2$C$\text{CO}_2^\theta$**

- **Ac**
  - **$\Delta$**
  - **$\square$**

- **Water removed and re-added**

- **ICDH**
  - **H$_2$C$\text{CO}_2^\theta$**
  - **HC$\text{CO}_2^\theta$**
  - **H$\text{CO}_2^\theta$**

- **IC (Iso-citrate)**

- **α-KGDH**
  - **$\Delta$**
  - **$\square$**

- **αKG looks like pyruvate with an acetate "decoration"**

- **αKGDH**

- **αKeto Glutarate**

- **PLP**

- **Glutamic Acid (E)**

- **More later**

- **Watch next page on stereochemical specificity of Aconitase (Ac)**

**B**

- **Label (△ & ◻) becomes scrambled!**

- **Because the molecule is symmetrical and SDH cannot tell the two ends apart.**

- **Succinyl CoA**
  - **H$_2$C$\text{CO}_2^\theta$**
  - **H$_2$C$\text{CO}_2^\theta$**

- **Succinate**

- **Succinyl CoA Synthetase**
  - **H$\text{SCoA}$**
  - **GDP (ADP)**
  - **GTP (ATP)**

- **Fumarase**

- **Fumarate**
  - **Note trans isomer**

- **Bound to SDH**
  - **which is embedded in mitochondrial inner membrane**
  - **SDH also known as Complex II**

- **Malate**

- **Asp (D)**

- **OA**

- **Cyce starts again**

- **Next AcCoA**

- **GAPDH**

- **GAPDH**

- **Symmetrical compound**

- **Bound to SDH**

- **Which is embedded in mitochondrial inner membrane**

- **SDH also known as Complex II**

- **Succinate Dehydrogenase**
**Detail on Stereochemical Specificity of Aconitase**

-- The hydroxyl group always moves to the ProR arm and never to the ProS, even though they are chemically identical, because \( \text{Ac} \) can distinguish the two arms (based on pro-chirality).

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-- The stereochemistry defined by \( \text{CS} \) generates only one isomer - where the -OH, \( \text{C}_2\text{O}_4^- \) and \( \text{CO}_2^- \) fit in a specific way in three docking locations on \( \text{Ac} \).

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-- The -OH, \( \text{C}_2\text{O}_4^- \) and \( \text{CO}_2^- \) make contact with \( \text{Ac} \) at three sites.
Anapleurotic Pathways

-- We know three Pathways -- look at Interactions

-- Definition: anapleurotic  "filling up"

-- Pathways that maintain catalytic amounts of TCA cycle intermediates

- Today we'll add more detail to this network
- Start with problem of how different life forms avoid running out of cytoplasmic NAD$^\circ$

Important
NAD$^\circ$ cannot enter mitochondrion