**Cellular Respiration**

**Stage 1: Glycolysis**

**What's the point?**

The point is to make ATP!

**ATP**

Glycolysis

- Breaking down glucose
  - "glyco – lysis" (splitting sugar)

**Overview**

10 reactions

- convert glucose (6C) to 2 pyruvate (3C)
- produces: 4 ATP & 2 NADH
- consumes: 2 ATP
- net yield: 2 ATP & 2 NADH

**Evolutionary perspective**

- Prokaryotes
  - first cells had no organelles
- Anaerobic atmosphere
  - life on Earth first evolved without free oxygen ($O_2$) in atmosphere
  - energy had to be captured from organic molecules in absence of $O_2$
- Prokaryotes that evolved glycolysis are ancestors of all modern life
  - ALL cells still utilize glycolysis

**Glycolysis**

- ancient pathway which harvests energy
- where energy transfer first evolved
- still is starting point for **ALL** cellular respiration
- but it’s inefficient
- generates only **2 ATP** for every **1 glucose**
- occurs in cytosol

**In the cytosol? Why does that make evolutionary sense?**

That’s not enough ATP for me!

Enzymes of glycolysis are "well-conserved"

**Glycolysis summary**

- endergonic invest some ATP
- exergonic harvest a little ATP & a little NADH

**Net yield**

- 2 ATP
- 2 NADH
1st half of glycolysis (5 reactions)

Glucose “priming”
- Get glucose ready to split
  - Phosphorylate glucose
  - Molecular rearrangement
- Split destabilized glucose

2nd half of glycolysis (5 reactions)

Energy Harvest
- NADH production
  - G3P donates H
  - Reduces NAD⁺
  - NAD⁺ → NADH
- ATP production
  - G3P → → pyruvate
  - PEP sugar donates P
  - "Substrate level phosphorylation"
  - ADP → ATP

Energy accounting of glycolysis
- Net gain = 2 ATP + 2 NADH
  - Some energy investment (2 ATP)
  - Small energy return (4 ATP + 2 NADH)
- 1 6C sugar → 2 3C sugars

Substrate-level Phosphorylation
- In the last steps of glycolysis, where did the P come from to make ATP?
  - The sugar substrate (PEP)

P is transferred from PEP to ADP
- Kinase enzyme
- ADP → ATP

But can’t stop there!

Glycolysis
- Going to run out of NAD⁺
  - Without regenerating NAD⁺, energy production would stop!
  - Another molecule must accept H from NADH
  - So NAD⁺ is freed up for another round

Is that all there is?
- Not a lot of energy...
  - For 1 billion years*, this is how life on Earth survived
    - No O₂ = slow growth, slow reproduction
    - Only harvest 3.5% of energy stored in glucose
    - More carbons to strip off = more energy to harvest

*Holmdel High School
How is NADH recycled to NAD\(^+\)?

Another molecule must accept H from NADH

\[ \text{Pyruvate} \rightarrow \text{Ethanol} + \text{CO}_2 \]

Fermentation (anaerobic)

- Bacteria, yeast
  - beer, wine, bread
  - Animals, some fungi
    - cheese, anaerobic exercise (no O\(_2\))

Alcohol Fermentation

- Dead end process
  - at ~12% ethanol, kills yeast
  - can't reverse the reaction

Lactic Acid Fermentation

- Reversible process
  - once O\(_2\) is available, lactate is converted back to pyruvate by the liver

Pyruvate is a branching point
And how do we do that?

- ATP synthase
  - set up a $H^+$ gradient
  - allow $H^+$ to flow through ATP synthase
  - powers bonding of $P_i$ to ADP

$$ADP + P_i \rightarrow ATP$$

But... Have we done that yet?

NO!
There’s still more to my story!
Any Questions?