Warm- Up

Objective:

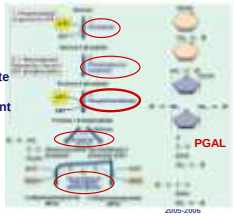
- Describe the role of ATP in coupling the cell's anabolic and catabolic processes.

Warm-up:

- **What cellular processes produces the carbon dioxide that you exhale?**

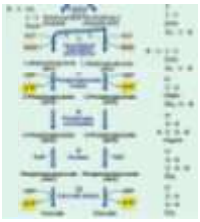
1st half of glycolysis (5 reactions)

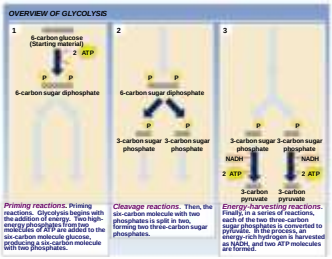
- **Glucose "priming"**
  - get glucose ready to split
    - phosphorylate glucose
    - rearrangement
  - split destabilized glucose



2nd half of glycolysis (5 reactions)

- **Oxidation**
  - G3P donates H
  - NAD → NADH
- **ATP generation**
  - G3P → pyruvate
  - donates P
  - ADP → ATP

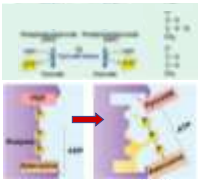




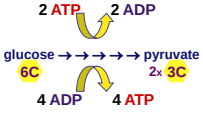
Substrate-level Phosphorylation

- **In the last step of glycolysis, where did the P come from to make ATP?**

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



Energy accounting of glycolysis



- **Net gain = 2 ATP**
  - some energy investment (2 ATP)
  - small energy return (4 ATP)
- **1 6C sugar → 2 3C sugars**

Is that all there is?

- **Not a lot of energy…**
  - for 1 billon years+ this is how life on Earth survived
    - only harvest 3.5% of energy stored in glucose
    - slow growth, slow reproduction

We can't stop there….

- **Glycolysis**

glucose + 2ADP + 2P_i + 2 NAD^+ → 2 pyruvate + 2ATP + 2NADH

- **Going to run out of NAD^+**
- **How is NADH recycled to NAD^+?**
  - without regenerating NAD+, energy production would stop
  - another molecule must accept H from NADH

How is NADH recycled to NAD^+?

- **Another molecule must accept H from NADH**
  - anaerobic respiration
    - ethanol fermentation
    - lactic acid fermentation
  - aerobic respiration

Anaerobic ethanol fermentation

- Bacteria, yeast

pyruvate → ethanol + CO_2
3C (NADH) 2C (NAD+) 1C

  - beer, wine, bread
  - at ~12% ethanol, kills yeast

- Animals, some fungi

pyruvate → lactic acid
3C (NADH) 3C (NAD+)

  - cheese, yogurt, anaerobic exercise (no O_2)

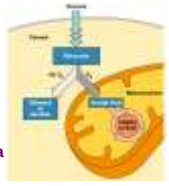
Pyruvate is a branching point

Pyruvate

O_2 O_2

fermentation

Kreb's cycle
mitochondria



What's the point?

ATP

The Point is to Make ATP!

Any Questions??

Chapter 9. Cellular Respiration

Oxidation of Pyruvate
Krebs Cycle

Glycolysis is only the start

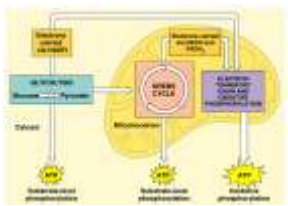
- Glycolysis

glucose → → → → pyruvate
6C 2x 3C

- Pyruvate has more energy to yield
  - 3 more C to strip off (to oxidize)
  - if O_2 is available, pyruvate enters mitochondria
  - enzymes of Krebs cycle complete oxidation of sugar to CO_2

pyruvate → → → → → CO_2
3C 1C

Cellular respiration



What's the point?

ATP

The Point is to Make ATP!

Oxidation of pyruvate

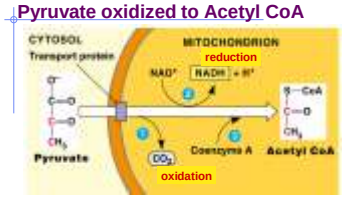
- Pyruvate enters mitochondria

2x [pyruvate → → → acetyl CoA + CO_2]
3C 2C 1C
NAD NADH

  - 3 step oxidation process
  - releases 1 CO_2 (count the carbons!)
  - reduces NAD → NADH (stores energy)
  - produces acetyl CoA

- Acetyl CoA enters Krebs cycle
  - where does CO_2 go?

Pyruvate oxidized to Acetyl CoA



Yield = 2C sugar + CO_2 + NADH

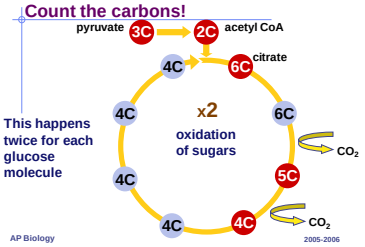
Krebs cycle

1937 | 1953

Hans Krebs
1900-1981

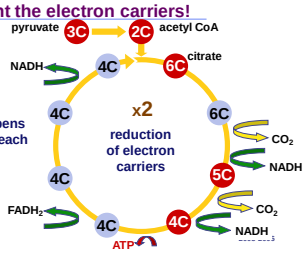
- aka Citric Acid Cycle
  - in mitochondrial matrix
  - 8 step pathway
    - each catalyzed by specific enzyme
    - step-wise catabolism of 6C citrate molecule
- Evolved later than glycolysis
  - does that make evolutionary sense?
    - bacteria →3.5 billion years ago (glycolysis)
    - free O_2 →2.7 billion years ago (photosynthesis)
    - eukaryotes →1.5 billion years ago (aerobic respiration (organelles)

Count the carbons!



This happens twice for each glucose molecule

Count the electron carriers!



This happens twice for each glucose molecule

Whassup?

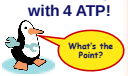
So we fully oxidized glucose

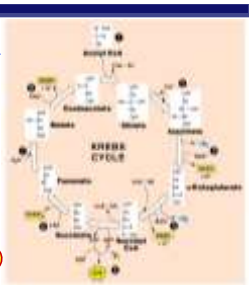
$C_6H_{12}O_6$

↓

CO_2

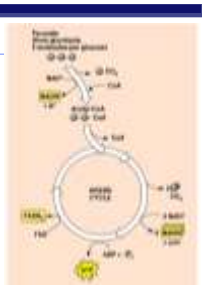
& ended up with 4 ATP!



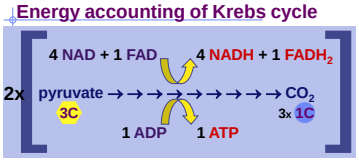


NADH & $FADH_2$

- Krebs cycle produces large quantities of electron carriers
  - NADH
  - $FADH_2$
  - stored energy!
  - go to ETC



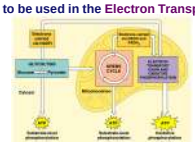
Energy accounting of Krebs cycle



- Net gain = 2 ATP
  = 8 NADH + 2 $FADH_2$

So why the Krebs cycle?

- If the yield is only 2 ATP, then why?
  - value of NADH & $FADH_2$
    - electron carriers
    - reduced molecules store energy!
    - to be used in the Electron Transport Chain



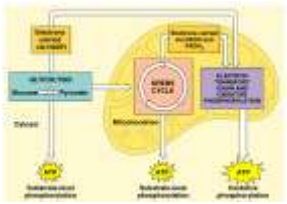
What's the point?

The Point is to Make ATP!

Any Questions??

Chapter 9.
Cellular Respiration
Electron Transport Chain

Cellular respiration



What's the point?

ATP

The Point is to Make ATP!

ATP accounting so far…

- Glycolysis → 2 ATP
- Kreb's cycle → 2 ATP

- Life takes a lot of energy to run, need to extract more energy than 4 ATP!

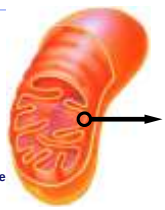
There's got to be a better way!

There is a better way!

- Electron Transport Chain
  - series of molecules built into inner mitochondrial membrane
    - mostly transport proteins
  - transport of electrons down ETC linked to ATP synthesis
  - yields ~34 ATP from 1 glucose!
  - only in presence of O_2 (aerobic)

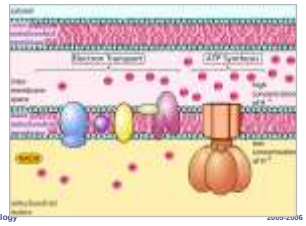
Mitochondria

- Double membrane
  - outer membrane
  - inner membrane
    - highly folded cristae*
    - fluid-filled space between membranes = intermembrane space
  - matrix
    - central fluid-filled space



*** form fits function!**

Electron Transport Chain



Remember the NADH?

Glycolysis

PGAL

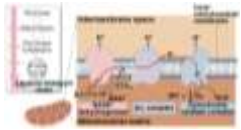
4 NADH

Kreb's cycle

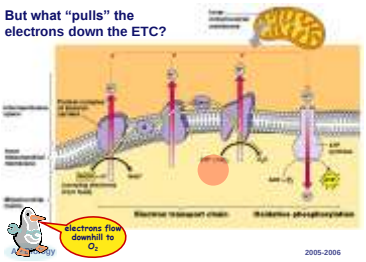
8 NADH
2 $FADH_2$

Electron Transport Chain

- NADH passes electrons to ETC
  - H cleaved off NADH & $FADH_2$
  - electrons stripped from H atoms → H^+ (H ions)
  - electrons passed from one electron carrier to next in mitochondrial membrane (ETC)
  - transport proteins in membrane pump H^+ across inner membrane to intermembrane space



But what "pulls" the electrons down the ETC?



Electrons flow downhill

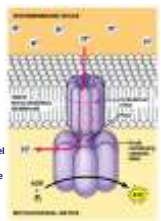
- Electrons move in steps from carrier to carrier downhill to O_2
  - each carrier more electronegative
  - controlled oxidation
  - controlled release of energy

Why the build up H^+?

- ATP synthase
  - enzyme in inner membrane of mitochondria

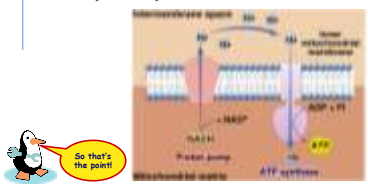
$$ADP + P_i \rightarrow ATP$$

  - only channel permeable to H^+
  - H^+ flow down concentration gradient = provides energy for ATP synthesis
    - molecular power generator!
    - flow like water over water wheel
    - flowing H+ cause change in shape of ATP synthase enzyme
    - powers bonding of P_i to ADP
    - "proton-motive" force



ATP synthesis

- Chemiosmosis couples ETC to ATP synthesis
  - build up of H+ gradient just so H+ could flow through ATP synthase enzyme to build ATP



1961 | 1978

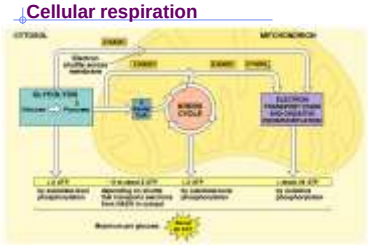
Peter Mitchell

- Proposed chemiosmotic hypothesis
  - revolutionary idea at the time

proton motive force

1920-1992

Cellular respiration



Summary of cellular respiration

$$C_6H_{12}O_6 + 6O_2 \rightarrow 6CO_2 + 6H_2O + \sim 36\ ATP$$

- Where did the glucose come from?
- Where did the O_2 come from?
- Where did the CO_2 come from?
- Where did the H_2O come from?
- Where did the ATP come from?
- What else is produced that is not listed in this equation?
- Why do we breathe?

Taking it beyond…

- What is the final electron acceptor in electron transport chain?

O_2

- So what happens if O_2 unavailable?
  - ETC backs up
  - ATP production ceases
  - cells run out of energy
  - and you die!

What's the point?

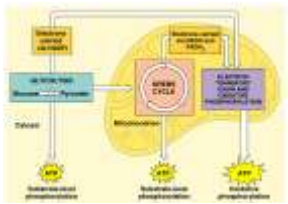
ATP

The Point is to Make ATP!

Any Questions??

Chapter 9.
Cellular Respiration
Other Metabolites & Control of Respiration

Cellular respiration

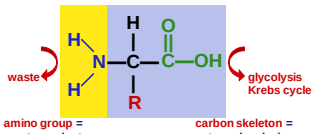


Beyond glucose: Other carbohydrates

- Glycolysis accepts a wide range of carbohydrates fuels
  - polysaccharides → → → glucose (hydrolysis)
    - ex. starch, glycogen
  - other 6C sugars → → → glucose (modified)
    - ex. galactose, fructose

Beyond glucose: Proteins

- Proteins → → → → amino acids (hydrolysis)

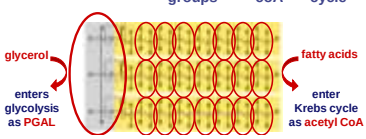


amino group = waste product excreted as ammonia, urea, or uric acid

carbon skeleton = enters glycolysis or Krebs cycle at different stages

Beyond glucose: Fats

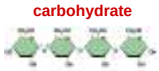
- Fats → → → → glycerol & fatty acids (hydrolysis)
  - glycerol (3C) → → PGAL → → glycolysis
  - fatty acids → 2C acetyl groups → acetyl coA → Krebs cycle



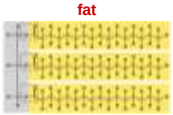
Carbohydrates vs. Fats

- Fat generates 2x ATP vs. carbohydrate
  - more C in gram of fat
  - more O in gram of carbohydrate
    - so it's already partly oxidized

carbohydrate

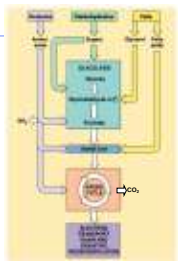


fat



Metabolism

- Coordination of digestion & synthesis
  - by regulating enzyme
- Digestion
  - digestion of carbohydrates, fats & proteins
    - all catabolized through same pathways
    - enter at different points
  - cell extracts energy from every source



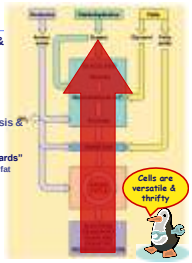
Metabolism

- Coordination of digestion & synthesis
  - by regulating enzyme
- Synthesis
  - enough energy? build stuff!
  - cell uses points in glycolysis & Krebs cycle as links to pathways for synthesis
    - run the pathways "backwards"
      - eat too much fuel, build fat

pyruvate → → glucose

Krebs cycle intermediaries → → amino acids

acetyl CoA → → fatty acids



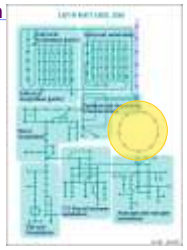
Carbohydrate Metabolism

- The many stops on the Carbohydrate Line

gluconeogenesis

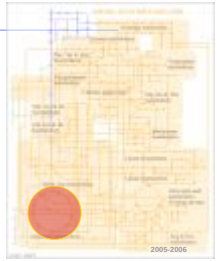
Lipid Metabolism

- The many stops on the Lipid Line



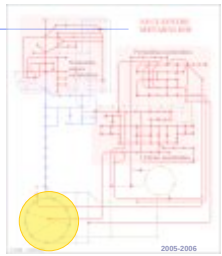
Amino Acid Metabolism

- The many stops on the AA Line



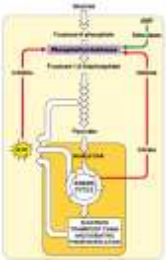
Nucleotide Metabolism

- The many stops on the GATC Line



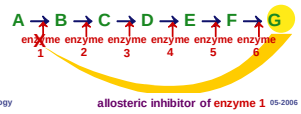
Control of Respiration

Feedback Control



Feedback Inhibition

- Regulation & coordination of production
  - production is self-limiting
  - final product is inhibitor of earlier step
    - allosteric inhibitor of earlier enzyme
  - no unnecessary accumulation of product

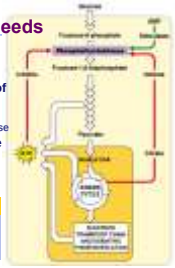


Respond to cell's needs

- Key points of control
  - phosphofructokinase
    - allosteric regulation of enzyme
      - "can't turn back" step before splitting glucose
    - AMP & ADP stimulate
    - ATP inhibits
    - citrate inhibits

Why is this regulation important?

Balancing act:
availability of raw materials vs.
energy demands vs. synthesis



A Metabolic economy

- Basic principles of supply & demand regulate metabolic economy
  - balance the supply of raw materials with the products produced
  - these molecules become feedback regulators
    - they control enzymes at strategic points in glycolysis & Krebs cycle
      - AMP, ADP, ATP
        - regulation by final products & raw materials
      - levels of intermediates compounds in the pathways
        - regulation of earlier steps in pathways
      - levels of other biomolecules in body
        - regulates rate of siphoning off to synthesis pathways

It's a Balancing Act

- Balancing synthesis with availability of both energy & raw materials is essential for survival!
  - do it well & you survive longer
  - you survive longer & you have more offspring
  - you have more offspring & you get to "take over the world"

Acetyl CoA is central to both energy production & synthesis make ATP or store it as fat

Any Questions??