#9: Carbohydrate Metabolism

BIOCHEM2280

Metabolism

Sum of the chemical reactions occurring in a living organism

- **Catabolism** = break down → provide energy, e^-
- **Anabolism** = building up → take energy, e^-

Metabolic Pathway = coordinated series of reactions that result in specific products

- Catalyzed by enzymes
- Occur in specific cells, locations (certain organs, tissues)

Flux = rate which molecules flow through each metabolic pathway

- Cell must change flux of molecules in each pathway to function
- Alter enzymatic activity
- Influenced by the concentration of metabolites
- First reaction in a metabolic pathway after a branch point is often irreversible → target for control
- Some reactions ΔG<<<0, but most ΔG=0

Formation + Breakdown of Glycogen

G6P ⇌ G1P is a reversible reaction

Formation: +ΔG

Glycogen Synthase makes α(1→ 4) linkages between G1P monomers to form glycogen using UTP as an energy source

Breakdown: -ΔG

In **skeletal muscles:** makes ATP for muscle function

In **liver:** maintains blood glucose

Glycogen Phosphorylase is what breaks down glycogen into G1P

*Separate enzymes are required to break the branch points

Pi comes from cytosol

Overall Reaction:

Glycogen (n residues) + G1P + UTP ⇒ Glycogen (n + 1 residues) + UDP + 2 Pi

Enzyme Activity

Synthase$^-$Ⓟ = inactive

Phosphorylase$^-$Ⓟ = active

Glycogen

- In liver + striated muscle
  - Liver: exists as G6P, makes ATP for muscle
- Absorbed from digestive tract
  - Circulates in blood (energy reserve for body → maintain blood glucose levels), enter cells via glucose transporters
  - Passively move by proteins from high → low glucose concentrations

Glycolysis

- Occurs in cytosol
- Results in ATP production
- 4 e^- transferred from 1 glucose → 2 NAD^+
- Process consumes NAD^+
- 2NAD^+ → 2NADH **REQUIRED** to regenerate NAD^+
- 2NADH transfer 2e^- to oxygen → pathway **blocked** if oxygen absent
- Other monosaccharides can enter glycolysis via conversion to G6P or F6P (glycolytic intermediates)

Overall Reaction: Glucose + 2 NAD^+ + 2 ADP + 2 Pi -> 2 Pyruvate + 2 NADH + 2 H^+ + 2 ATP + 2 H_2O

Glycolysis Regulation

- Reactions 1, 3, and 10 are irreversible (ΔG<<<<0)
  - These reactions are targets for the control of flux
- Control of flux regulates hexokinase (1), PFK (3), pyruvate kinase (10)

PFK

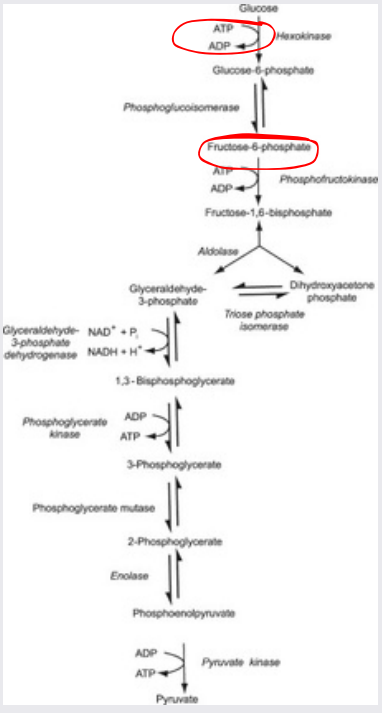
- Catalyzes **F6P + ATP → F1,6P + ADP**
- Commits cell to metabolizing glucose
- No storage, conversion to other sugars

AMP, ADP, Pi, F26P = allosteric activators

- AMP, ADP, Pi production indicates cell is low on energy → increases glycolysis to produce energy
- F26P production is a response to low insulin which signals low blood glucose → indicates cell is in a low energy state → F2P increases glycolysis

Citrate, ATP = allosteric inhibitors

- Cell has lots of energy
- Slow krebs cycle = low ATP demand
- Inhibits change in enzyme conformation
- Reduce its affinity for PFK

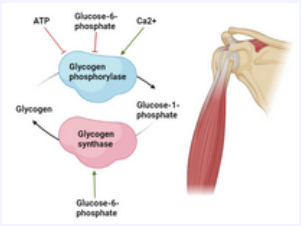


Modified from https://mgcub.ac.in/pdf/material/20200428105362 1e311a9a5.pdf

Skeletal Muscle

- **Insulin** causes **dephosphorylation**
- **Epinephrine** causes **phosphorylation (+Ⓟ)**
- Skeletal muscle is "selfish": it does not respond to glucagon changes, i.e. it ignores signals to release glucose into the bloodstream
  - Won't break down glycogen stores if glucose is low, i.e. it keeps all its glucose storage to itself

Low insulin = phosphorylation (low glucose)	Epinephrine
• Synthase-Ⓟ ○ Less active ○ No G1P → glycogen • Phosphorylase-Ⓟ ○ More active ○ Glycogen → G1P	• Synthase-Ⓟ ○ Less active ○ No G1P → glycogen • Phosphorylase-Ⓟ ○ More active ○ Glycogen → G1P
High insulin = Dephosphorylation	**ATP**
• Synthase ○ Active ○ G1P → glycogen • Phosphorylase ○ Less active ○ Glycogen storage	• Causes phosphorylase to be dephosphorylated • Allosteric inhibitor • Less active • Glycogen storage
	AMP
	• Causes phosphorylase to be dephosphorylated • Allosteric activator • More active • Glycogen → G1P

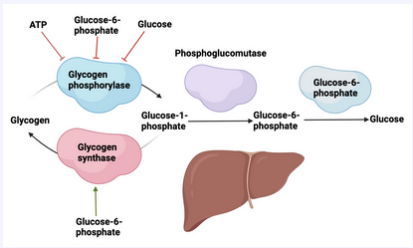


Created using BioRender.com

Liver

- **Insulin** causes **dephosphorylation**
- **Glucagon** and **Epinephrine** cause **phosphorylation (Ⓟ)**
- Hormones bind to receptors, don't directly cause phosphorylation

Low insulin, high glucagon (low glucose)	Epinephrine
• Synthase-Ⓟ ○ Less active ○ No G1P → glycogen • Phosphorylase-Ⓟ ○ More active ○ Glycogen → G1P	• Synthase-Ⓟ ○ Less active ○ No G1P → glycogen • Phosphorylase-Ⓟ ○ More active ○ Glycogen → G1P
High insulin, low glucagon	**G6P**
• Synthase ○ Active ○ G1P → glycogen using UTP • Phosphorylase ○ Less active ○ Glycogen storage	• Causes synthase to be dephosphorylated • Allosteric activator • Active • G1P → glycogen
	Glucose
	• Causes phosphorylase to be dephosphorylated • Allosteric inhibitor • Less active • Glycogen storage



Created using BioRender.com

#9: Carbohydrate Metabolism

BIOCHEM2280

Fermentation

- Anaerobic respiration → no O_2 present
- Produce ATP without changing net oxidation state of carbon
- Pyruvate reduced to lactate or ethanol

1. Lactate formation

Pyruvate + NADH → Lactate + NAD^+

[Glucose + 2 ADP + 2 Pi → 2 Lactate + 2 ATP]

- e^- come from NADH earlier to make ATP
- Regenerates NAD^+
- Occur in many microorganisms
- Occur in higher organisms when little O_2 present

2. Ethanol Formation (2 step reaction)

Pyruvate + H^+ → CO_2 + Acetaldehyde

[Glucose + 2 ADP + 2 Pi → 2 Ethanol + 2 CO_2 + 2 ATP]

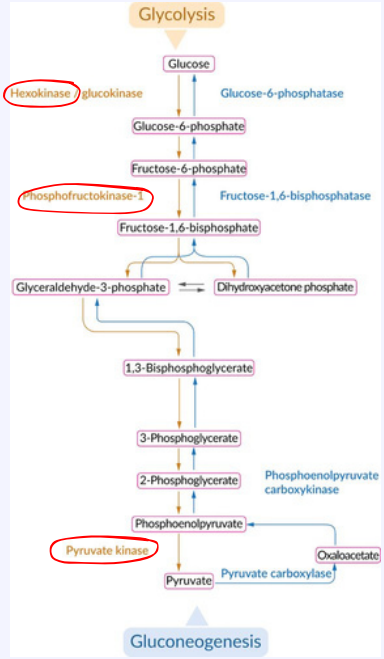
- Ethanol → brewing purposes
- CO_2 → making bread
- Cells in higher eukaryotes can switch between aerobic and anaerobic respiration
- Some cells are strict aerobes, need oxygen (e.g. brain cells)

Gluconeogenesis (-ΔG)

- Synthesizes glucose to maintain blood glucose levels
- Mostly in the liver
- Occurs in the cytosol
- Reductive process (e^- from NADH)
- Reaction costumes 4 more ATP/GTP to convert 2 pyruvate molecules
- **NOT** the reverse of glycolysis

Overall Reaction:

2 Pyruvate + 4 ATP + 2 GTP + 2 NADH → Glucose + 4 ADP + 2 GDP + 6 Pi + 2 NAD^+



- For **ΔG ~ 0** reactions, the **same** enzymes must be used for both processes
- For **ΔG<<<0** reactions, **different** enzymes must be used in both pathways
- Favored direction depends on metabolite concentration
- Compounds that activate glycolysis enzymes will inhibit gluconeogenesis enzymes
- **CANNOT** be turned on simultaneously (reactions will rapidly interconvert)
- Glycerol, lactate, krebs cycle intermediates, many amino acids can be used as raw materials for gluconeogenesis

Pentose Phosphate Pathway

- Carbohydrates can either enter glycolysis (G6P → Pyruvate) or the PPP (G6P → Ribose-5-phosphate → PPP compounds)
- Uses G6P (from glycolysis) to make NADPH
- e^- transfer from NADP+ → NADPH
- When NADPH is needed, cells don't pick one pathway over the other → a **mix** of the 2 is more likely, depending on conditions
- Promotes biosynthesis
  - R5P makes nucleotides, which form DNA and RNA
  - DNA and RNA also break down to form nucleotides

When cells need ATP and NADPH:

3 G6P + 6 NADP+ → 2 F6P + glyceraldehyde phosphate (G3P) + 6 NADPH + 3 CO_2

- For every 3 G6P, 3 carbons are oxidized to CO_2
- F6P and G3P = glycolysis intermediates
- CO_2 = waste
- NADPH = e^- sourse
  - Make 6 NADPH → the other 15 enter glycolysis

When cells need nucleotides:

G6P + 2 NADP+ → ribose-5-phosphate (R5P) + CO_2 + 2 NADPH

- R5P = nucleotide synthesis
- CO_2 = waste
- NADPH = e^- source

Gluconeogenesis Regulation

PFK

- Increased ADP, Pi, AMP, F2,6P will activate it
- Decreased citrate and/or ATP will inhibit it

Fructose Bisphosphate

- AMP, F2,6P will inhibit it

Modified from https://www.amboss.com/us/knowledge/glycolysis-and-gluconeogenesis

♡ LETTER TO THE STUDENT

Dear Student,

Thank you for opening this Biochemistry 2280A guidebook. This resource has been created by the Education Team at WebStraw. The Education Team consists of students that have previously taken and/or are currently taking Biochemistry 2280A.

Created by students for other students, this resource aims to provide a comprehensive view of material taught within this course. Our goal is to help students develop, solidify, and refine their understanding of course content. Our resource is also open access meaning there are no financial or legal barriers to students who wish to access and use our resource.

To maximize the benefits of this resource, we recommend that you read carefully through the topics, focusing on *bolded terminology, compound structures, and diagrams.* Although this resource ideally will cover all testable content as of the 2024-2025 academic year, we cannot guarantee this and strongly encourage you to cross-reference with class material and notes.

Disclaimer
This resource is supplementary to your course content and is not meant to (1) replace any of the resources provided to you by your instructor nor is it meant to (2) be used as a tool to learn the course material from scratch. We assume that students who use this resource will have a basic understanding of the course content. This resource does not contain everything you need to know for your evaluations. Please refer to the course material provided by your instructors if there are any discrepancies between our resource and your course content.

We appreciate you using our resource! Best of luck on your exams :)

-The WebStraw team

♡ Note to Instructors: If this resource has been created for your course and you would like to collaborate with us, please email us at team@webstraw.org

Note: Marvin was used for drawing, displaying and characterizing chemical structures, substructures and reactions, Marvin 24.4.1, Chemaxon (https://www.chemaxon.com)

biochem 2280.

a handmade guide

BROUGHT TO YOU
BY WEBSTRAW

MADE WITH LOVE BY

Ali Alimorad
Sara Cordoba Reyes
Lucy Yang
Quynh Phi

Questions? Ask us at team@webstraw.org