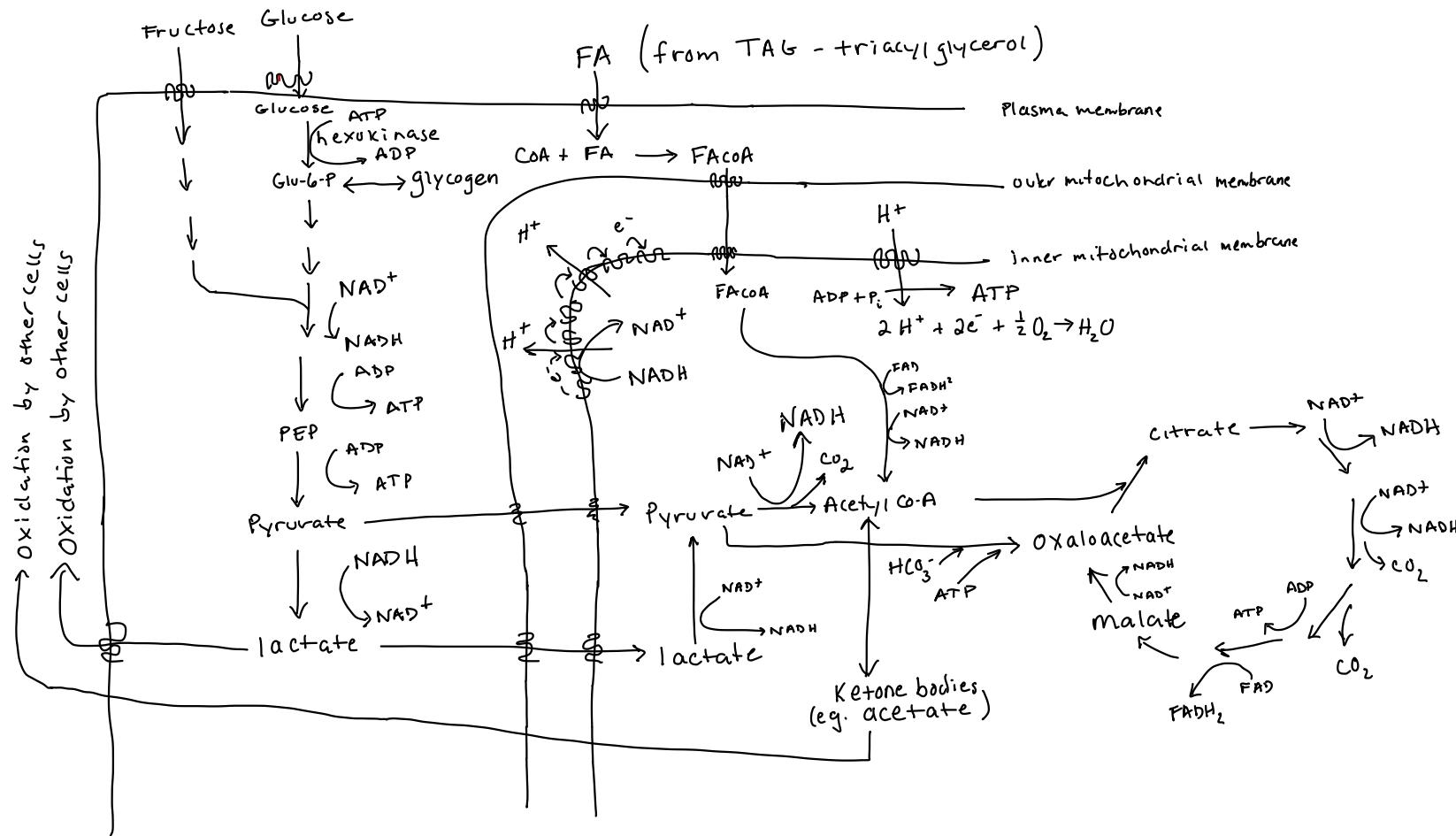
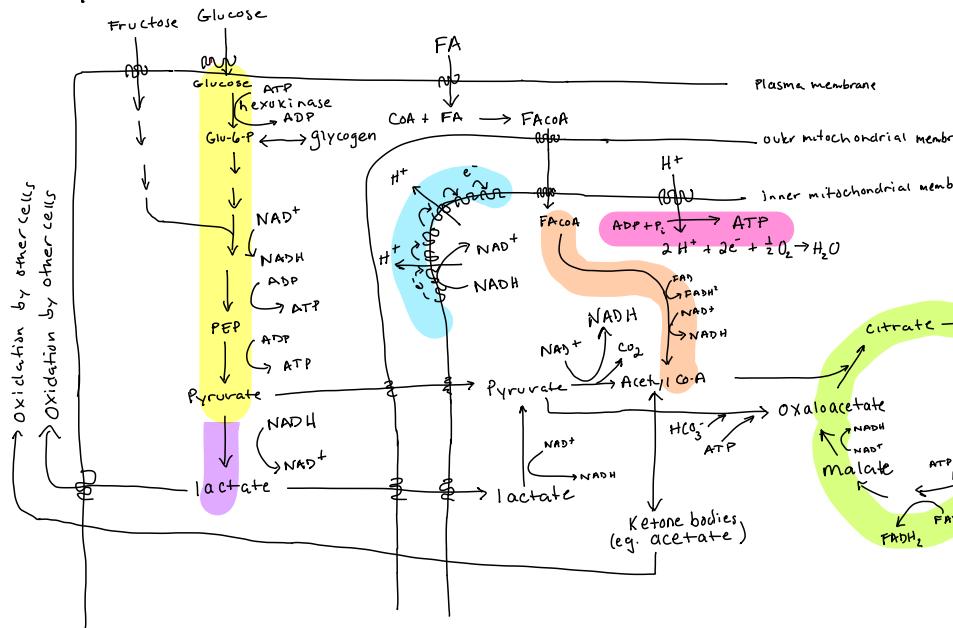


ATP Synthesis



junk going on in cytoplasm:

(i) Glycolysis



(2) fermentation

Junk Going on in mitochondria

(a) Oxidative Phosphorylation

(5) Citrate Cycle

AKA

Citric acid cycle

Kreb's Cycle

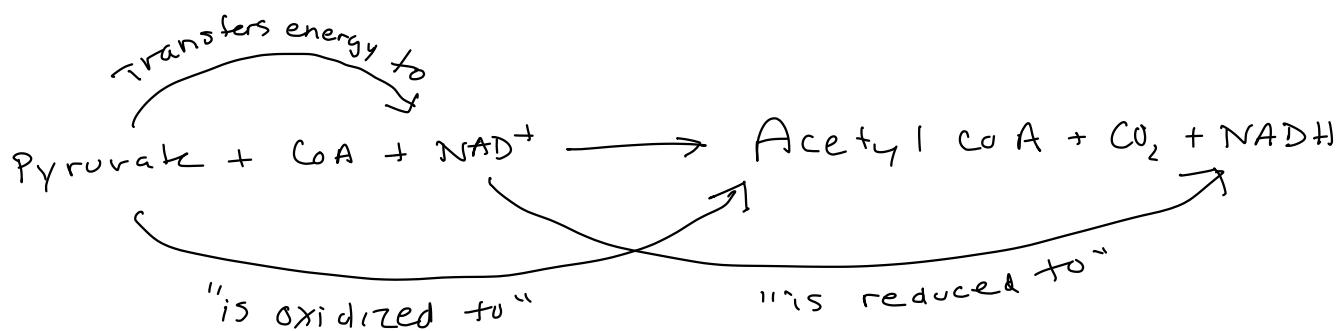
TCA Cycle

(c) Electron transport Chain

(d) β -oxidation

ATP Synthesis

- set of reactions many of which are oxidation-reduction reactions. A non-technical way to define this is a reaction that transfers energy in the form of an electron from one substrate to the other

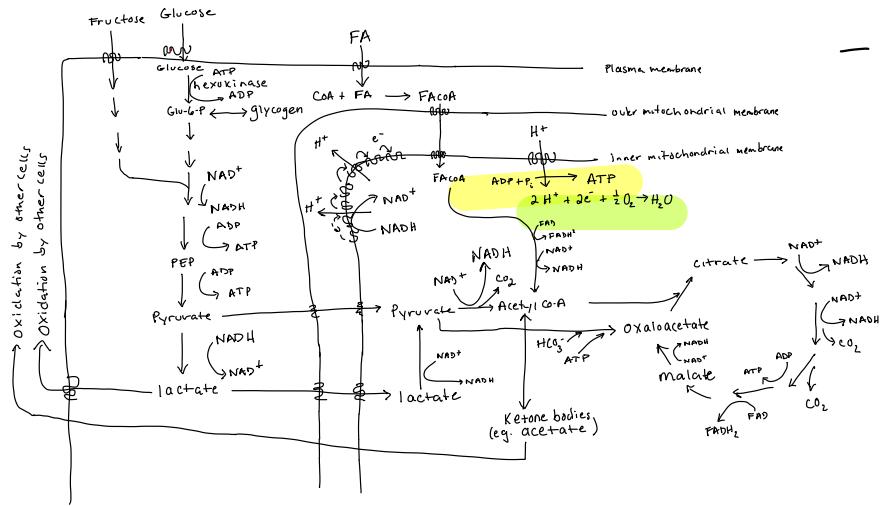


Glycolysis

- ① reactions occur in cytoplasm (NOT mitoch.)
- * ② Anaerobic path for ATP Synthesis because O₂ is not a substrate in reactions
- ③ first step is key because the enzyme hexokinase only catalyzes in direction → G-6-P so once in cell, glu stays in cell
- ④ multiple reactions - This is NOT an assembly line. The products of one reaction are substrates for multiple reactions and which reaction entered has a big stochastic component
-
- The diagram illustrates the glycolytic pathway. It starts with Glucose at the top, which is converted to Glu-6-P by Hexokinase (using ATP to ADP). This is followed by a series of reactions: conversion to NADH (using NAD⁺ to NAD), conversion to ADP (using ATP to ADP), conversion to PEP (using ADP to ATP), and finally conversion to Pyruvate (using ADP to ATP).

* Anaerobic does NOT mean in absence of O₂. Your cells always have lots of O₂

ATP synthesis in mitochondria

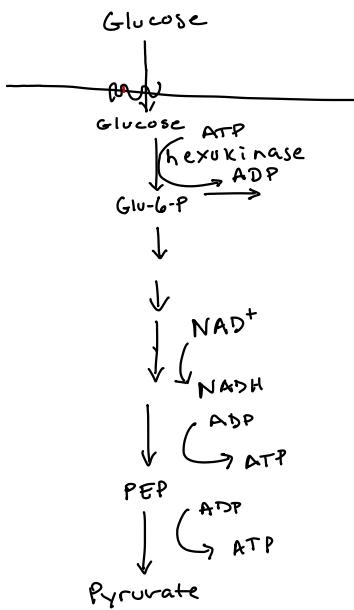


- **Aerobic** - meaning O₂ is part of reaction

- most ATP synthesized by direct phosphorylation by an inorganic phosphate (NOT bound to an organic molecule.)
- Known as **Oxidative Phosphorylation** because O₂ is part of this reaction.

- The Energy for oxidative phosphorylation comes from the H⁺ gradient across the inner mitochondrial membrane
- The Energy to generate the H⁺ gradient comes from e⁻ in the ETC
- These e⁻ are transferred from NADH and FADH₂ to the ETC. This is the "purpose" of NADH and FADH₂

Think about glycolysis in terms of energy transfer



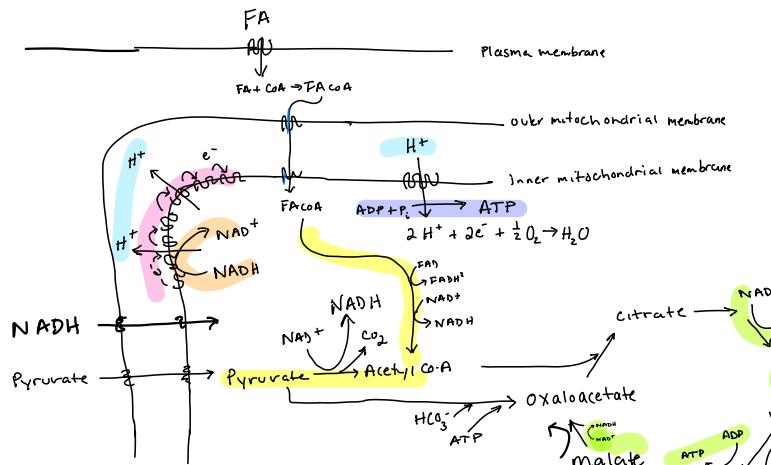
The chemical energy in glucose is transferred into

(1) 2 ATP +

(2) 2 NADH + → This can diffuse into Mitochondria and Transf. Energy to ETC

(3) 2 Pyruvate

↳ This can diffuse into Mitochondria and Transfer Energy to Citrate cycle



Energy Flow in the mitochondria

Energy in FA and pyruvate transferred to

- acetyl Co A +
- NADH, FADH₂

Chemical energy in acetyl co A transferred to

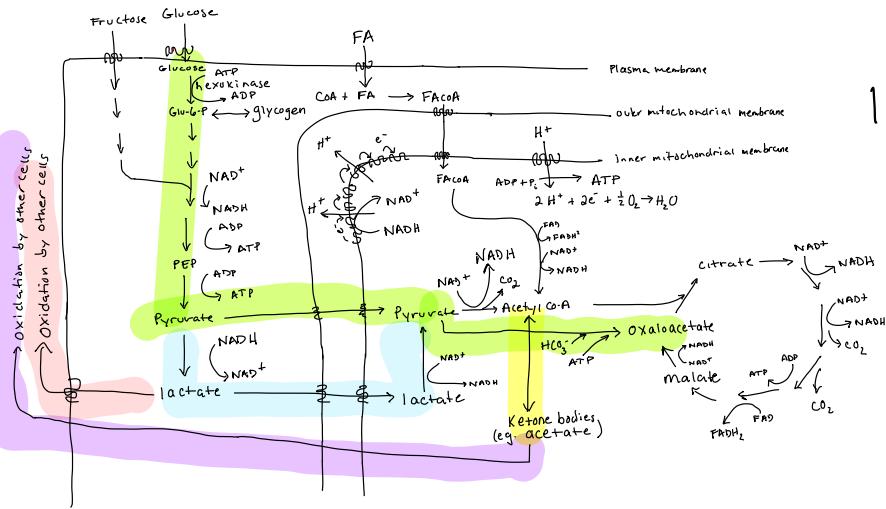
- 3 NADH +
- 1 FADH₂ +
- 1 ATP

(3) Chemical energy in NADH/FADH₂ transferred to ETC, which transfers Energy to

(4) H⁺ gradient, which transfers

(5) Energy to ATP

Metabolic inputs to ATP synthesis



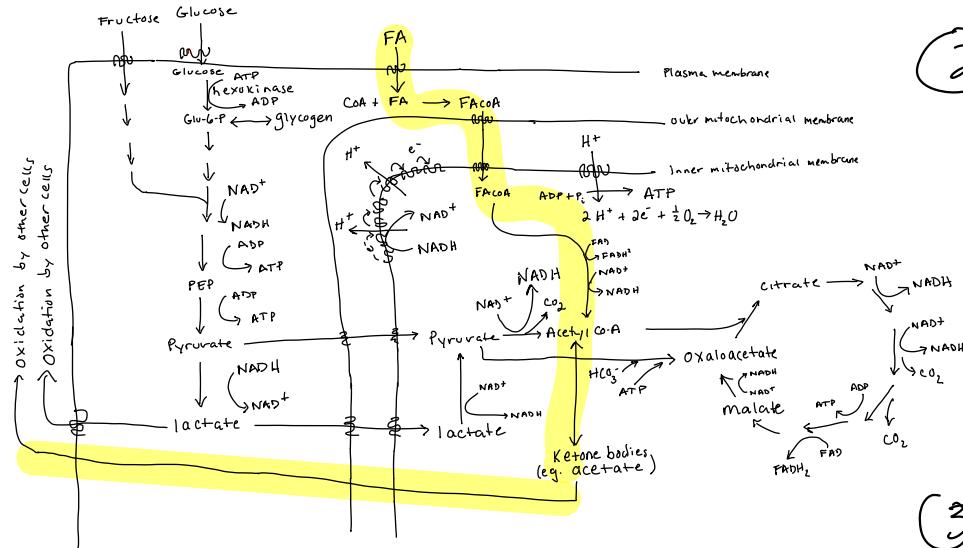
1. Ketone bodies -- oxidation of FA (as opposed to glucose) tends to result in more Ketone bodies: $FA \rightarrow Acetyl\text{-}coA \rightarrow KB$

(a reason: w/ less pyruvate from glycolysis there is less oxaloacetate for the citrate cycle).

EXCESS KB diffuse into the blood and are used by other tissues (e.g. heart, brain). This is good, but see ketoacidosis next page.

2. Lactate, which is formed by reduction of pyruvate can enter Aerobic pathway in own cell or diffuse into blood and be oxidized (synthesize ATP) by other tissue (e.g. heart)

Ketoacidosis



(1) - in unregulated Type I diabetes, in muscle cells:
 ↓ glucose → ↓ Pyruvate
 results in
 ↓ results in
 ↓ oxaloacetate

(2) Consequently, most ATP synthesis is from FA → Acetyl-CoA. But because limited Oxaloacetate. There is a high rate of Acetyl-CoA → Ketone Bodies

(3) KB are always synthesized in small to moderate amounts, especially between meals (post-absorptive state). but in T1 diabetes, this is excessive KB synthesis. KB are acids and this excessive KB create Ketoacidosis.

Hormonal regulation of metabolism

Absorptive state - The energy-rich condition following a meal / absorption when anabolic pathways are stimulated and catabolic pathways are inhibited

Post-absorptive state - the energy poor condition following a fast when catabolic pathways are stimulated and anabolic pathways are inhibited

Anabolism - Synthesize large molecules from small molecules

Catabolism - breaking down large molecules into small molecules

absorptive vs postabsorptive paths

glyogenesis — synthesis of glycogen (glucose storage)

lipogenesis - synthesis of lipids including TAG (FA storage)

de novo lipogenesis - synthesis of lipids from non-lipid source

protein synthesis - synthesis of proteins

transamination - transforming one kind of amino acid to another

Glycogenolysis - breakdown of glycogen to glucose

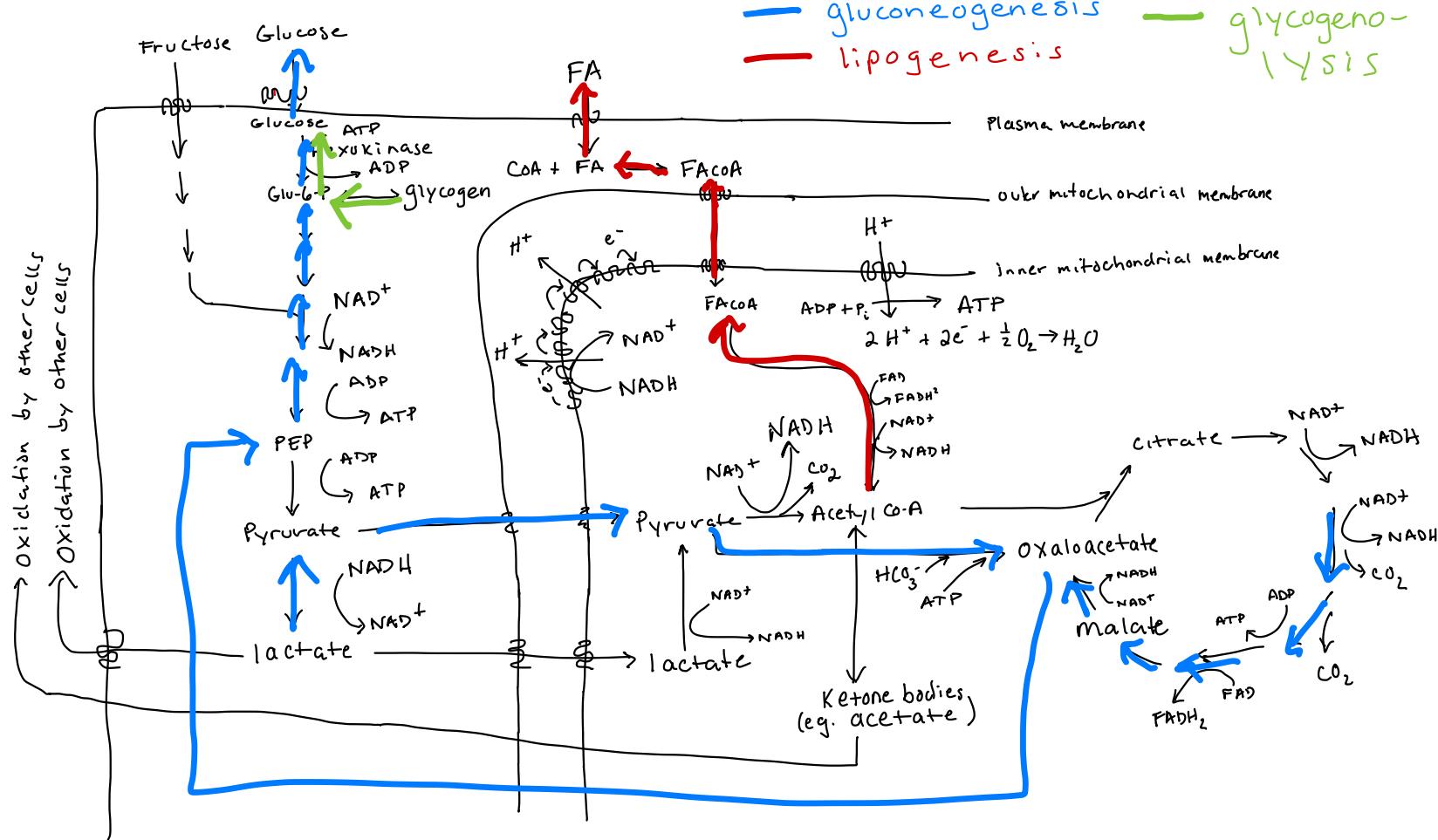
Gluconeogenesis - synthesis of glucose

Lipolysis - breakdown of TG

Ketogenesis - synthesis of ketone bodies

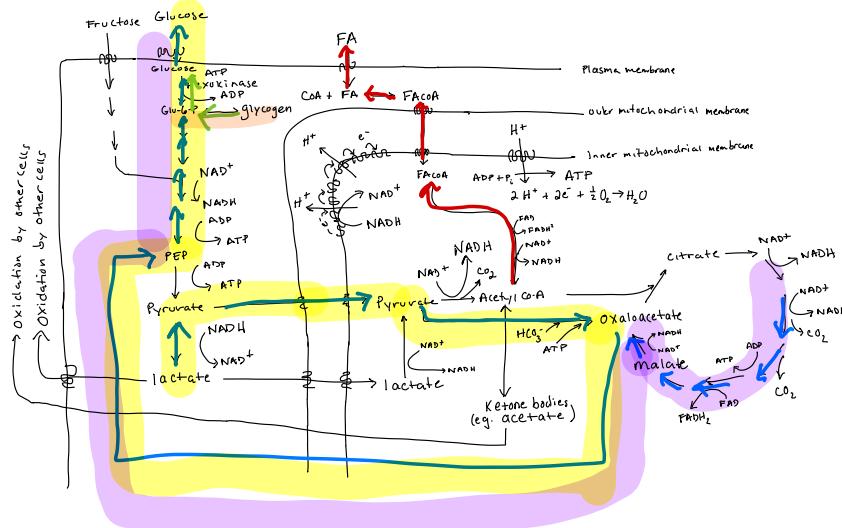
Protein hydrolysis - breakdown of protein

deamination - removal of N from AA for input to CC
and gluconeogenesis



I Gluconeogenesis

- "The birth of new glucose"
- To make glucose from non-carbohydrates
- principal substrates are
 - 1) lactate (this is Cori cycle)
 - 2) glycerol from TAG (not shown)
 - 3) most amino acids, which are converted to oxaloacetate via Citrate cycle



The final step is $\text{Glu-6-P} \rightarrow \text{Glu}$. The enzyme that catalyzes this is glucose 6 phosphatase, which is expressed in the liver but not many other cell types. The liver synthesizes glucose for rest of body.

II Glycogenolysis - many cells do this but liver does this to supply glucose to rest of body

Lipogenesis

"birth of fat"

- Source is acetyl CoA

- carbohydrates are a

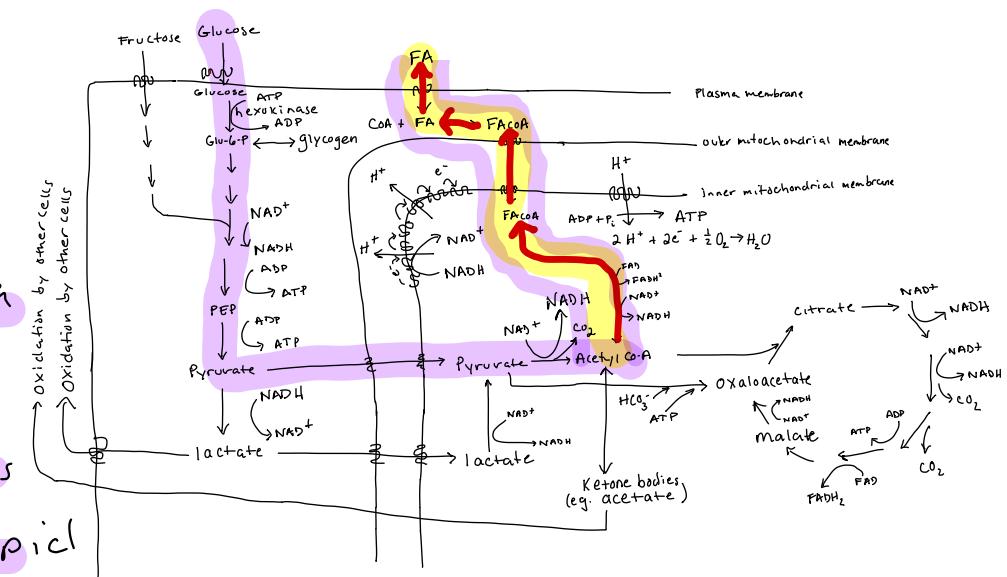
non-lipid source of

acetyl-CoA. Synthesis

of FA from non-lipid

source (principally Carbs)

is de novo lipogenesis, a super important metabolic process in modern America.



absorptive state

sm. intestine

Glucose

FA

AA

Liver

ATP

glycogen

TAG → VLDL

urea

Protein

interconversion

Skel. muscle

ATP

glycogen

ATP

glycogen

TAG

protein

Adipose

ATP

TG

protein

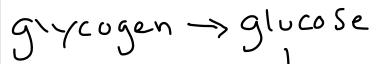
other tissue

ATP

Protein

Post absorptive state

SKEI. muscle



lactate

ATP



FA

AA ← Protein

Liver

glycogen



Lactate → glucose

ATP



AA



glycerol



ATP



FA



Ketone
Bodies

Nervous

glucose → ATP

Ketone
Bodies



blood glucose

other tissues

AA ← Protein

ATP ← FA

ATP ← Ketone
Bodies

Adipose

glycerol



TAG

FA



ATP



AA



Protein



ATP



FA



Ketone
Bodies



ATP



FA



Ketone
Bodies



ATP



FA

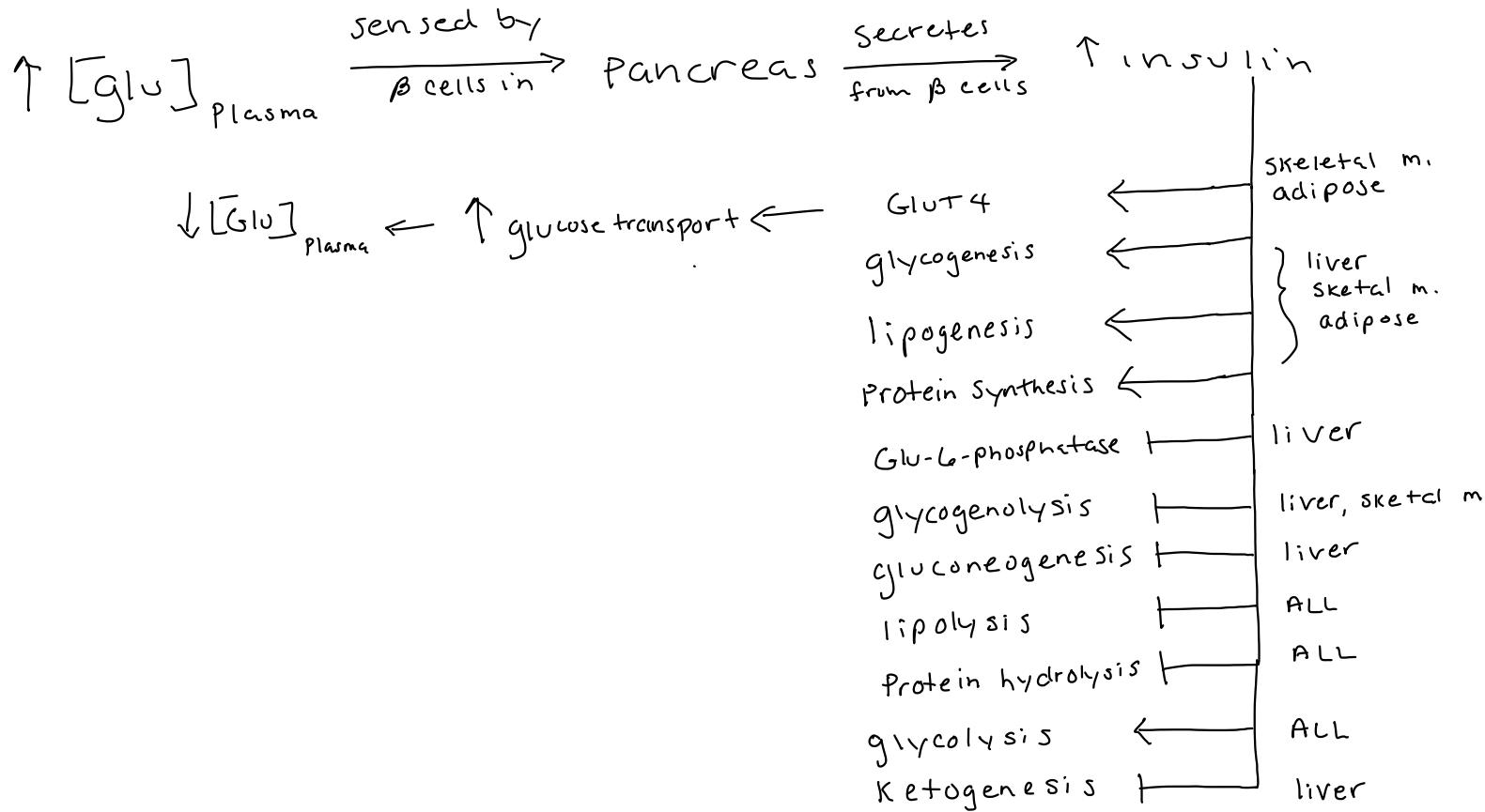


Ketone
Bodies

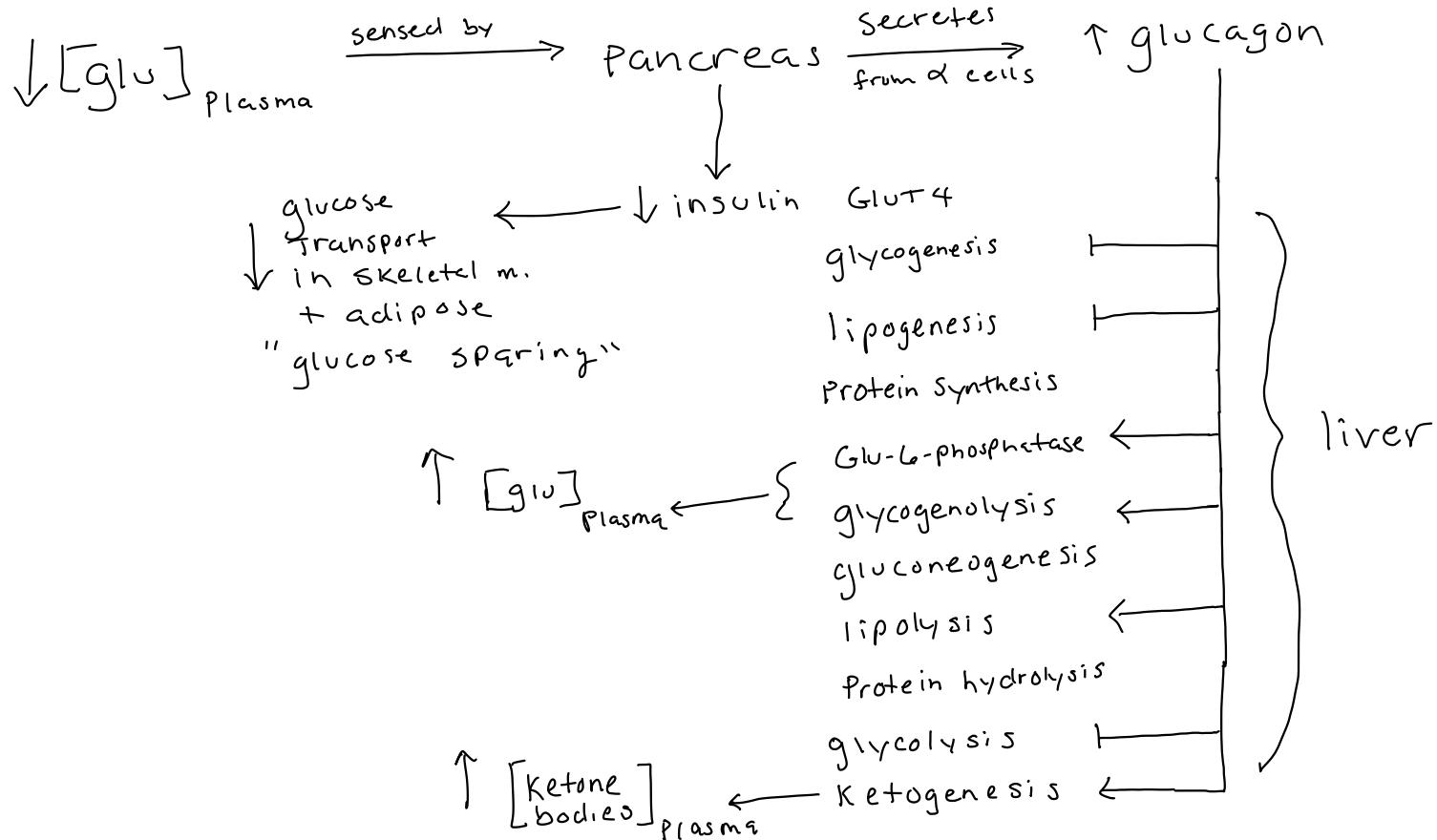


ATP

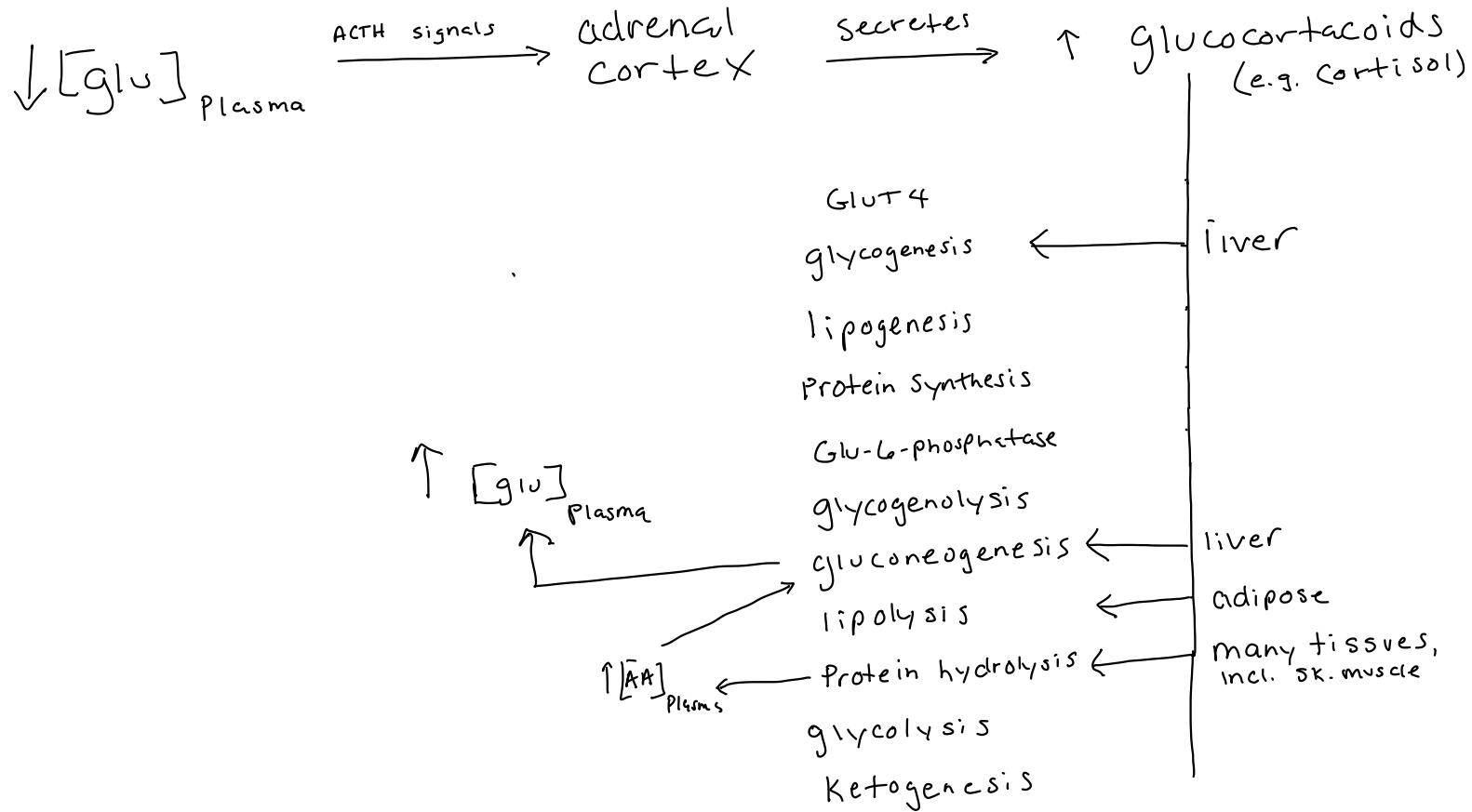
Absorptive state - Insulin Signals Liver, Adipose, + skeletal muscle to store energy



post-absorptive state → glucagon ↑ hepatic secretion of glucose via glycogenolysis



Prolonged fasting - glucocorticoids \uparrow [glu]_{plasma}
via gluconeogenesis



Summary

