

GEROSCIENCE EDUCATION & TRAINING

Energy and Metabolism: Core Energy Metabolism and Signaling



Brought to you



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Core energy metabolism and signaling

- How carbohydrates and lipids are mobilized and used at the systemic and cellular levels



Learning Objectives

Understand storage and mobilization of glucose and fat (lipids)

Learn cellular pathways to take up and harvest energy from these molecules

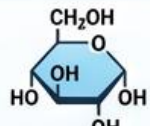
Become familiar with two key intracellular energy sensors, mTORC1 and AMPK

Understand storage and mobilization
of glucose and fat (lipids)

Objective 1

COMPARATIVE GUIDE: MACRONUTRIENTS

CARBOHYDRATES



Glucose molecule
($C_6H_{12}O_6$)



Glycogen chain

PRIMARY ENERGY SOURCE



Quick Fuel



Simple Sugars



Complex Starches

Examples: Bread, pasta, potatoes, fruit, oats

Provides fast energy (glucose) for muscles and brain. Stored as Glycogen. 4 Cal/g.



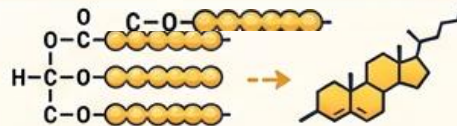
Chain of sugar



Athletes running/biking

ENERGY FOR EXERCISE

LIPIDS / FATS



Triglyceride molecule
(Glycerol + 3 Fatty Acids)

Cholesterol

LONG-TERM STORAGE & INSULATION



Stored Fat



Cell Membranes



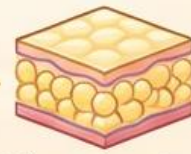
Hormones

Avocado, nuts, oils, butter, cheese, fatty fish

Concentrated energy reserve (storage). Major component of cell membranes (phospholipids). Protects organs. 9 Cal/g.



Fat cells (Adipocytes)



Adipose tissue layer

SUSTAINED ENERGY & PROTECTION

PROTEINS



Amino Acids



Polypeptide chain

BUILDING BLOCKS & STRUCTURE



Muscle Repair



Enzymes



Hormones



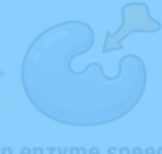
Immunity

Chicken, fish, eggs, beef, beans, tofu, milk

Essential for growth, repair, and maintenance of all body tissues. Transports substances. 4 Cal/g.



Muscle fibers
(contracting)

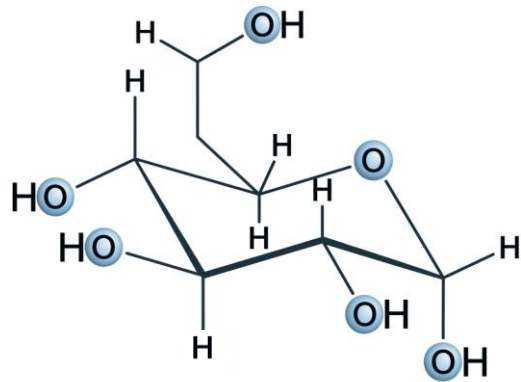


An enzyme speeds
speeding a reaction

TISSUE GROWTH & FUNCTION

● Carbs (Glycogen) ● Lipids (Adipose) ● Protein (Muscle)

Glucose is the main sugar in blood

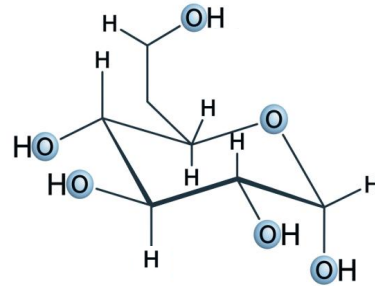
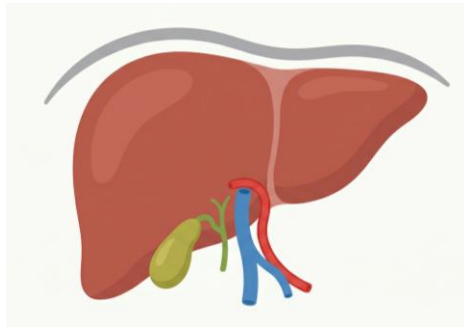


Glucose

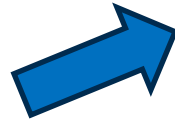
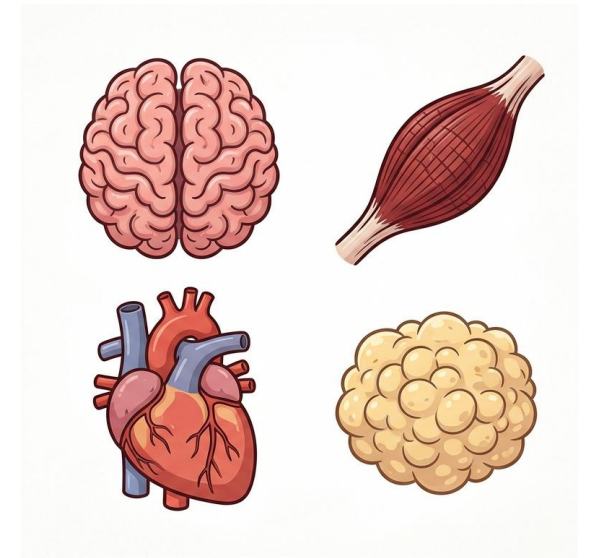
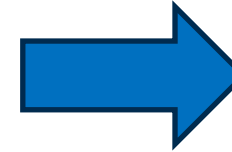
Fasting **Blood Sugar Ranges** (mg/dL)



Glucose comes from food and the liver



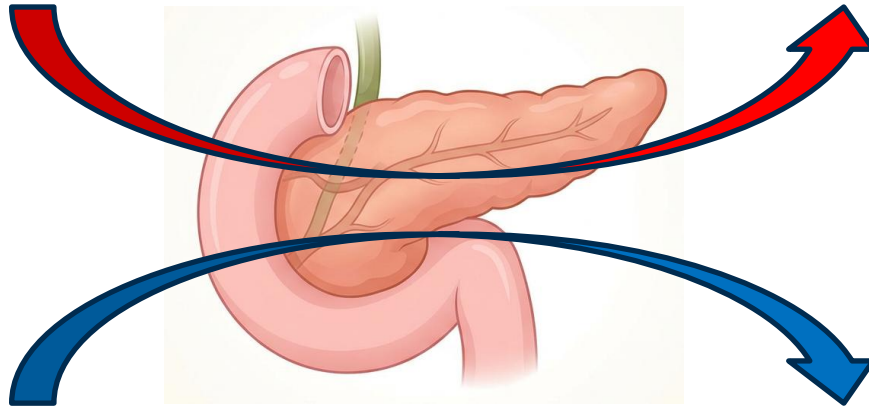
Glucose



Insulin and glucagon from the pancreas regulate glucose

High glucose

Low glucose



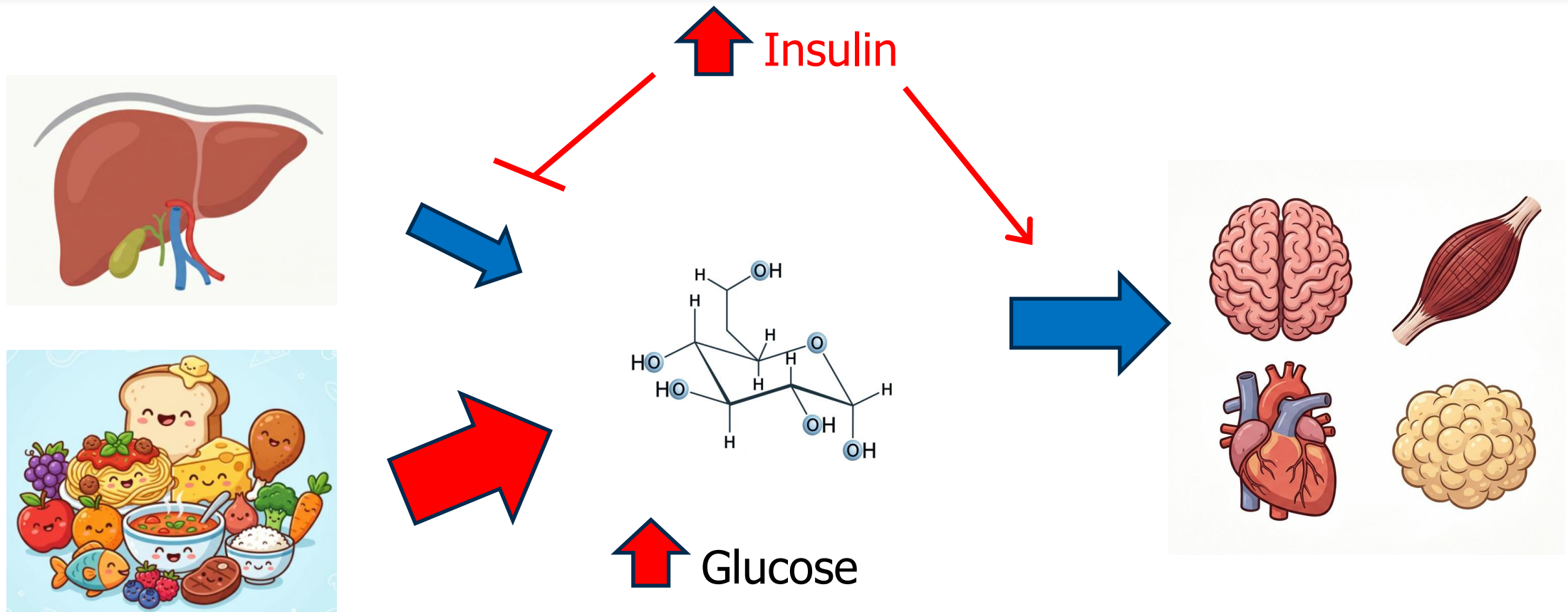
Insulin

- Increases tissue uptake
- Decreases liver production

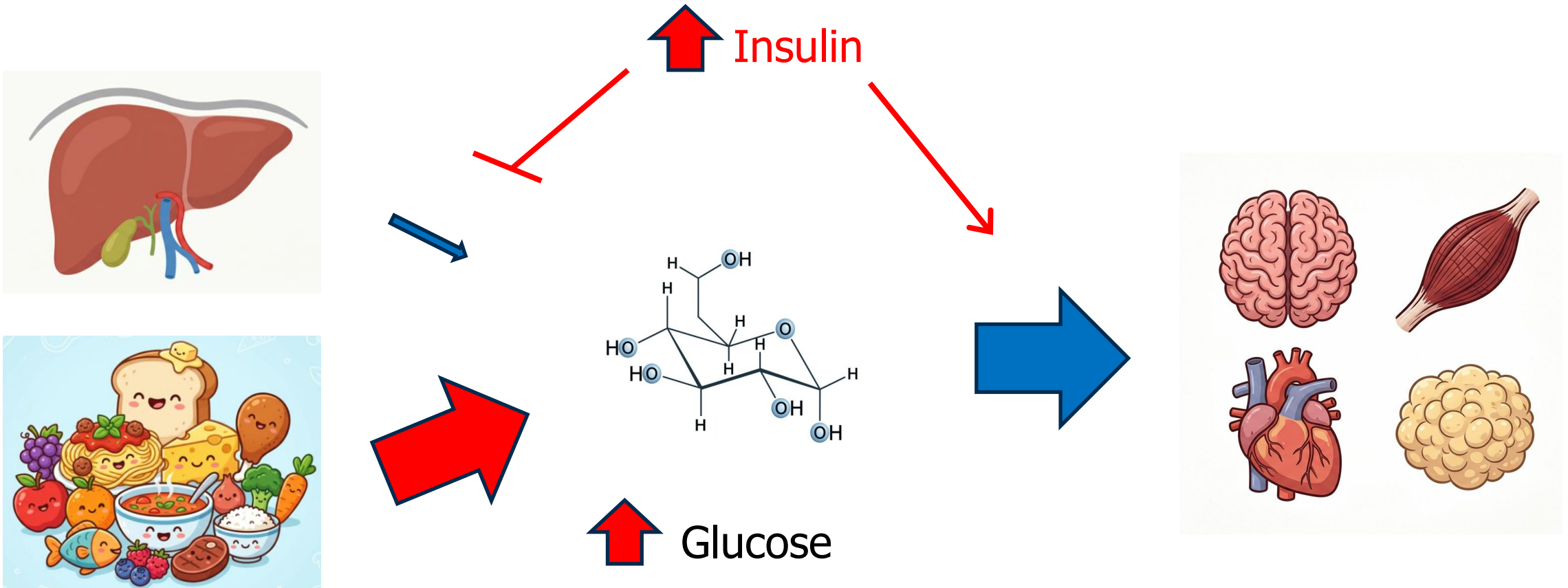
Glucagon

- Increases liver production

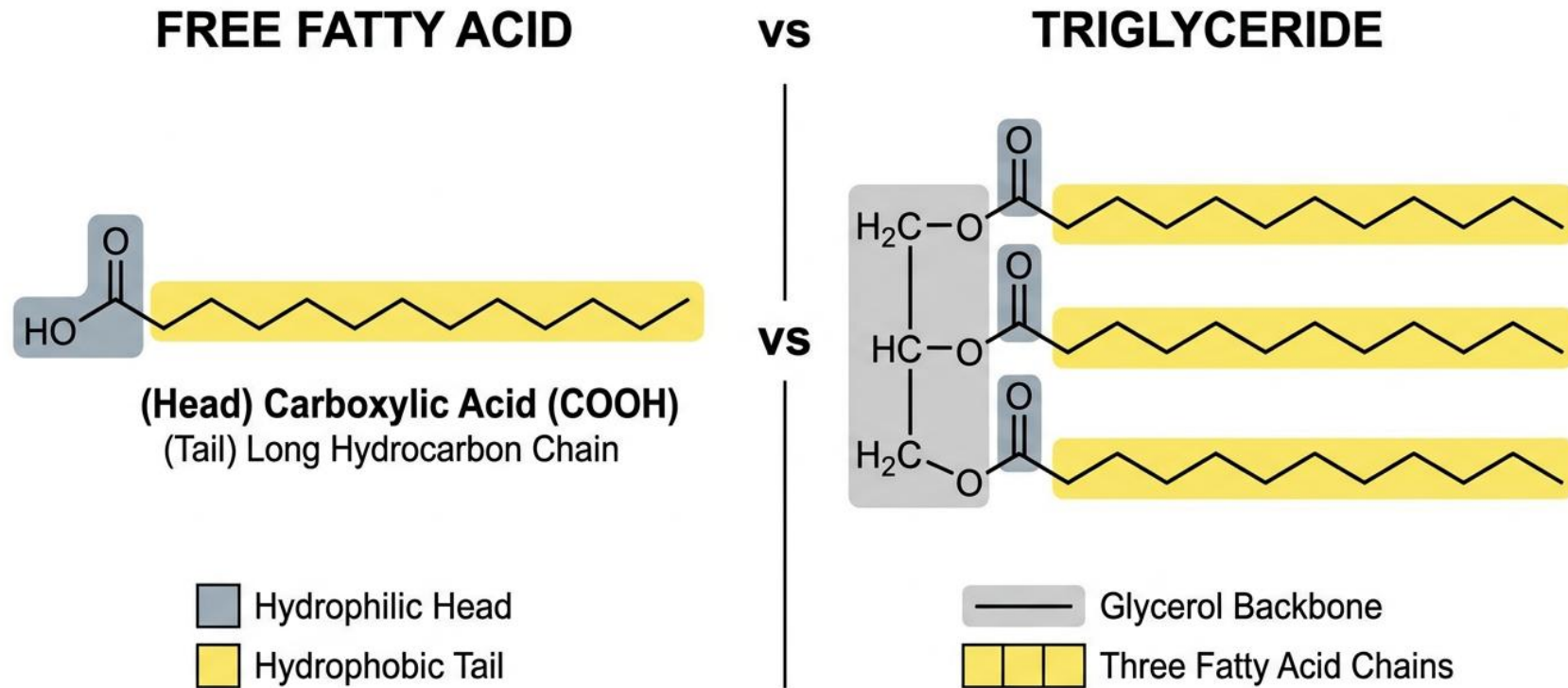
Insulin maintains glucose levels



Insulin maintains glucose levels



Main circulating lipids (fats)

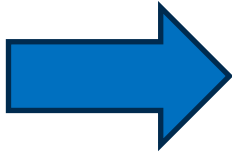


Free Fatty Acid (left): Single unesterified molecule	vs	Triglyceride (right): Glycerol + Three (3) Fatty Acids (Storage Fat)
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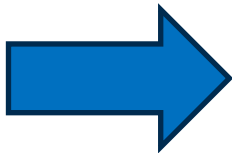
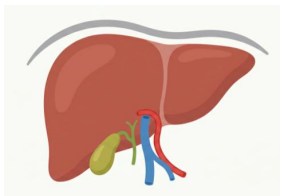
Circulating Lipids in fasting and feeding

Fasting

Fed



Free Fatty
Acids



Triglycerides
(VLDL)

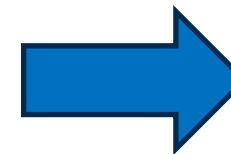


Free Fatty
Acids

Insulin

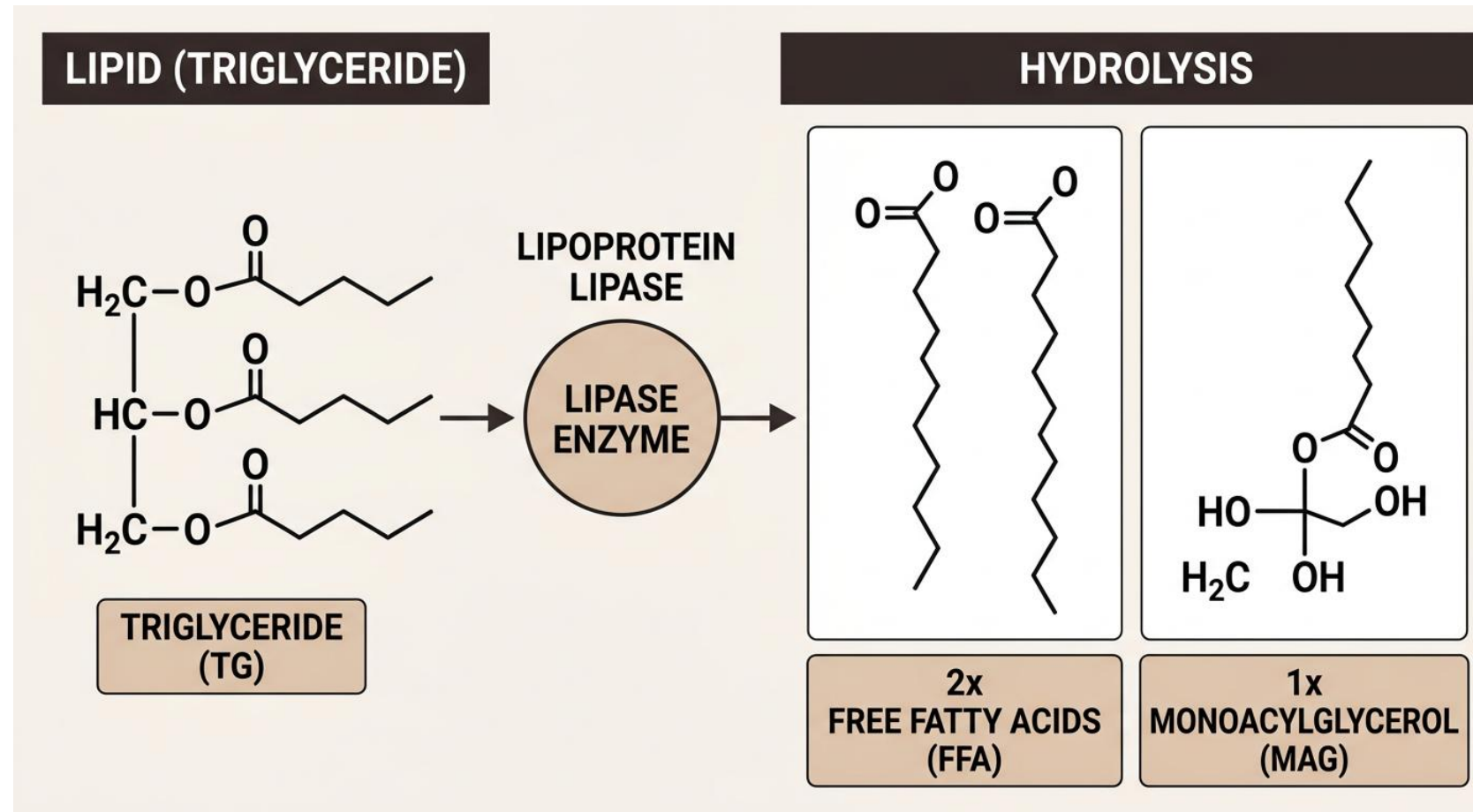


Triglycerides
(VLDL)



Triglycerides
(Chylomicrons)

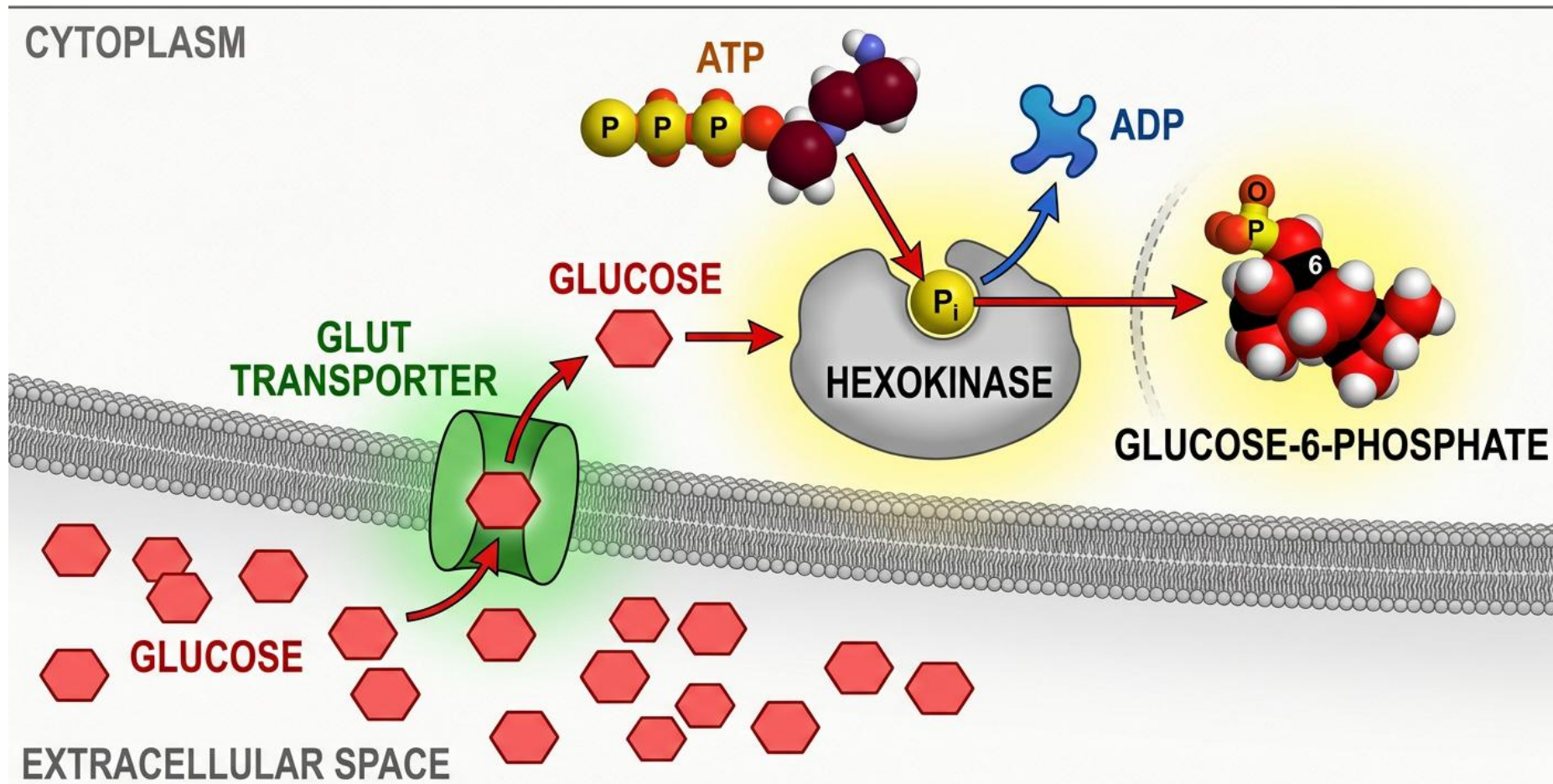
Triglycerides are hydrolyzed for uptake



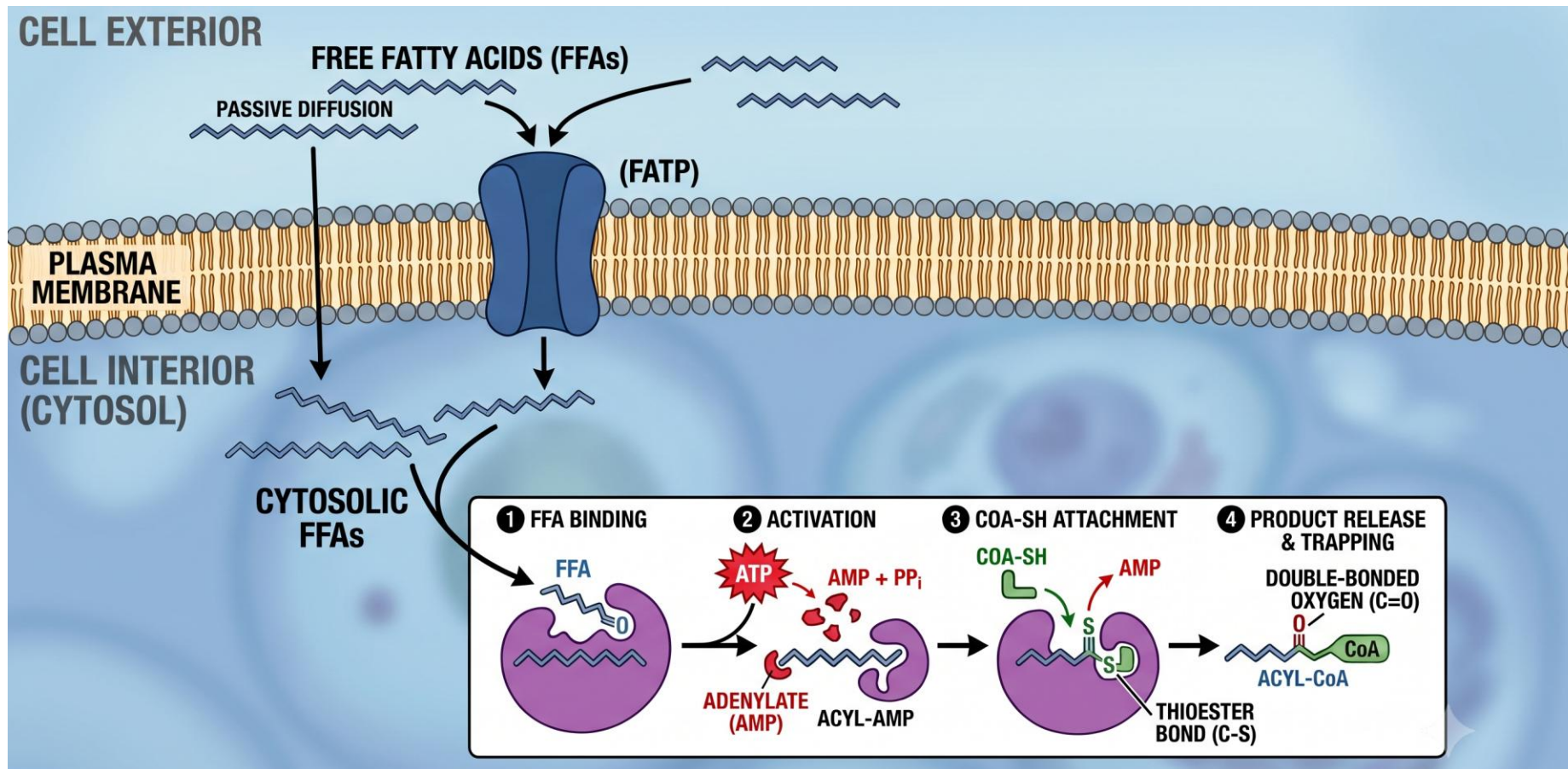
Learn cellular pathways to take up
and harvest energy from these
molecules

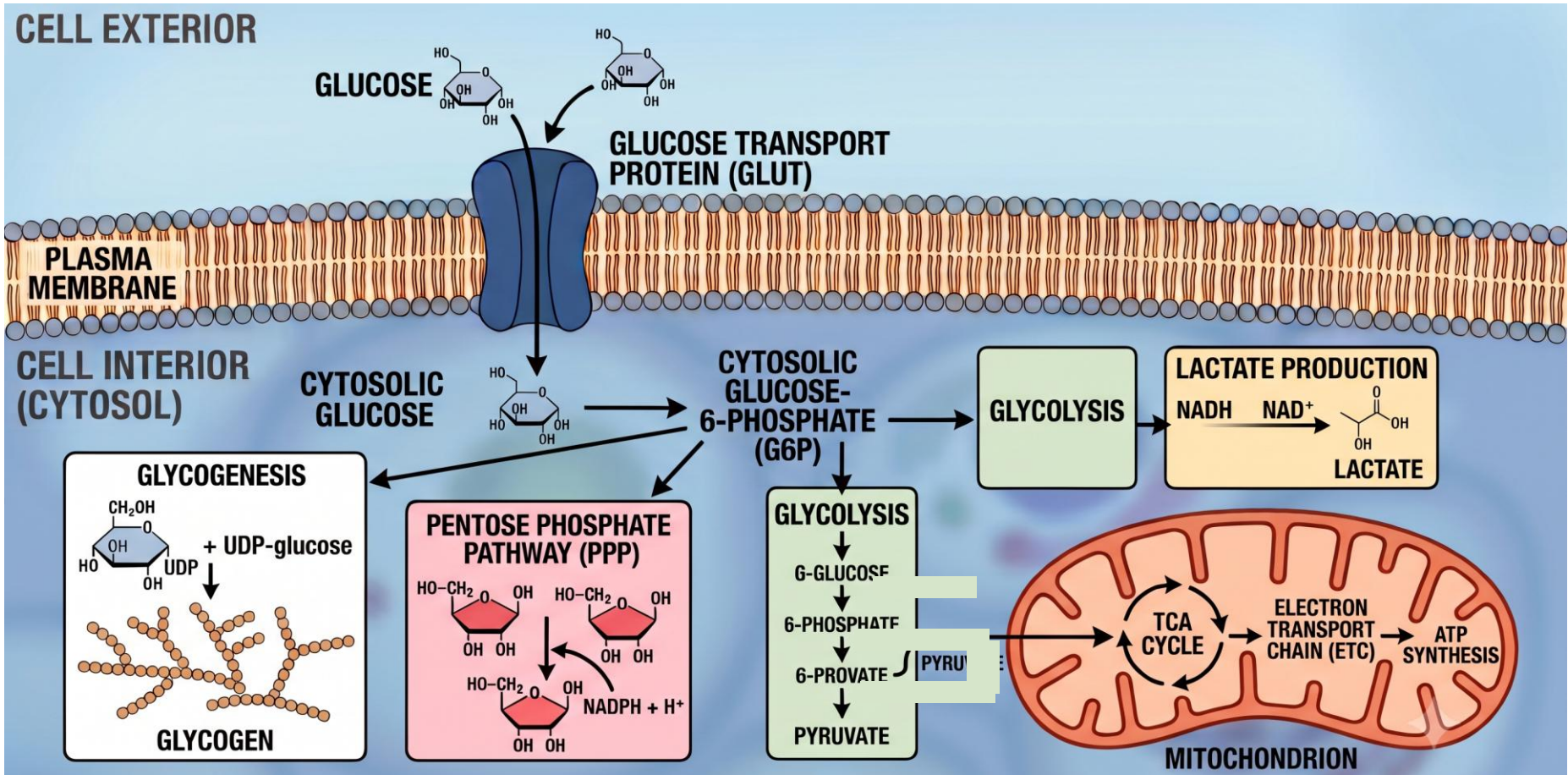
Objective 2

Glucose is trapped by phosphorylation

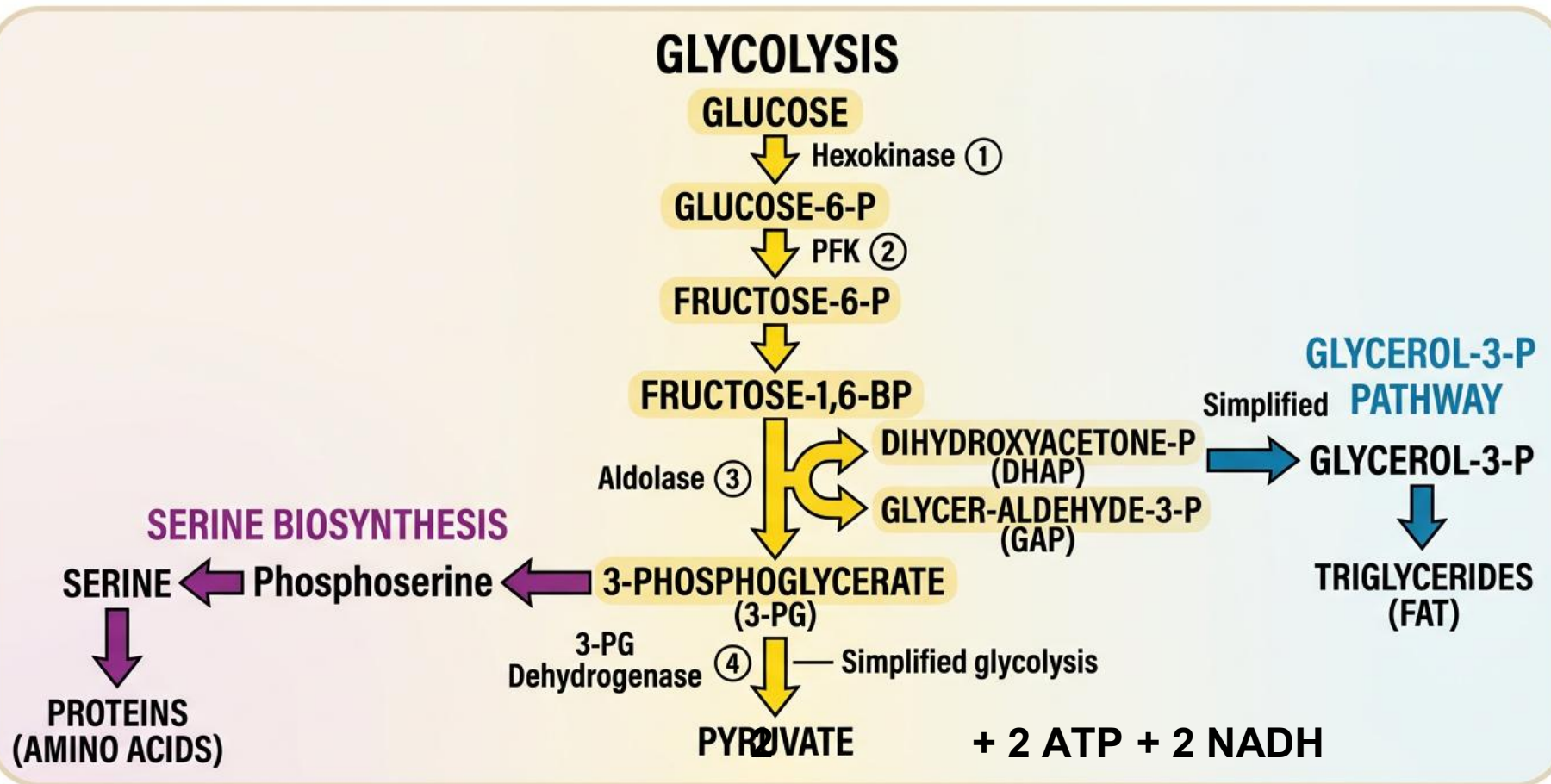


Fatty acids are trapped by CoA addition

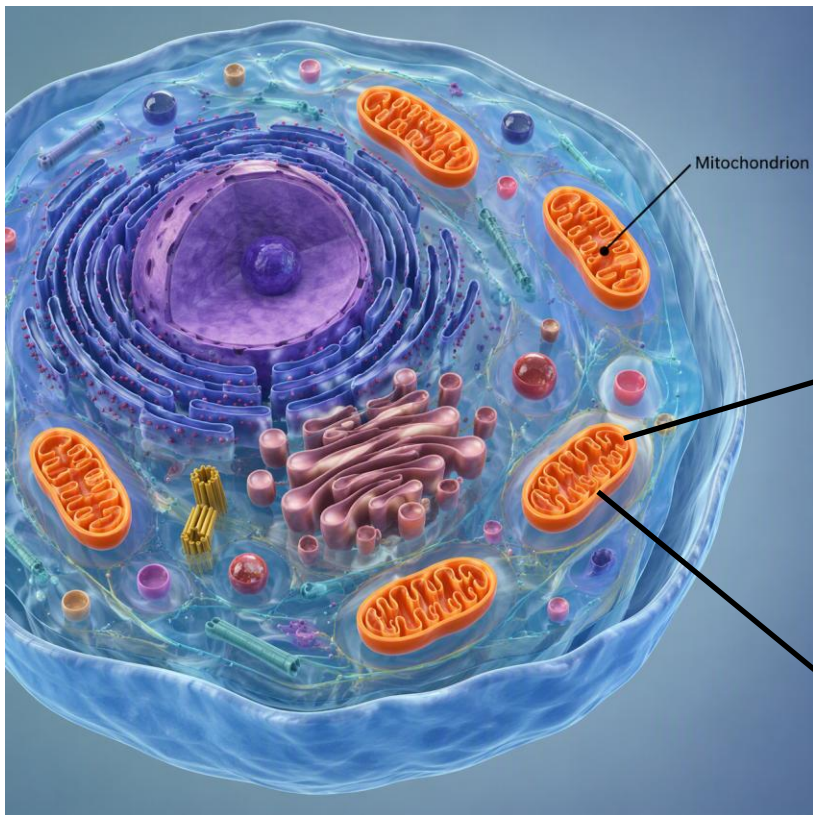




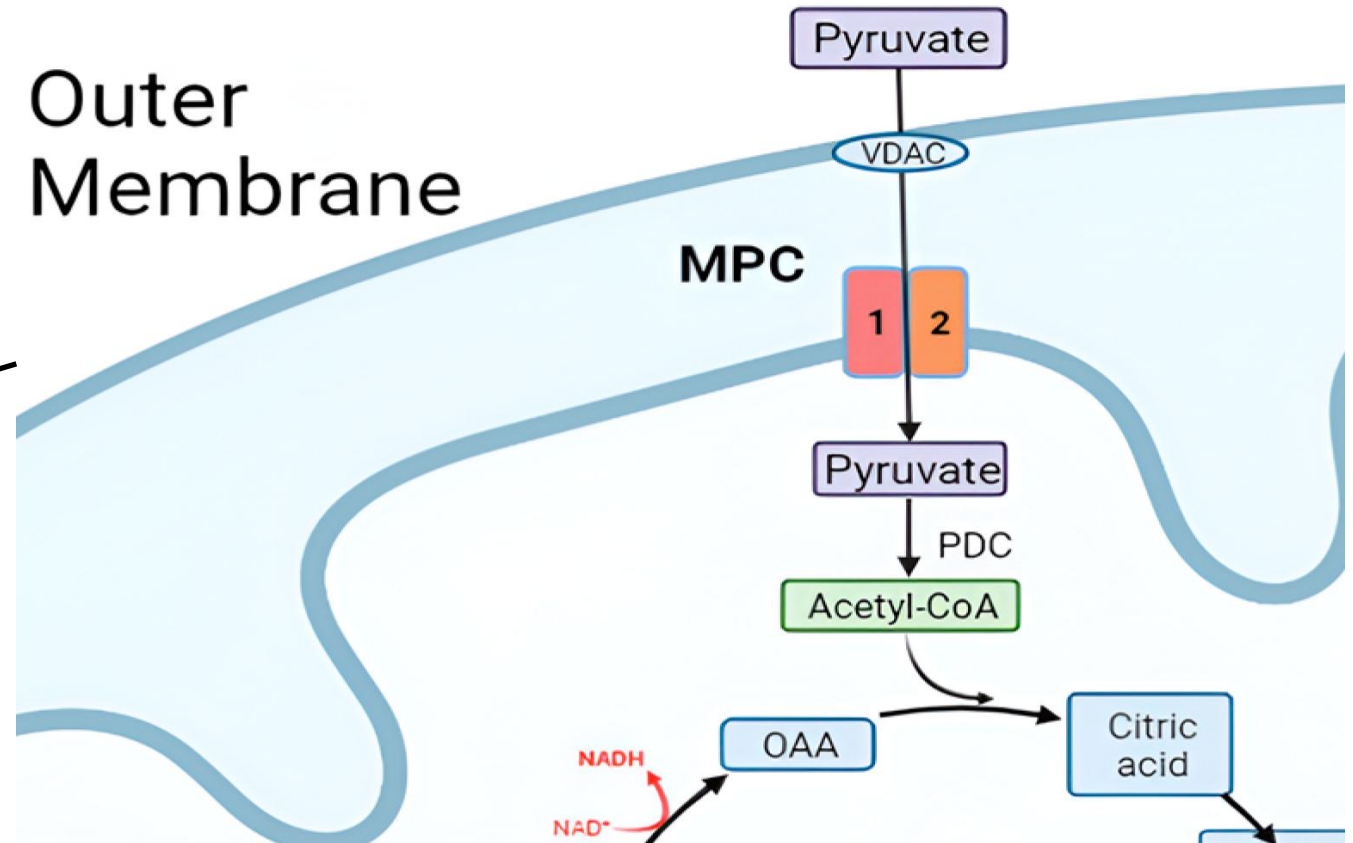
Metabolic pathways branch

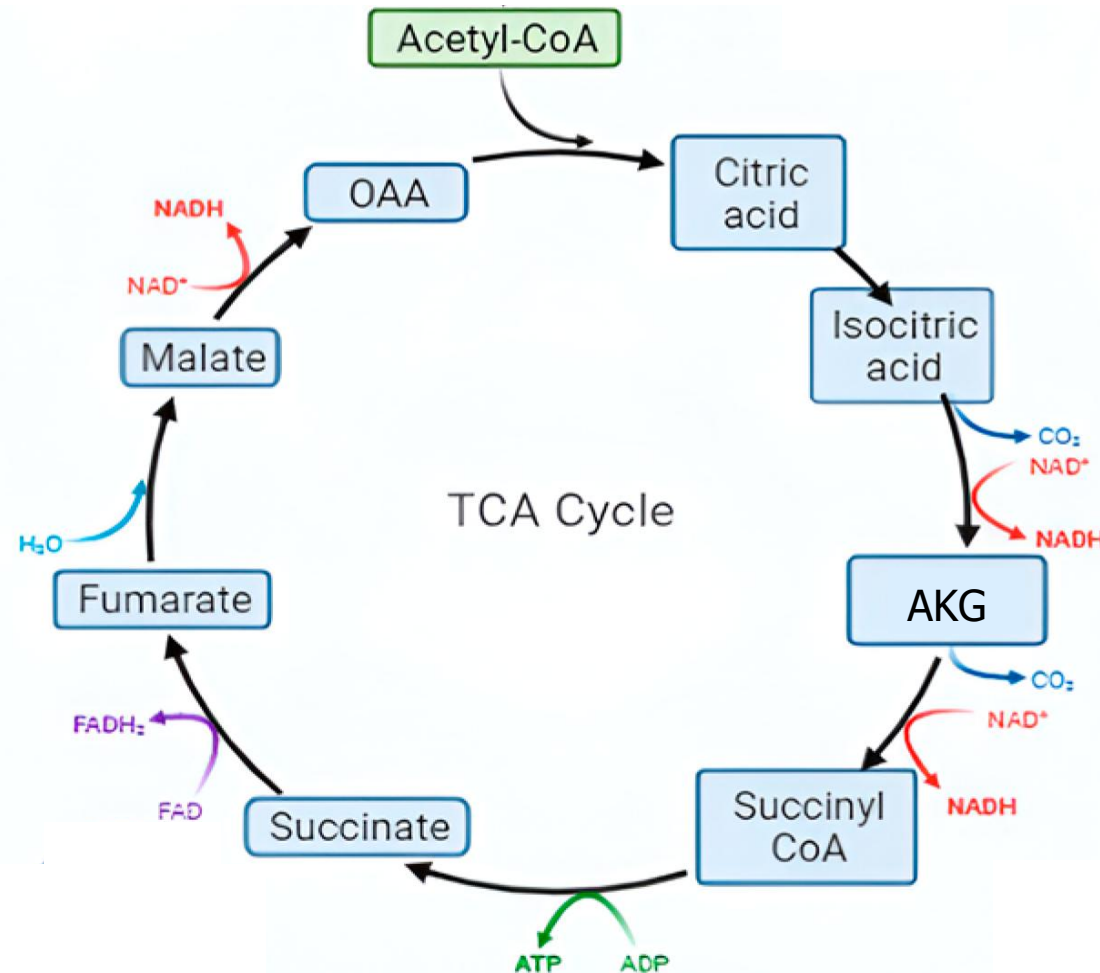


Mitochondria oxidize pyruvate



Outer
Membrane





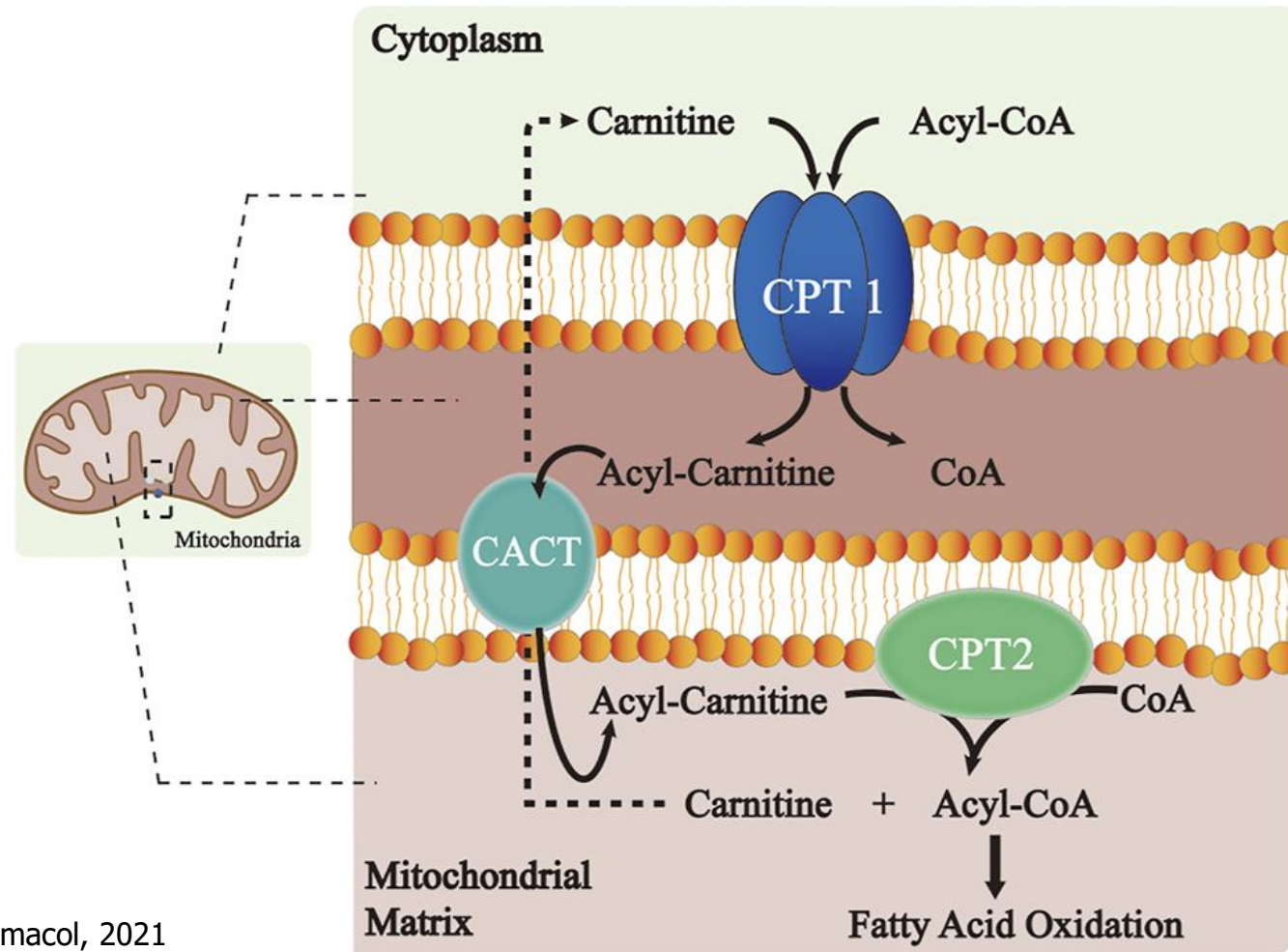
Each Acetyl-CoA:

3 NADH

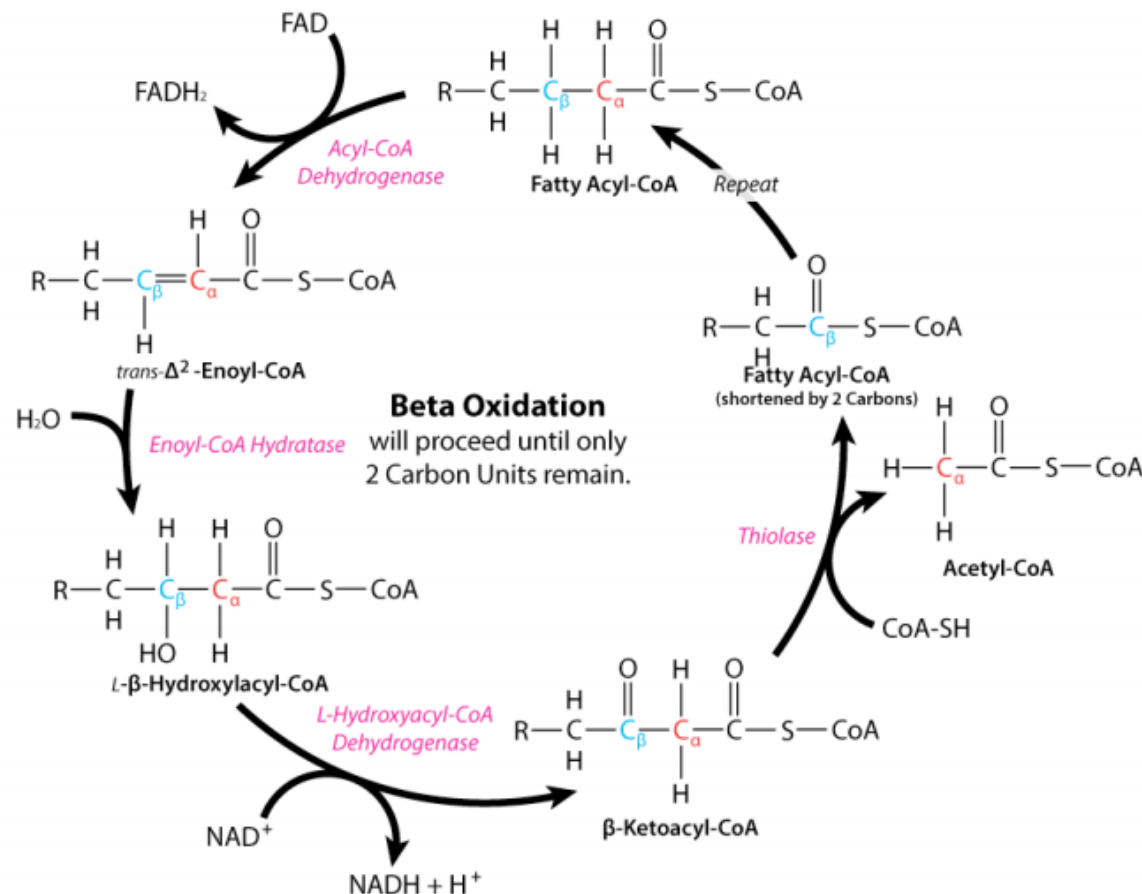
1 FADH₂

1 ATP (or GTP)

Mitochondria import fatty acids via Cpt1



Mitochondria oxidize fatty acids to Acetyl-CoA



(Tricarboxylic acid cycle)

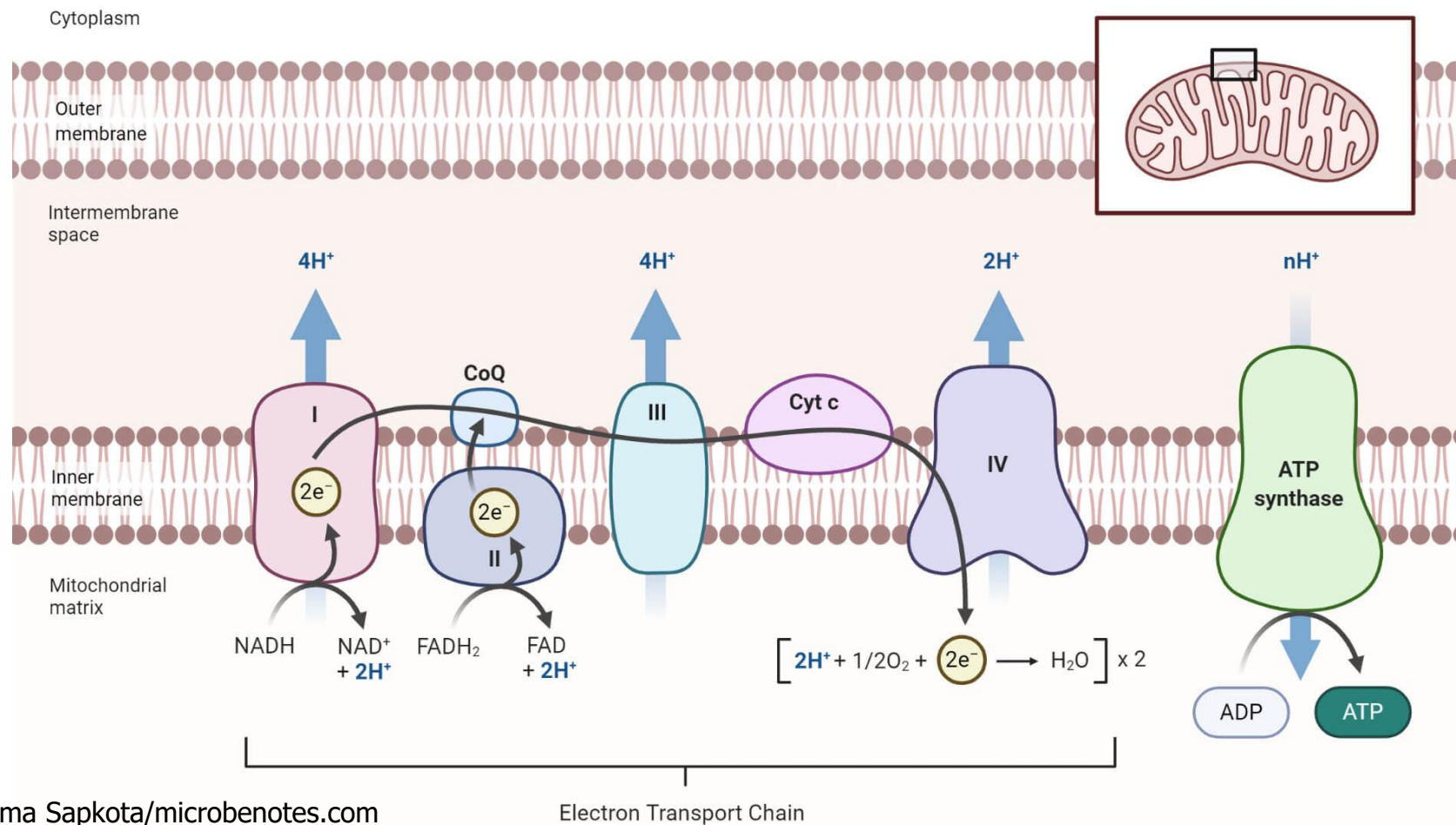
Each Acetyl-CoA:

3 NADH

1 FADH₂

1 ATP (or GTP)

Electron transport chain (ETC) generates ATP



Intracellular sensing of nutrients and energy

Each Acetyl-CoA:

3 NADH ~2.5 ATP each = 7.5 ATP
1 FADH₂ ~1.5 ATP
1 ATP (or GTP) 1 ATP (or GTP)
10 ATP

Starting from Glucose:

Glycolysis 2 ATP
 2 NADH (~5 ATP)

Pyruvate dehydrogenase 2 NADH (~5 ATP)

2 Acetyl-CoA 20 ATP

~32 ATP/glucose

Become familiar with two key intracellular energy sensors, mTORC1 and AMPK

Objective 3

Intracellular sensing of nutrients and energy

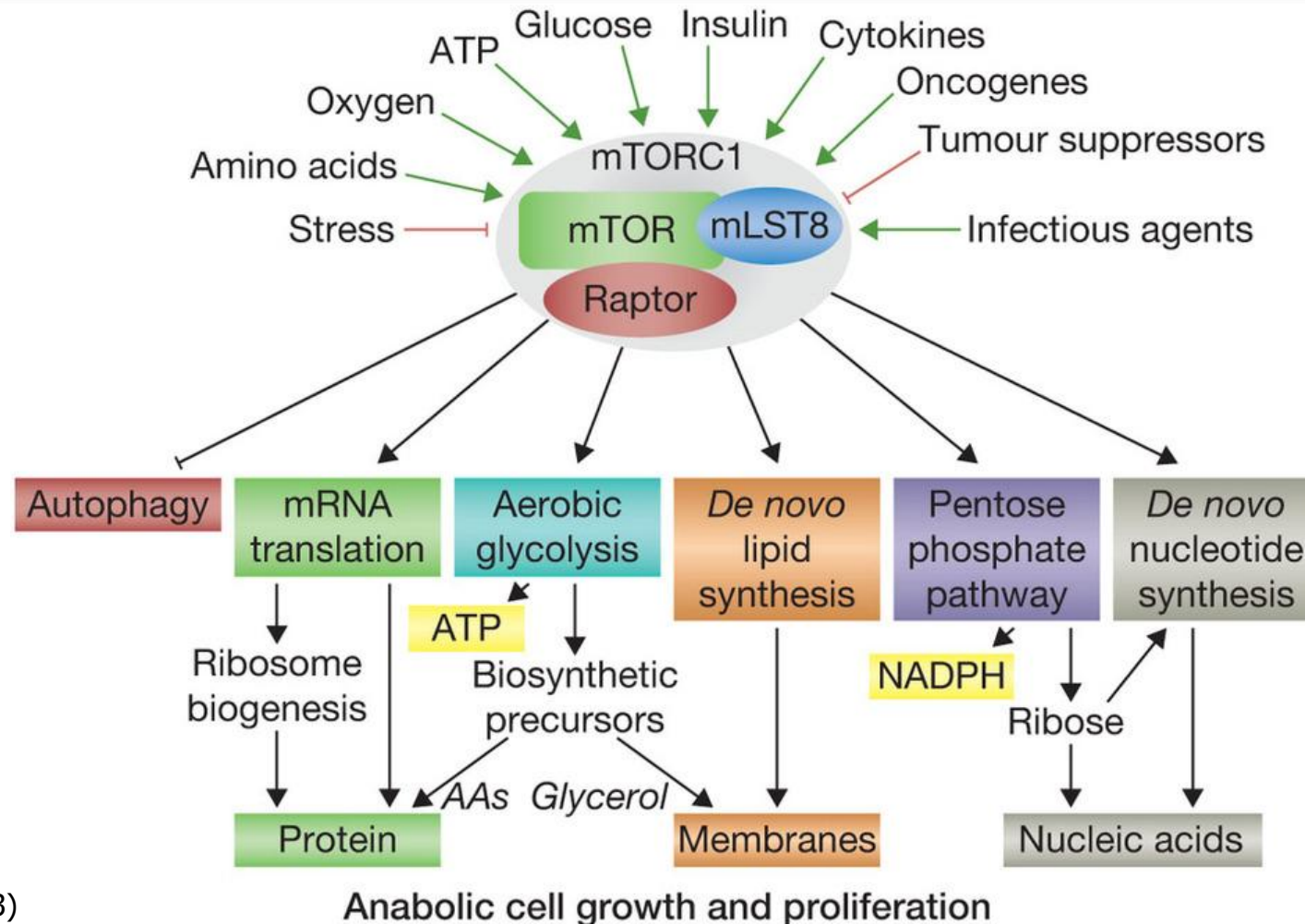
Cells need to adapt to:

- Availability of nutrients
- Energetic demands
- Presence or absence of key building blocks
- Damage/stress

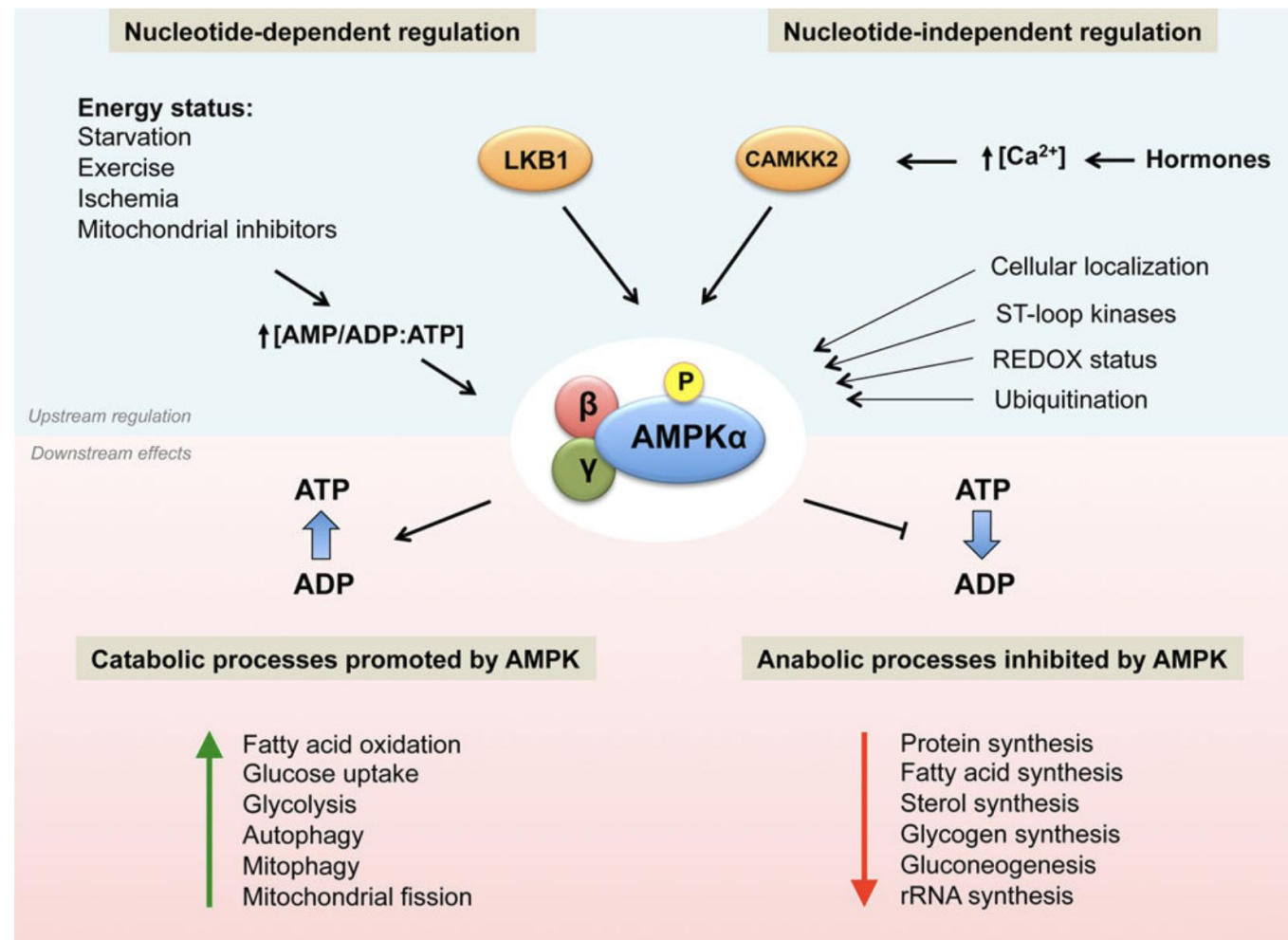
mTORC1 is a key indicator of nutrient sufficiency/growth

AMPK is a key indicator of energetic stress

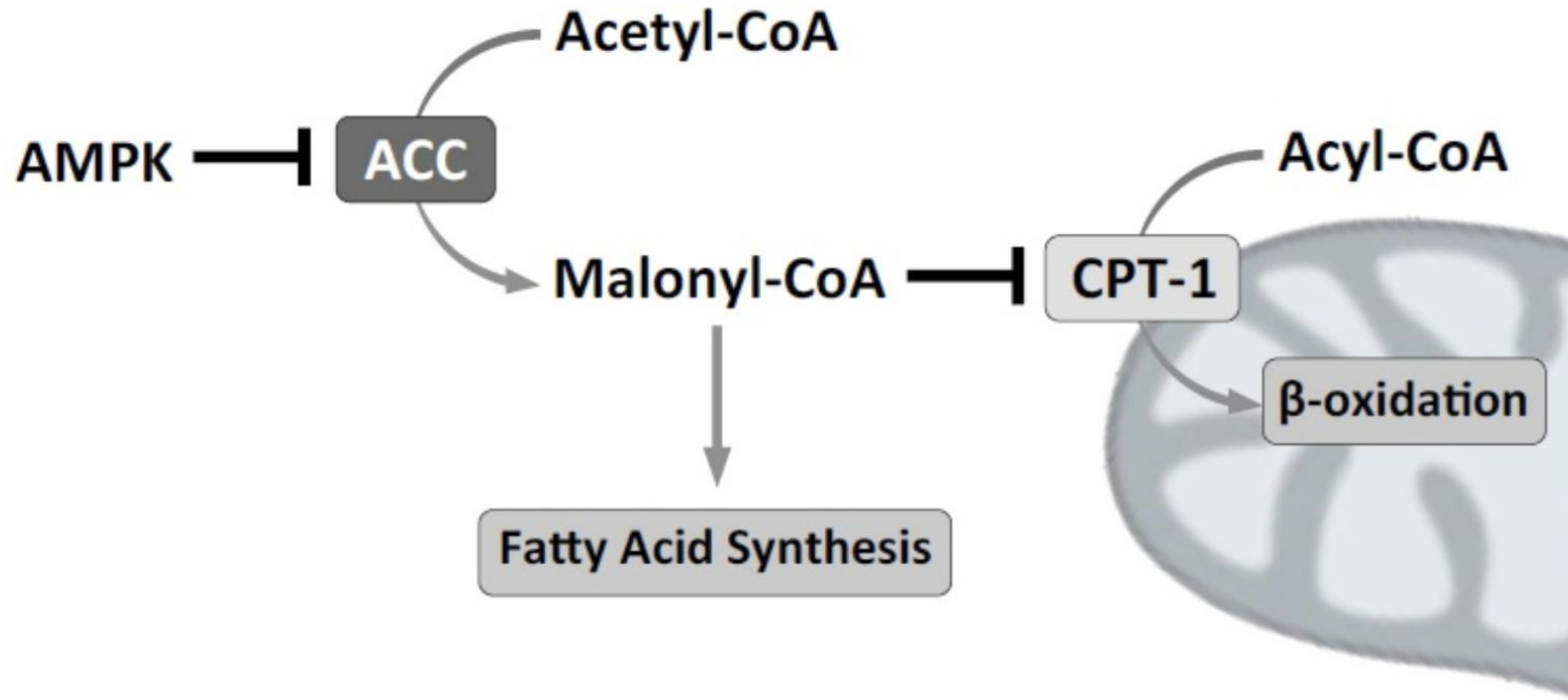
mTORC1 senses nutrients and promotes growth



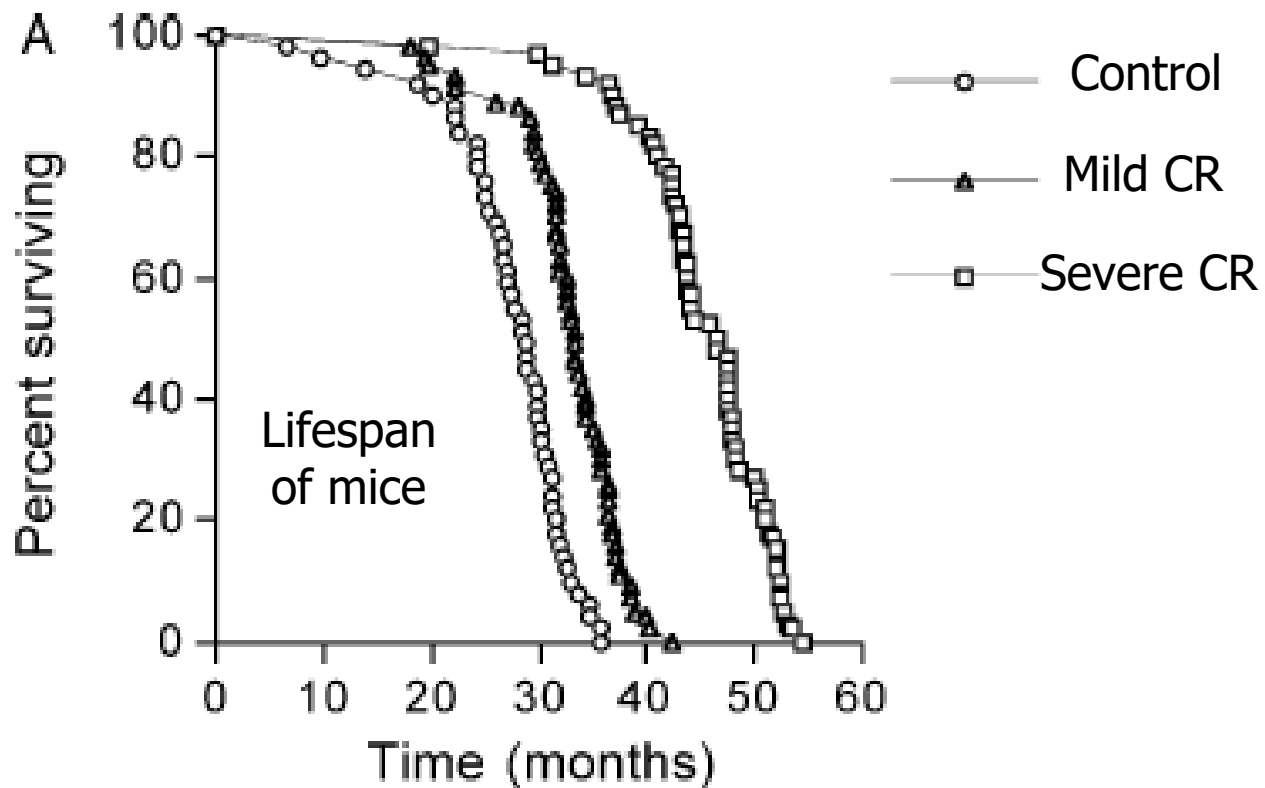
AMPK primarily senses energetic stress



AMPK switches from fat synthesis to oxidation



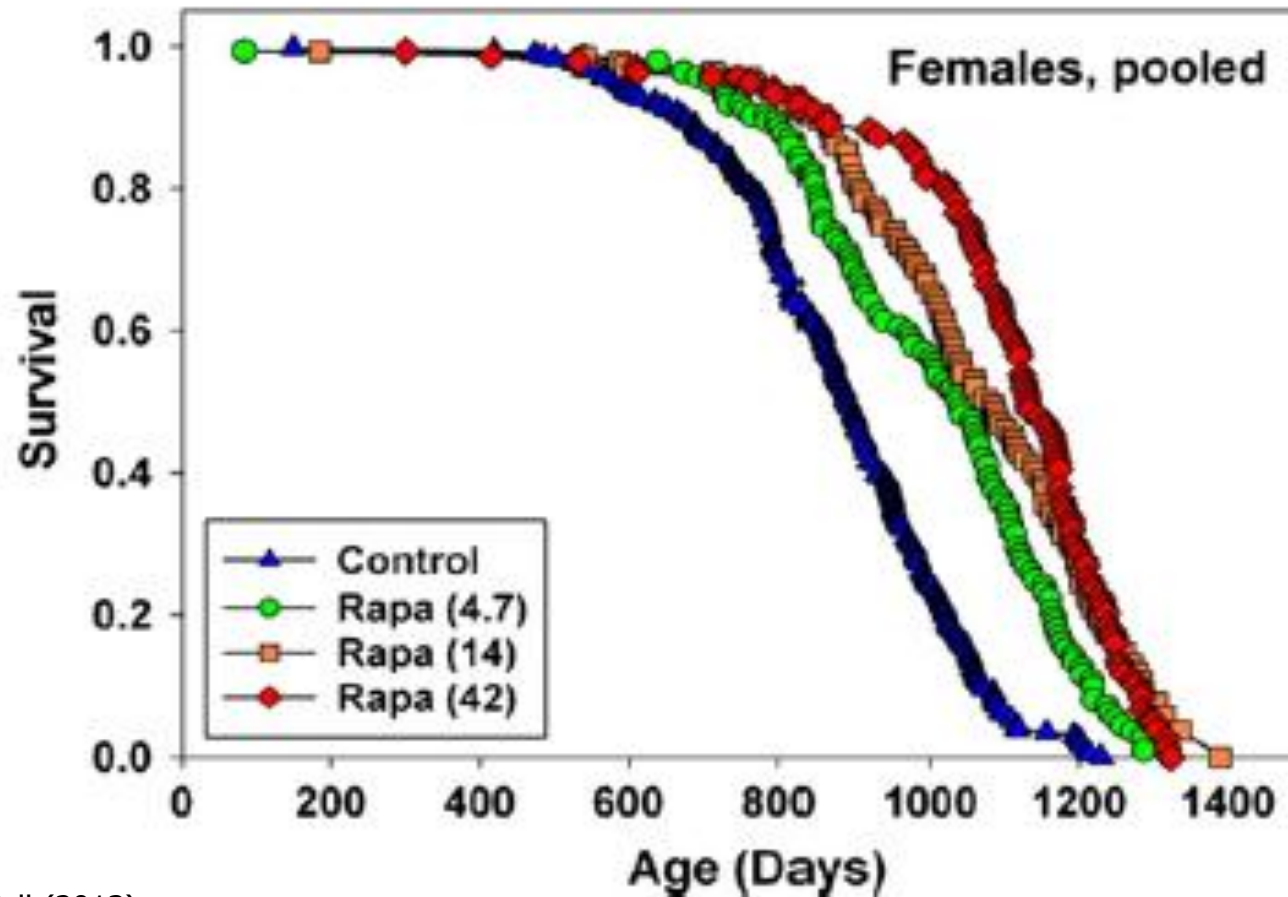
Can targeting mTORC1/AMPK mimic caloric restriction?



mTORC1 

AMPK 

mTORC1 inhibitor rapamycin extends mouse lifespan



Miller et al, Aging Cell (2013)

But may act differently from CR



Journals of Gerontology: Biological Sciences
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doi:10.1093/gerona/glz060
Advance Access publication March 11, 2019



Special Issue: Is vicTORy in sight? New advances in mTOR, rapalogs and aging

Is Rapamycin a Dietary Restriction Mimetic?

Archana Unnikrishnan, PhD,¹ Kavitha Kurup, PhD,¹ Adam B. Salmon, PhD,^{2,3} and Arlan Richardson, PhD^{1,4,*}

“...while dietary restriction and rapamycin may have similar effects on some pathways and processes; overall, they affect many pathways/processes quite differently.”

Summary

Glucose and lipid metabolism

- Blood glucose is dynamically maintained in a tight range as readily available fuel
- Lipids contain more energy and are essential to meet sustained demand
- Both are metabolized to fuel the TCA in mitochondria (and glucose generates additional ATP through glycolysis)
- Cellular sensors can respond to nutrient and energy availability

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