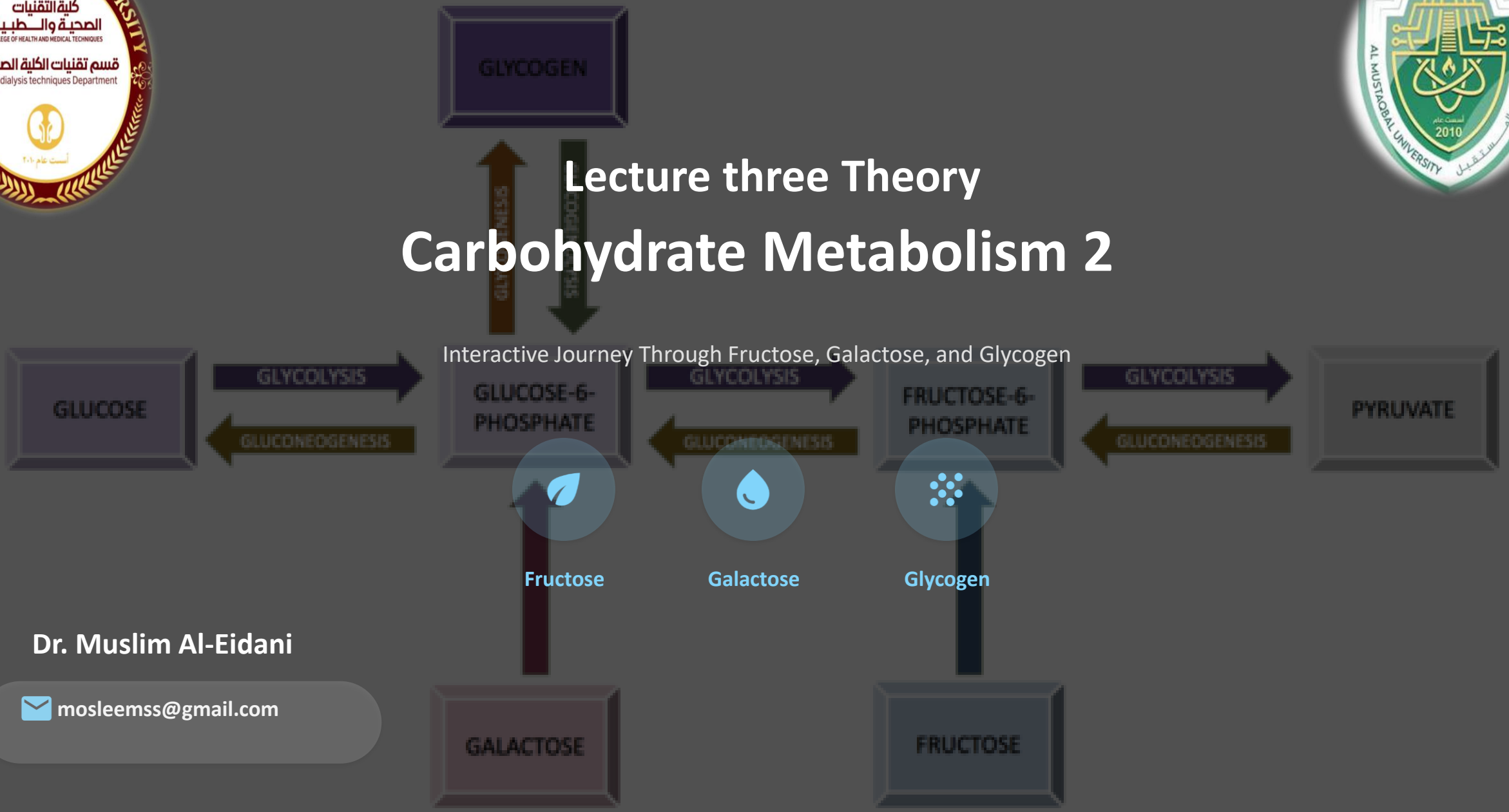
Lecture three Theory

Carbohydrate Metabolism 2

Interactive Journey Through Fructose, Galactose, and Glycogen



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Overview of Carbohydrate Metabolism

Primary Energy Source

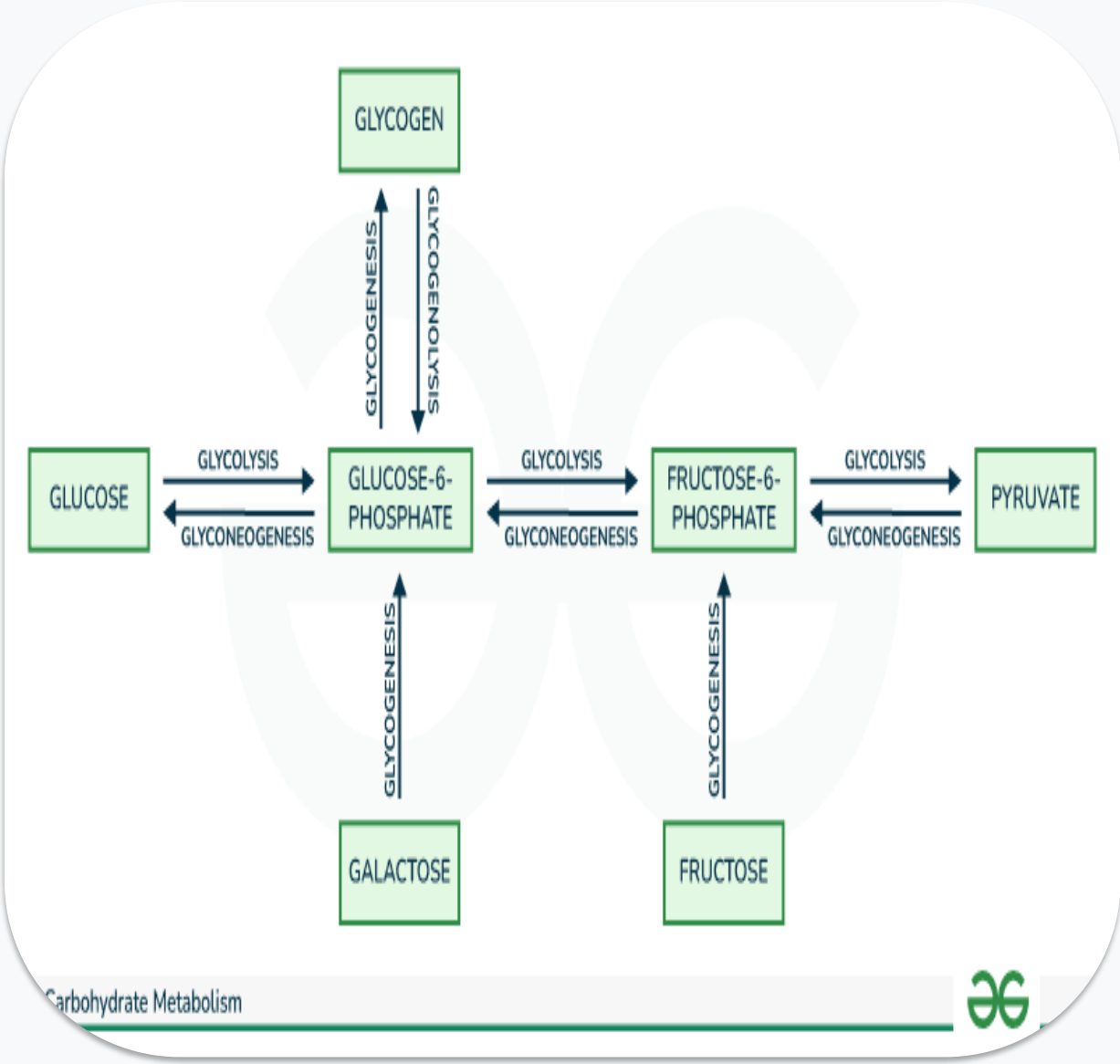
Essential for cellular functions and ATP production

Brain Function

Critical for cognitive processes and red blood cells

Biomolecule Precursors

Building blocks for nucleotides and glycoproteins



Main Types of Carbohydrates

Monosaccharides

Glucose	Primary energy source
Fructose	Fruit sugar
Galactose	Milk sugar component

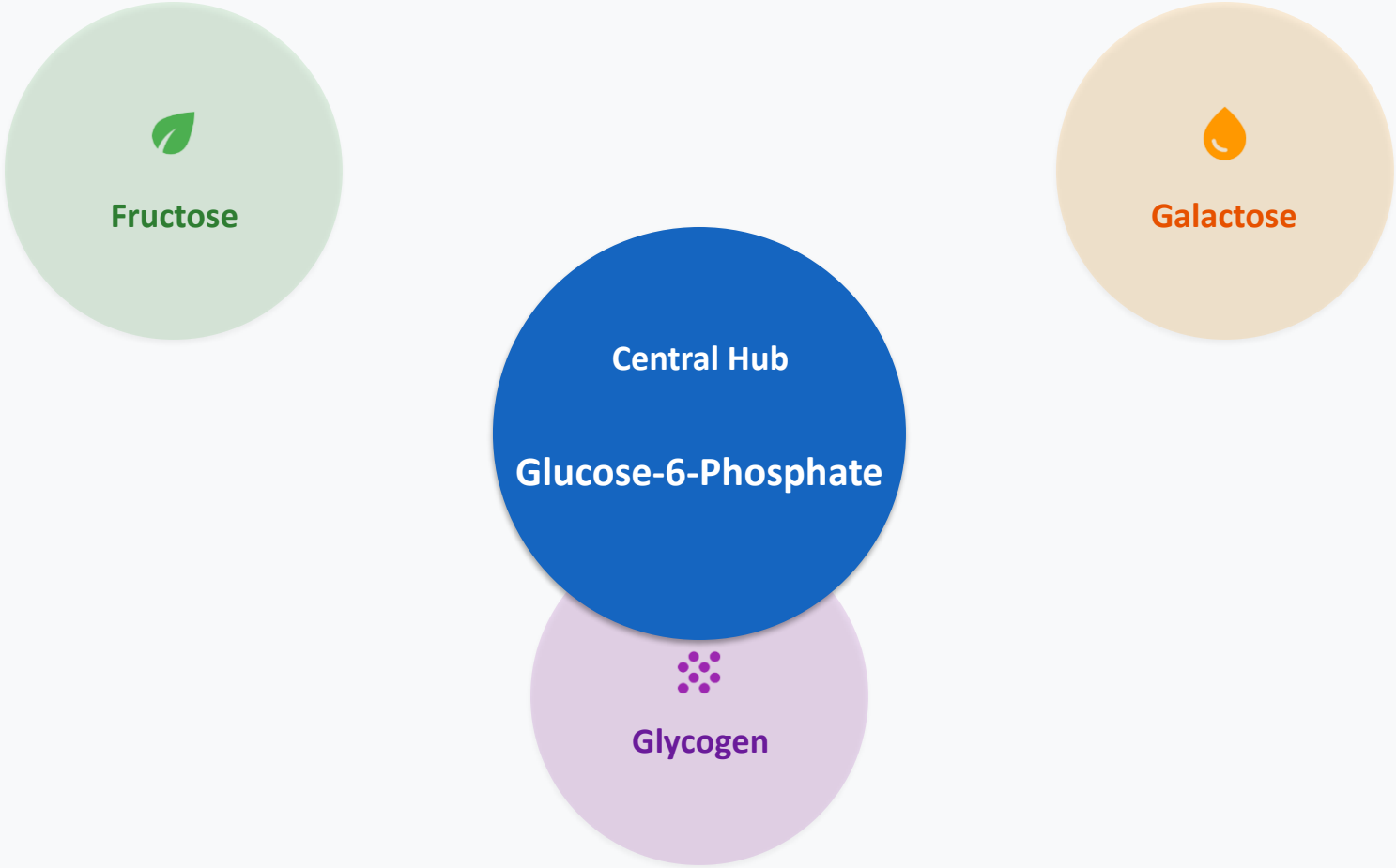
Disaccharides

Sucrose	Table sugar
Lactose	Milk sugar
Maltose	Malt sugar

Polysaccharides

Glycogen	Animal energy storage
Starch	Plant energy storage
Cellulose	Structural component

Metabolic Pathways Convergence



All three pathways converge at glucose-6-phosphate — the central hub for energy distribution

General Metabolic Fates

Immediate Energy

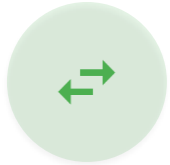
Rapid ATP production through glycolysis pathway

Fast energy source

Glycogen Storage

Short-term energy storage in liver and muscle cells

Readily accessible



Fatty Acid Conversion

Long-term energy storage as triglycerides in adipose tissue

High energy density

Fructose Metabolism - Dietary Sources

Fruits & Vegetables

Natural sources of fructose in whole foods

Honey

Natural sweetener with high fructose content

High-Fructose Corn Syrup

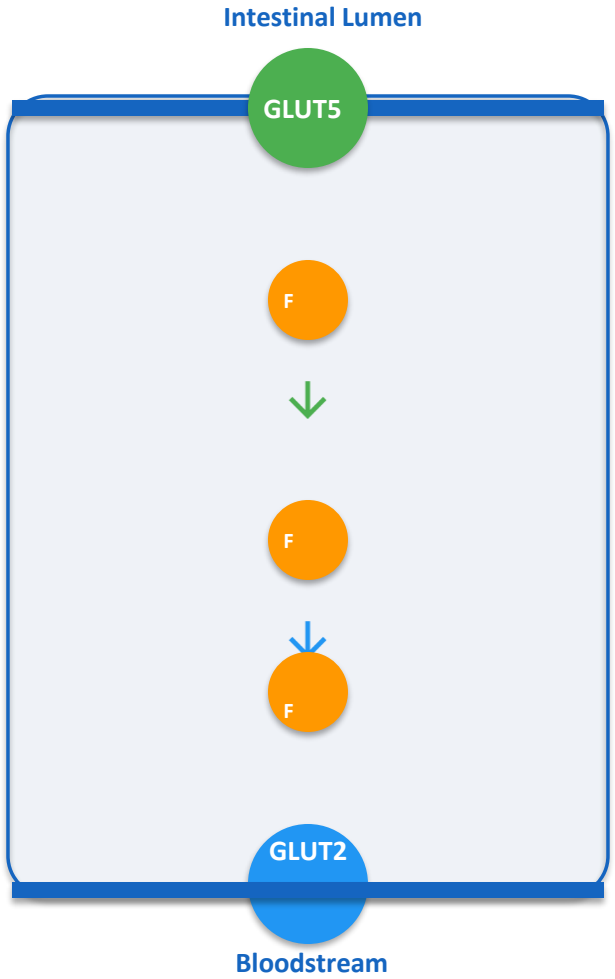
Common sweetener in processed foods and beverages

Table Sugar (Sucrose)

Disaccharide composed of glucose and fructose

Unlike glucose, fructose metabolism does not require insulin for transport into cells

Fructose Metabolism - Absorption & Transport



GLUT5 (SLC2A5)

High affinity for fructose

Apical membrane of enterocytes

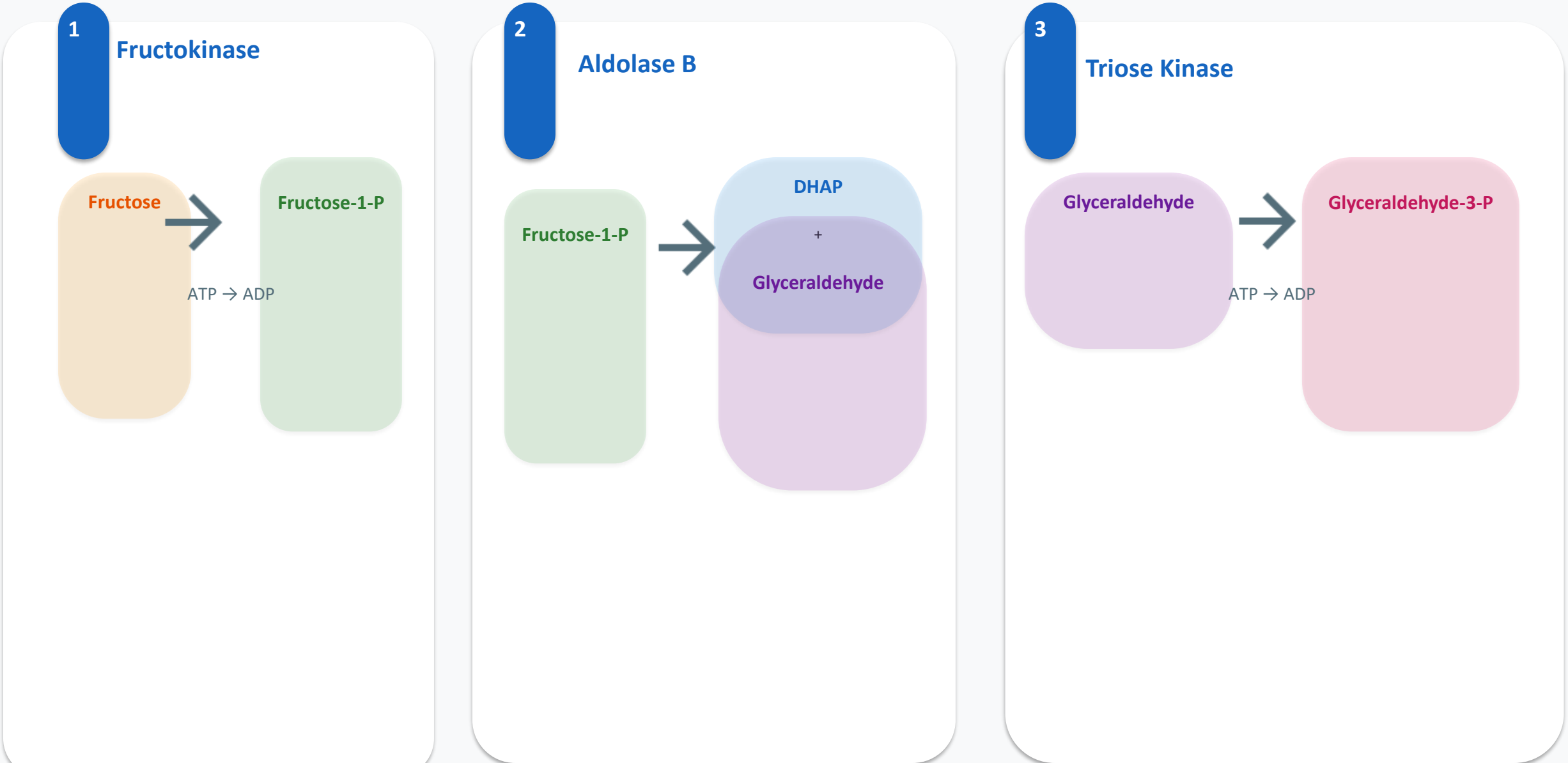
GLUT2 (SLC2A2)

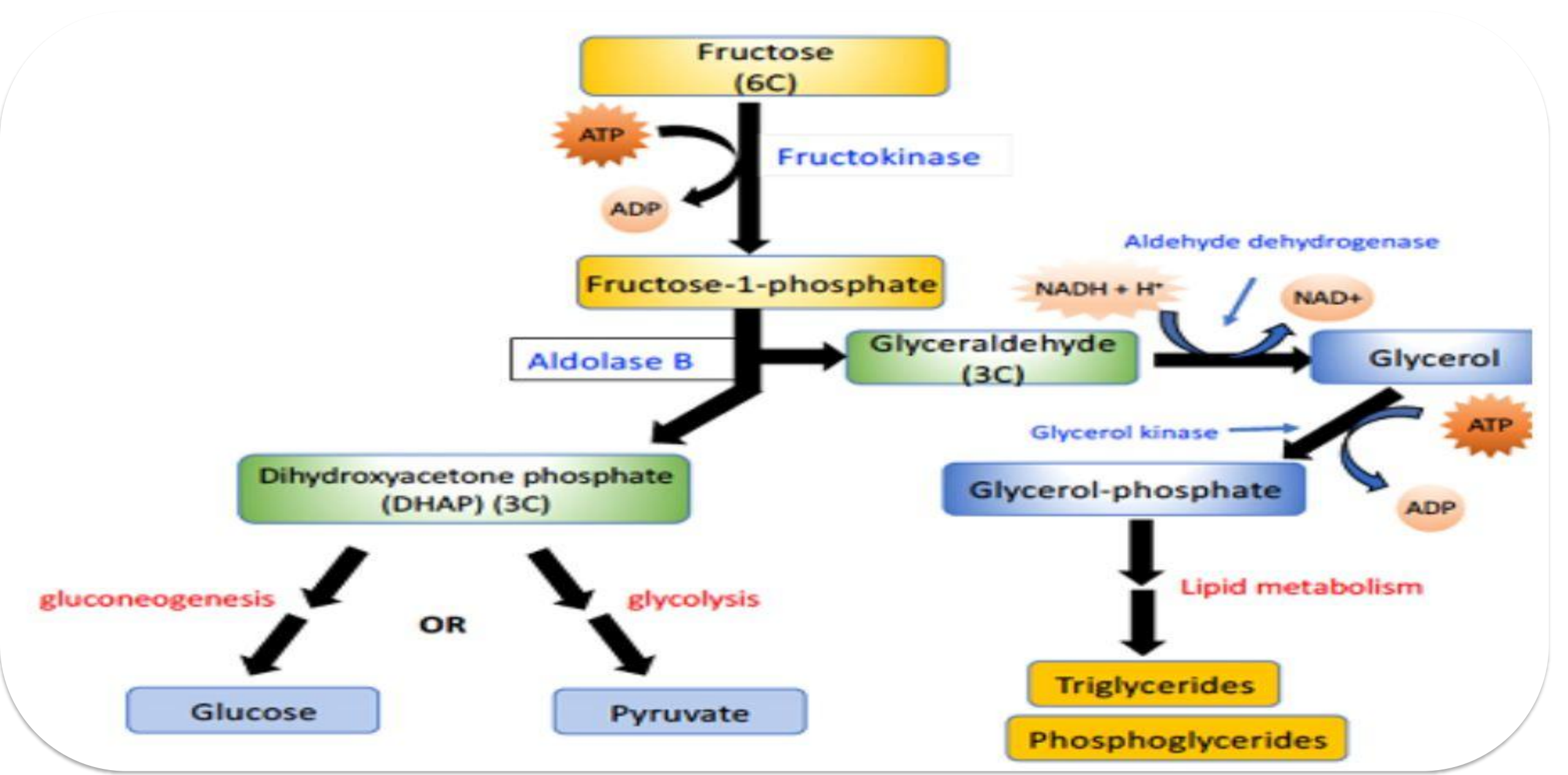
Transports fructose into bloodstream

Basolateral membrane

Unlike glucose, fructose metabolism does not require insulin for transport into cells

Fructose Metabolism - Metabolic Pathway





Fructose metabolism bypasses the rate-limiting step of glycolysis (PFK-1), allowing rapid metabolism

Fructose Metabolism - Regulation & Physiological Functions

Bypasses PFK-1

Avoids the rate-limiting step of glycolysis

No Hormonal Regulation

Not controlled by insulin or glucagon

Promotes Hepatic Uptake

Enhances glucose uptake and glycogen storage in liver

Accelerates Oxidation

Speeds up carbohydrate oxidation after meals

Fructose metabolism provides rapid energy without the normal regulatory controls of glucose metabolism

Fructose Metabolism - Clinical Significance

Hereditary Fructose Intolerance

Genetic Basis

Autosomal recessive disorder caused by **aldolase B deficiency**

Prevalence

Affects approximately **1 in 20,000** people worldwide

Onset

Symptoms appear after weaning when fructose is introduced to diet

Biochemical Basis

Fructose-1-phosphate accumulation in liver and kidney

Depletion of inorganic phosphate & ATP

Inhibition of gluconeogenesis & glycogenolysis

Case Study

Patient:	8-month-old infant
Symptoms:	Vomiting after fruit introduction, failure to thrive
Diagnosis:	Genetic testing confirmed ALDOB mutation
Treatment:	Fructose-restricted diet

Management Strategies

- Fructose-restricted diet
- Early diagnosis crucial for preventing complications
- Avoid sucrose, sorbitol, and fructose-containing foods
- Regular monitoring of liver function and growth

Galactose Metabolism - Dietary Sources

Lactose in Milk & Dairy

Primary source of galactose in adult diet

Some Fruits & Vegetables

Minor sources of galactose in whole foods

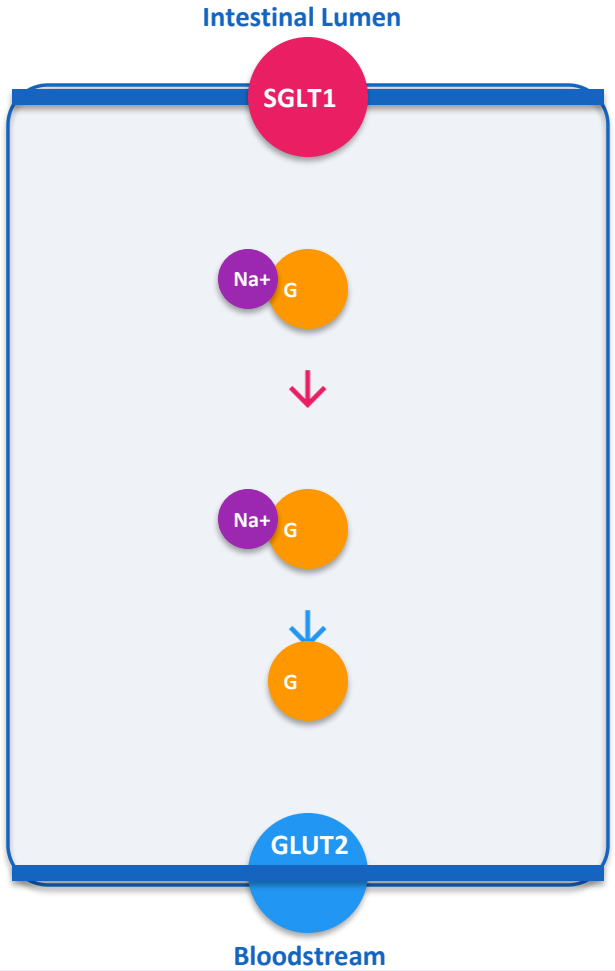
Galactose shares transport mechanisms with glucose, explaining efficient intestinal absorption

Infant Nutrition

Galactose is the **primary carbohydrate source** in breast milk, making it essential for infant development

- Essential for brain development
- Building block for glycoproteins
- Critical for cell signaling

Galactose Metabolism - Absorption & Transport



SGLT1

Active transport with sodium

Apical membrane

GLUT2

Facilitated diffusion

Basolateral membrane

Galactose shares transport mechanisms with glucose, explaining efficient intestinal absorption

Galactose Metabolism - Leloir Pathway

1

Galactokinase (GALK)

Galactose → Gal-1-P

ATP → ADP

2

Galactose-1-P Uridylyltransferase (GALT)

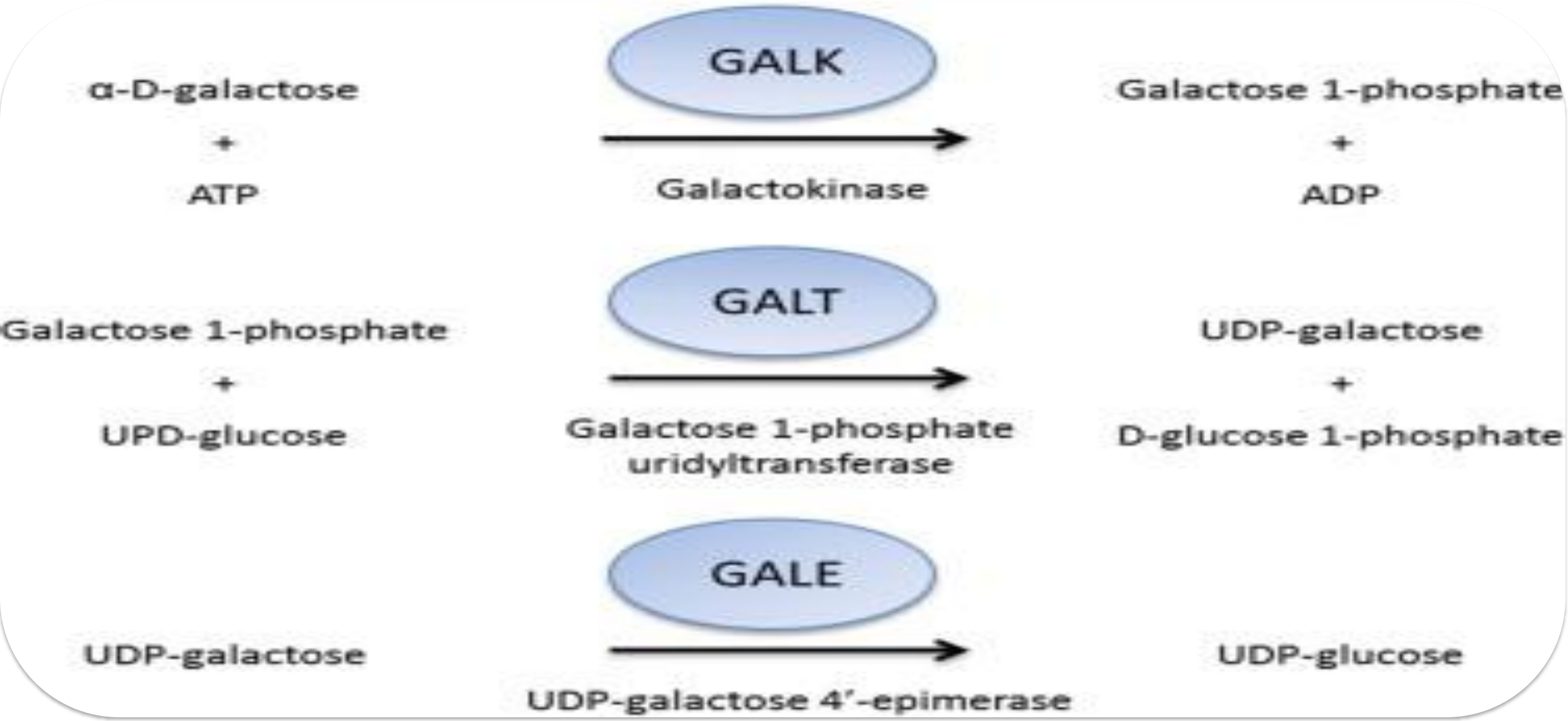
Gal-1-P + UDP-Glc → UDP-Gal + Glc-1-P

3

UDP-Galactose 4-Epimerase (GALE)

UDP-Gal ⇄ UDP-Glc

Reversible reaction



Leloir pathway converts galactose to glucose-6-phosphate, allowing entry into glycolysis or glycogen storage

Galactose Metabolism - Clinical Significance

I

Classic Type

GALT deficiency (most severe)

II

Type II

Galactokinase deficiency

III

Type III

UDP-galactose 4-epimerase deficiency

Affects 1 in 30,000-60,000 newborns • Included in newborn screening programs

Clinical Management

Galactosemia requires **lifelong dietary management** to prevent serious complications affecting multiple organ systems

Common Symptoms

- Jaundice
- Vomiting
- Hepatomegaly
- Hypoglycemia
- Cataracts
- Developmental delay

Glycogen Metabolism - Structural Features

α-1,4 Linear Chains

Linear chains of glucose units form the backbone structure

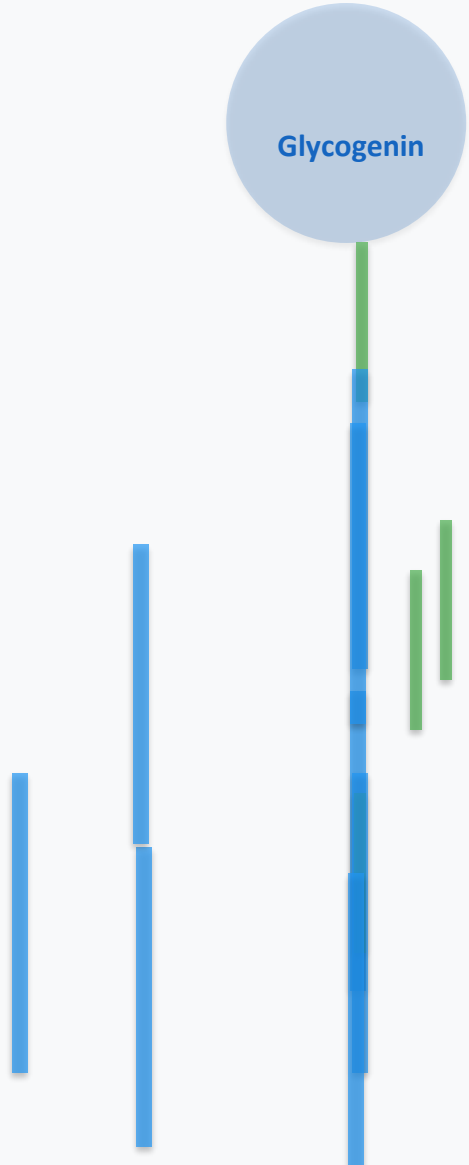
α-1,6 Branch Points

Branch points occur every **8-12 residues**

Compact Storage

Branched structure allows up to **10,000 glucose molecules** in soluble form

Highly branched structure maximizes storage efficiency and accessibility



Glycogen Metabolism - Storage Locations

Liver

4-6%

of liver weight

Primary Function

Maintains blood glucose levels

Muscle

1-2%

of muscle weight

Primary Function

Provides local energy for muscle contraction

Dynamic Equilibrium

Balance between synthesis and breakdown • Hormonal regulation by **insulin** and **glucagon**

Glycogen Metabolism - Glycogenolysis (Breakdown)

1

Glycogen Phosphorylase

Glycogen → Glucose-1-P

Rate-limiting enzyme • Activated by phosphorylation

2

α-1,4 →α-1,4 Glucan Transferase

Trisaccharide → Branch Point

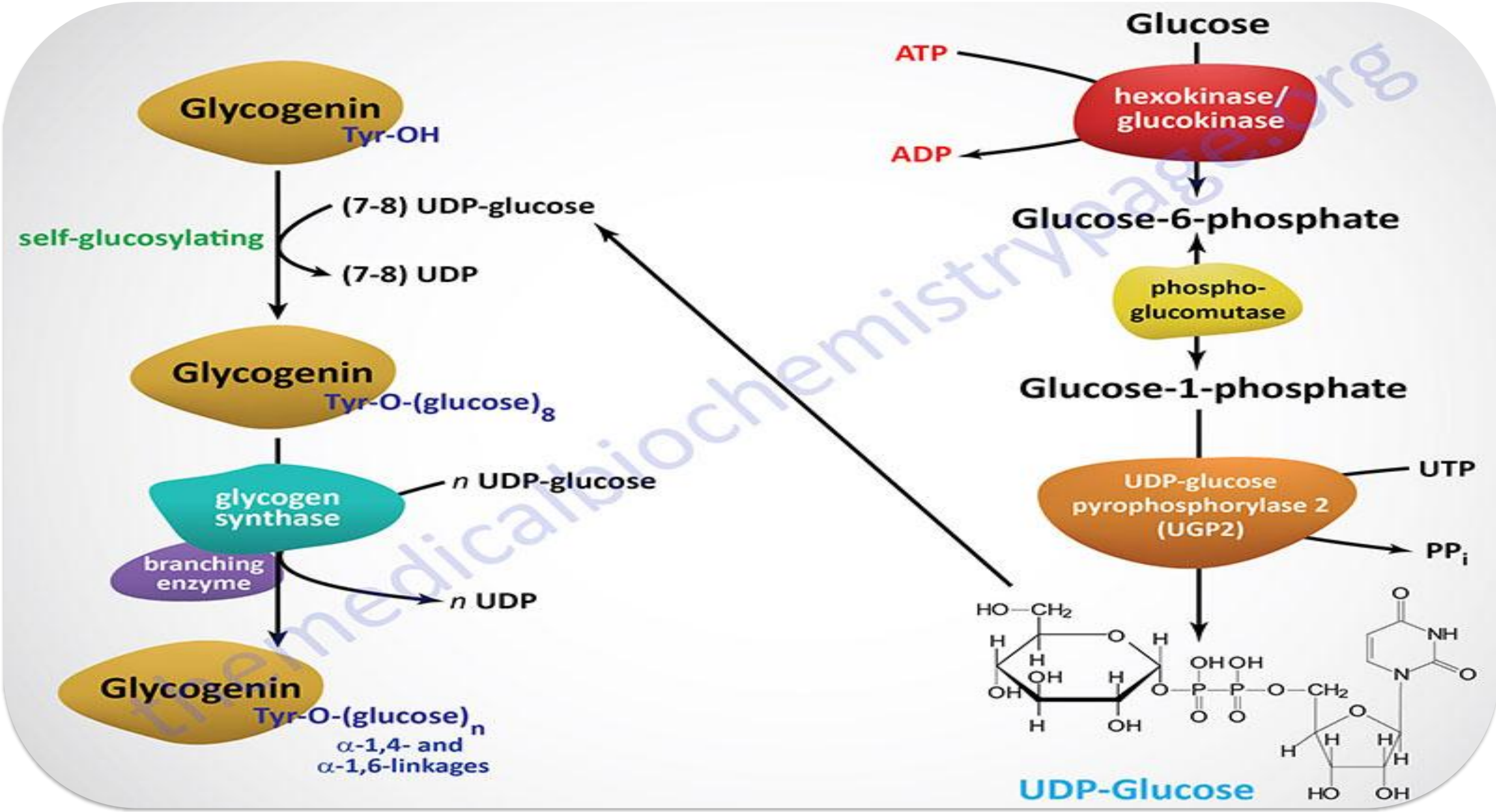
Transfers 3 glucose units to expose branch point

3

Debranching Enzyme

α-1,6 Linkage → Free Glucose

Hydrolyzes α-1,6 linkage to release free glucose



Glycogen Metabolism - Hormonal Regulation

Glucagon

Stimulates liver glycogenolysis during fasting

Epinephrine

Stimulates muscle & liver glycogenolysis (fight-or-flight)

Insulin

Inhibits glycogenolysis, stimulates glycogenesis

Signal Cascade

1. Hormone
2. Receptor
3. Adenylate Cyclase
4. cAMP
5. PKA
6. Phosphorylase Kinase
7. Glycogen Phosphorylase

Hormonal regulation maintains glucose homeostasis through precise control of glycogen synthesis and breakdown

Glycogen Metabolism - Clinical Significance

I

Von Gierke Disease

Glucose-6-phosphatase deficiency

- Severe hypoglycemia
- Hepatomegaly

II

Pompe Disease

Acid maltase deficiency

- Lysosomal glycogen accumulation
- Cardiomegaly

III

Cori Disease

Debranching enzyme deficiency

- Mild hypoglycemia
- Hepatomegaly

V

McArdle Disease

Muscle phosphorylase deficiency

- Exercise intolerance
- Myoglobinuria

Management Strategies

Dietary modifications • Enzyme replacement therapy • Gene therapy (experimental) • **Early diagnosis crucial** for preventing complications

Integration of Metabolic Pathways

Glycolysis

Glycogen Storage

Pentose Phosphate Pathway

All three carbohydrate pathways converge at glucose-6-phosphate, serving as a central metabolic hub for flexible energy distribution based on cellular needs

Summary: Metabolic Pathway Comparison

Fructose Metabolism

- Bypasses PFK-1
- No hormonal regulation
- Hereditary intolerance

Galactose Metabolism

- Essential for infants
- Leloir pathway
- Galactosemia types

Glycogen Metabolism

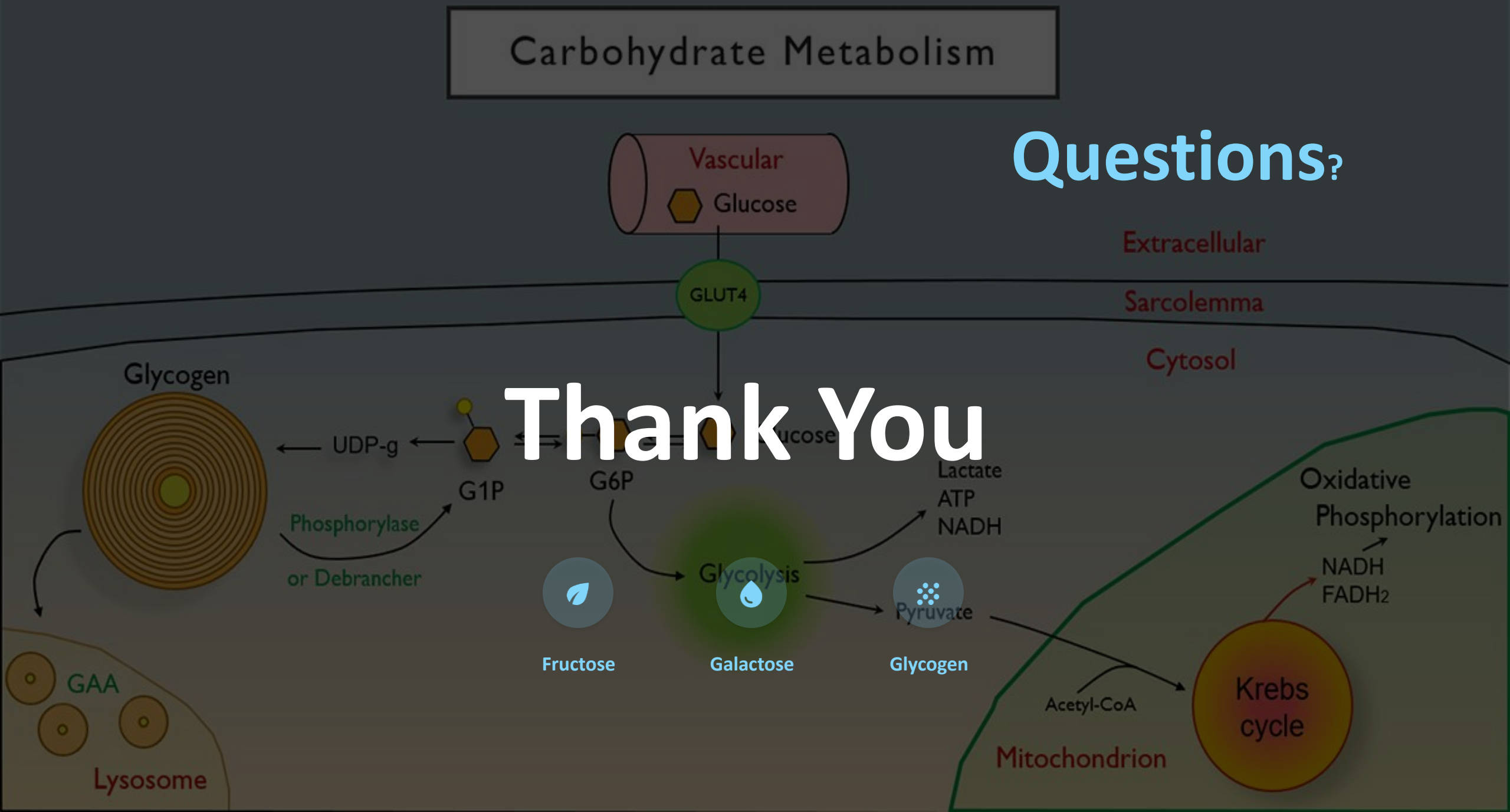
- Branched structure
- Hormonal regulation
- Storage diseases

Central Metabolic Hub

Glucose-6-Phosphate

All three pathways converge at **G6P**, allowing flexible energy distribution based on cellular needs

Understanding these metabolic processes is crucial for maintaining energy homeostasis and managing related clinical disorders



Questions?

Thank You