Author(s): Arno Kumagai, M.D., 2009

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Islet Cell Hormones

And

Hormonal Regulation of Fuel Metabolism

M2-Endocrine Sequence
Arno K. Kumagai, M.D
Dept. of Internal Medicine

Winter 2009

University of Michigan
Medical School

Normal Physiology

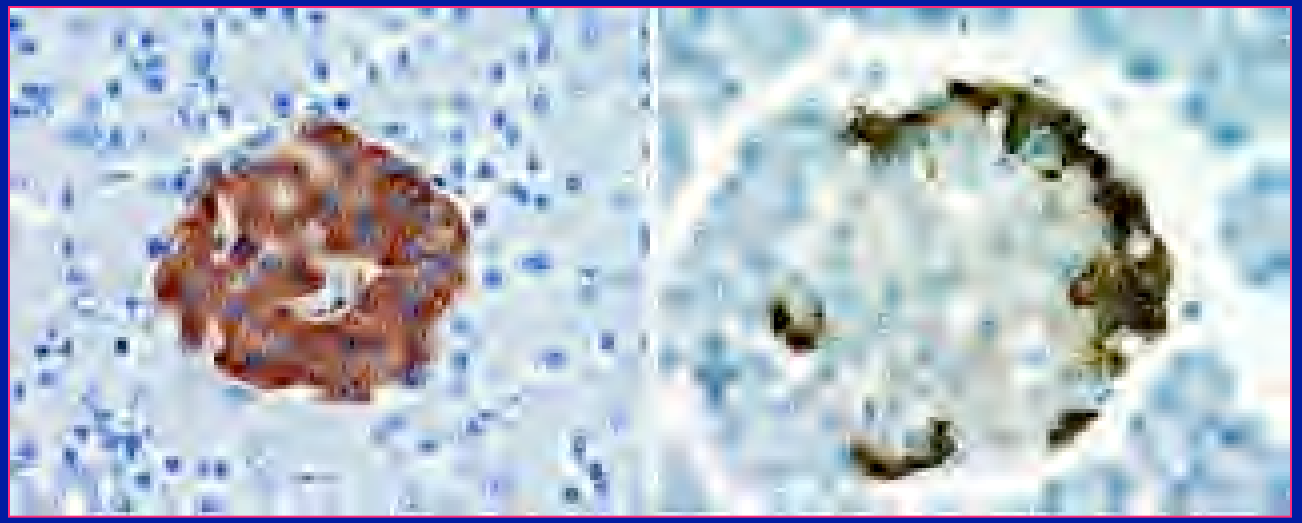
ISLET CELL HORMONES

Alpha Cells:
GLUCAGON

Beta Cells:
INSULIN
(AND AMYLIN)

Normal Physiology

ISLET CELL HORMONES



Alpha Cells:
GLUCAGON

Beta Cells:
INSULIN
(AND AMYLIN)

Response to a meal

Islet hormone secretion varies with circulating glucose levels

Meal increases:

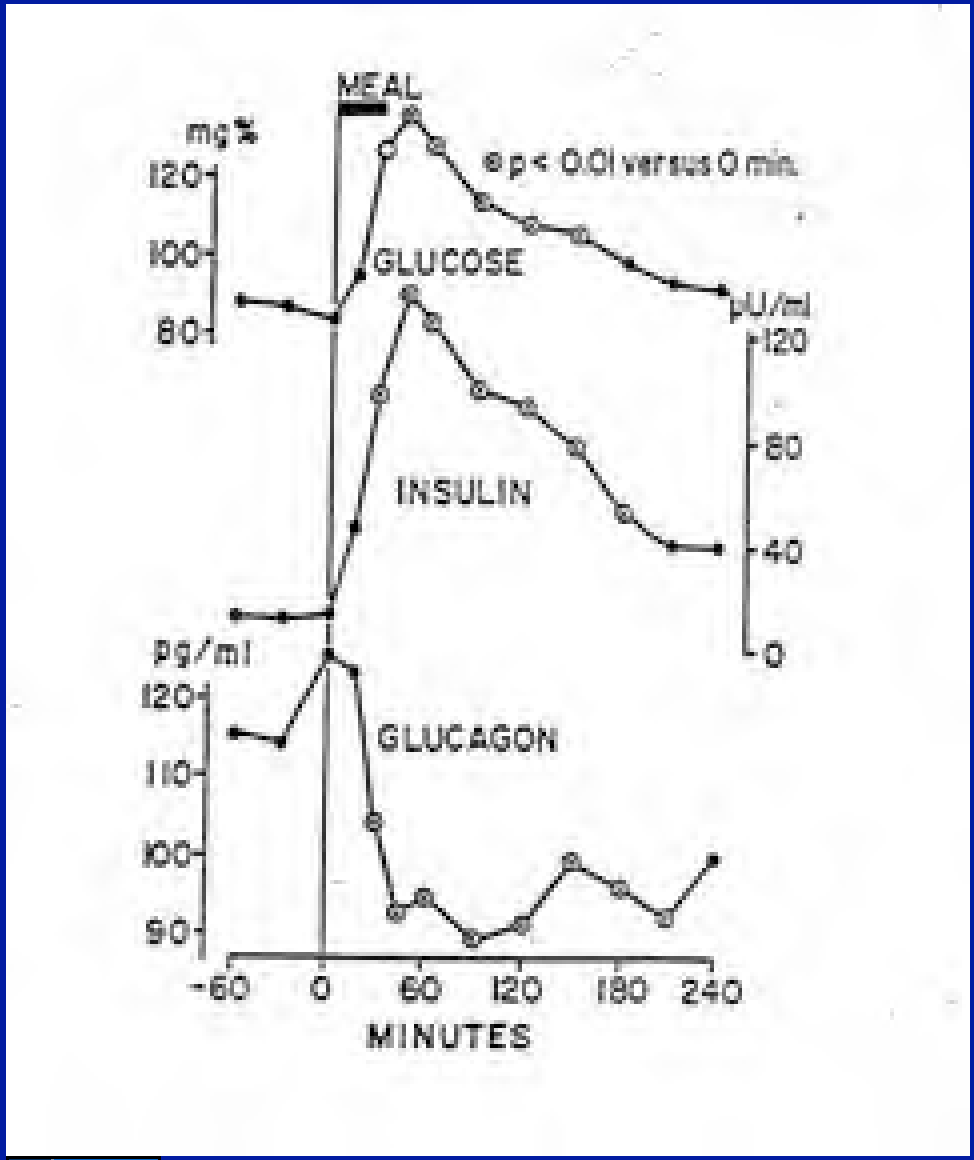
Glucose

⟶ increased **insulin**

⟶ decreased **glucagon**

Amino acids, FA

⟶ increased **insulin**



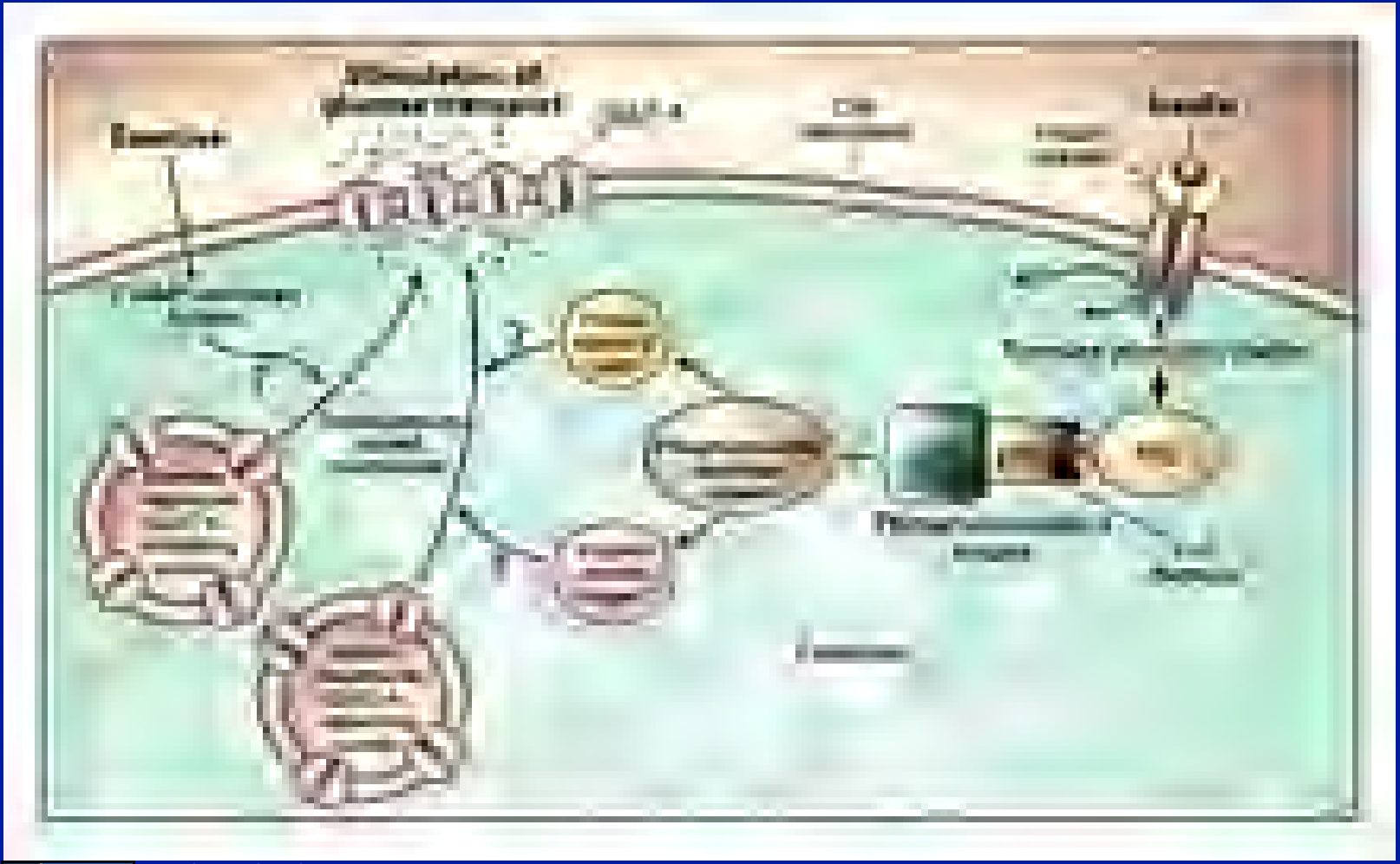
Normal Insulin Physiology

STIMULI FOR INSULIN SECRETION:

GLUCOSE
Amino Acids
Fatty Acids

INSULIN

Insulin Action



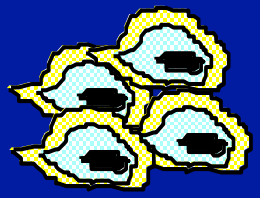
Insulin Actions

Insulin stores stuff…

Insulin Action

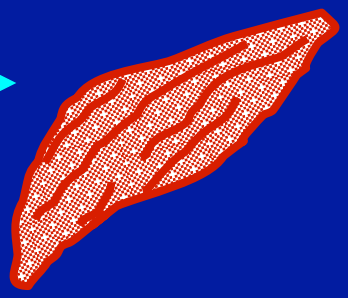
INSULIN

- Increases glycogen synthesis
- Increases glycolysis
- Inhibits gluconeogenesis



FAT

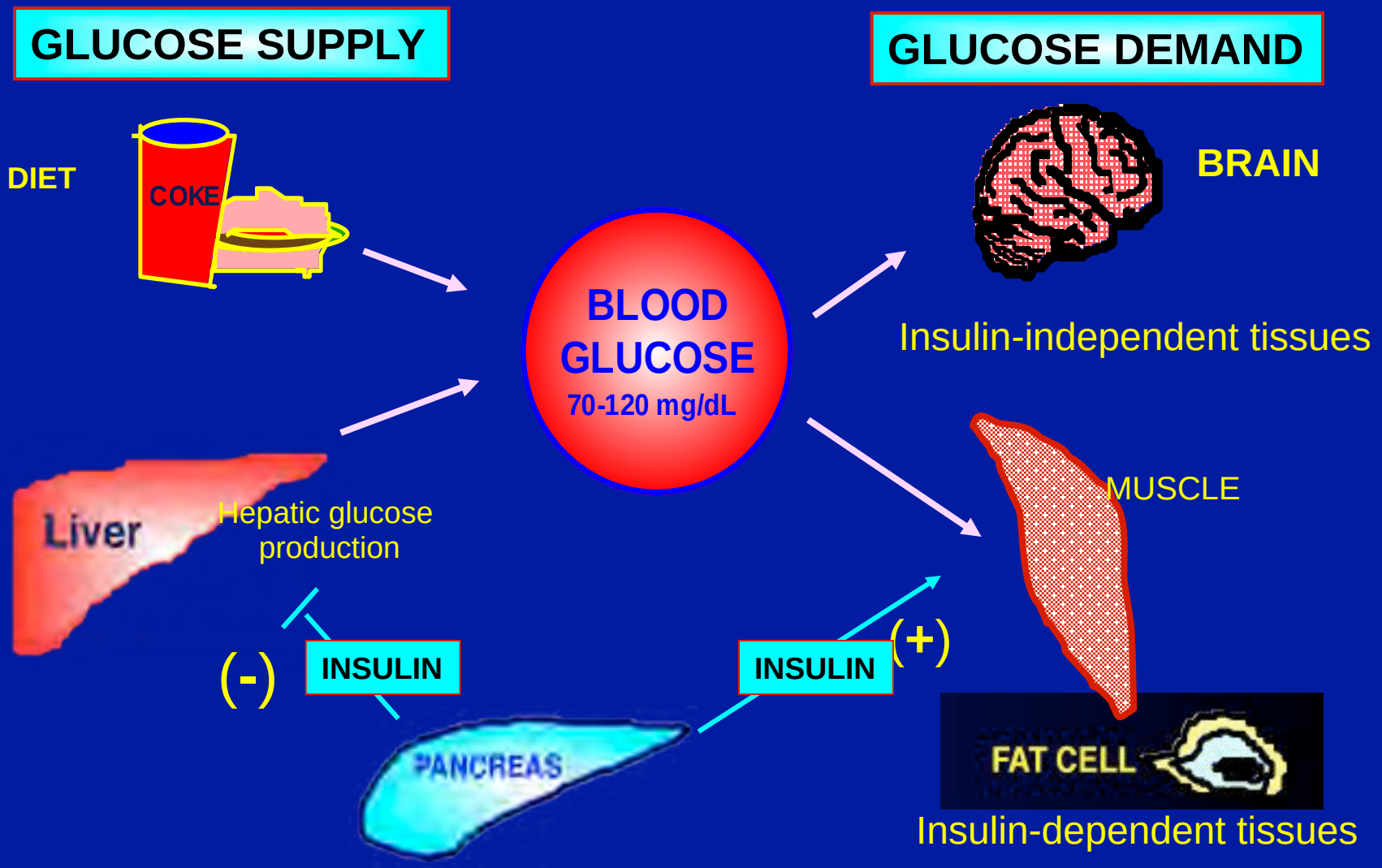
- Increases glucose transport
- Increases lipogenesis
- Inhibits lipolysis



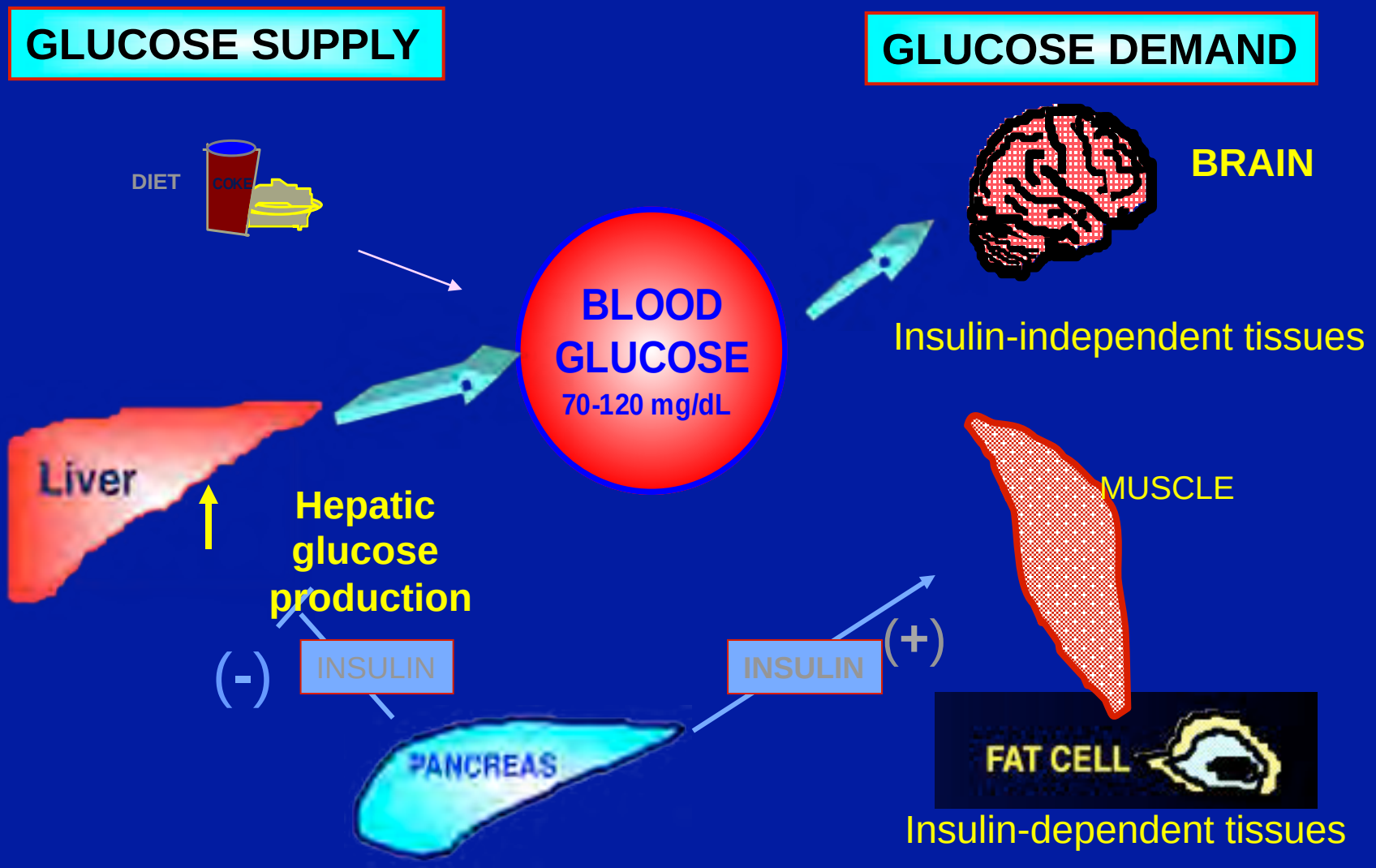
SKELETAL MUSCLE

- Increases glucose transport
- Increases glycogen synthesis
- Inhibits gluconeogenesis

Normal Glucose Metabolism

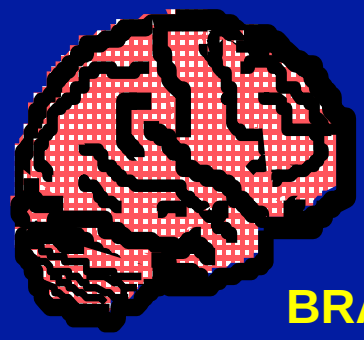


Normal Glucose Metabolism:
The Fasting State or "Feeding the Head"



 A. Kumagai

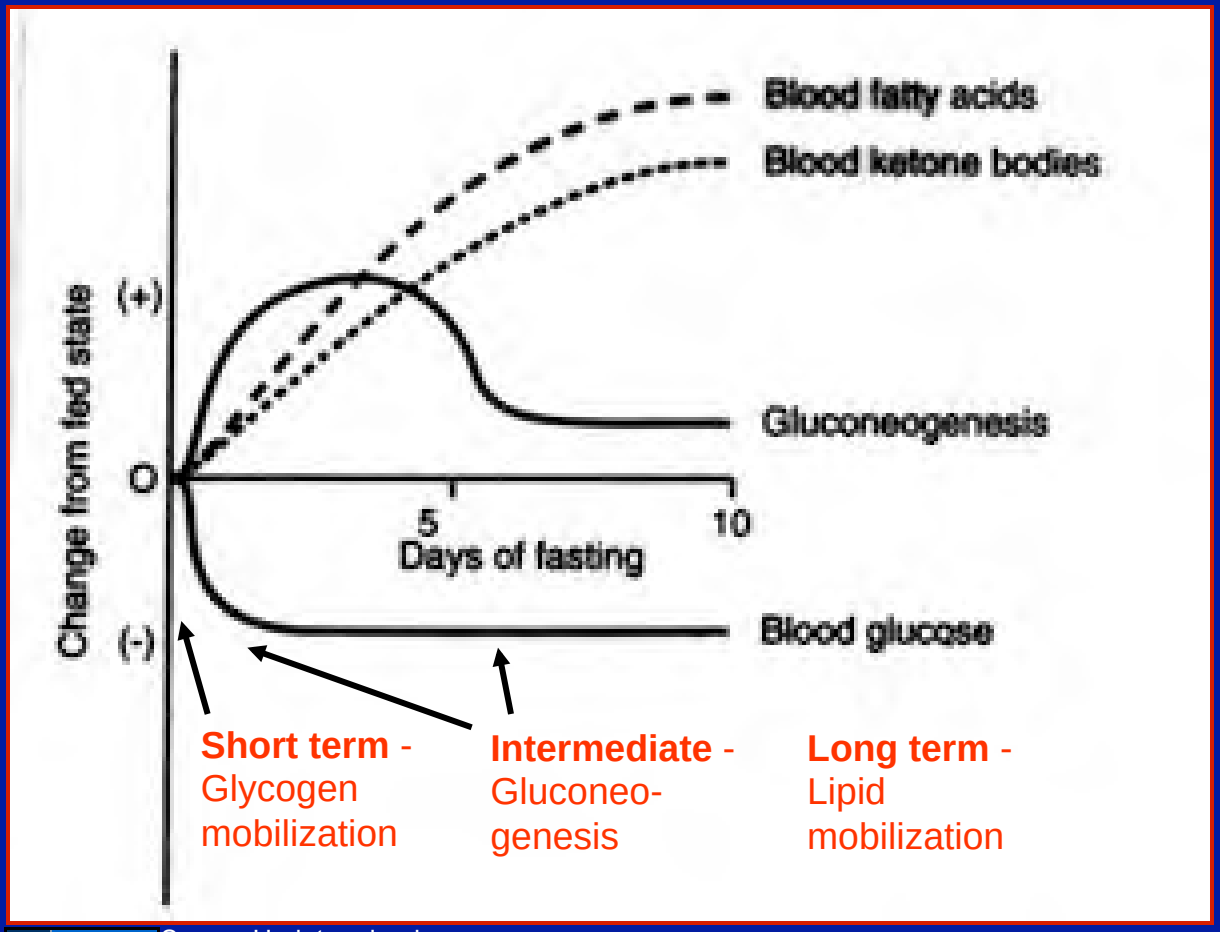
The Brain = Obligate Glucose Consumer



BRAIN

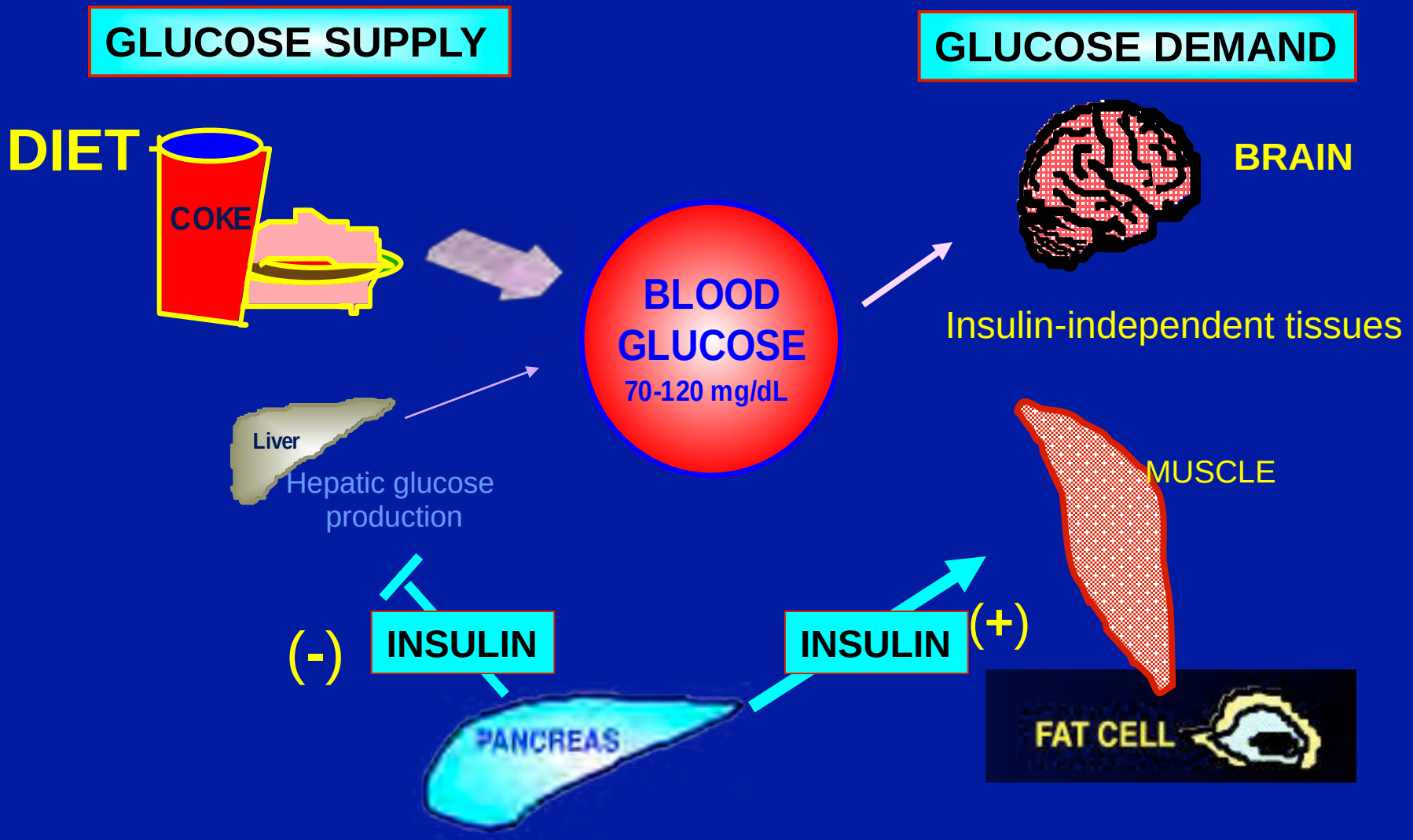
The adult brain is completely dependent on glucose for normal metabolism until >5 days into a fast

Metabolic Changes During Fasting



PD-INCL Source Undetermined

Normal Glucose Metabolism: The Fed State



INSULIN-GLUCAGON RELATIONSHIPS

STORAGE

MOBILIZATION

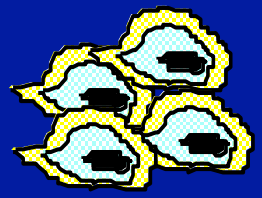
Glycogenesis and decreased blood glucose

Glucoenogenesis and increased blood glucose

Insulin Action

INSULIN

- Increases glycogen synthesis
- Increases glycolysis
- Inhibits gluconeogenesis



FAT

- Increases glucose transport
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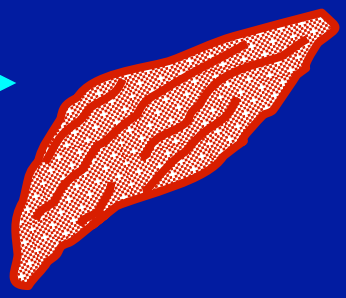
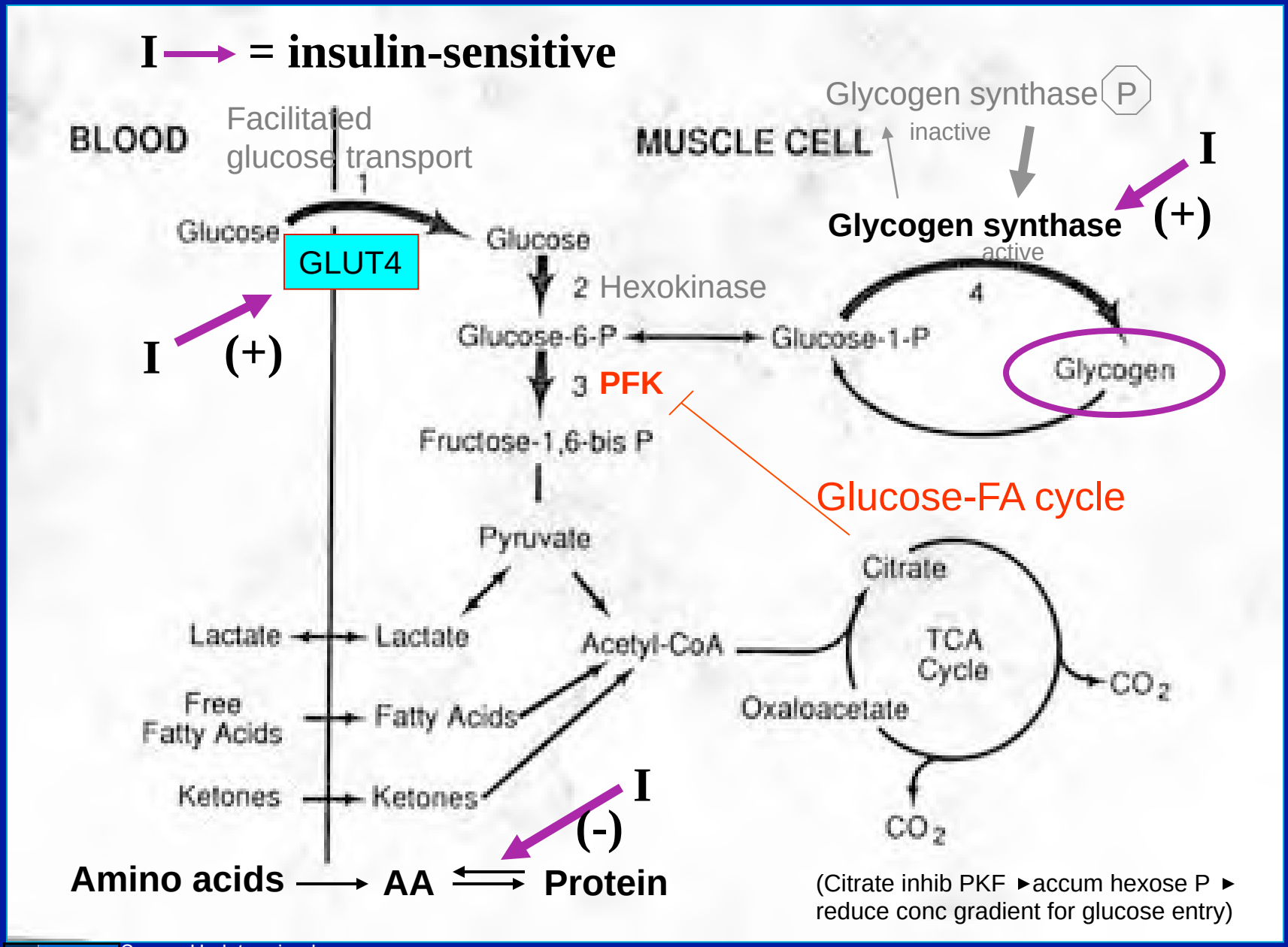
- Inhibits lipolysis



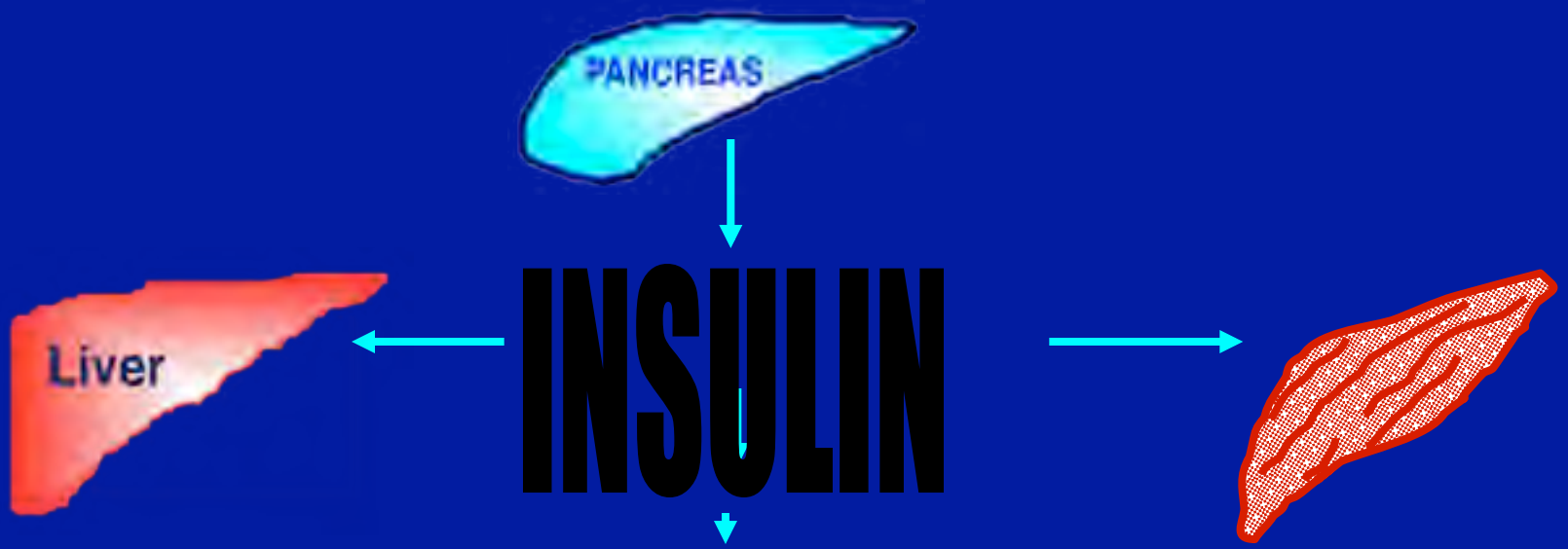
SKELETAL MUSCLE

- Increases glucose transport
- Increases glycogen synthesis
- Inhibits gluconeogenesis

Insulin-regulated steps in muscle carbohydrate metabolism



Insulin Action



- Increases glycogen synthesis
- Increases glycolysis
- Inhibits gluconeogenesis

FAT

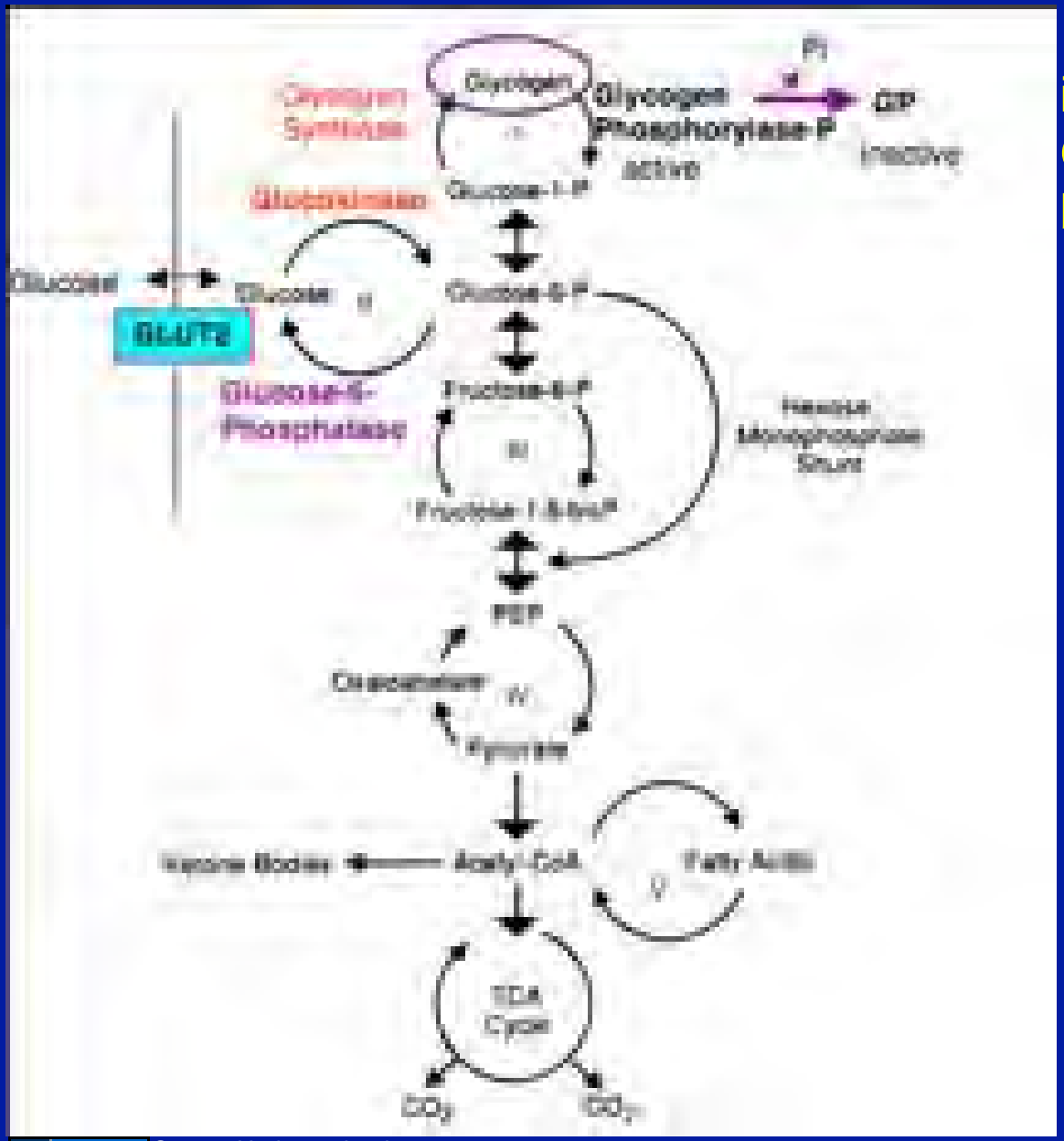
- Increases glucose transport
- Increases lipogenesis
- Inhibits lipolysis

SKELETAL MUSCLE

- Increases glucose transport
- Increases glycogen synthesis
- Inhibits gluconeogenesis

Carbohydrate Metabolism in Hepatocytes
Insulin inhibits glucose production

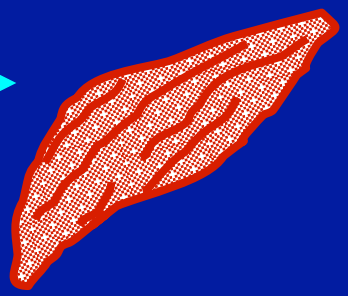
Insulin
Stimulates
glycogen storage

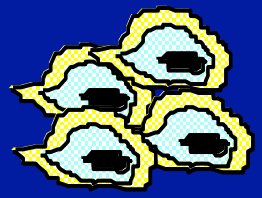


Insulin
inhibits
Glycogen
breakdown

Insulin Action

INSULIN





FAT

- Increases glucose transport
- Increases lipogenesis
- Inhibits lipolysis

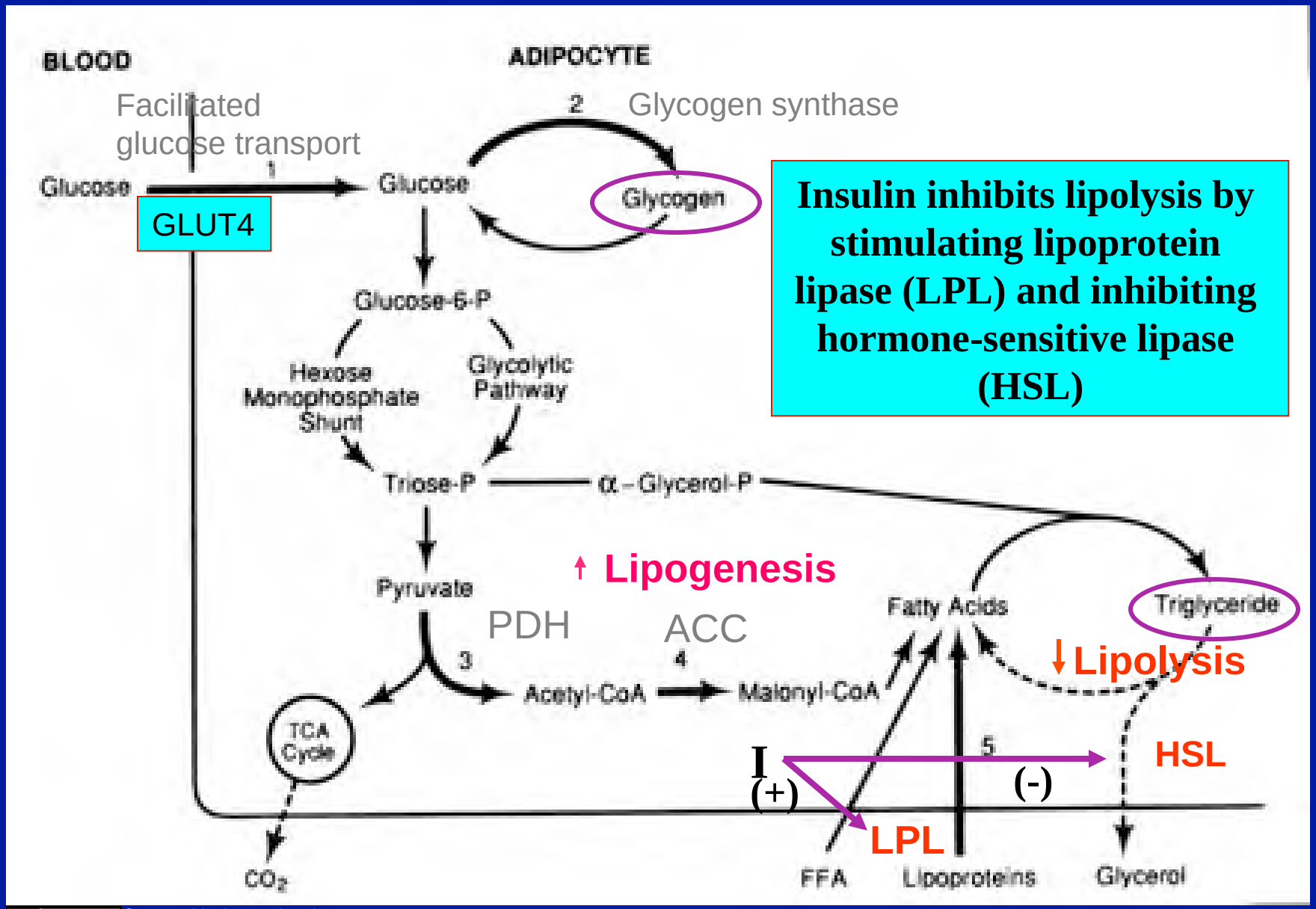
SKELETAL MUSCLE

- Increases glucose transport
- Increases glycogen synthesis
- Inhibits gluconeogenesis

LIVER

- Increases glycogen synthesis
- Increases glycolysis
- Inhibits gluconeogenesis

Insulin-regulated carbohydrate metabolism: adipocyte



Insulin inhibits lipolysis by stimulating lipoprotein lipase (LPL) and inhibiting hormone-sensitive lipase (HSL)

Fuel Metabolism: Take-Home Points

Understand:

1. That insulin binding to its receptor initiates a cascade of signaling pathways that results in translocation of the insulin-sensitive GLUT4 to the plasma membrane and increased glucose uptake.
2. The changes in insulin secretion in fasting and fed states and the physiologic "rationale" for preserving brain glucose uptake.

Fuel Metabolism: Take-Home Points

Understand:

3. The actions of insulin on skeletal muscle, liver, and fat.
4. The biochemistry: understand that insulin *stores* (e.g., stimulates glycogen synthase and lipoprotein lipase) and inhibits catabolism (e.g., inhibits HSL).

Additional Source Information

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