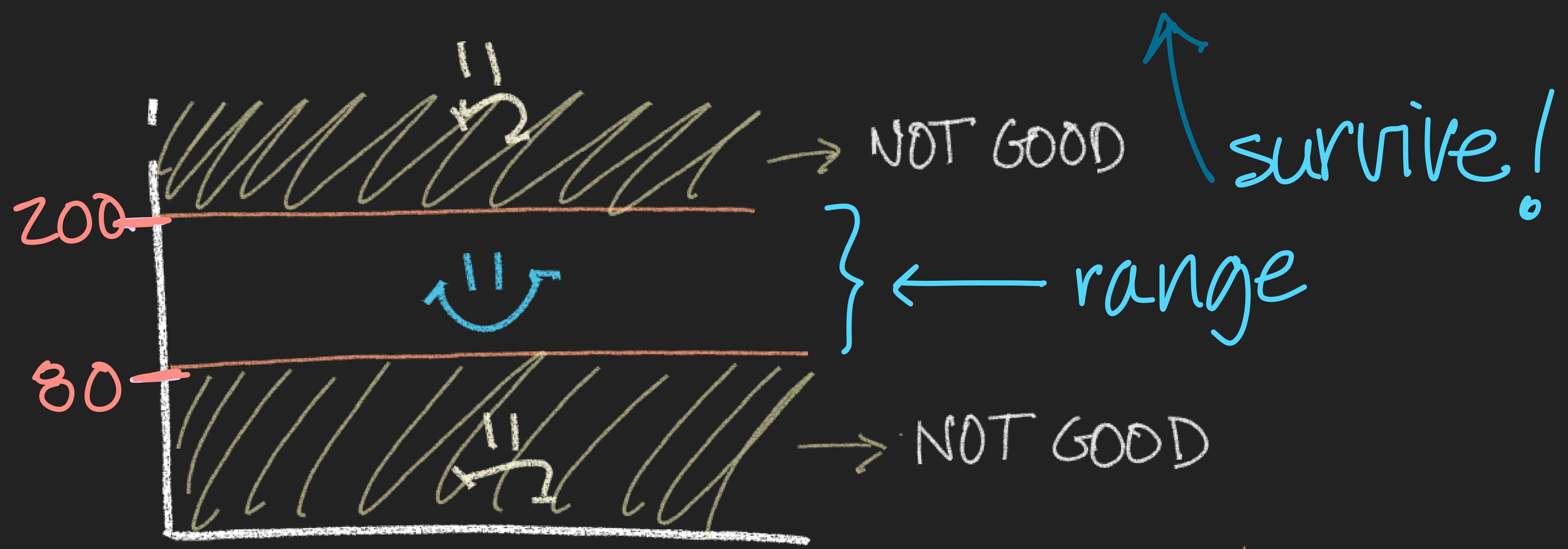
BOYLE - METABOLIC BRAIN DISORDERS

INSULIN BASICS

Maintain Blood Glucose Levels



BLOOD GLUCOSE LEVELS (mg/dL)

FASTING RANGE: ≈ 80-100

AFTER EATING: 170-200

How does your body do this?

NEED GLUCOSE:

1. Glycogen – QUICKLY CONVERTS into glucose
   - skeletal muscle
   - liver

GLUCAGON!

2. make glucose!
   - gluconeogenesis (uses amino acids)

3. use alternative energy sources
   - Fatty Acid oxidation!

Ketones!

How does your body do this?

TOO MUCH GLUCOSE?

INSULIN!

(*) call insulin – hormone
- β cells
- pancreas

T1D: TYPE 1 DIABETES

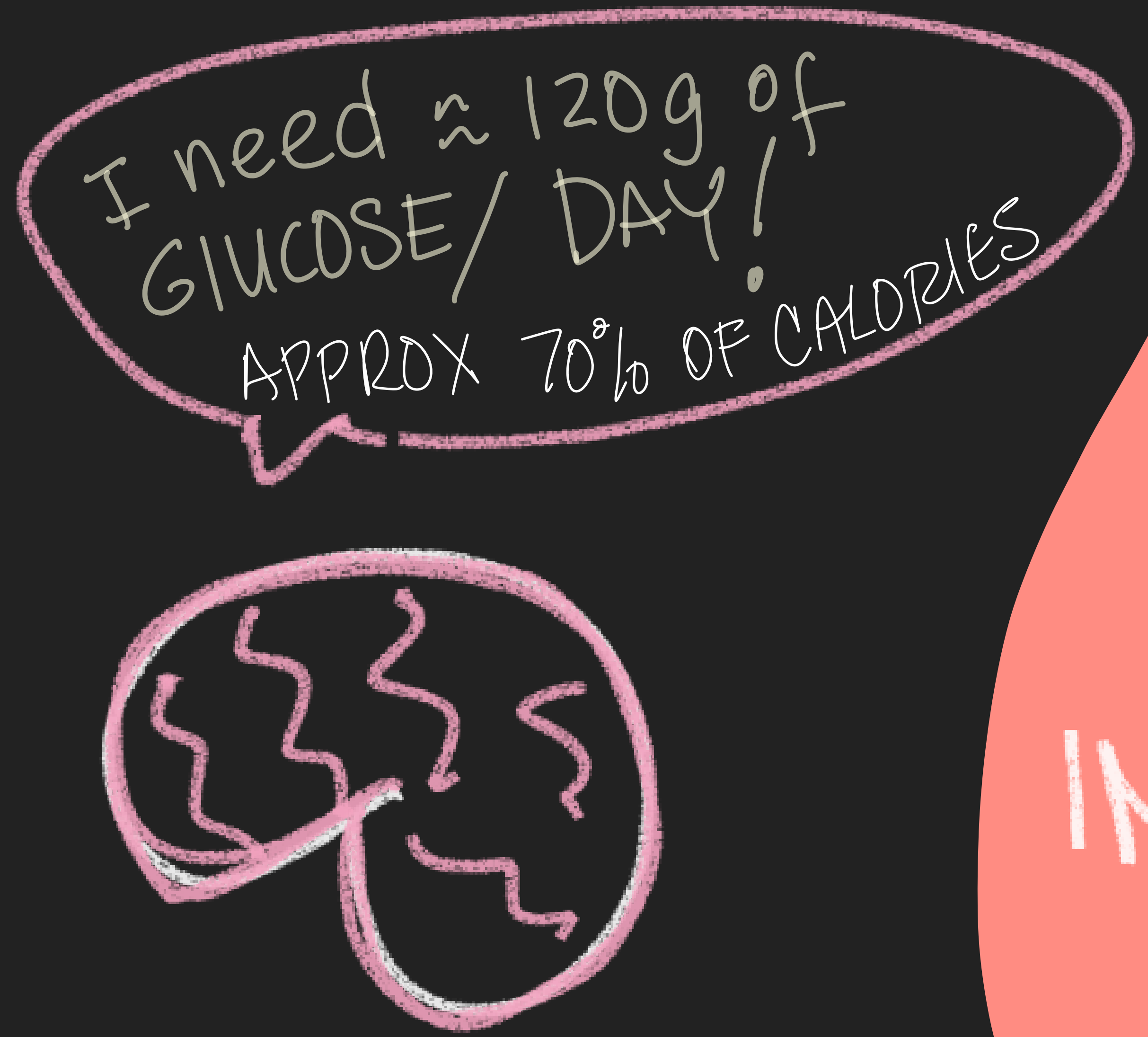
T1D: β cells die

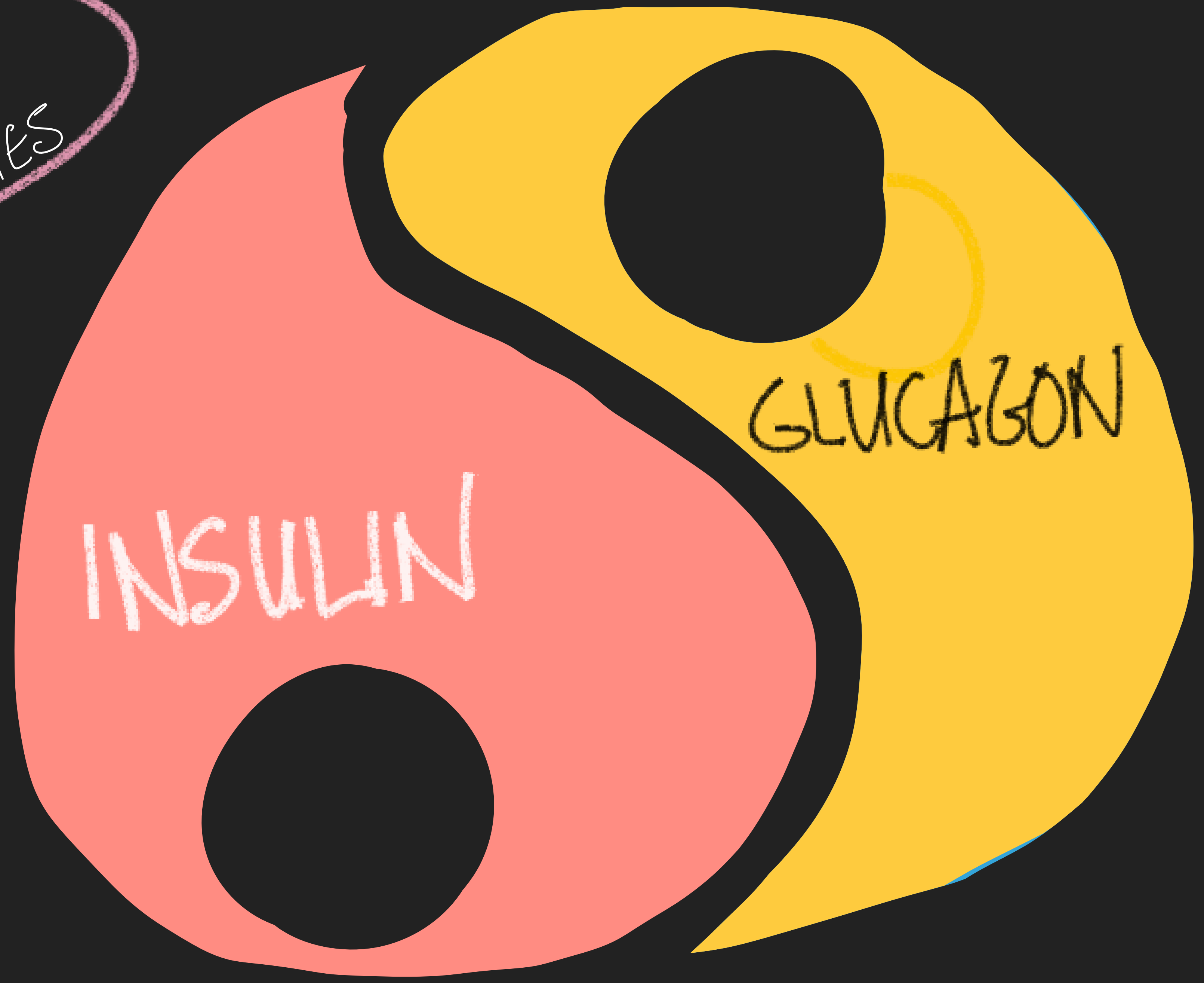
no insulin available

INSULIN RESISTANCE

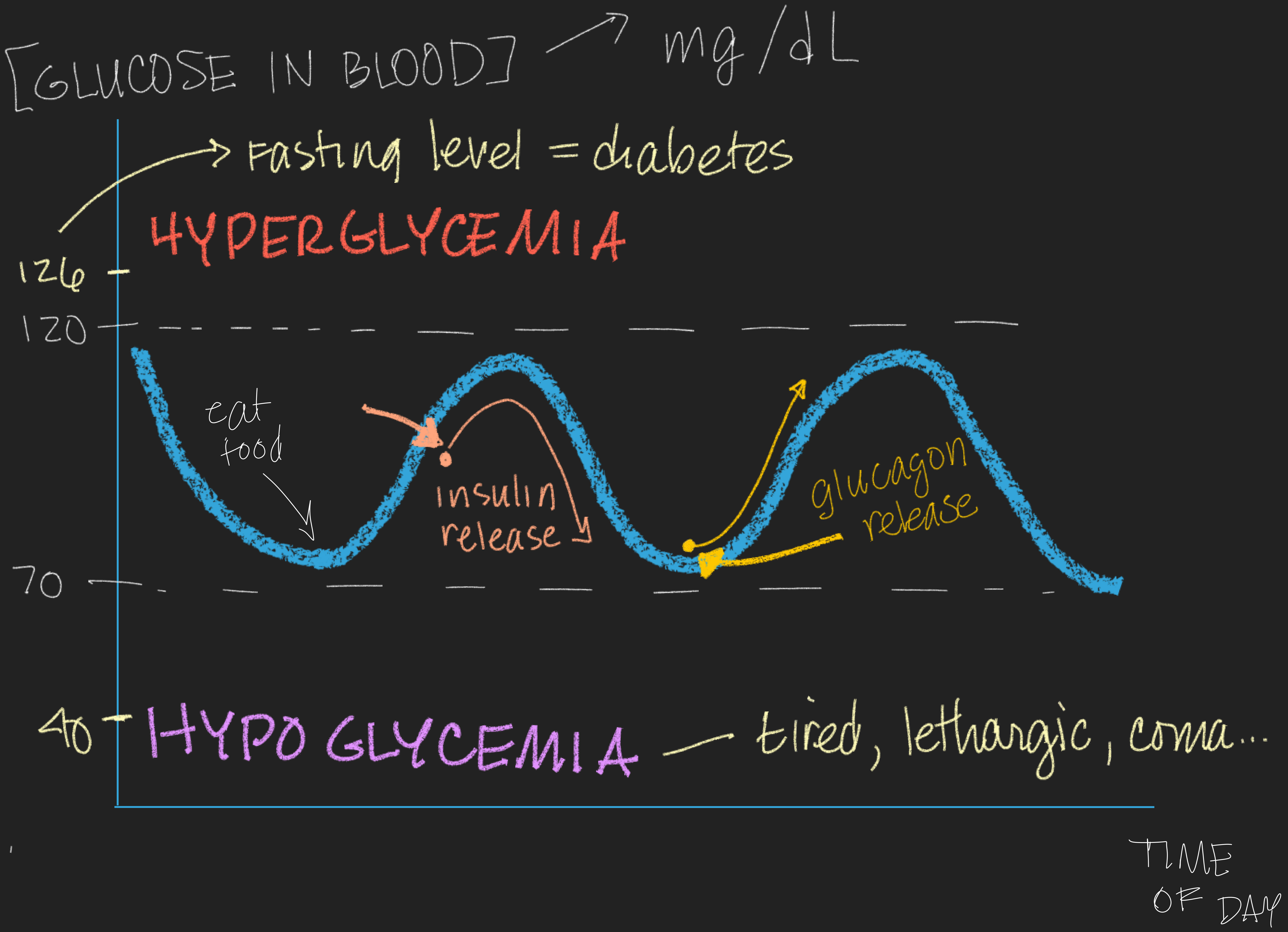
insulin does not work anymore

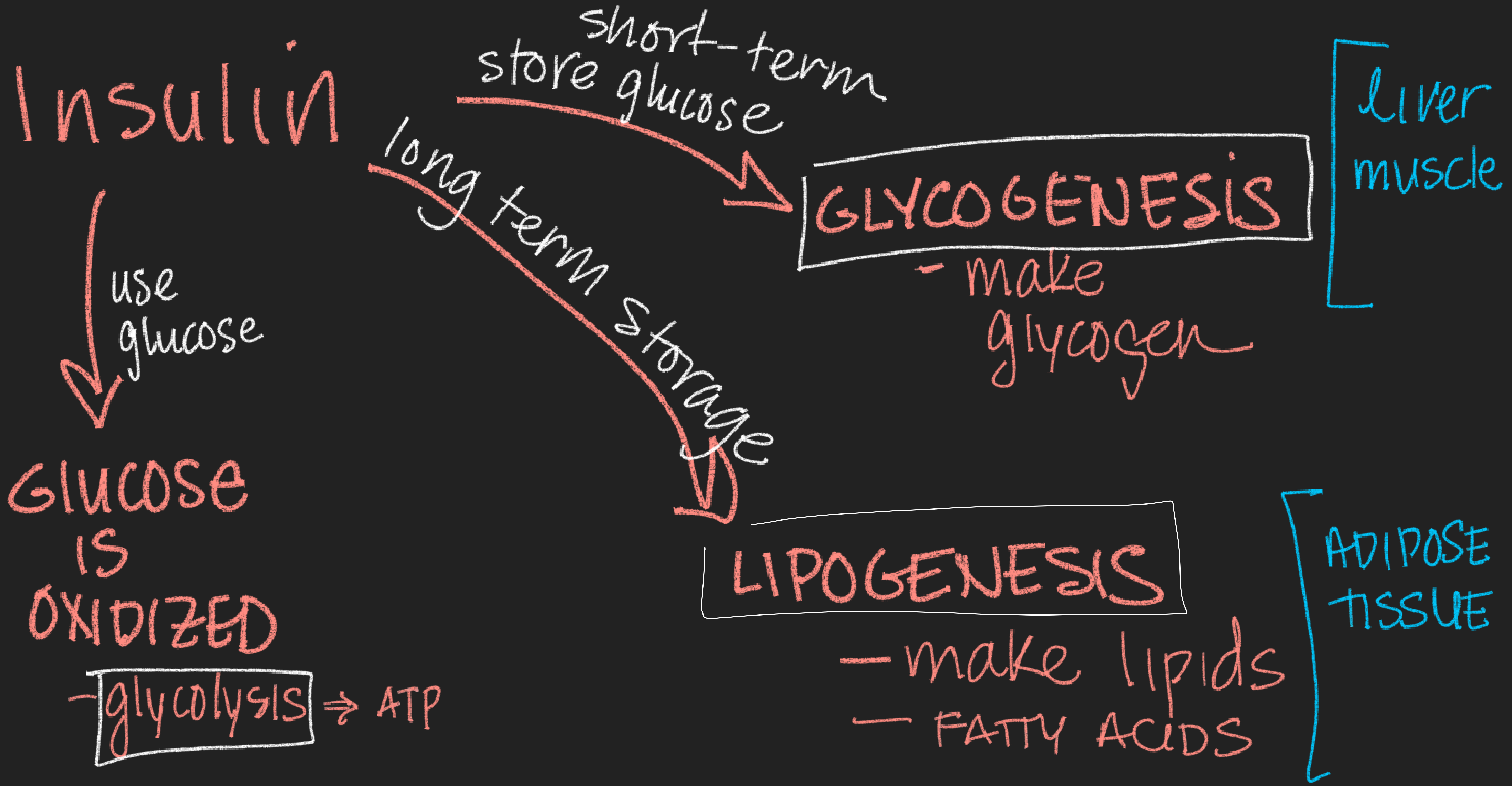
HOMONES DEDICATED FOR GLUCOSE IN BLOOD





YIN+YANG OF GLUCOSE MANAGEMENT


[GLUCOSE IN BLOOD]
mg/dL
Fasting level = diabetes
HYPERGLYCEMIA
126
120
70
40
eat food
insulin release
glucagon release
HYPOGLYCEMIA
tired, lethargic, coma...
TIME OF DAY


Insulin
short-term
store glucose
GLYCOGENESIS
- make glycogen
liver
muscle
long term storage
LIPOGENESIS
- make lipids
- FATTY ACIDS
ADIPOSE TISSUE
use glucose
Glucose is OXIDIZED
- glycolysis ⇒ ATP

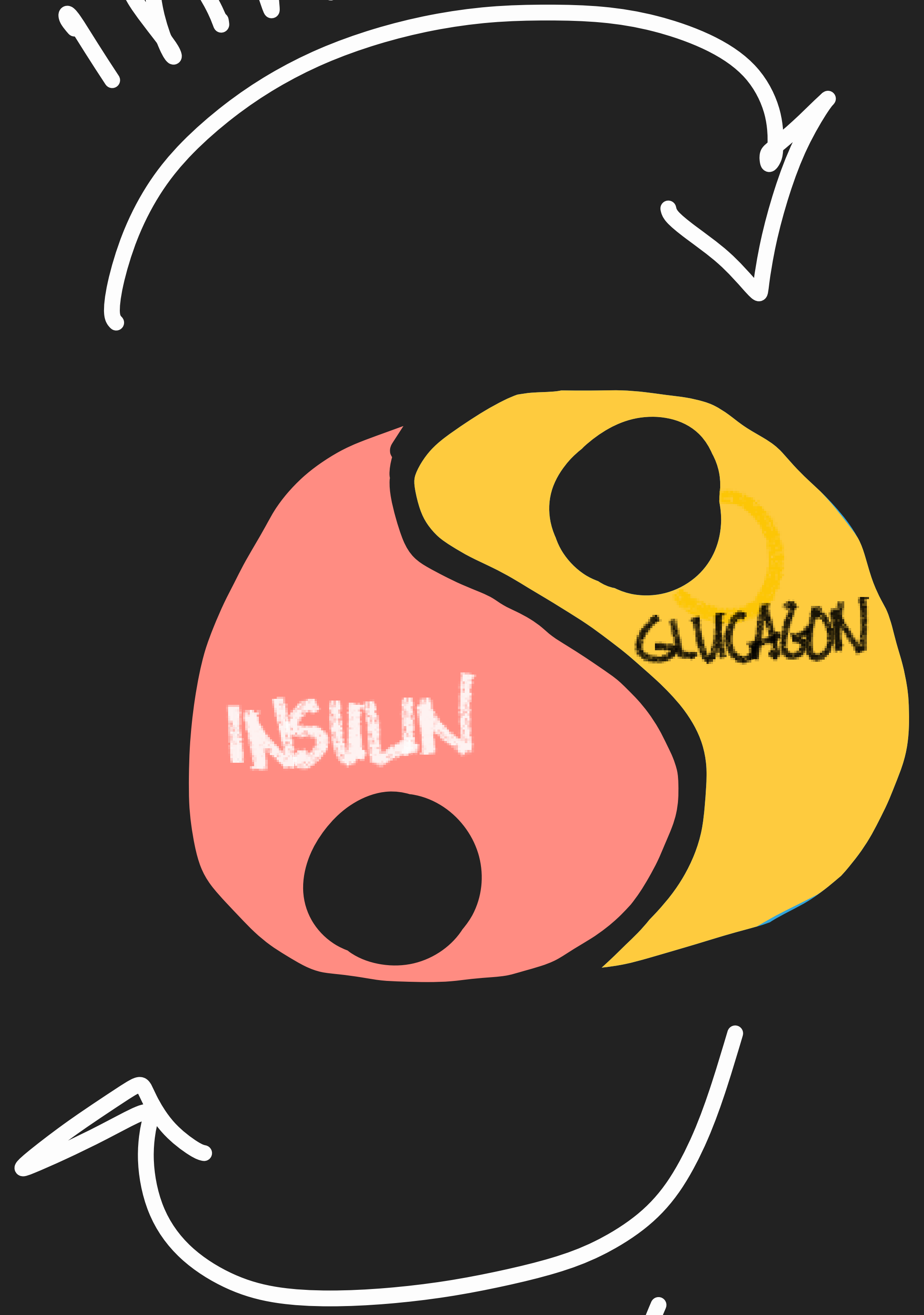
Glucagon

glycogen —glycogen→ glucose ← glycogenolysis
breaking down glycogen

amino acids —glycogen→ glucose ← gluconeogenesis
making glucose from AA

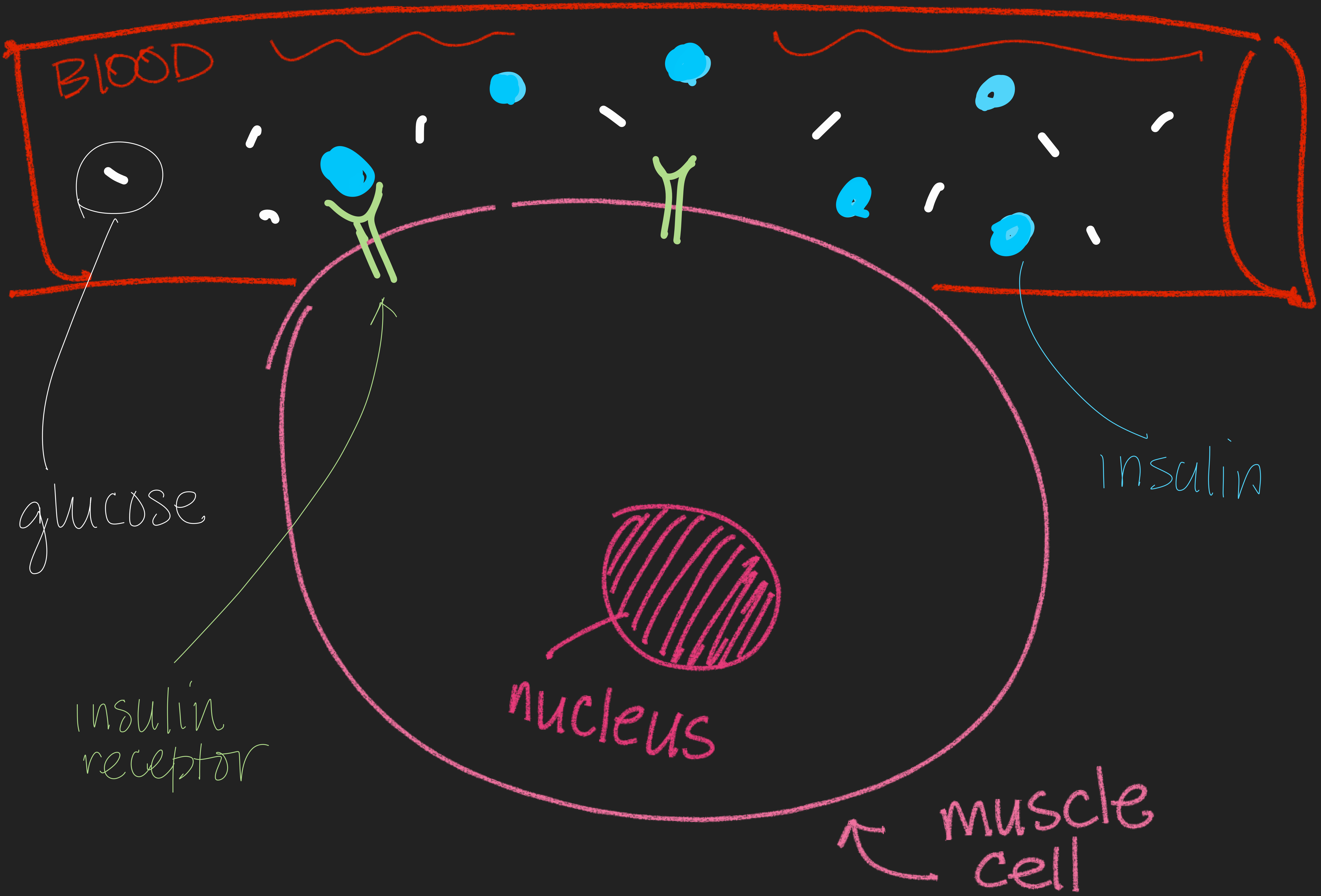
Fatty acids —glycogen→ Ketone bodies ← Ketogenesis
"starvation energy"
← used by brain

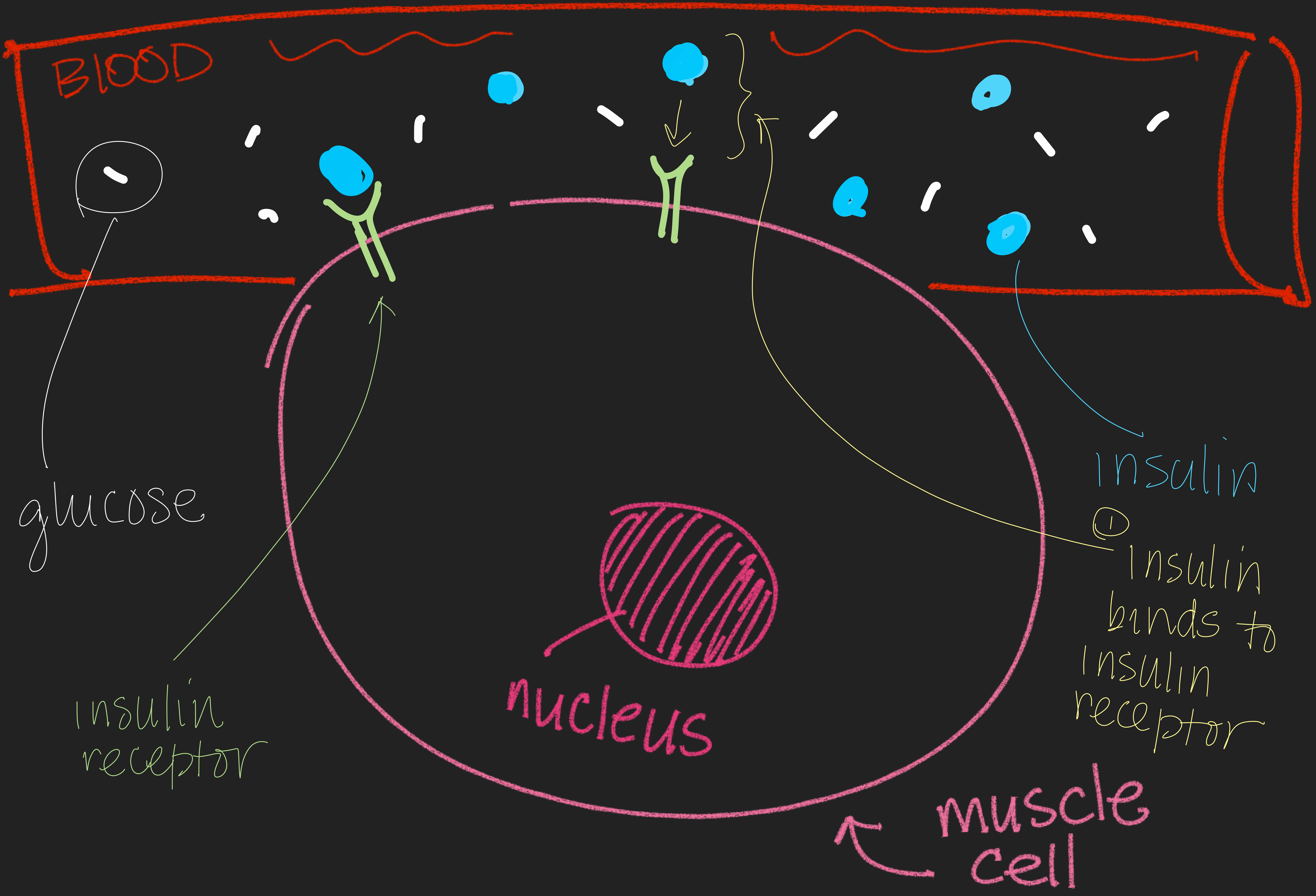
inhibit

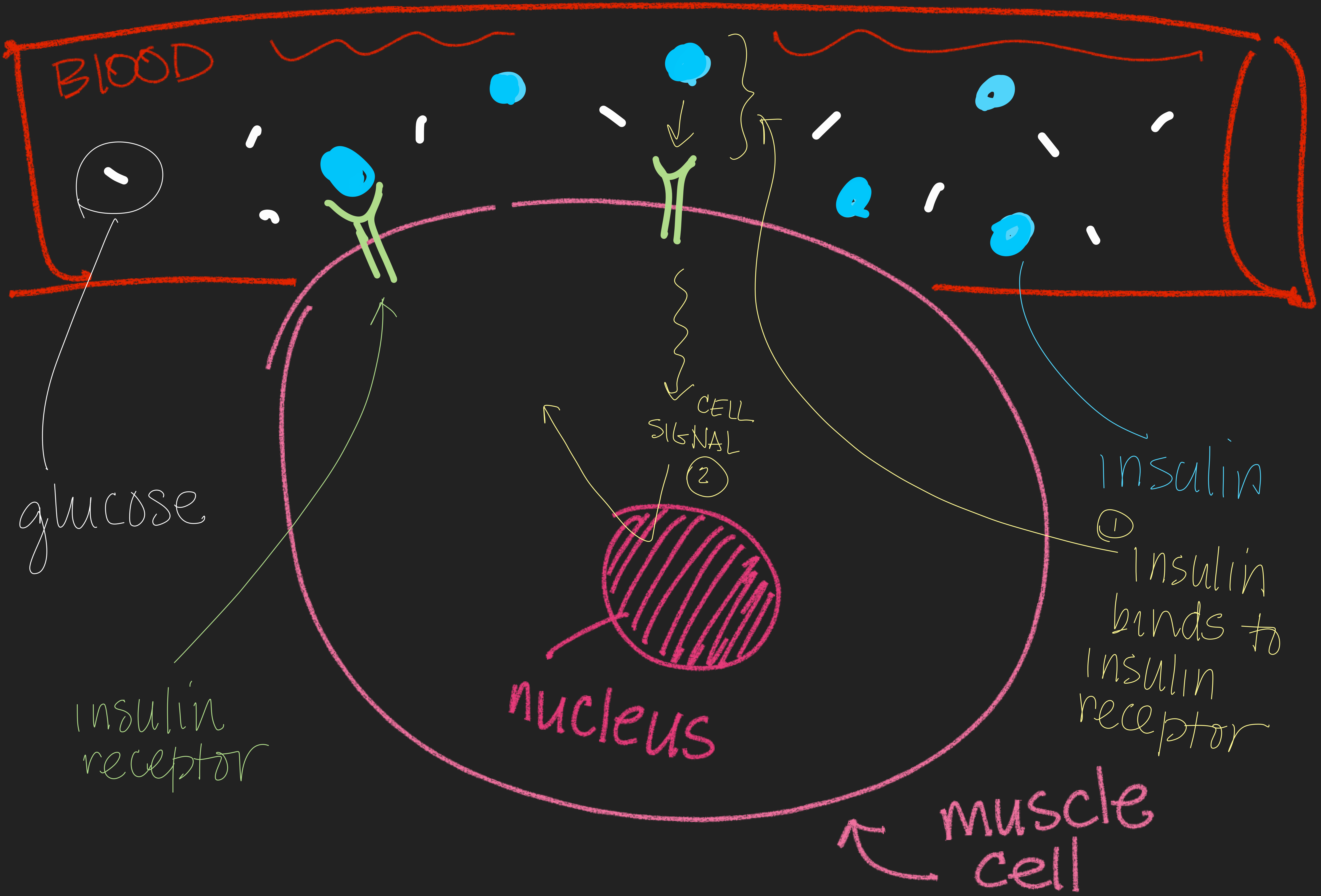


each other

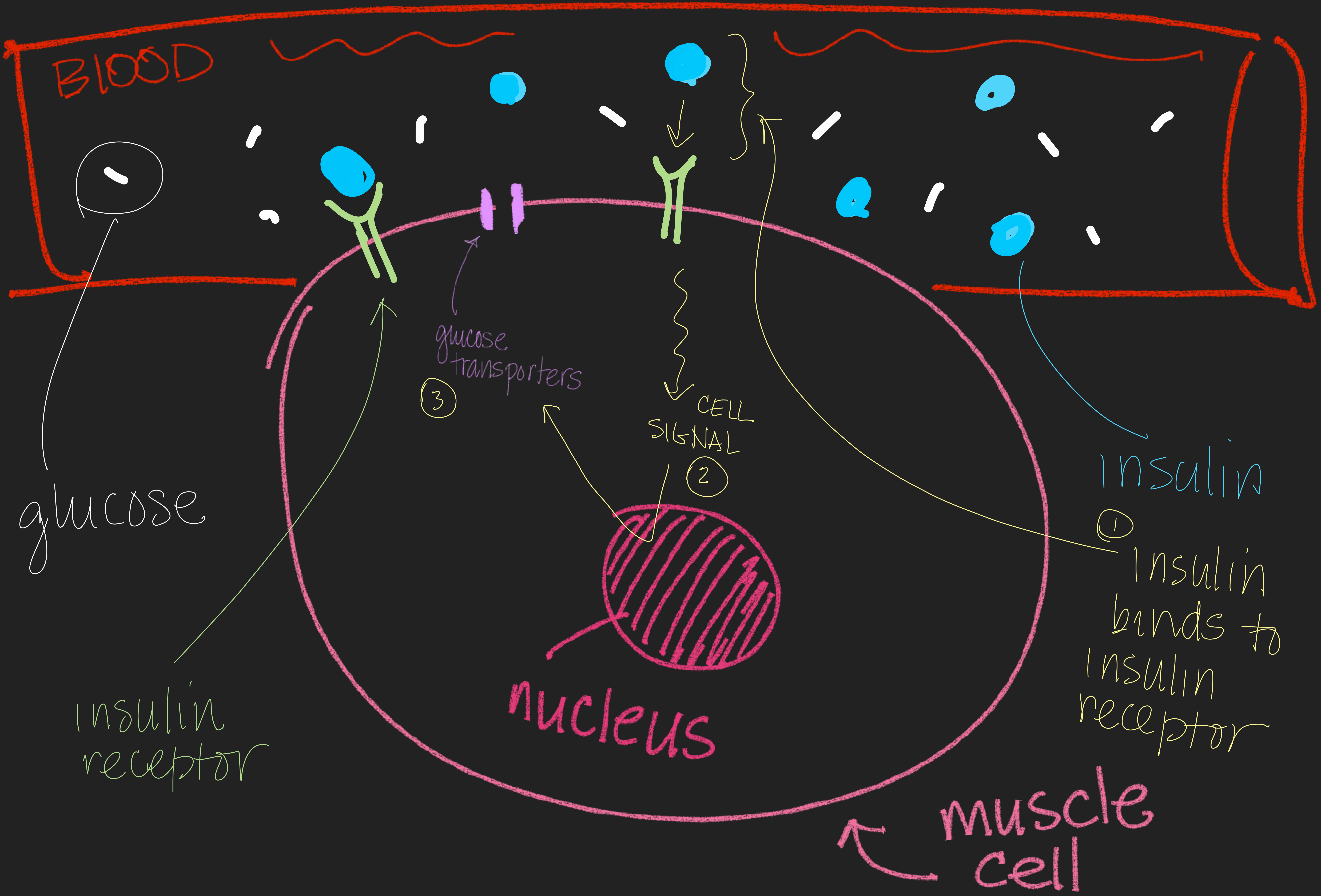
*mostly.

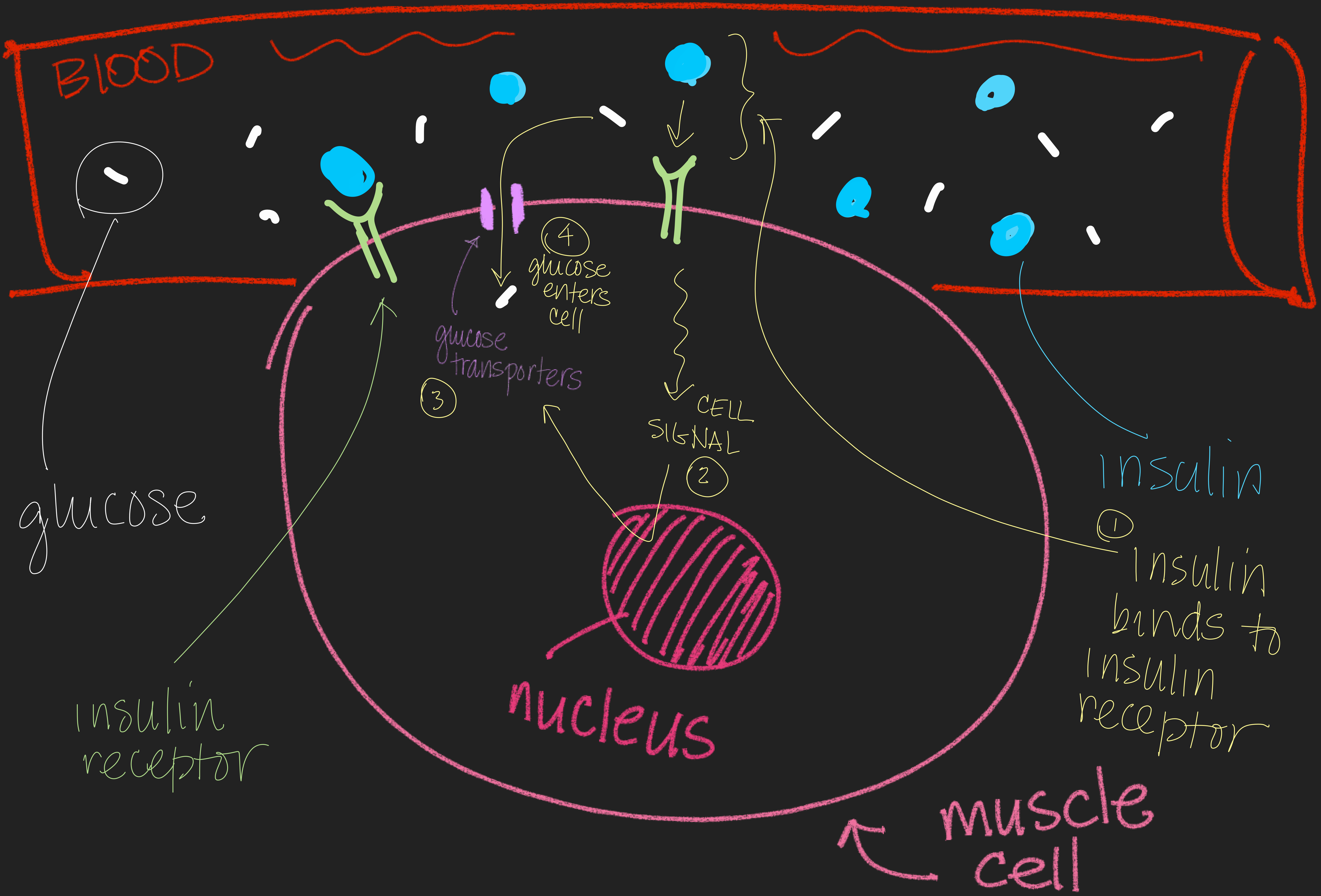

BLOOD
glucose
insulin
insulin receptor
nucleus
muscle cell

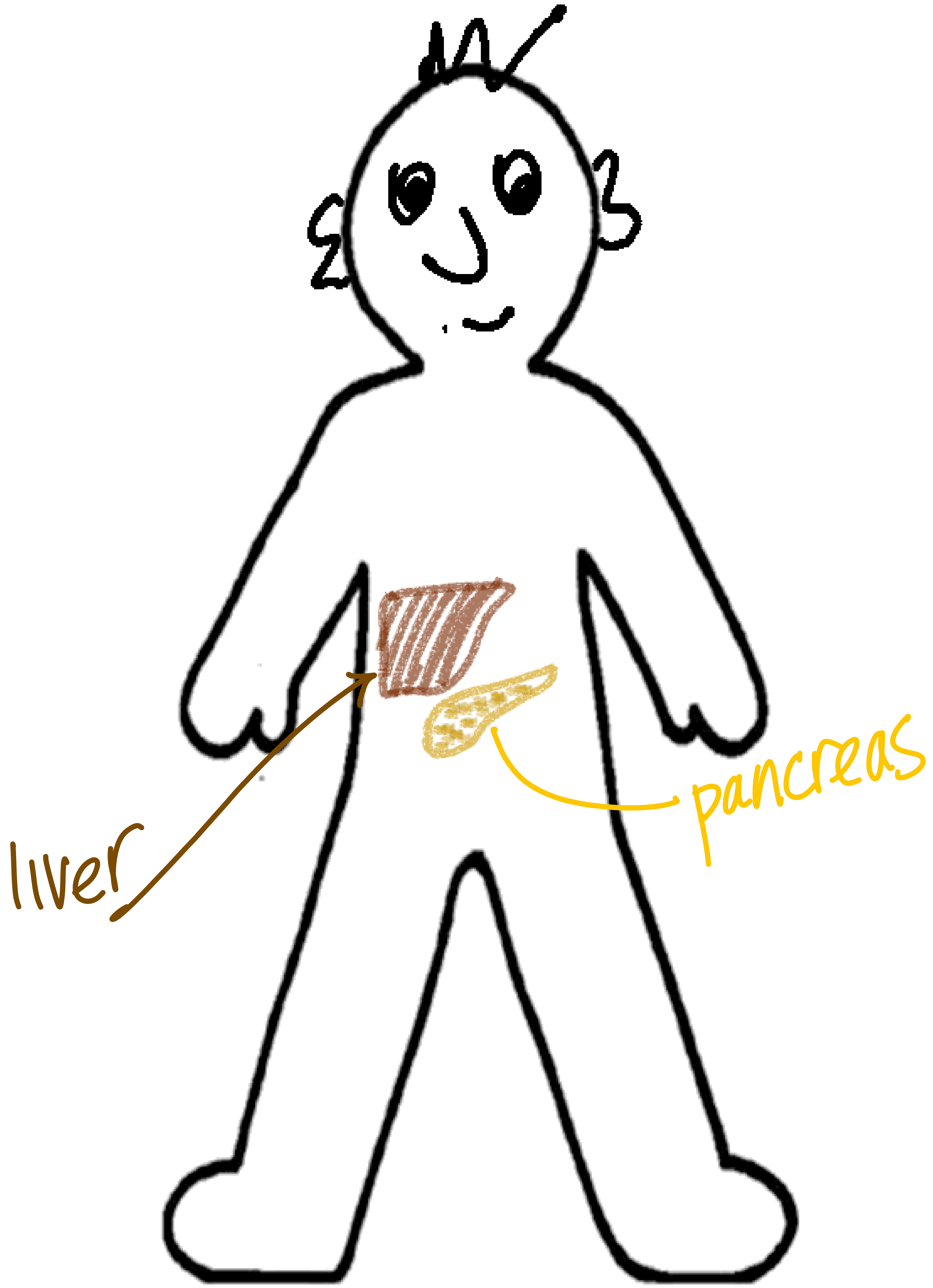

BLOOD
glucose
insulin receptor
nucleus
insulin
① insulin binds to insulin receptor
muscle cell

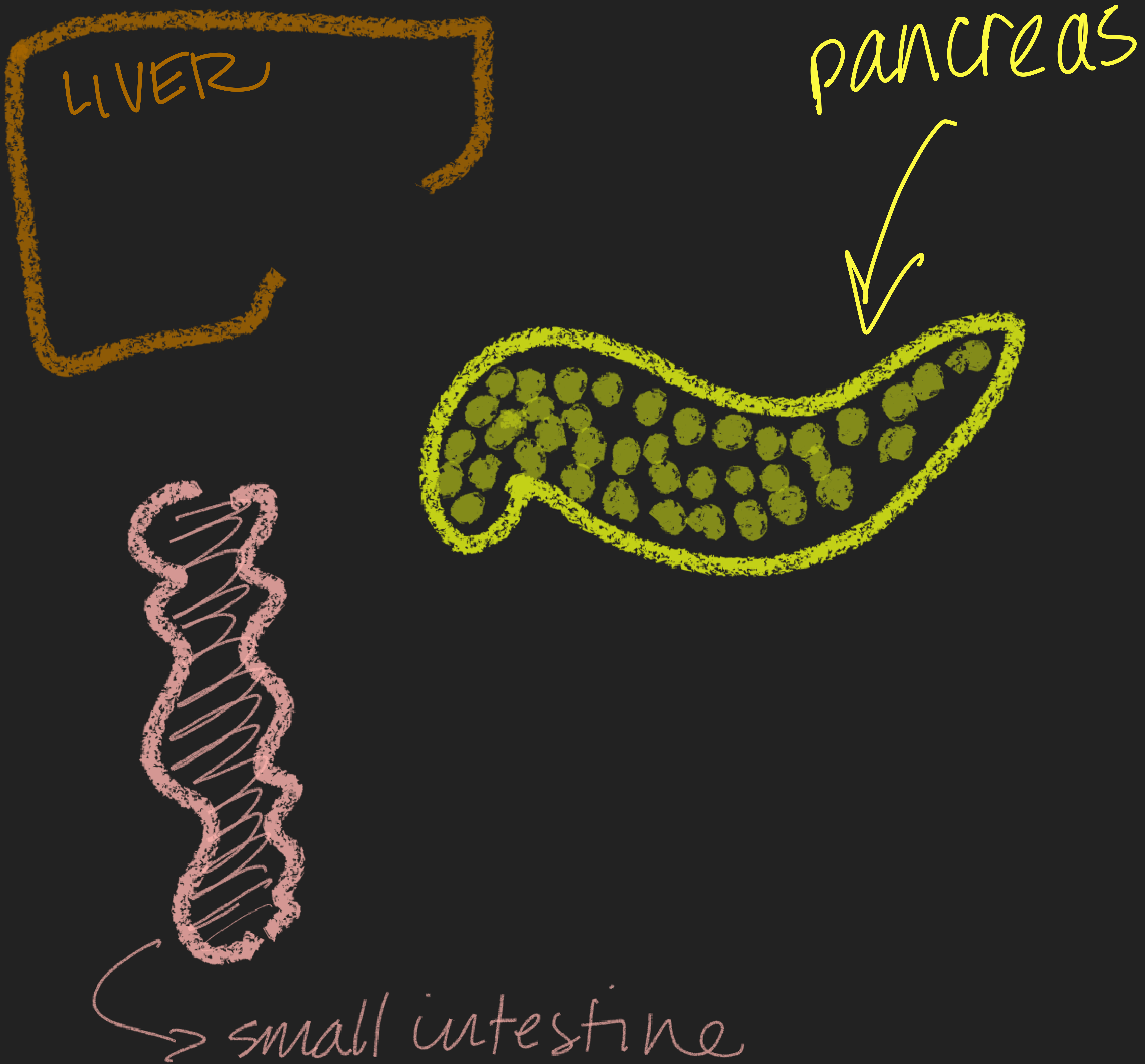


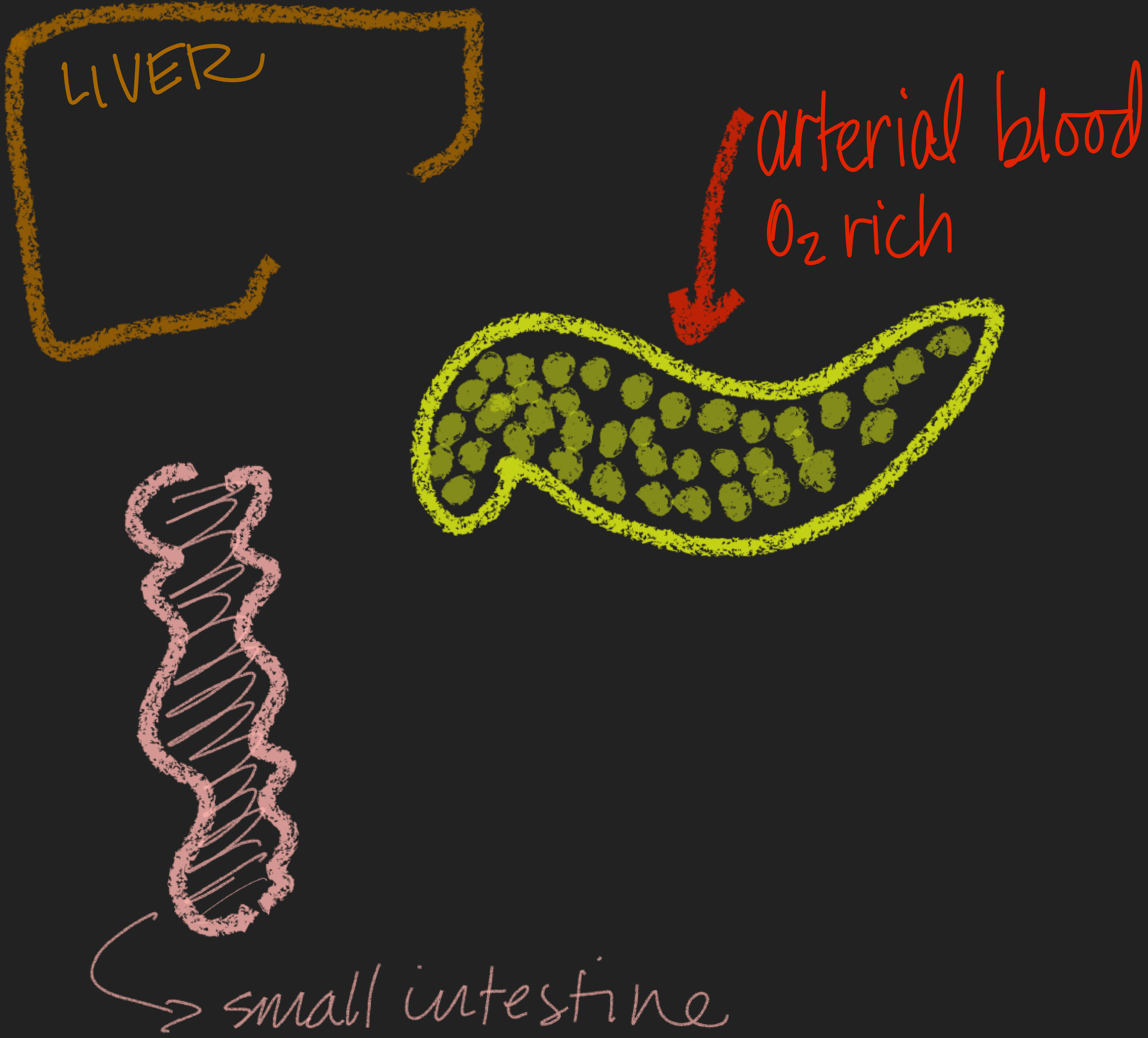
BLOOD
glucose
insulin receptor
CELL SIGNAL
2
nucleus
insulin
1
insulin binds to insulin receptor
muscle cell

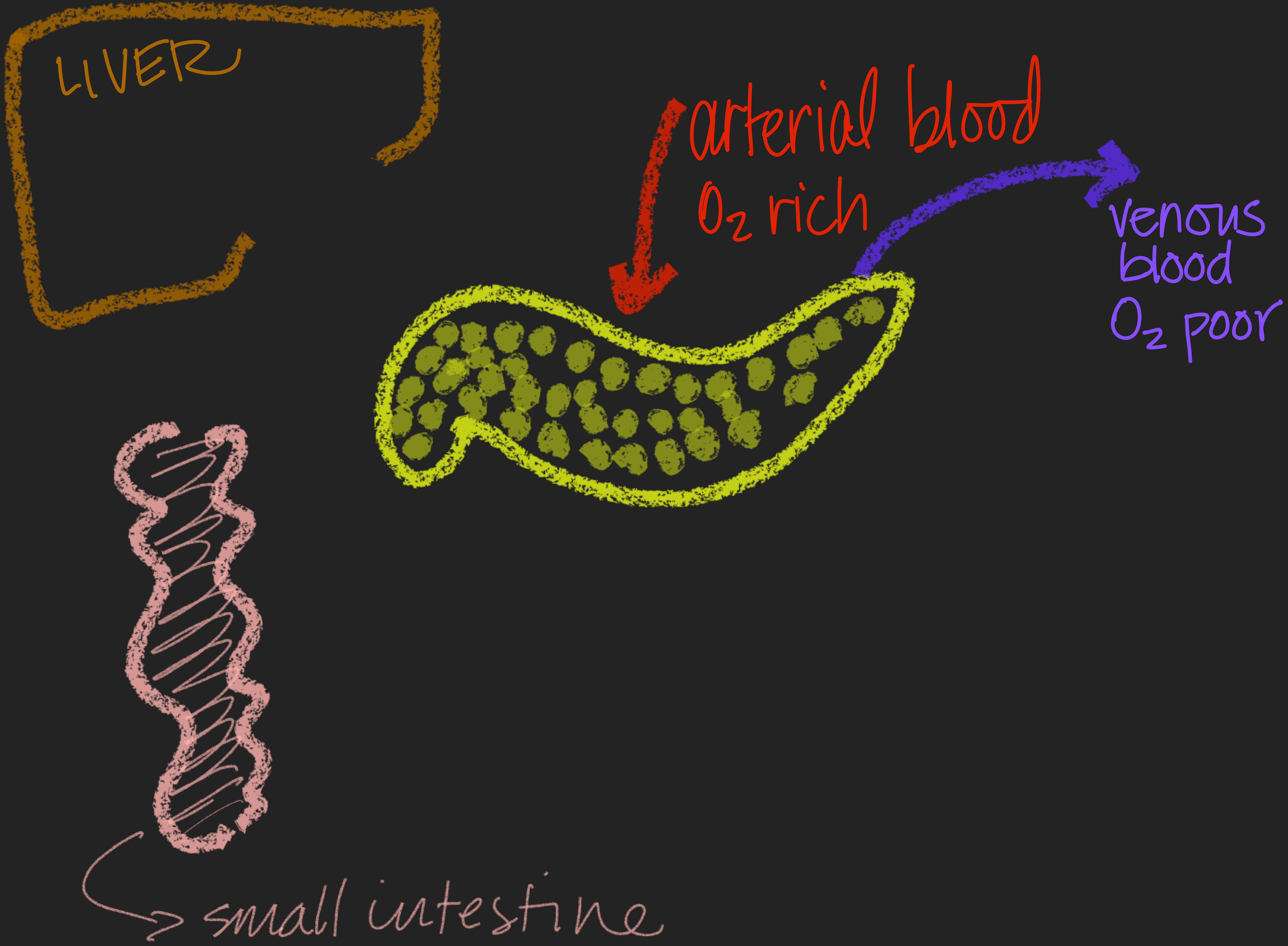

BLOOD
glucose
insulin receptor
glucose transporters
③
CELL SIGNAL
②
insulin
①
Insulin binds to Insulin receptor
nucleus
muscle cell

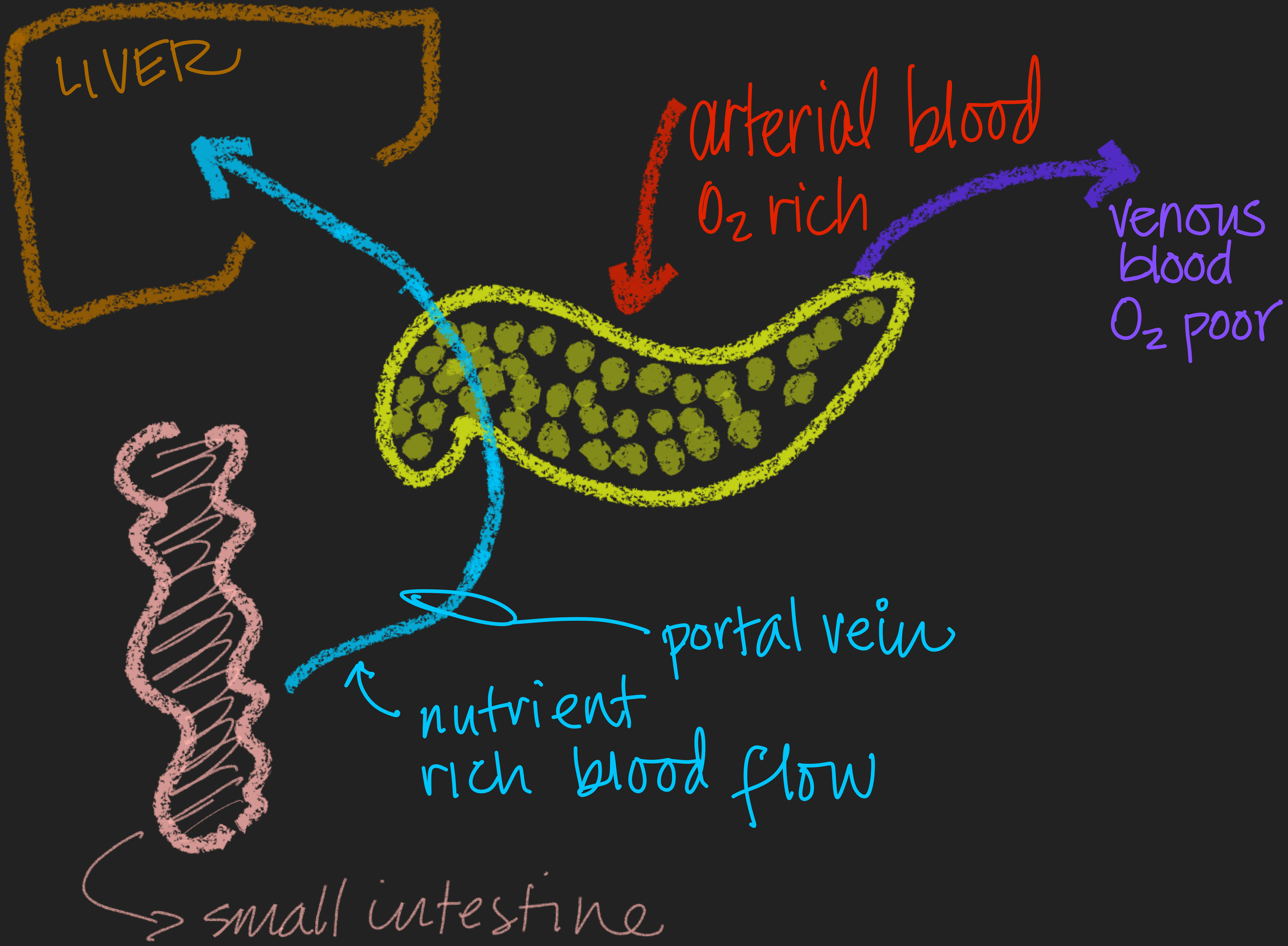

BLOOD
glucose
insulin receptor
glucose transporters
③
④ glucose enters cell
CELL SIGNAL ②
insulin
① insulin binds to insulin receptor
nucleus
muscle cell

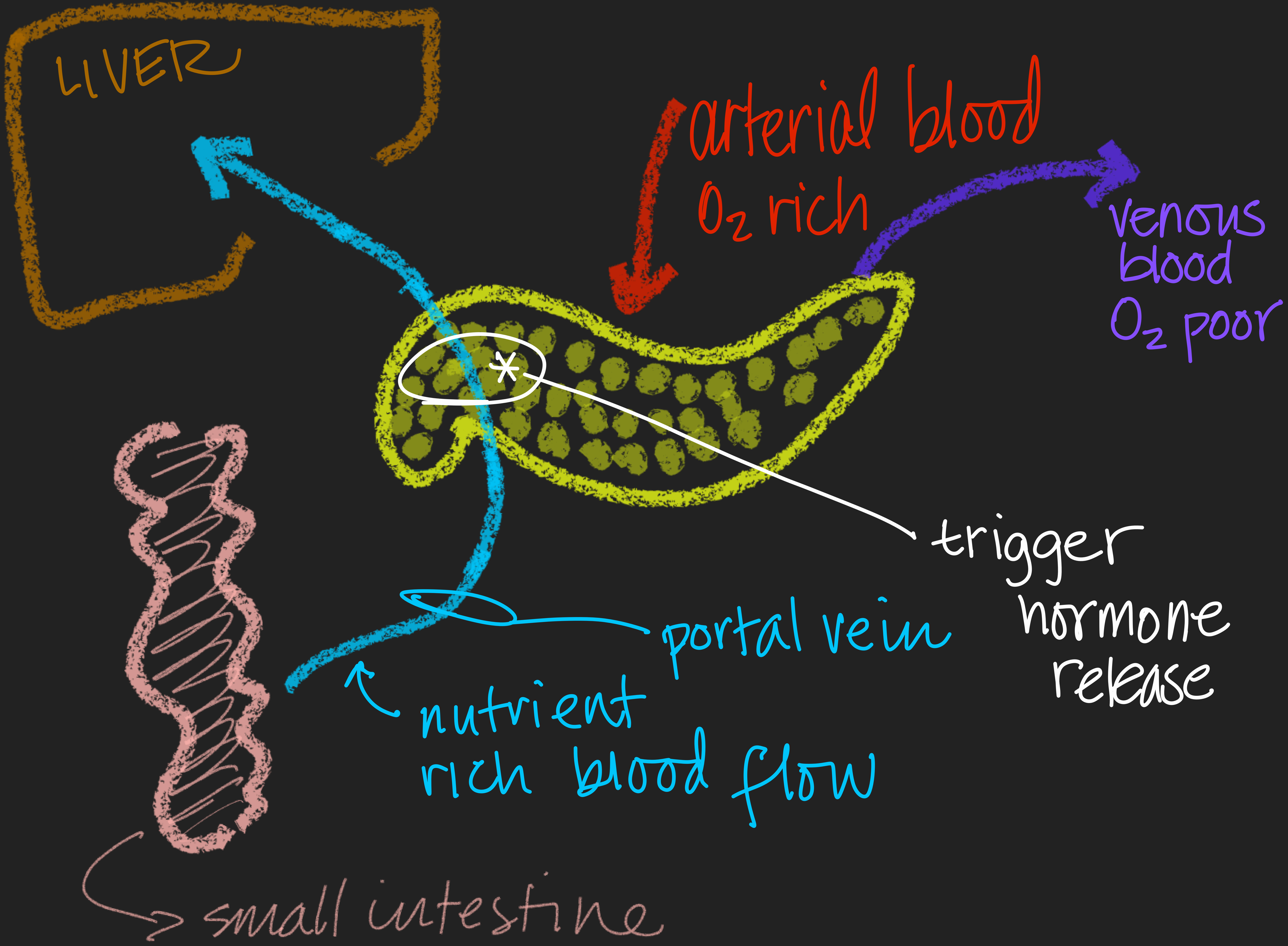

liver
pancreas

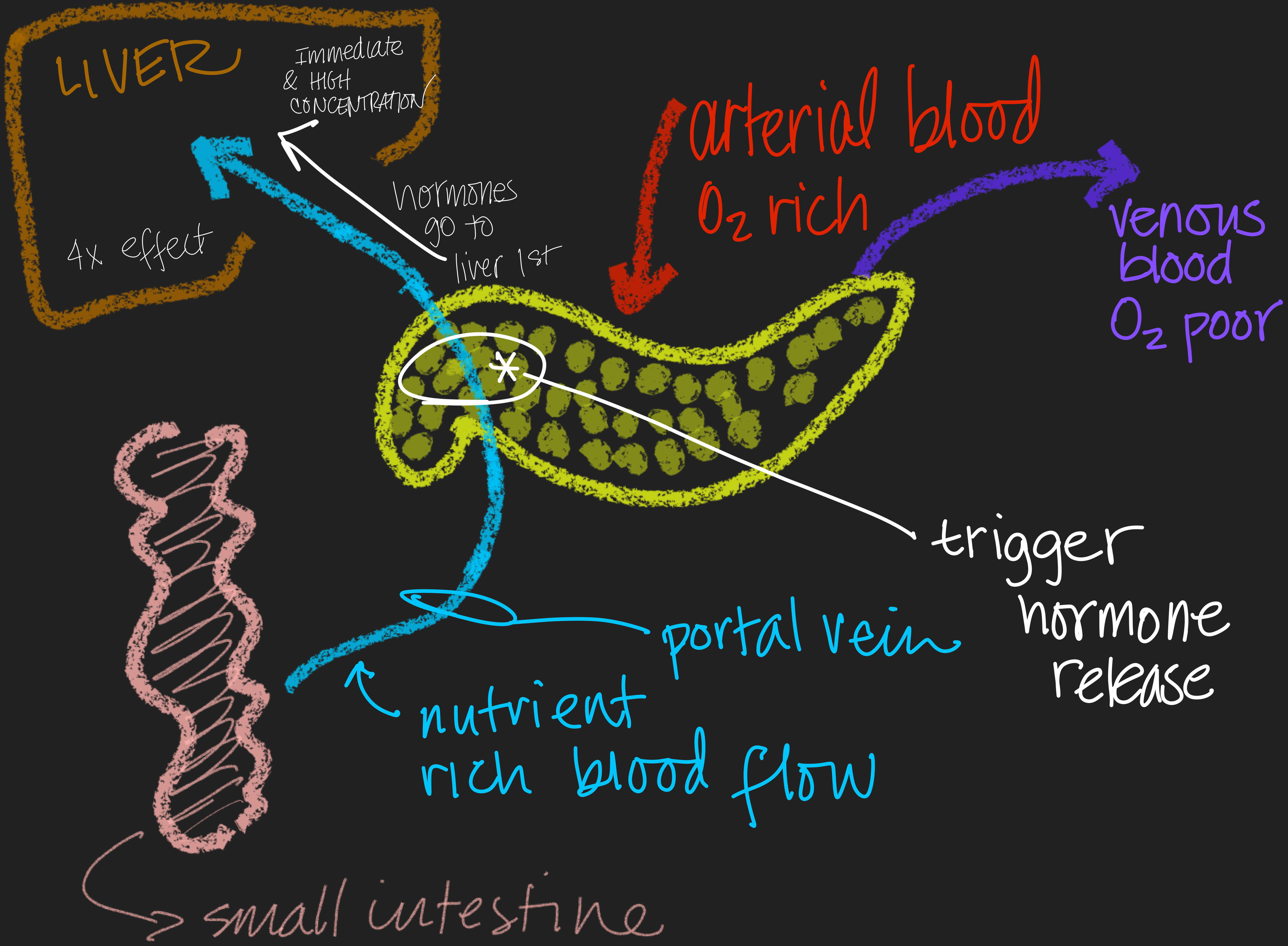

LIVER
pancreas
small intestine


LIVER
arterial blood
O_2 rich
small intestine


LIVER
arterial blood
O_2 rich
venous
blood
O_2 poor
small intestine

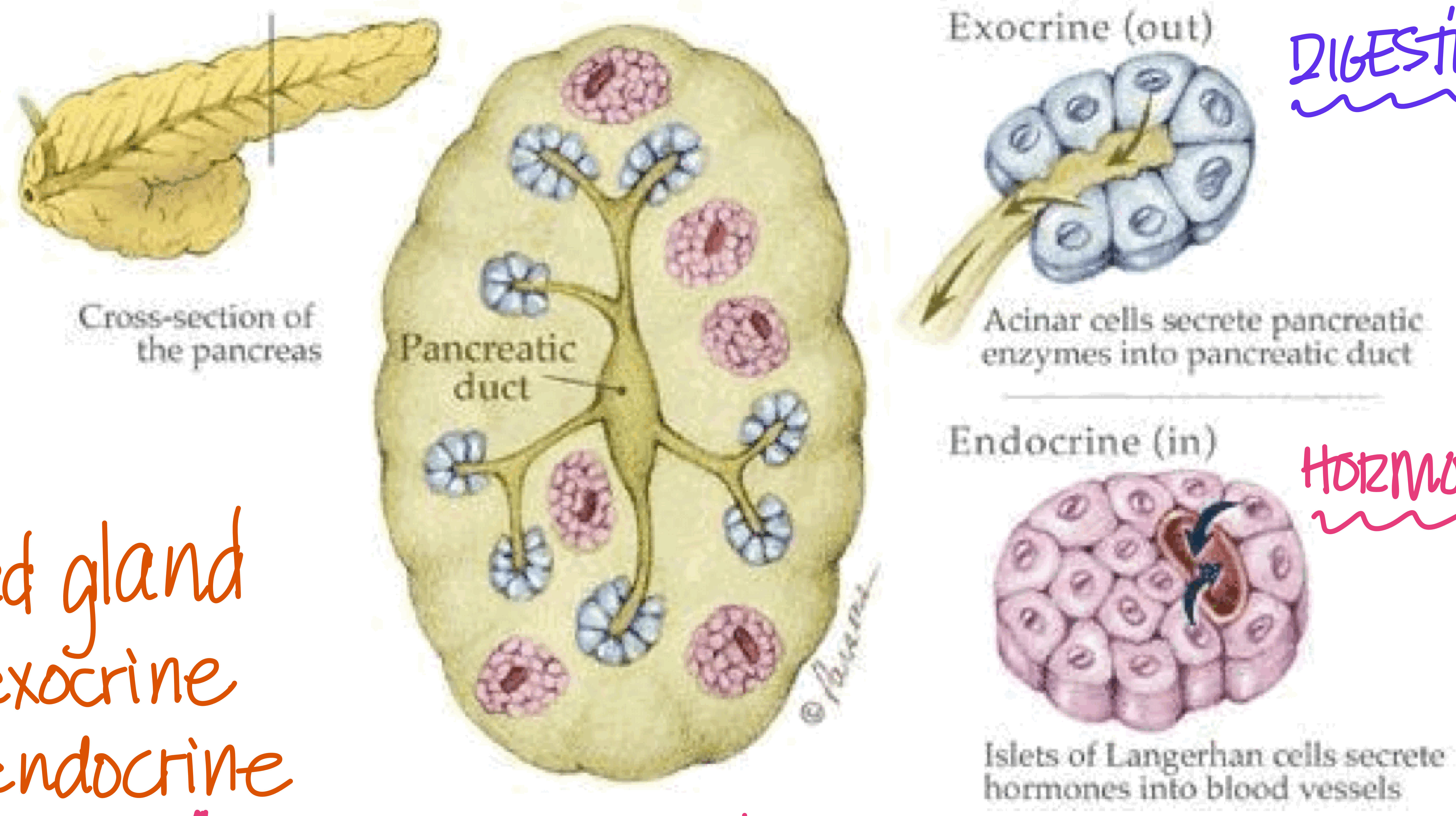

LIVER
arterial blood
O_2 rich
venous blood
O_2 poor
portal vein
nutrient rich blood flow
small intestine


LIVER
arterial blood
O2 rich
venous
blood
O2 poor
trigger
hormone
release
portal vein
nutrient
rich blood flow
small intestine



LIVER
Immediate & HIGH CONCENTRATION
4x effect
hormones go to liver 1st
arterial blood
O2 rich
venous blood
O2 poor
trigger hormone release
portal vein
nutrient rich blood flow
small intestine

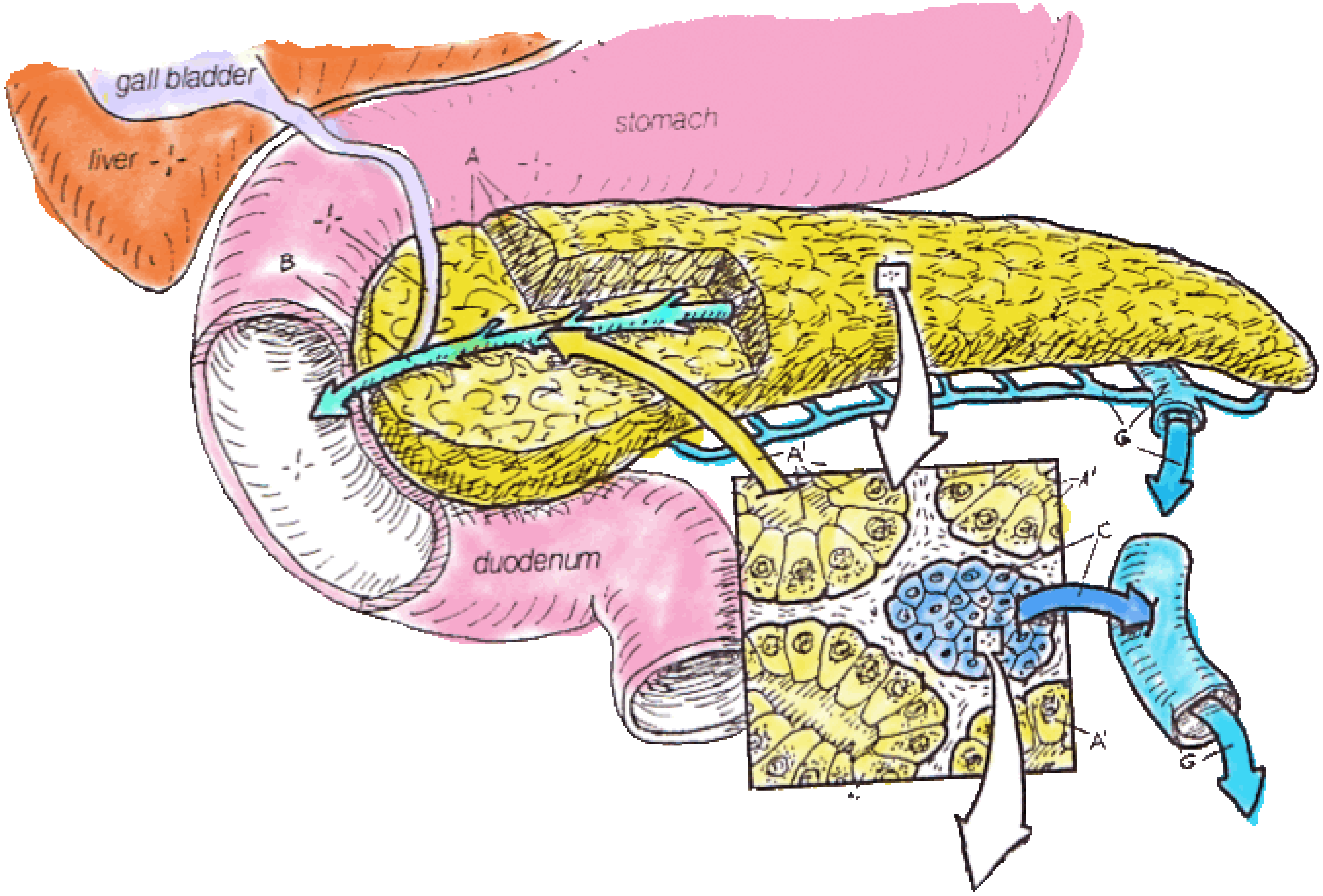
CROSS-SECTION OF THE PANCREAS:

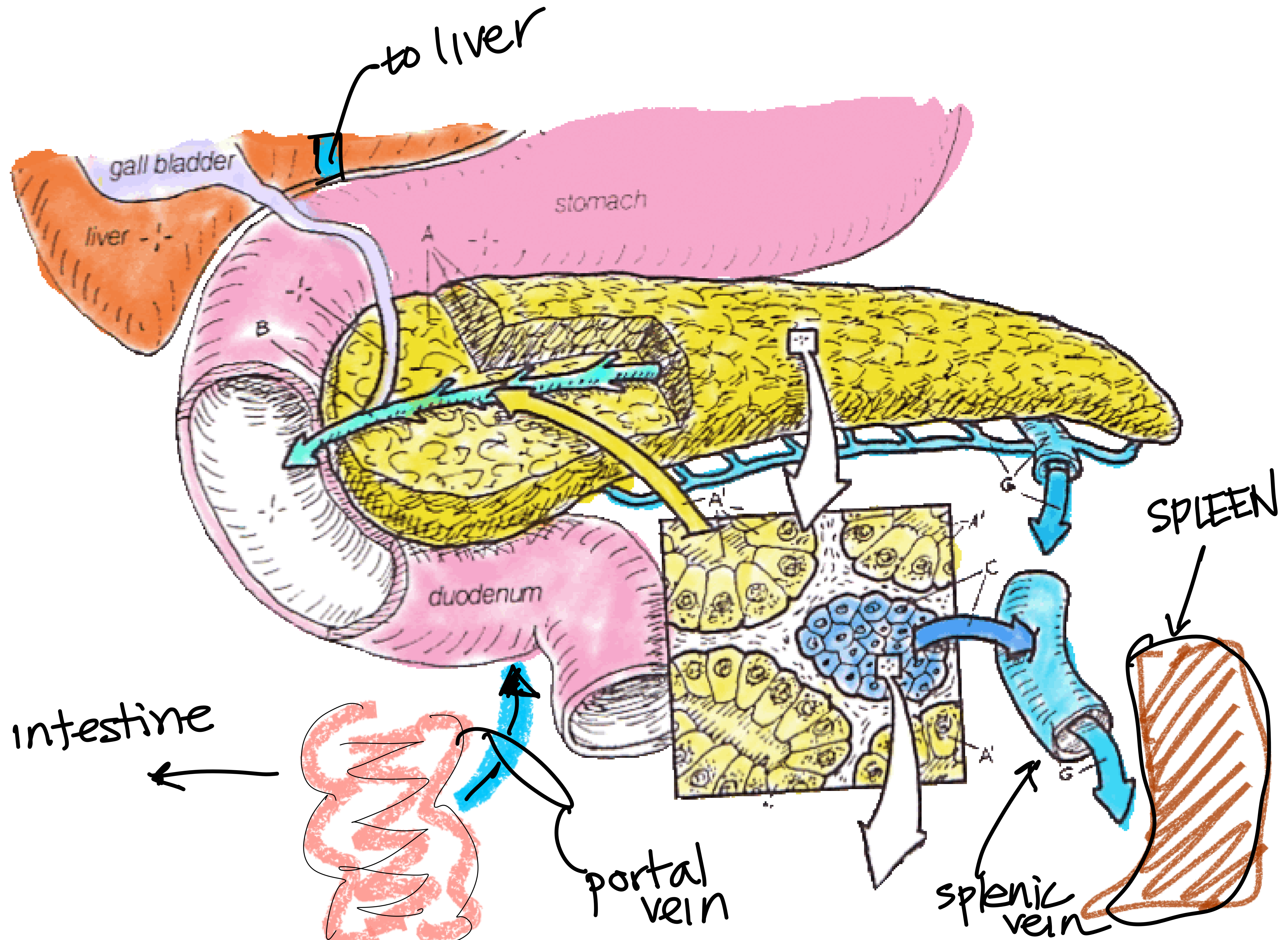


DIGESTION

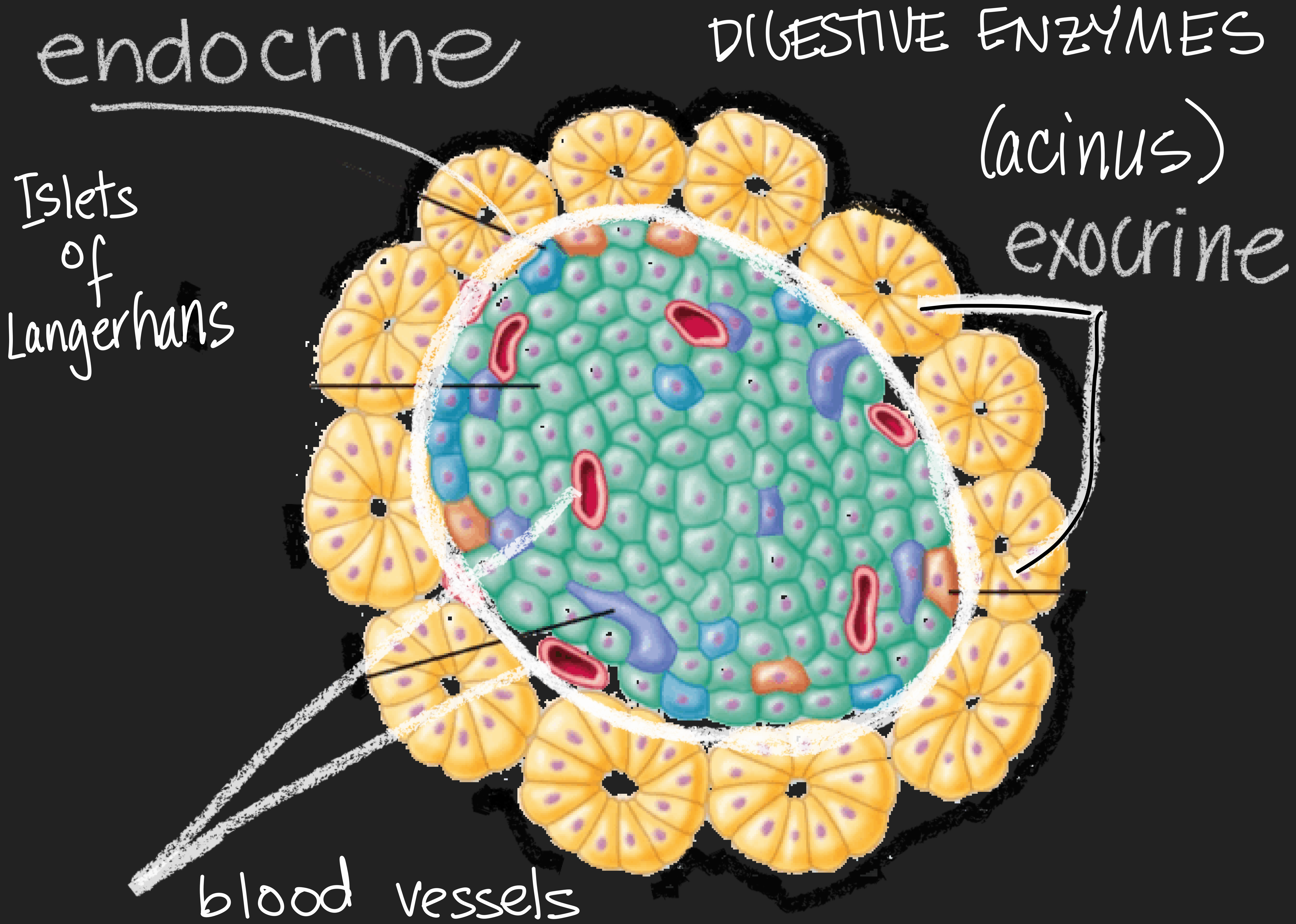
HORMONAL

mixed gland
⊛ 1. exocrine
2. endocrine
↖ glucose regulation!


gall bladder
liver
stomach
A
B
duodenum
A'
A'
C
A'
G
G



to liver
gall bladder
liver
stomach
A
B
duodenum
A'
C
G
SPLEEN
intestine
portal vein
splenic vein

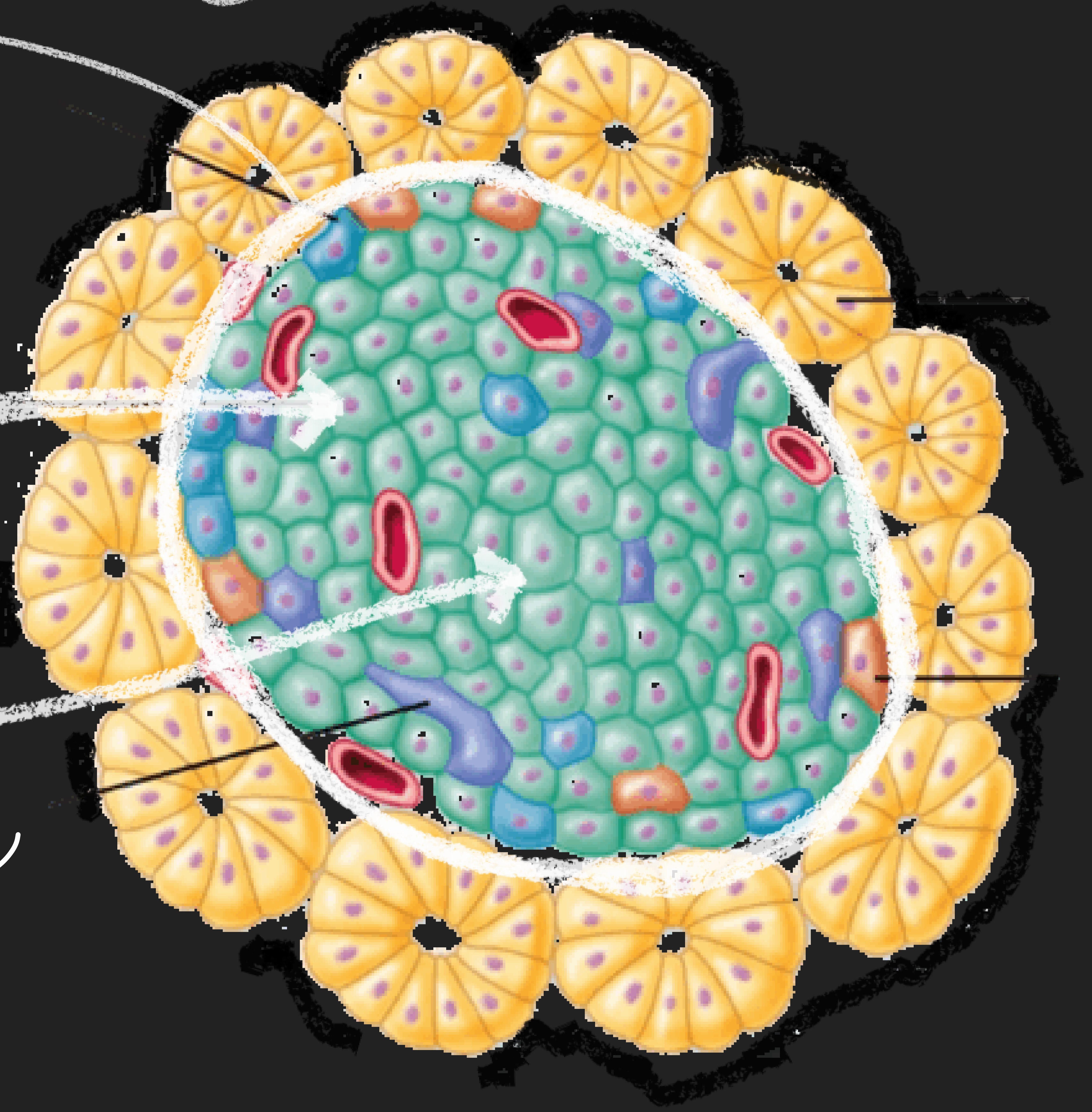

endocrine
DIGESTIVE ENZYMES
(acinus)
exocrine
Islets of Langerhans
blood vessels

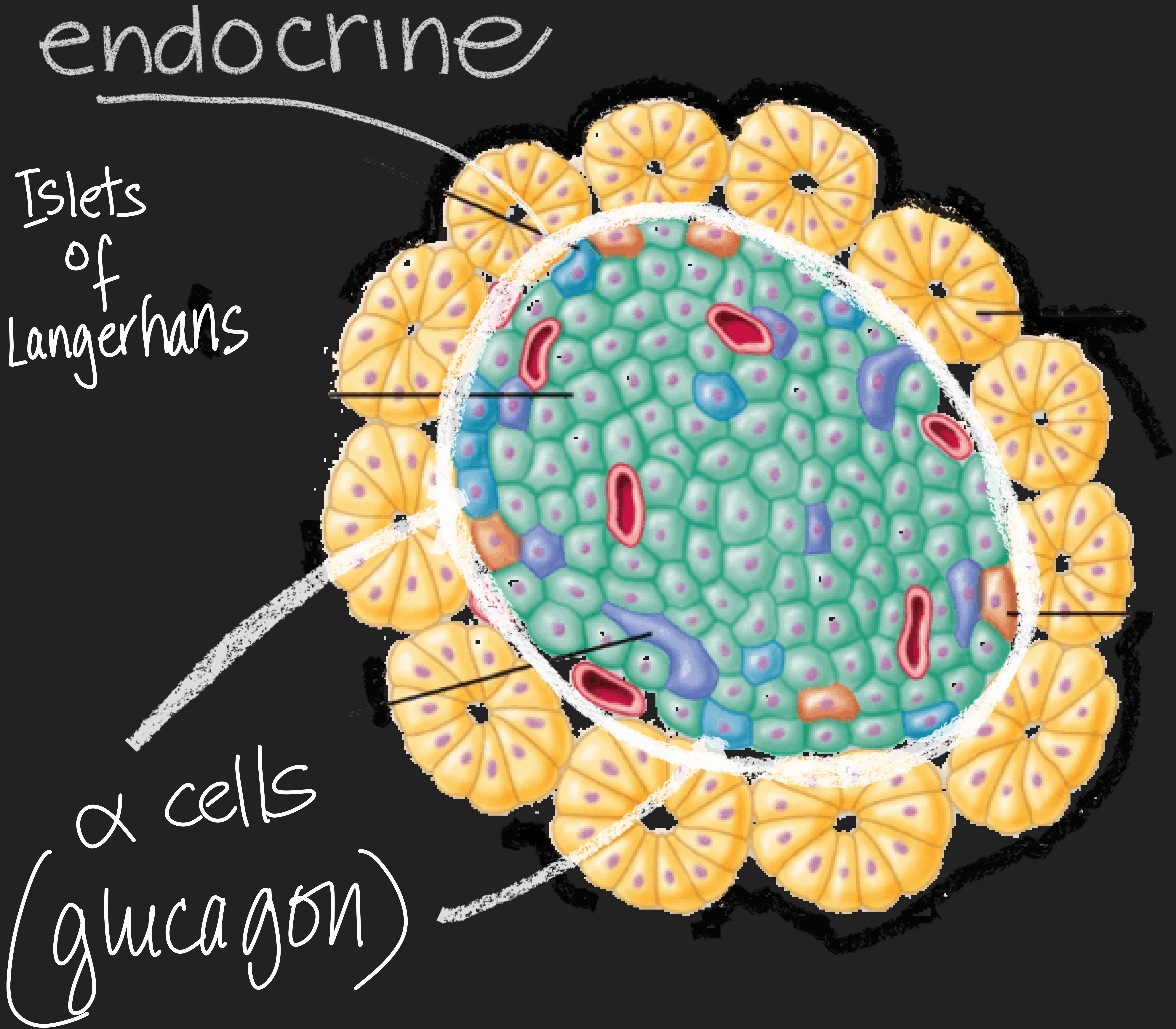
endocrine

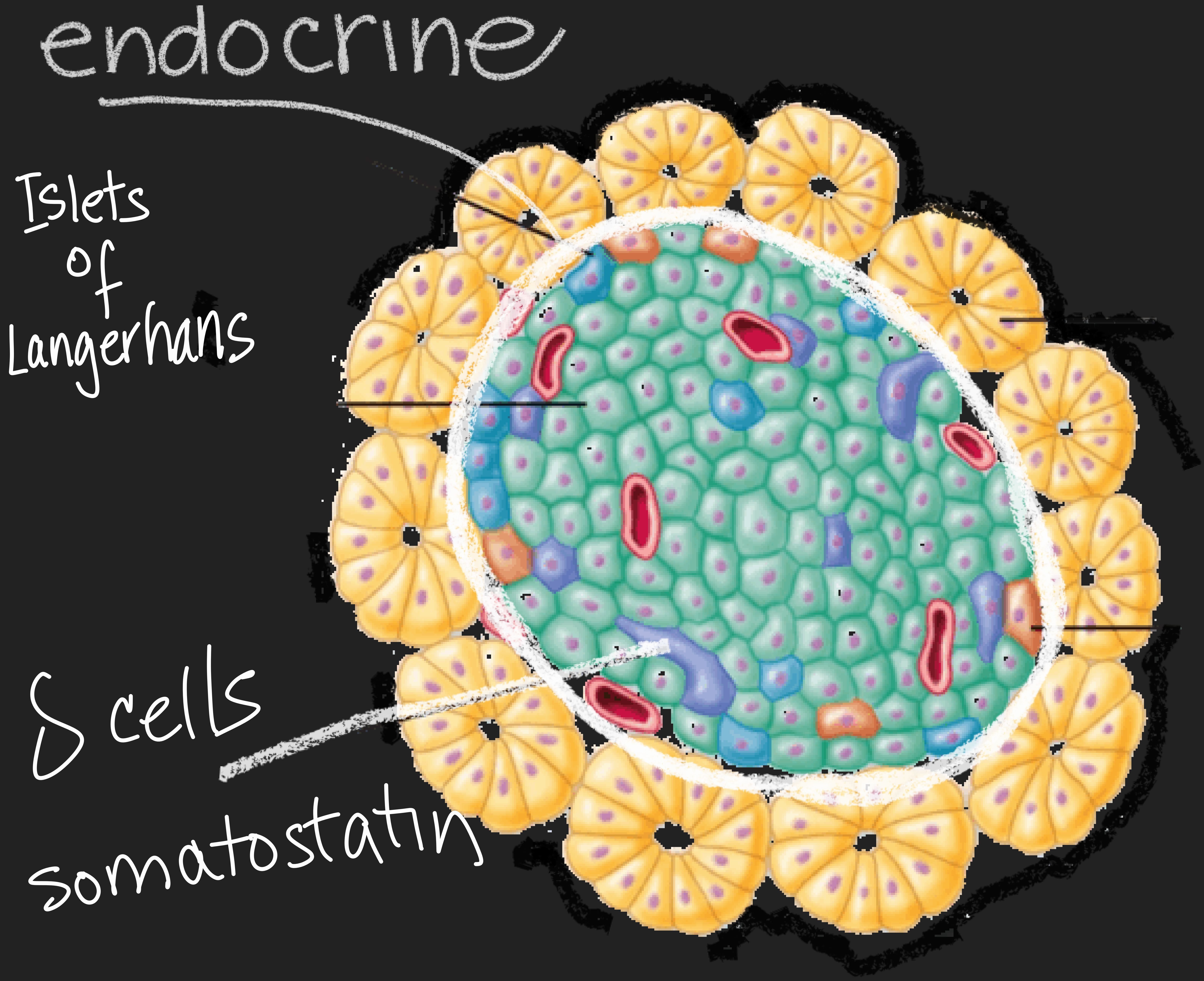
Islets of Langerhans

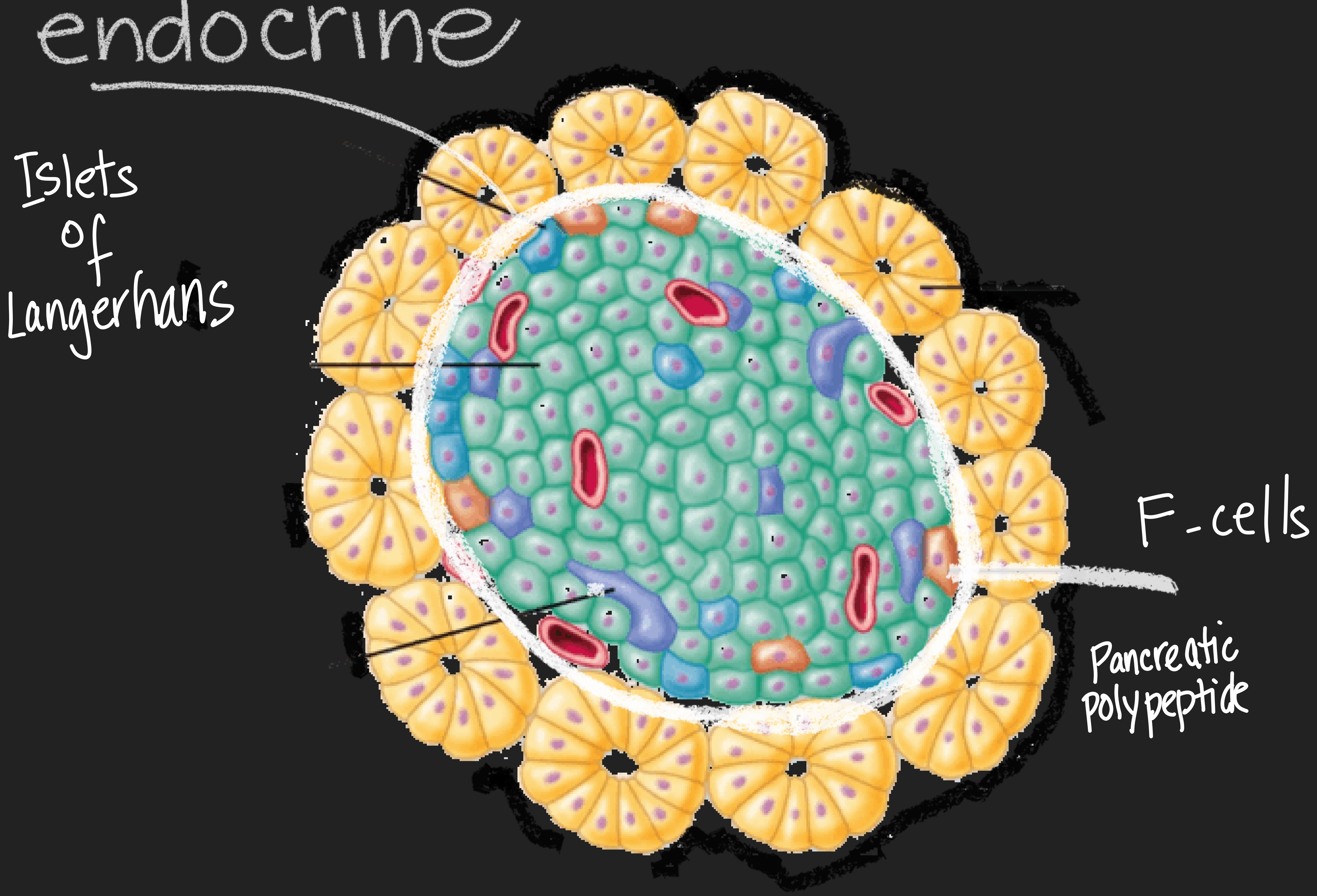
β cells

insulin

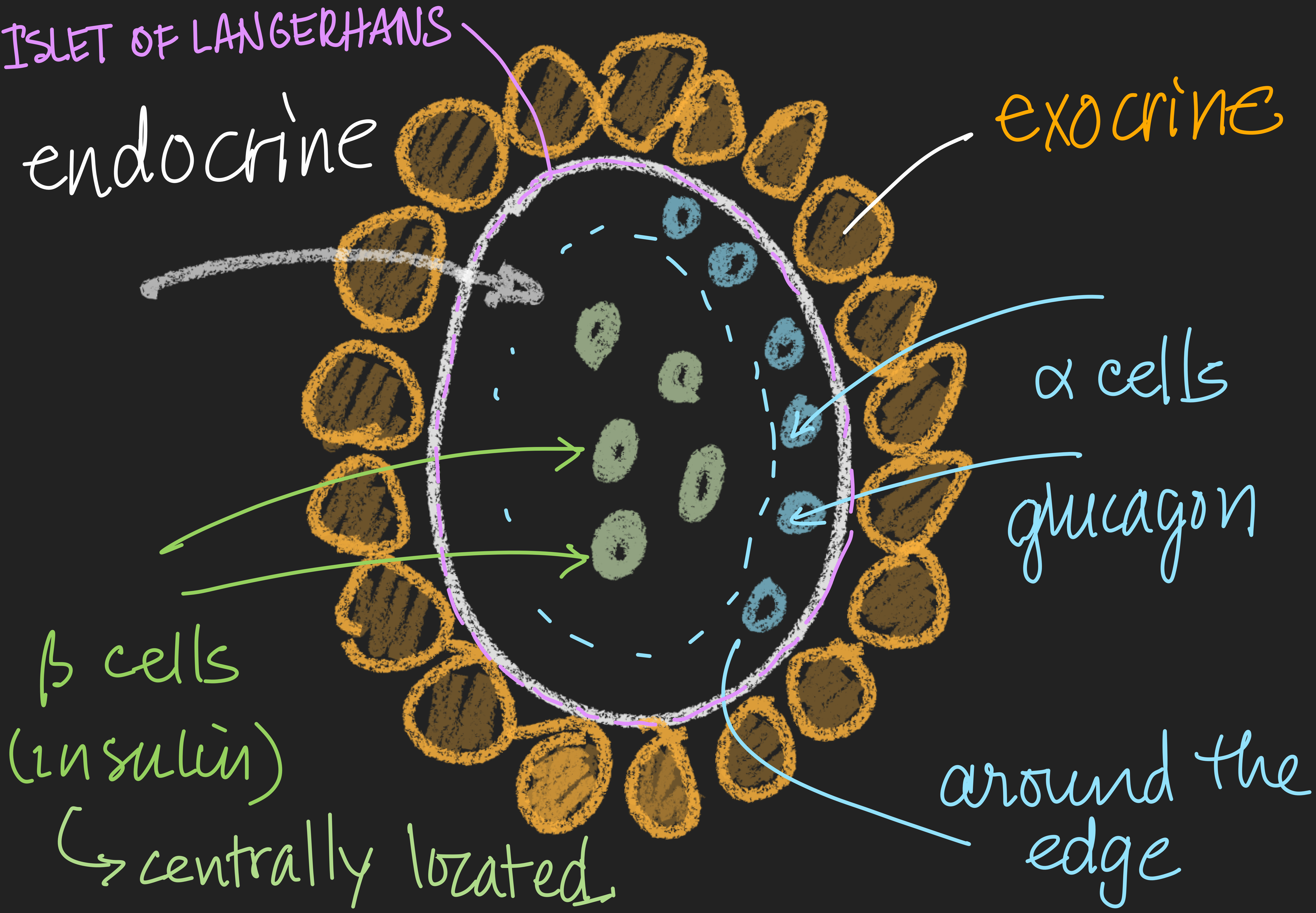



endocrine
Islets of Langerhans
α cells
(glucagon)

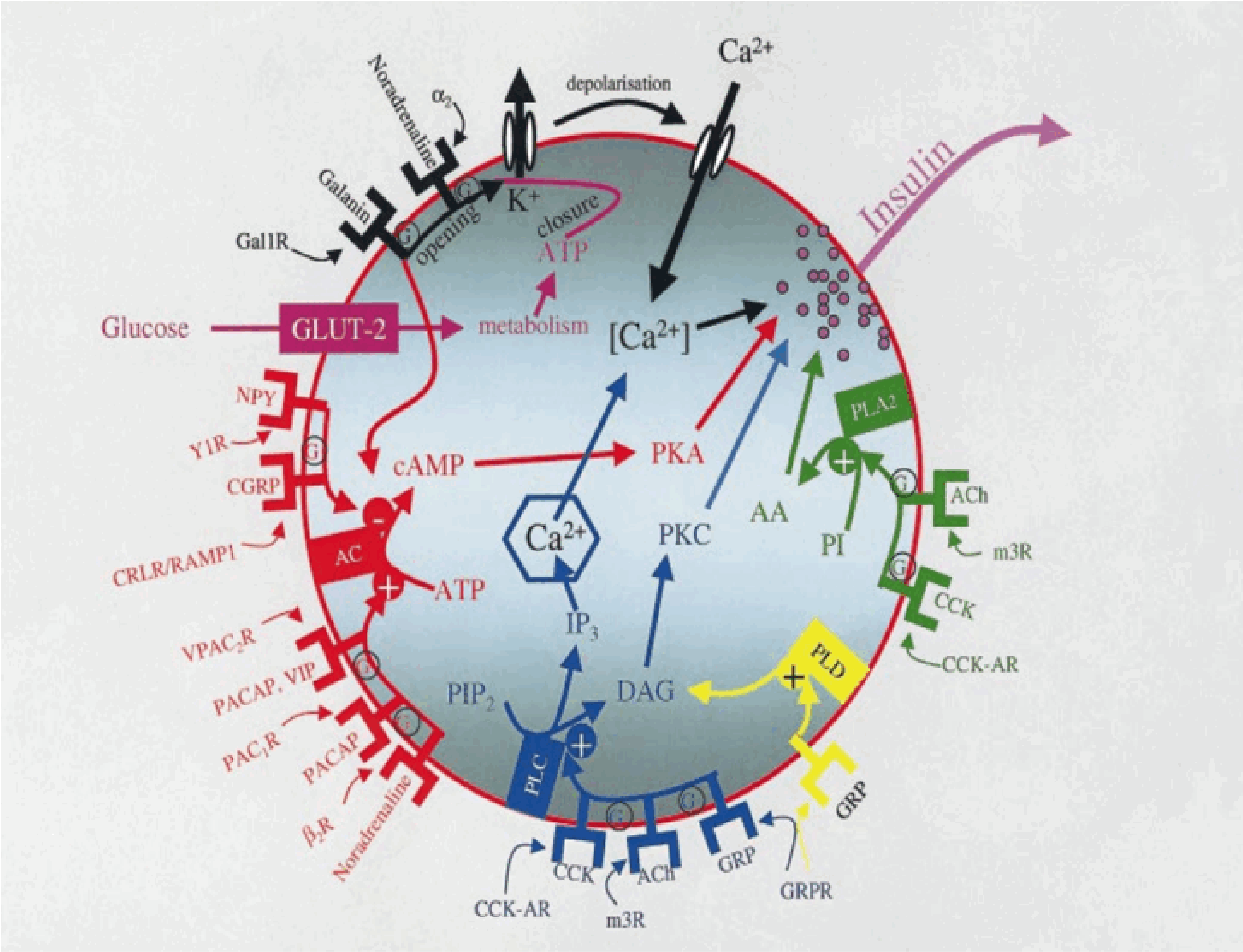

endocrine
Islets of Langerhans
δ cells
somatostatin


endocrine
Islets of Langerhans
F-cells
Pancreatic polypeptide

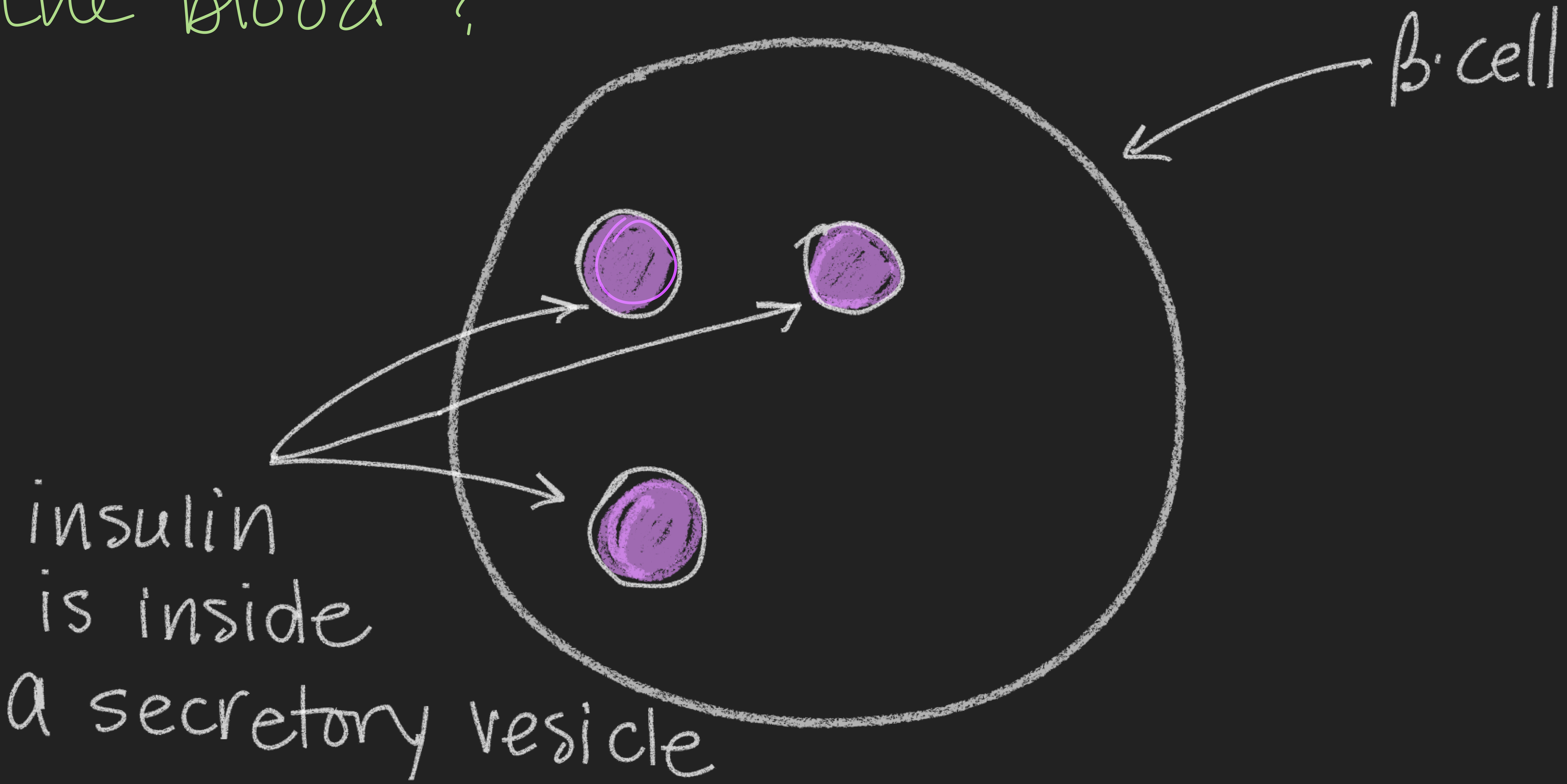
ORGANIZATIONAL STRUCTURE:



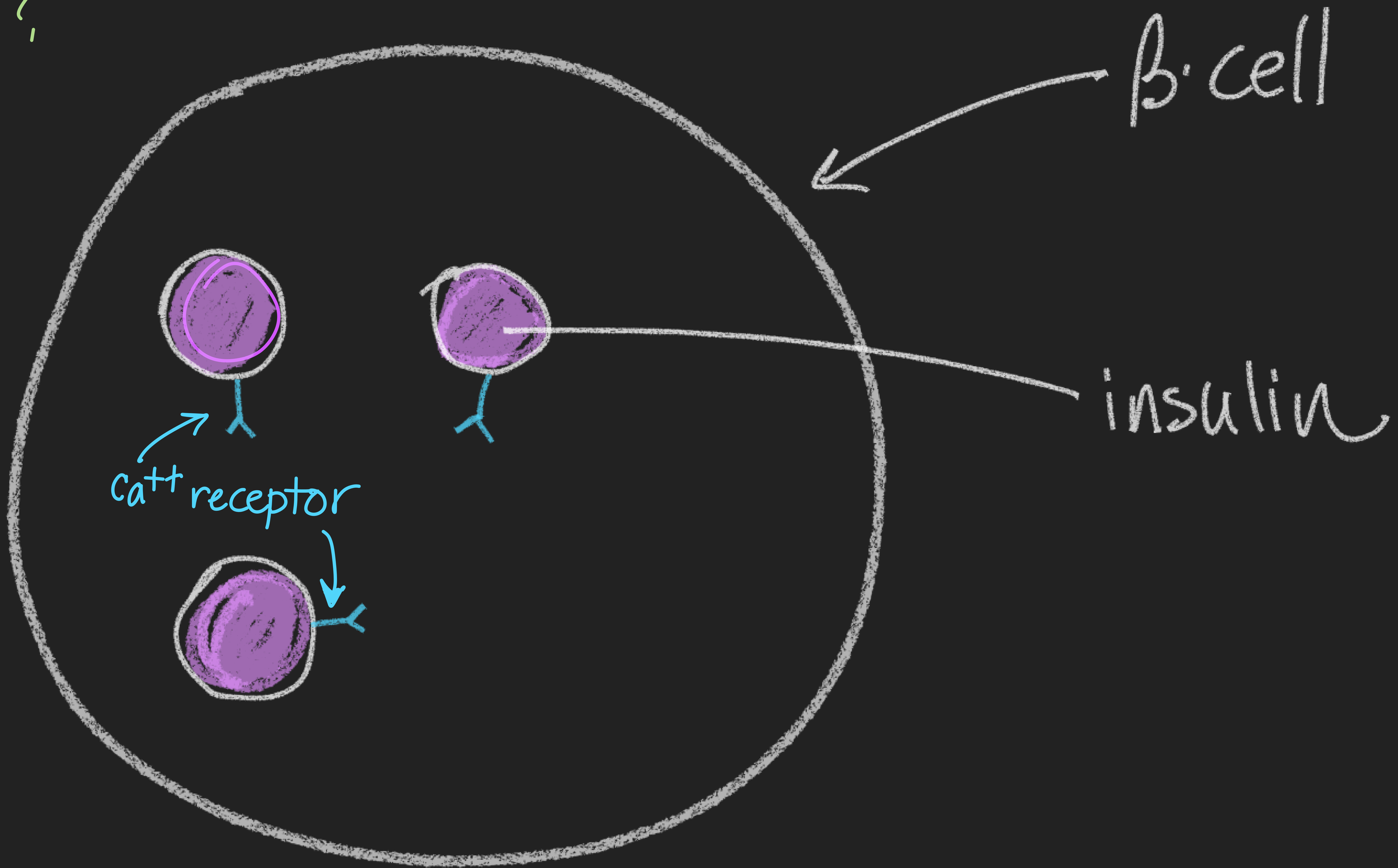
INSULIN SECRETION β cells:



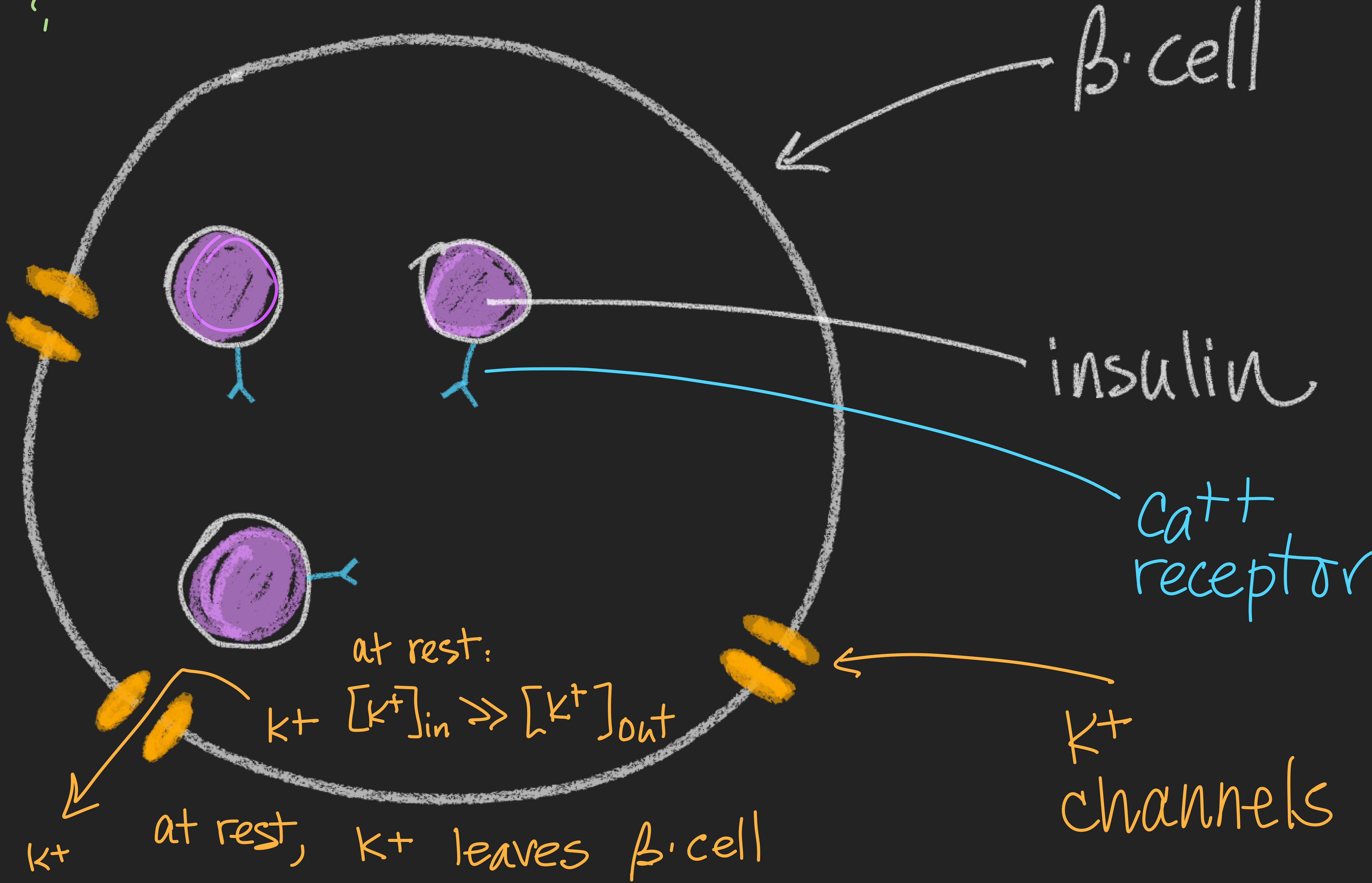
How does a β-cell secrete insulin into the blood ?



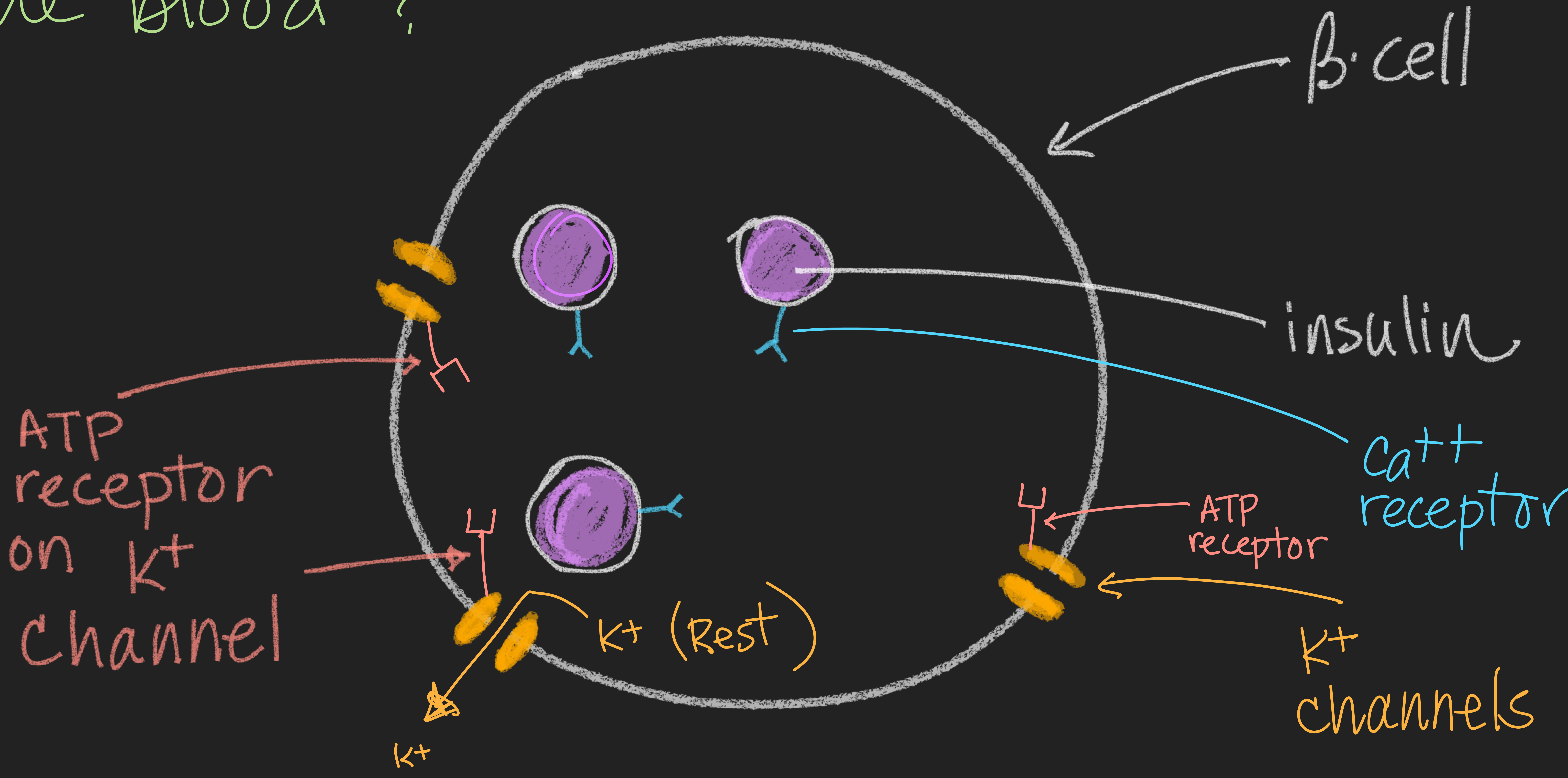
How does a β-cell secrete insulin into the blood?



How does a β-cell secrete insulin into the blood?



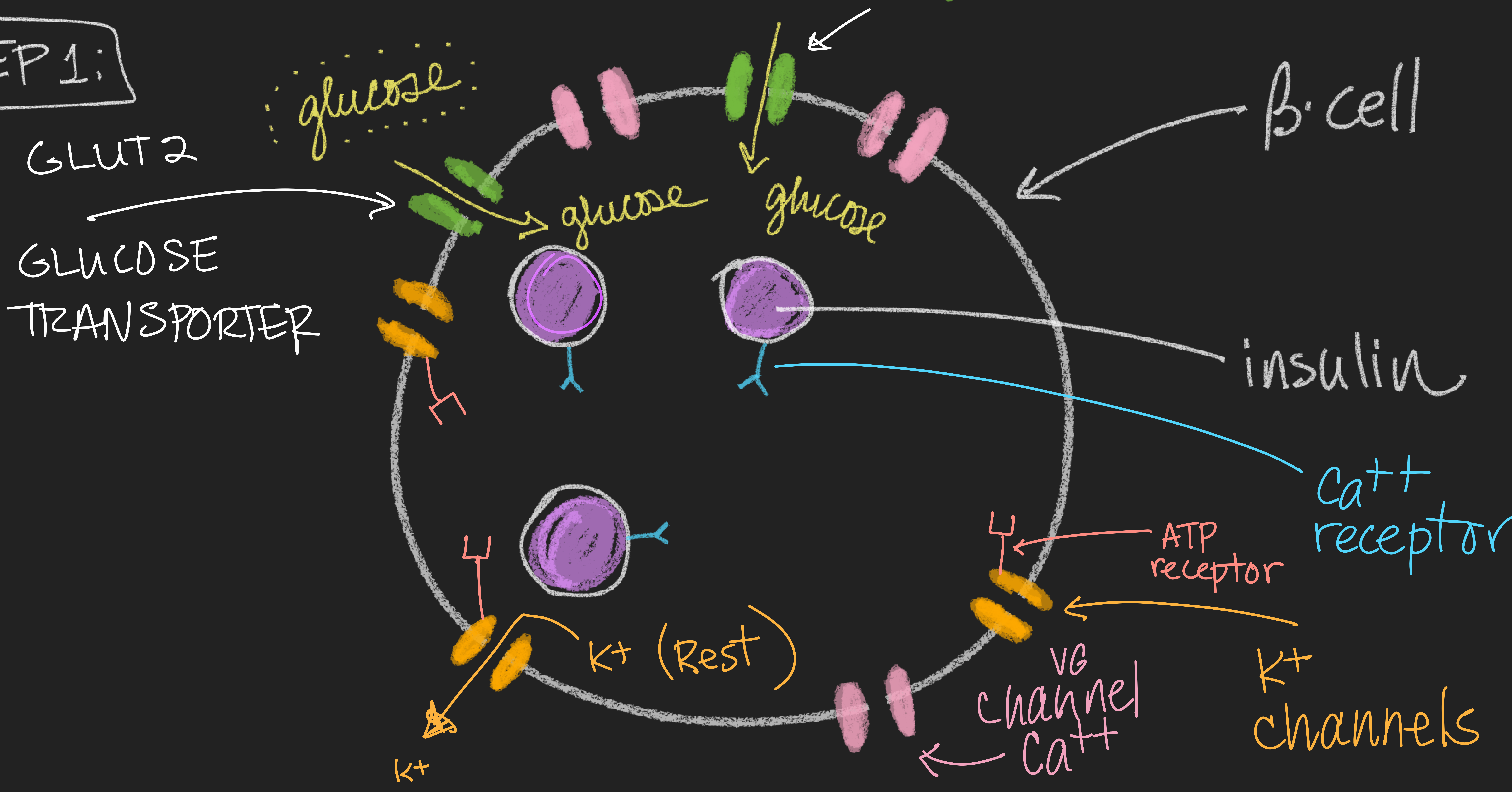
How does a β-cell secrete insulin into the blood ?



How does a β-cell secrete insulin into the blood ?

GLUCOSE ENTERS VIA GLUT2

STEP 1:



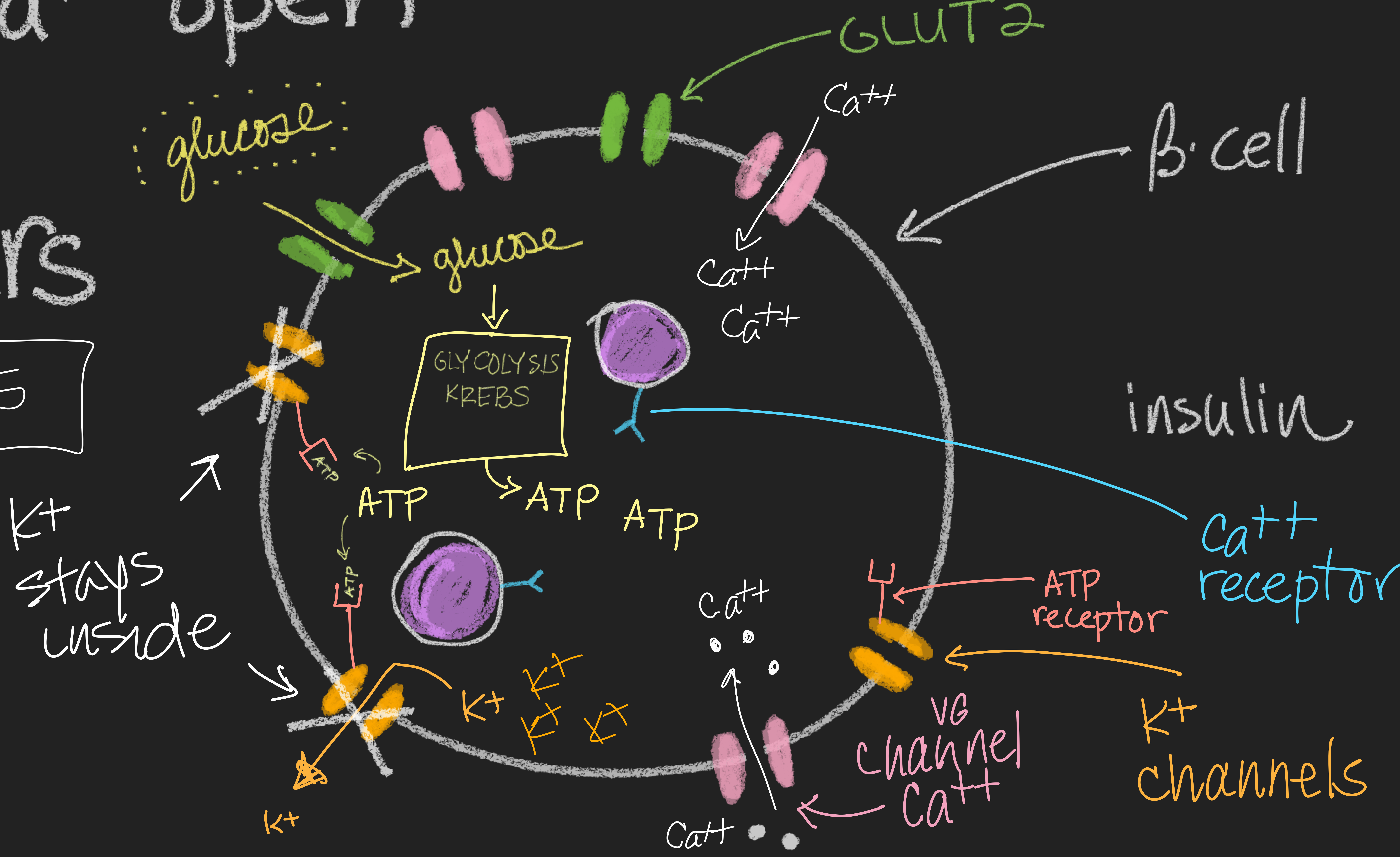
GLUCOSE IS OXIDIZED

ATP BINDS TO K+ CHANNEL


STEP 4
ATP-K+
CLOSES
K+
CHANNEL
DEPOLARIZE
glucose
GLUT2
β·cell
glucose
GLYCOLYSIS
KREBS
ATP
ATP
ATP
ATP
ATP
insulin
Ca++
receptor
ATP
receptor
K+
stays
inside
K+ (Rest)
K+
VG
channel
Ca++
K+
channels

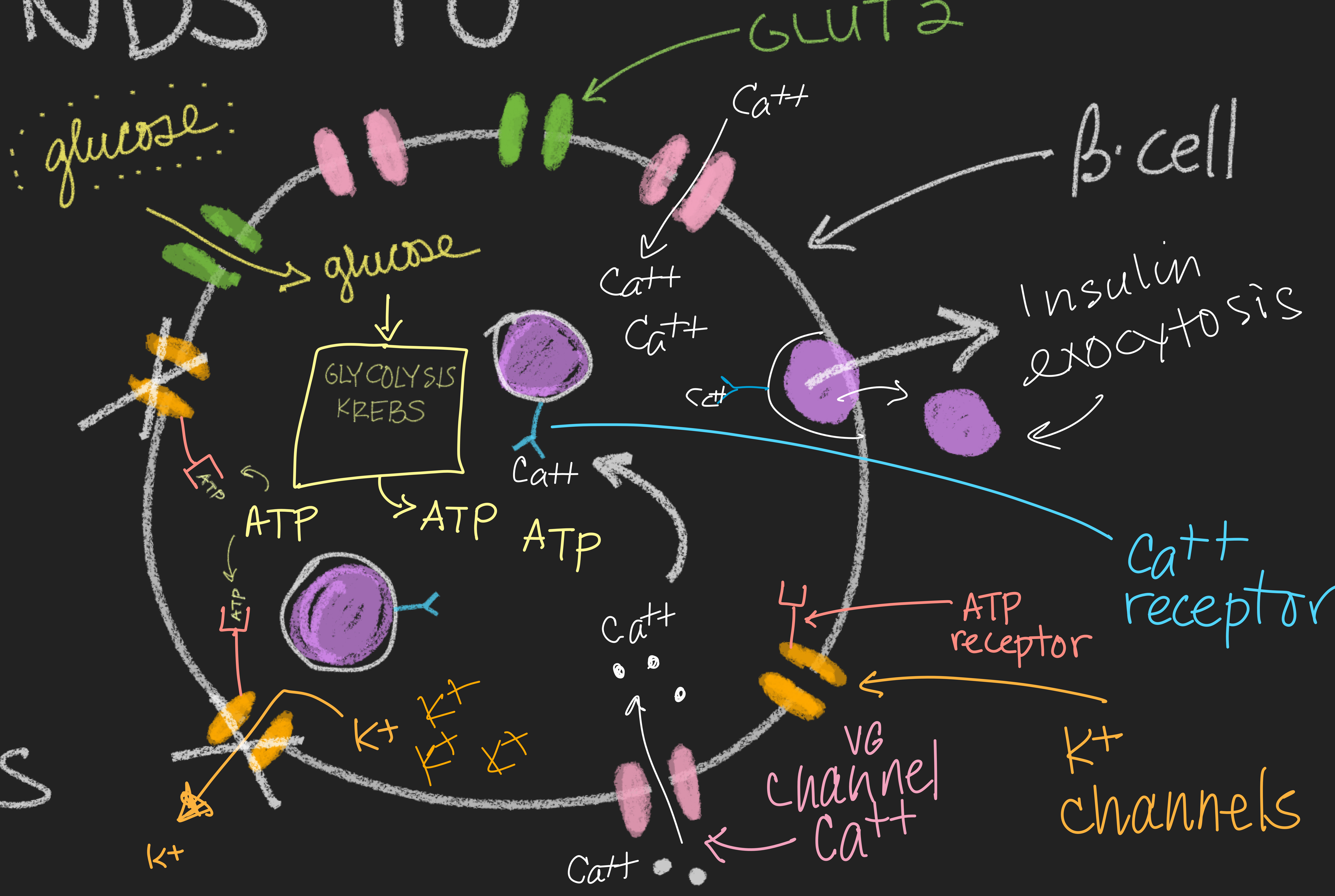
VG Ca++ open
Ca++ enters

STEP 5



Ca++ BINDS TO INSULIN & VESICLE FUSES => endocytosis

STEP 6




β-cell INSULIN release
LIVER
GLUT2
glucose
glucose
GLYCOLYSIS
KREBS
ATP
ATP
ATP
ATP
ATP
Ca++
Ca++
Ca++
Ca++
Ca++
Ca++
Ca++
Insulin
portal
venus
blood
ATP
receptor
VG
channel
Ca++
K+
channels
K+
K+
K+
K+
K+