

ENDOCRINE FUNCTION OF PANCREAS

OBJECTIVES

- **Structure, mechanism of secretion and functions of insulin**
- **How glucose enters into cells of the body**
- **The effects of insulin deficiency**
- **Role of different hormones in glucose homeostasis**

PANCREAS: FUNCTIONAL ANATOMY

⊗ Ducts and blood vessels

☞ 18%

⊗ Exocrine portion

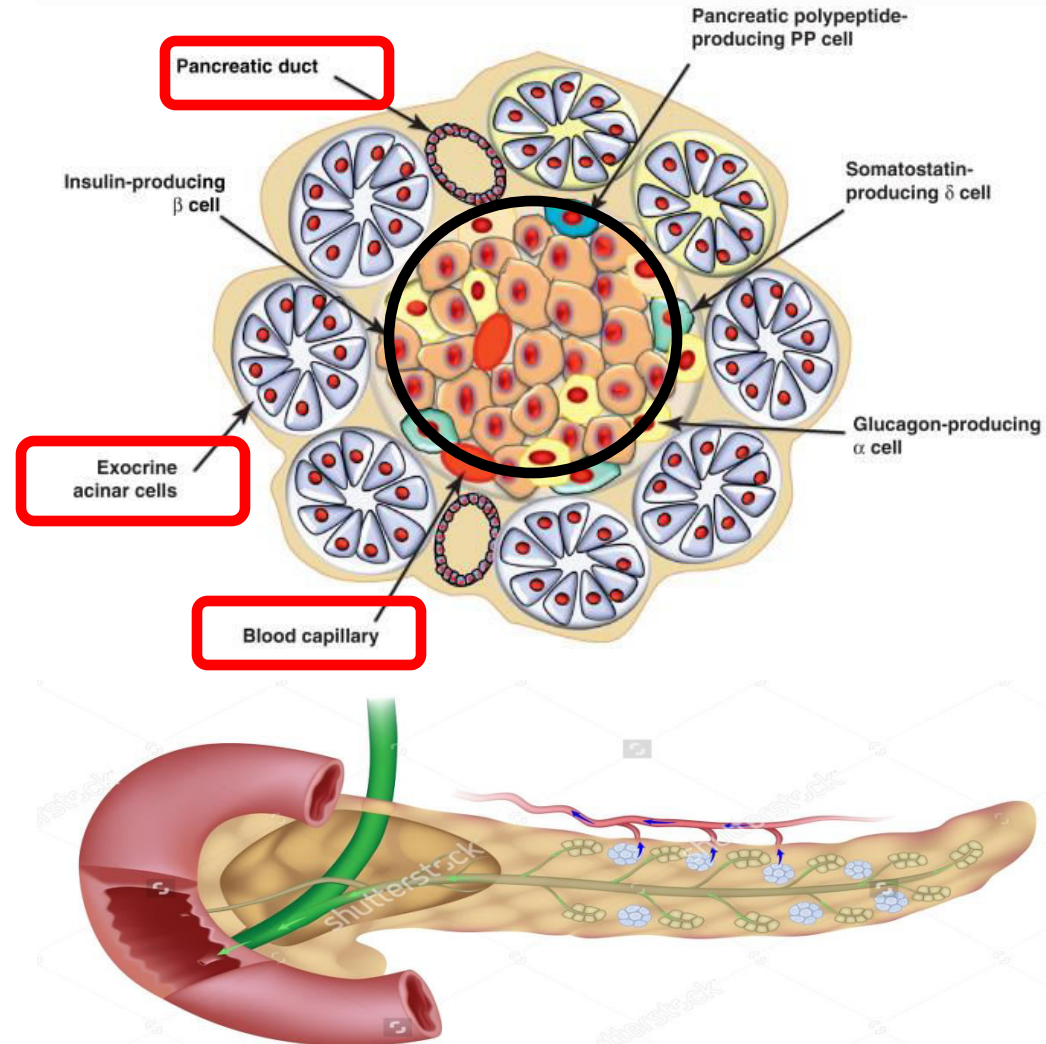
☞ 80%

- Digestive enzymes

⊗ Endocrine portion

☞ 2%

- Hormones



Islets of Langerhans

⊗ 1-2 million islets/pancreas

⊗ Secrete polypeptide hormones

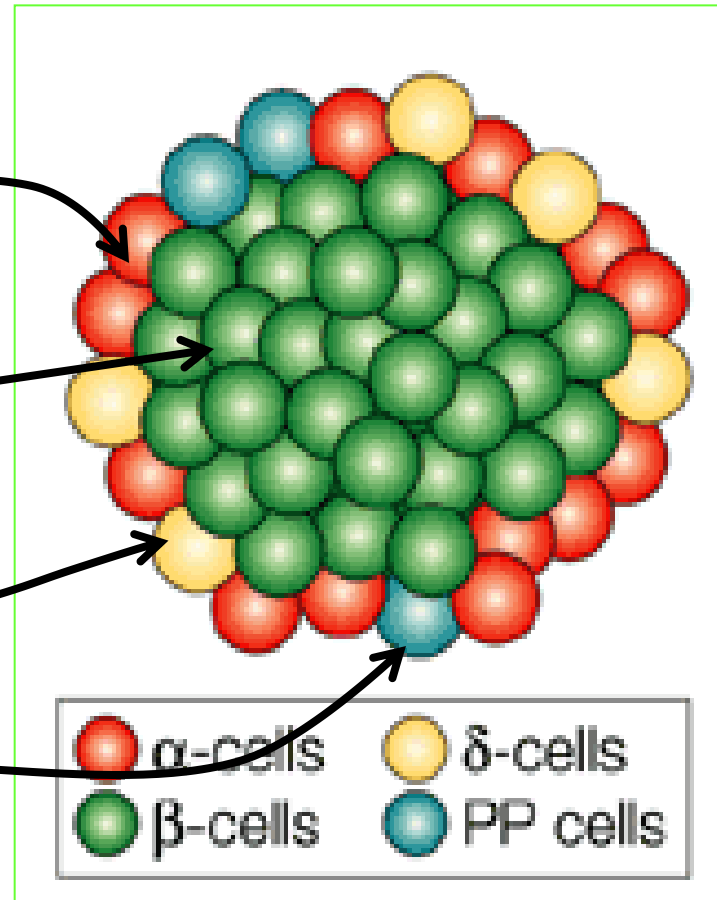
1) **Alpha (α) cells** → glucagon

2) **Beta (β) cells** → insulin

☞ Most common cell type

3) **Delta (δ) cells** → somatostatin

3) **Gamma (γ) cells (pp)** → pancreatic polypeptide



INSULIN STRUCTURE & SPECIES SPECIFICITY

☉ **Chemistry:** polypeptide [51-AA]

☛ A chain 21AA

☛ B chain 30 AA

☉ **Species Specificity:**

☛ Bovine insulin:

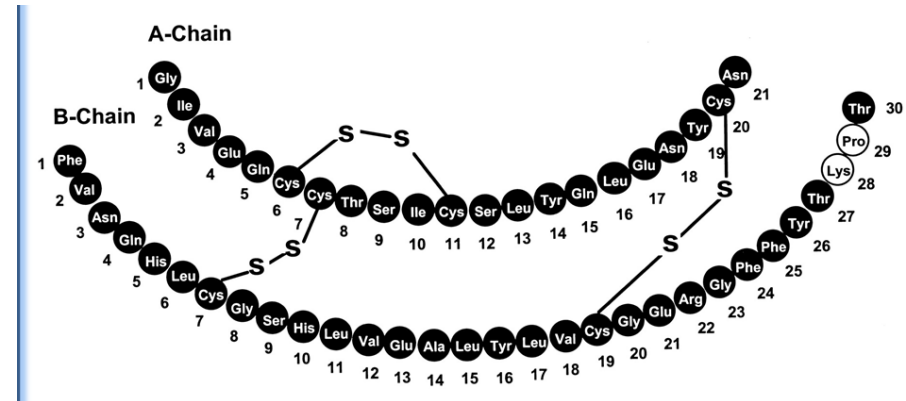
- Biologically active
- Antigenic (Ab production)

☛ Porcine insulin:

- 1 AA difference less antigenic

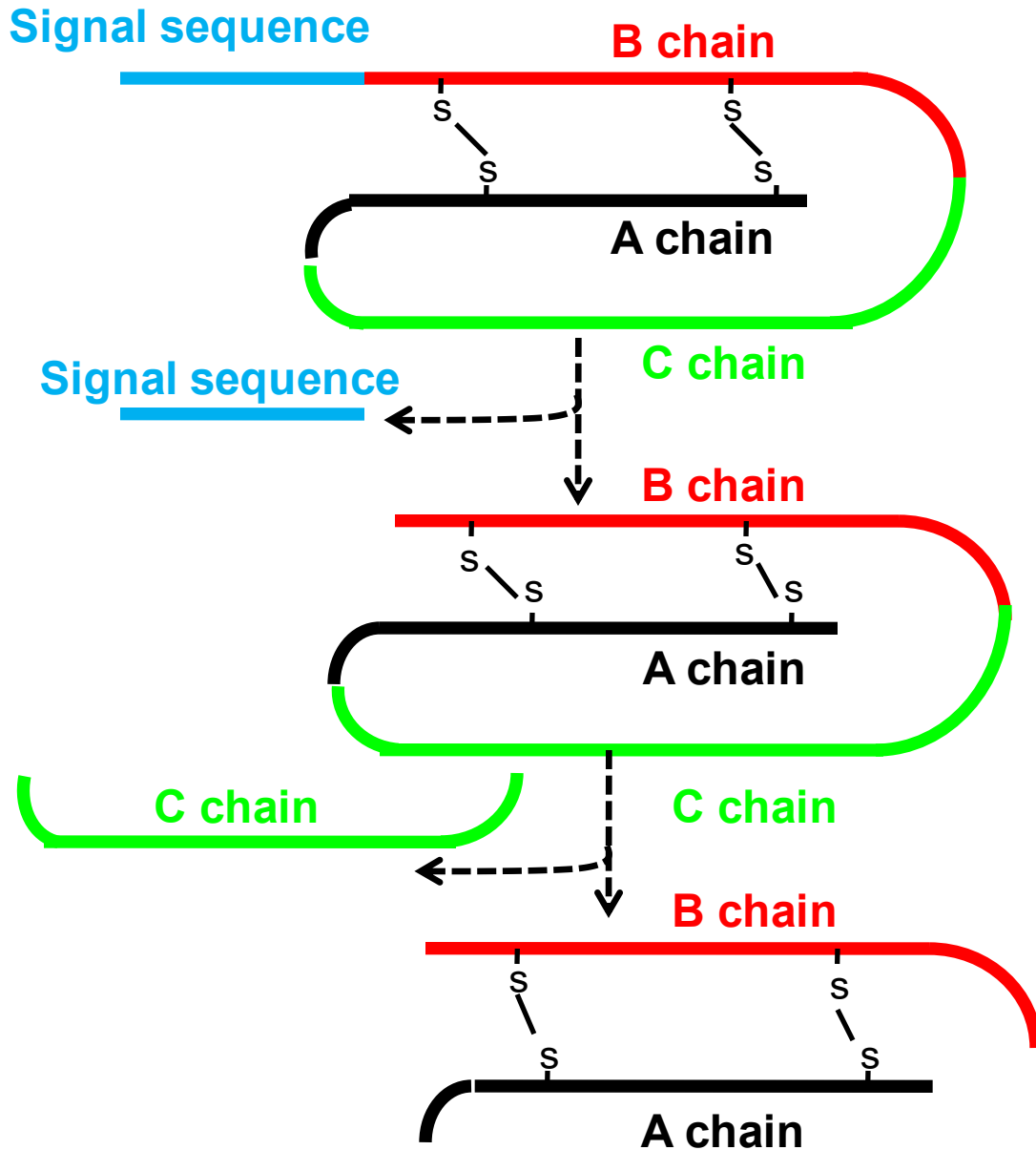
☛ Human insulin:

- Produced in bacteria by recombinant DNA technology is now widely used to avoid antibody formation



BIOSYNTHESIS & SECRETION

- Secretion from β cells:
- 90–97% insulin along with equimolar amounts of C peptide
 - 3-10% proinsulin (little biological activity)



Preproinsulin (4 peptides)

Rough ER

Proinsulin (3 peptides)

Golgi apparatus

Insulin (2 peptides)

TRANSPORT

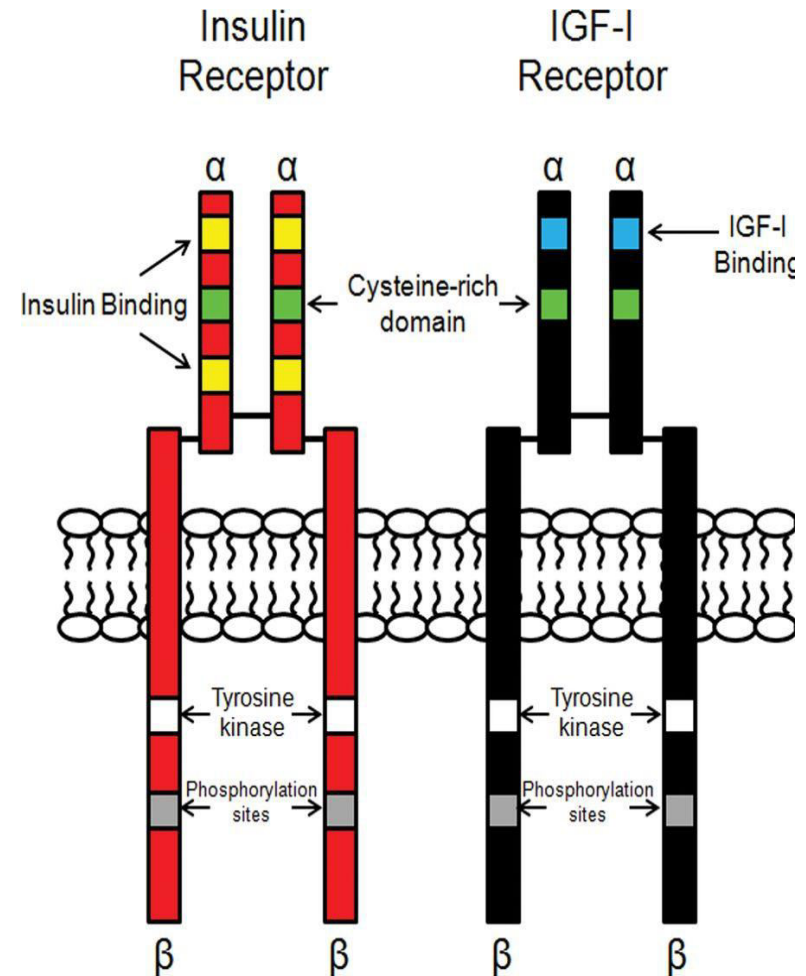
- Free in plasma (short half life) 5min

INACTIVATION

- Insulinase

INSULIN RECEPTORS

- 4 subunits held by disulfide link
- 2 α subunits (outside) insulin binding
- 2 β subunits (inside) tyrosine kinase



CELLULAR EFFECT

Rapid (sec)
membrane

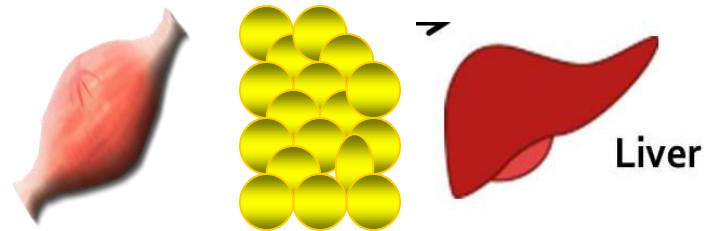
Intermediate (min)
cytoplasm

Delayed (hr)
nucleus

⊙ ↑ Membrane permeability to Glucose, AA & K^+ (insulin sensitive cells)

⊙ Phosphorylation and dephosphorylation of enzymes

⊙ ↑ or ↓ DNA & RNA → protein synthesis



HORMONE OF ABUNDANCE

HOW GLUCOSE ENTERS INTO THE CELLS

```
graph TD; A[HOW GLUCOSE ENTERS INTO THE CELLS] --> B[Secondary active transport with Na+  
(Na+ dependent glucose transporter)  
SGLT1,2]; A --> C[Facilitated diffusion  
(Glucose transporter)  
GLUT 1-7]; B --> D[SGLT 1  
▪ Small Intestine, Renal Tubules  
SGLT 2:  
▪ Renal Tubules];
```

Secondary active transport with Na⁺
(Na⁺ dependent glucose transporter)
SGLT1,2

Facilitated diffusion
(Glucose transporter)
GLUT 1-7

SGLT 1

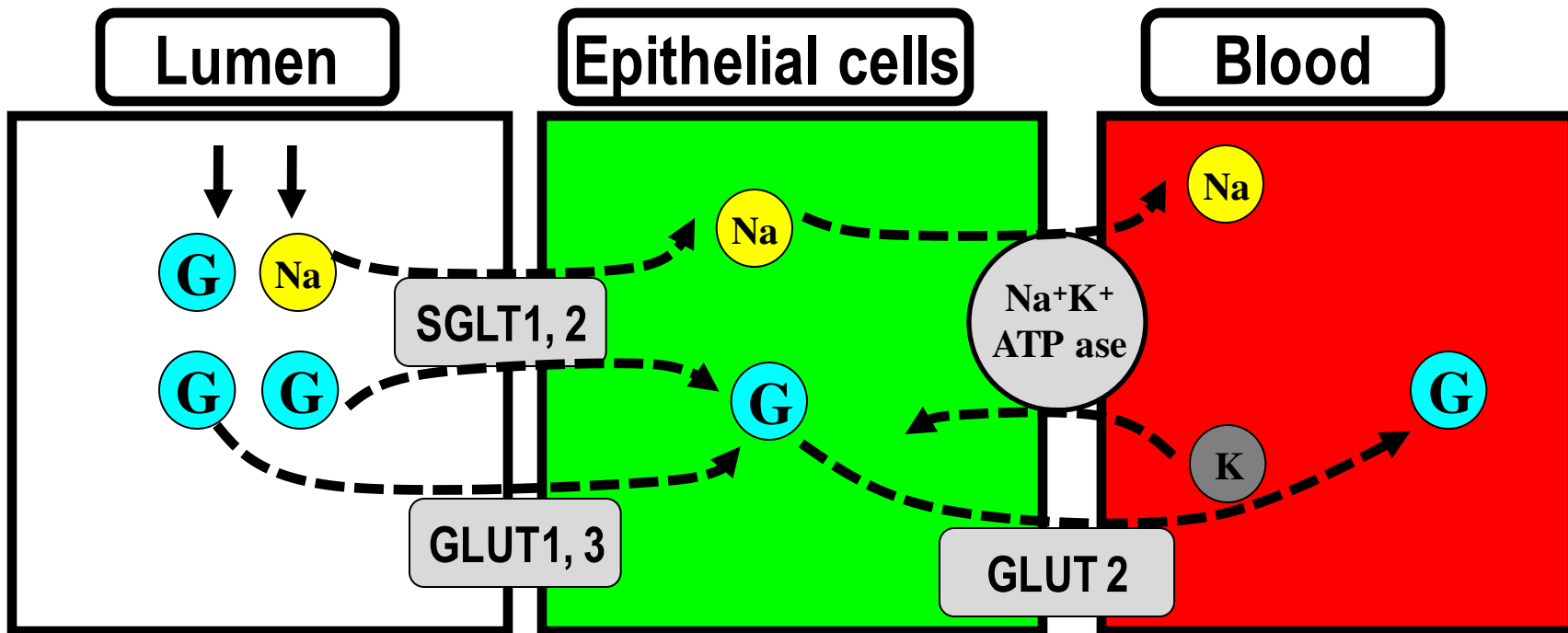
- Small Intestine, Renal Tubules

SGLT 2:

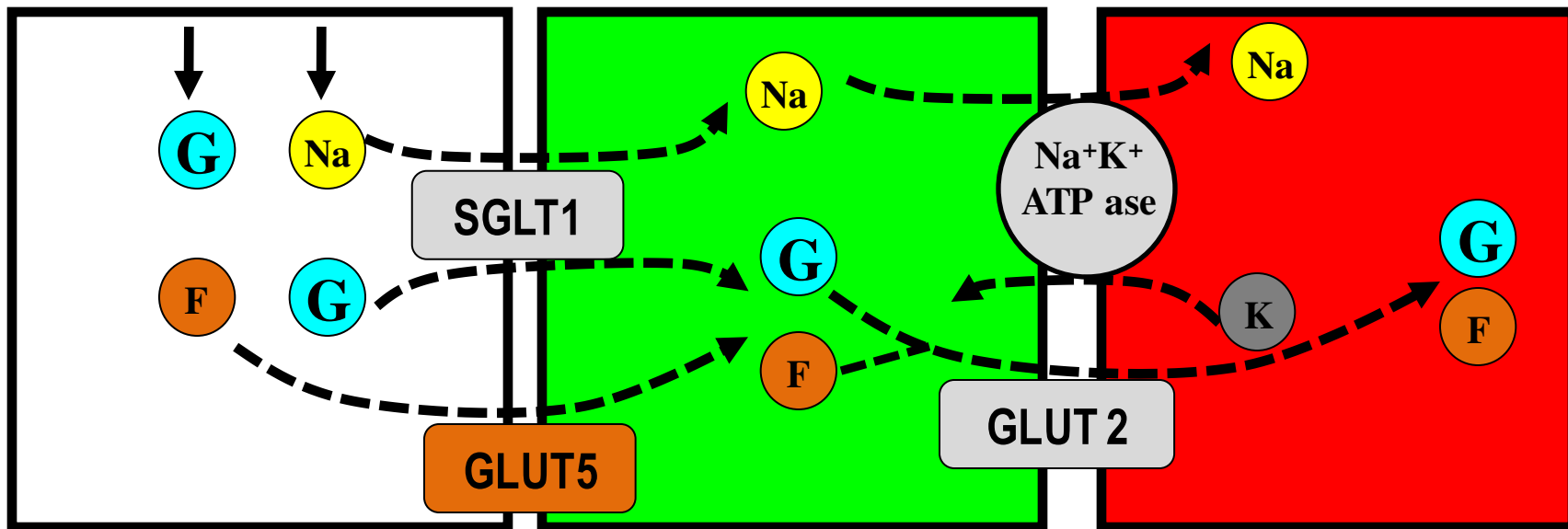
- Renal Tubules

GLUCOSE REABSORPTION IN NEPHRON AND INTESTINE

NEPHRON



INTESTINE



GLUT 1

GLUT 2

GLUT 3

GLUT 4



GLUT 5

GLUT 6

GLUT 7

GLUT 1: Basal glucose uptake

⇒ BBB, brain, Placenta, kidneys & RBCs

GLUT 2: B cell glucose sensor, intestine and renal epith. (out of)

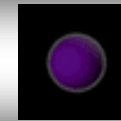
⇒ B cells of islets, liver & epithelial cells of SI & kidneys

GLUT 3: Basal glucose uptake

⇒ Brain, placenta & kidneys

GLUT 4: Insulin stimulated glucose uptake

⇒ Skeletal, cardiac muscles & adipose tissue



GLUT 5: Fructose transport

⇒ Jejunum & sperm

GLUT 6: None

GLUT 7: Glucose 6 phosphate transporter in ER

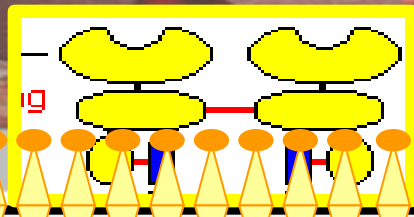
⇒ Liver & other tissues

MECHANISM OF ACTION (insulin)

ECF

Ins

Ins

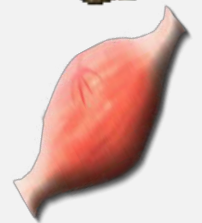
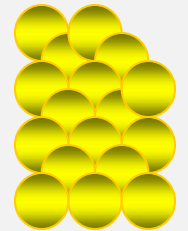
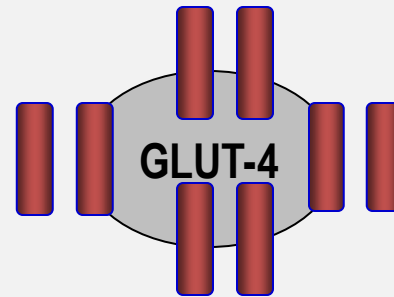


Tyrosine Kinase

P

Tyrosine Kinase

P



IRS-1

Phospho Kinase

ICF

