# Chapter 11 Insulin
## Lecture 16

Pancreas

most of organ: exocrine secretion digestive enzymes & $HCO_3^-$

endocrine cells only 2% of total organ

surrounded by capillaries & parasympathetic/sympathetic

A. Islets of Langerhans

1869 Paul Langerhans German anatomist

B. four cell types

1. β type: 75% cells

insulin & amylin

2. α type: 20% cells

glucagon

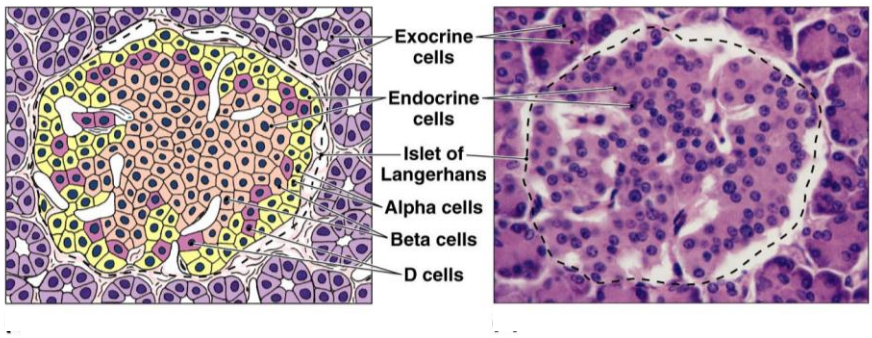
3. D type: ~5% cells

somatostatin

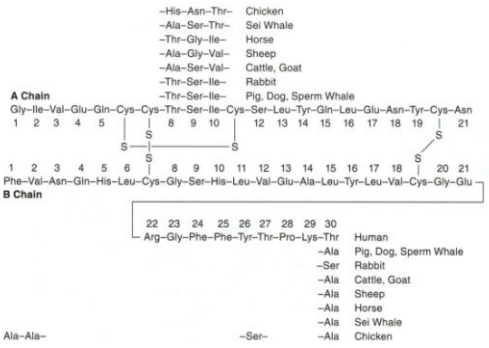
4. F (PP) type: ~<1% cells

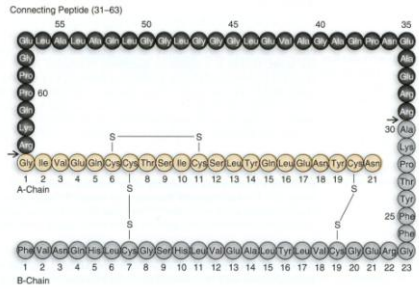
pancreatic polypeptide

| CELL | SECRETES: |
|---|---|
| Alpha cells | Glucagon |
| D cells | Somatostatin |
| Beta cells | Insulin, amylin |



## Chemical Structure of Insulin



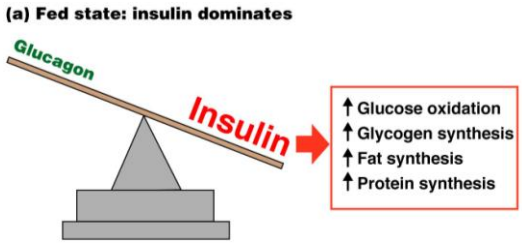

**Insulin secretion stimulated by:**

1) ↑ glucose concentrations
2) ↑ amino acids concentrations
3) feed forward effects of GI hormones
4) parasympathetic activity
5) sympathetic activity

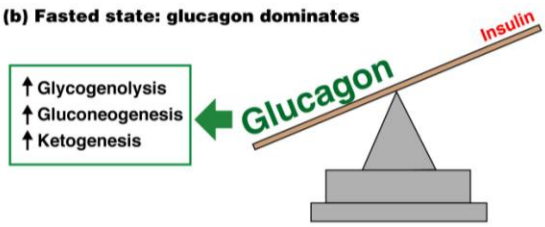
Insulin & Glucagon antagonistic

ratio titers determines dominance of hormonal action

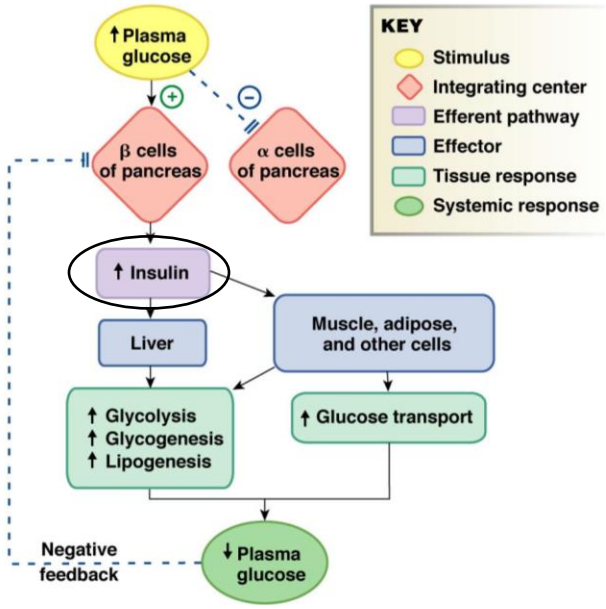
a) fed state? insulin



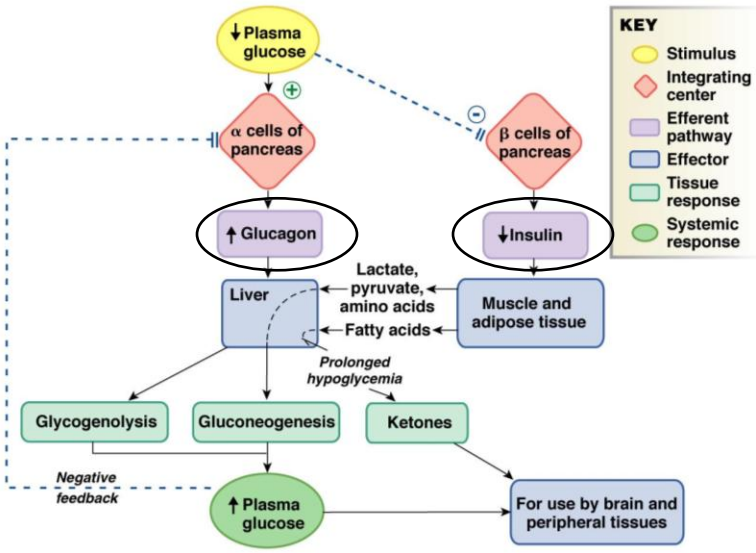

b) fasted state? hypoglycemia (low plasma glucose) glucagon



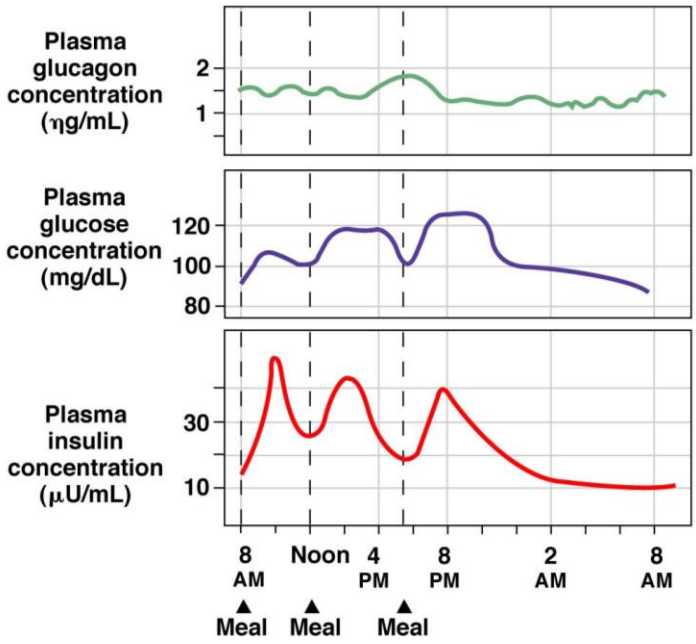
## Fed State



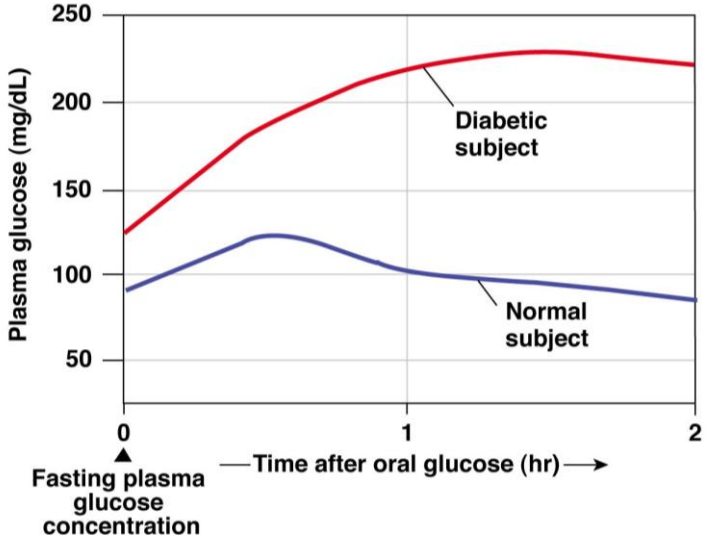

## Starved State: hypoglycemia



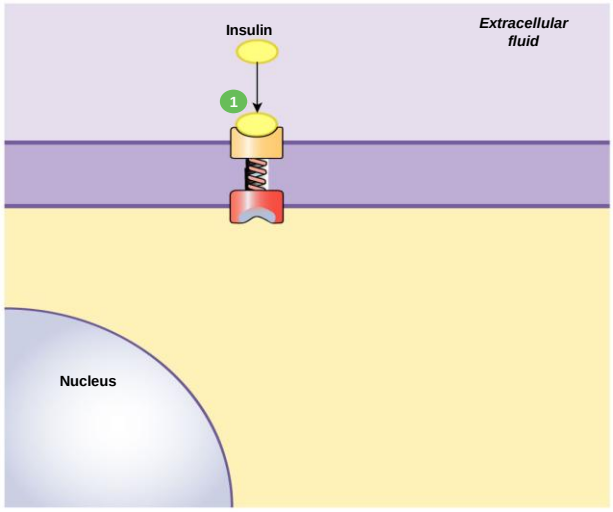
**Glucagon-glucose-insulin titers over 24 hr period**




**Normal & Abnormal Results of Glucose Tolerance Test**

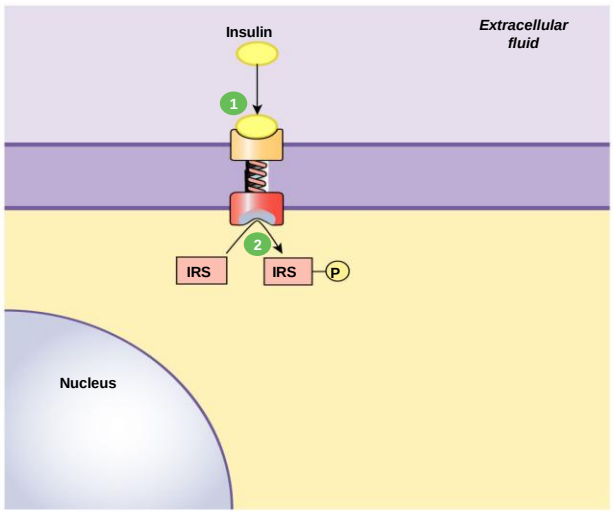


## Insulin: Cellular Mechanism of Action




1 Insulin binds to tyrosine kinase receptor.

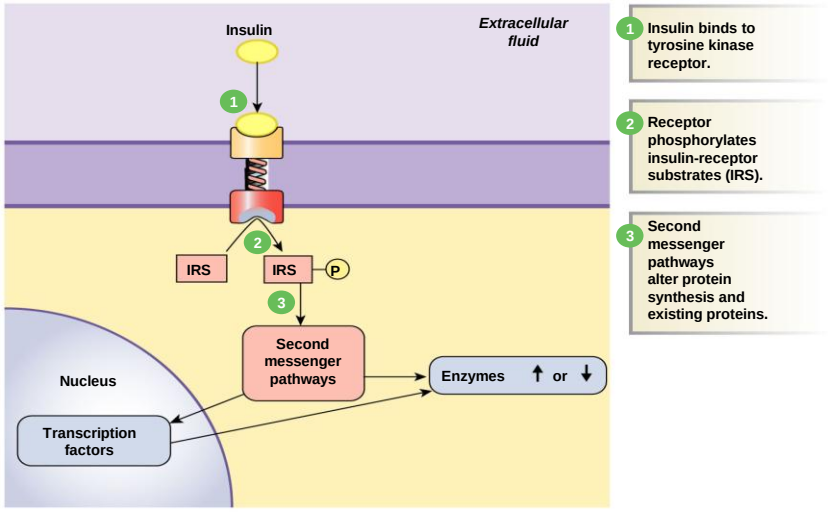
## Insulin: Cellular Mechanism of Action



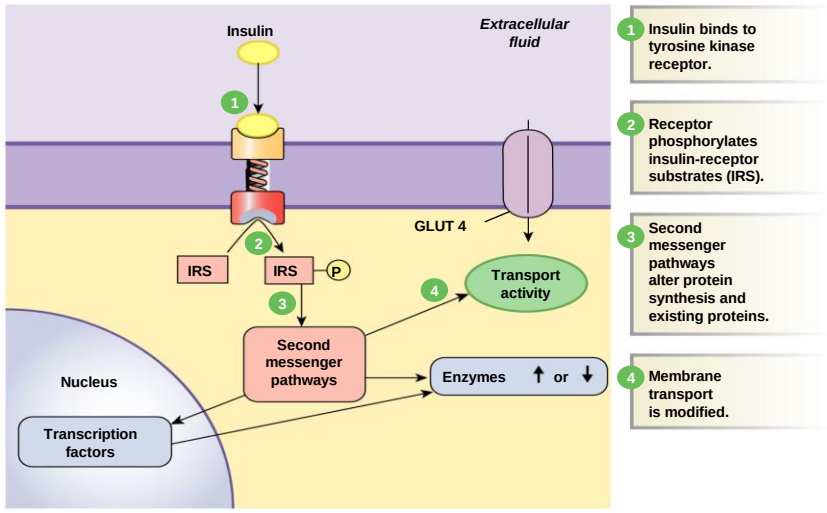

1 Insulin binds to tyrosine kinase receptor.

2 Receptor phosphorylates insulin-receptor substrates (IRS).

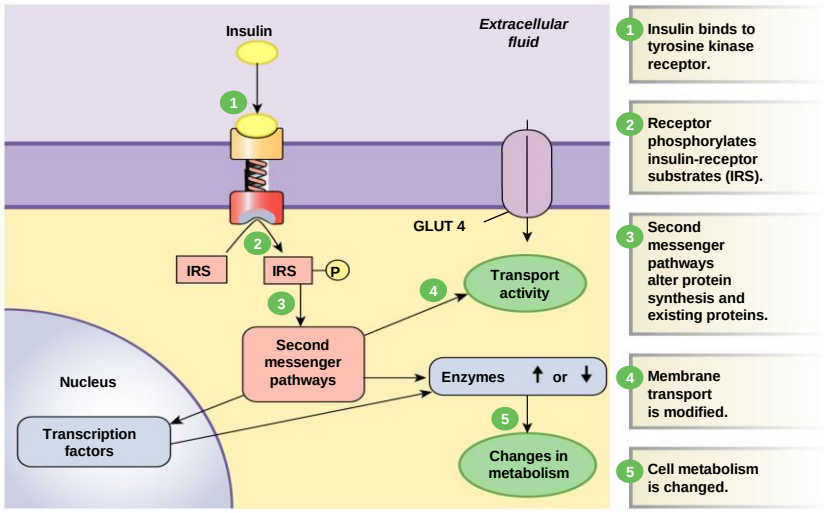
## Insulin: Cellular Mechanism of Action




## Insulin: Cellular Mechanism of Action



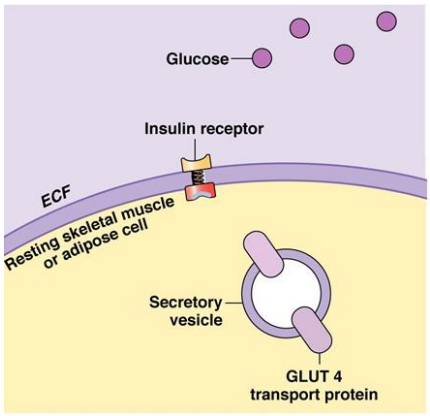
## Insulin: Cellular Mechanism of Action



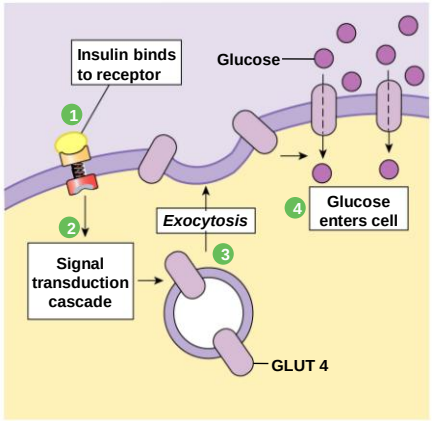

## Insulin: promotes anabolism

1) ↑ glucose transport into most, but not all, insulin-sensitive cells
2) enhances cellular utilization & storage of glucose
3) enhances utilization of amino acids
4) promotes fat synthesis

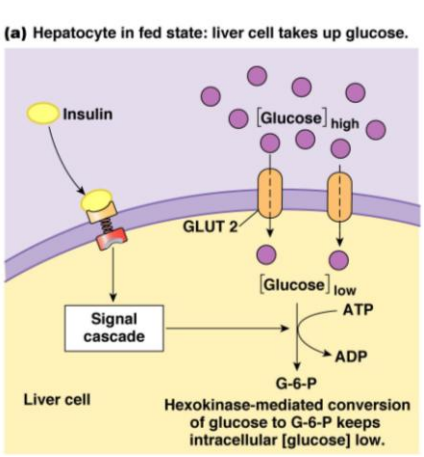
# Insulin promotes cellular glucose uptake

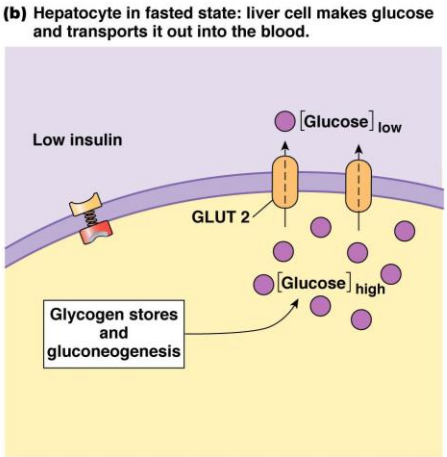



without insulin

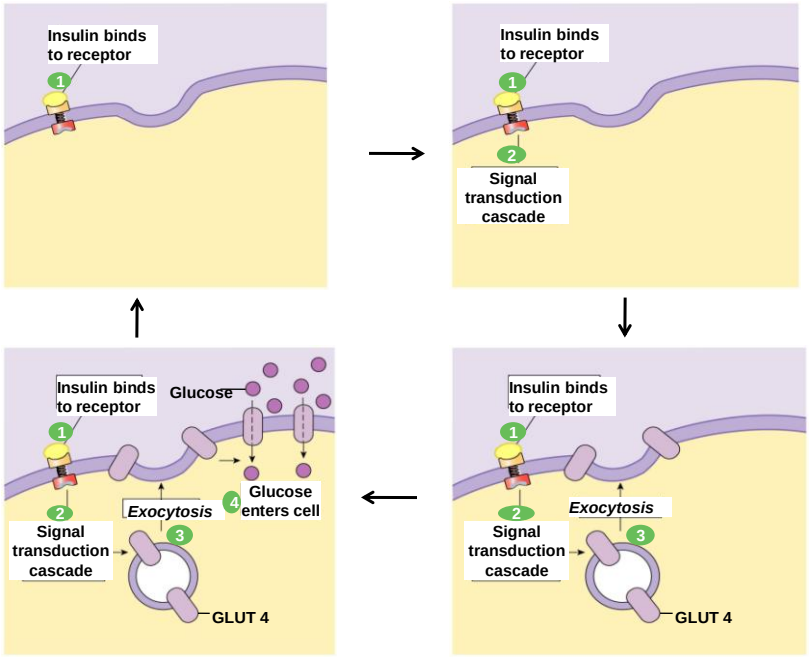



with insulin




Insulin acts **indirectly** to alter glucose uptake in hepatocytes




## Summary of Insulin

| | |
|---|---|
| Cell of origin | Beta cells of pancreas |
| Chemical nature | 51-amino acid peptide |
| Biosynthesis | Typical peptide |
| Transport in the circulation | Dissolved in plasma |
| Half-life | 5 minutes |
| Factors affecting release | Plasma [glucose] > 100 mg/dL; ↑ blood amino acids; GLP-1 (feedforward reflex); and parasympathetic activity amplifies. Sympathetic activity inhibits. |
| Target cells or tissues | Liver, muscle, and adipose tissue primarily; brain, kidney, and intestine not insulin dependent |
| Target receptor | Membrane receptor with tyrosine kinase activity; pathway with insulin-receptor substrates |
| Whole body or tissue action | ↓ Plasma [glucose] by ↑ transport into cells or ↑ metabolic use of glucose |
| Action at cellular level | ↑ Glycogen synthesis; ↑ aerobic metabolism of glucose; ↑ protein and triglyceride synthesis |
| Action at molecular level | Inserts GLUT transporters in muscle and adipose cells; alters enzyme activity. Complex signal transduction pathway involved. |
| Feedback regulation | ↓ Plasma [glucose] shuts off insulin release. |
| Other information | Growth hormone and cortisol are antagonistic. |

## Summary of Glucagon

| | |
|---|---|
| Cell of origin | Alpha cells of pancreas |
| Chemical nature | 29-amino acid peptide |
| Biosynthesis | Typical peptide |
| Transport in the circulation | Dissolved in plasma |
| Half-life | 4–6 minutes |
| Factors affecting release | Stimulated by plasma [glucose] < 200 mg/dL, with maximum secretion below 50 mg/dL; ↑ blood amino acids |
| Target cells or tissues | Liver primarily |
| Target receptor/ second messenger | G protein-coupled receptor linked to cAMP |
| Whole body or tissue action | ↑ Plasma [glucose] by glycogenolysis and gluconeogenesis; ↑ lipolysis leads to ketogenesis in liver |
| Action at molecular level | Alters existing enzymes and stimulates synthesis of new enzymes |
| Feedback regulation | ↑ Plasma [glucose] shuts off glucagon secretion |
| Other information | Member of secretin family (along with VIP, GIP, and GLP-1) |