

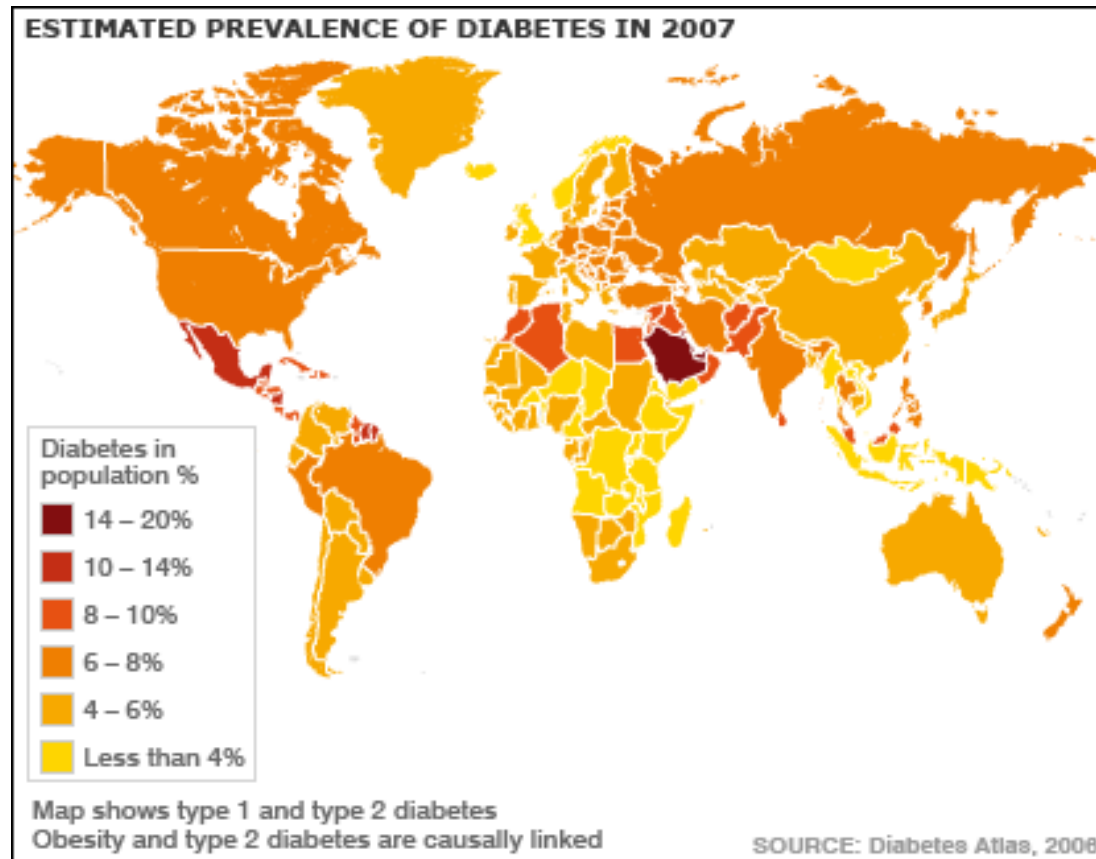
# The Endocrine Pancreas

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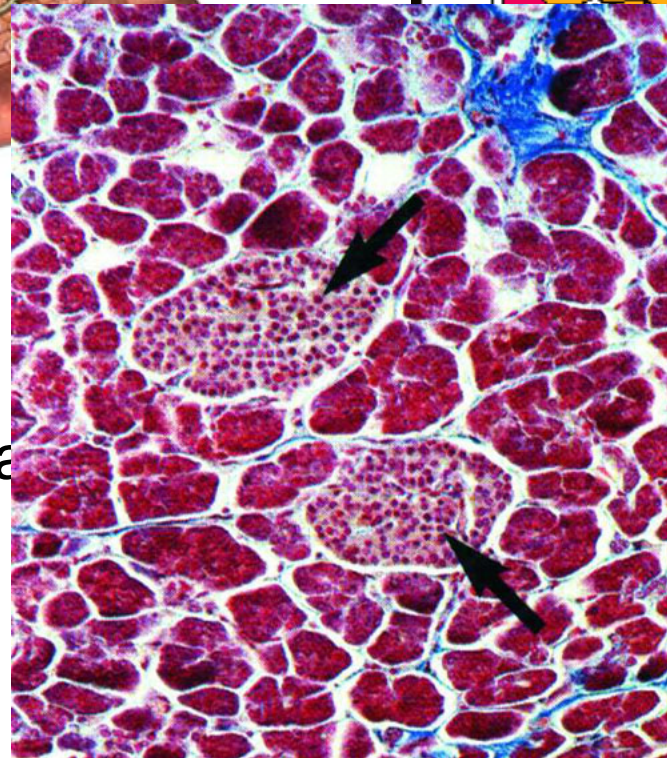
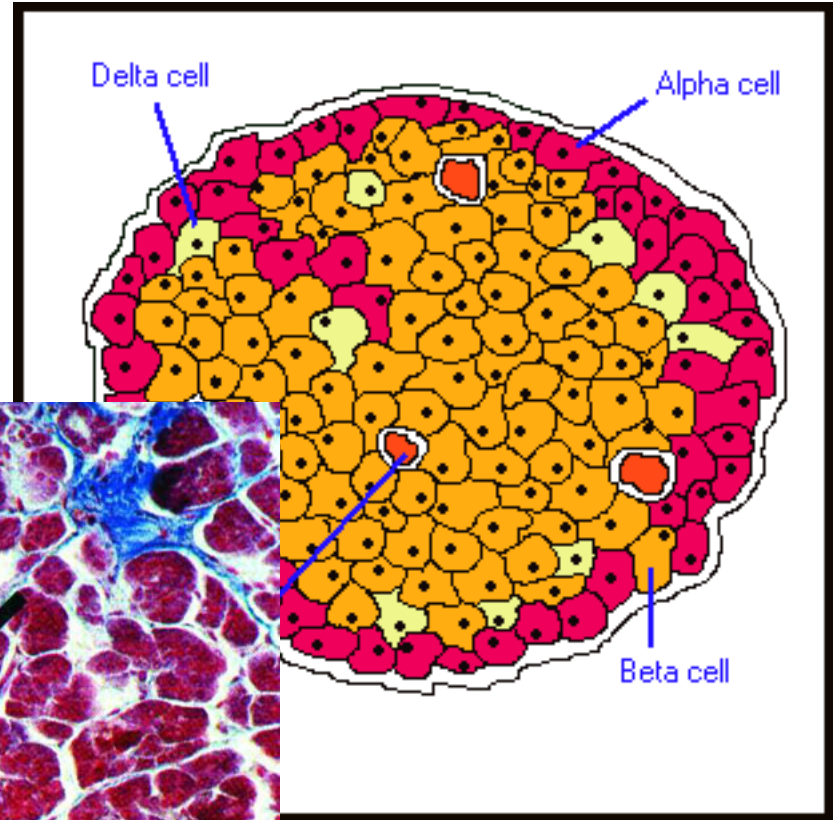
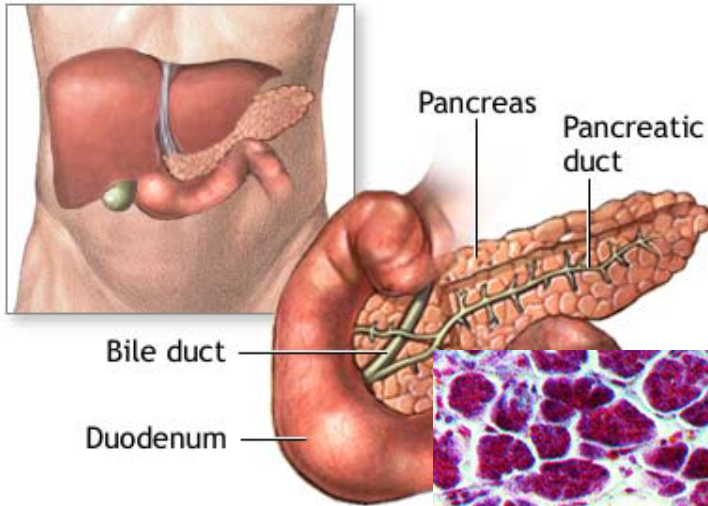
Worldwide, there are 170 million people with diabetes mellitus



- This prevalence will double before 2030
- 2.7 million with diabetes mellitus in UK
- 3.2 million deaths annually directly attributable to diabetes
- Commonest cause of end stage renal failure, blindness and non-traumatic amputations

- **Aims:**
  - To explain the endocrine pancreas and how it regulates carbohydrate, lipid and protein metabolism
- **Learning outcomes:**
  - Know the anatomy, embryology and physiology of the endocrine pancreas
  - Be able to describe functioning of alpha and beta cells ie regulation of insulin and glucagon secretion
  - Describe glucose sensing by the beta cell
  - List the principal actions of insulin and glucagon
  - Integrate the actions of insulin on intermediary metabolism

# Pancreas - Anatomy

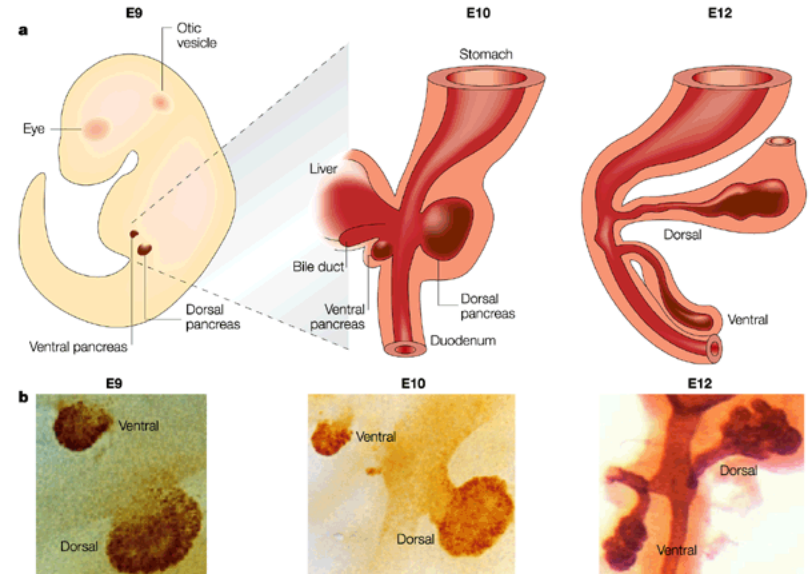


$\beta$  cell - insulin  
 $\alpha$  cell - glucagon  
 $\delta$  cell - somatostatin

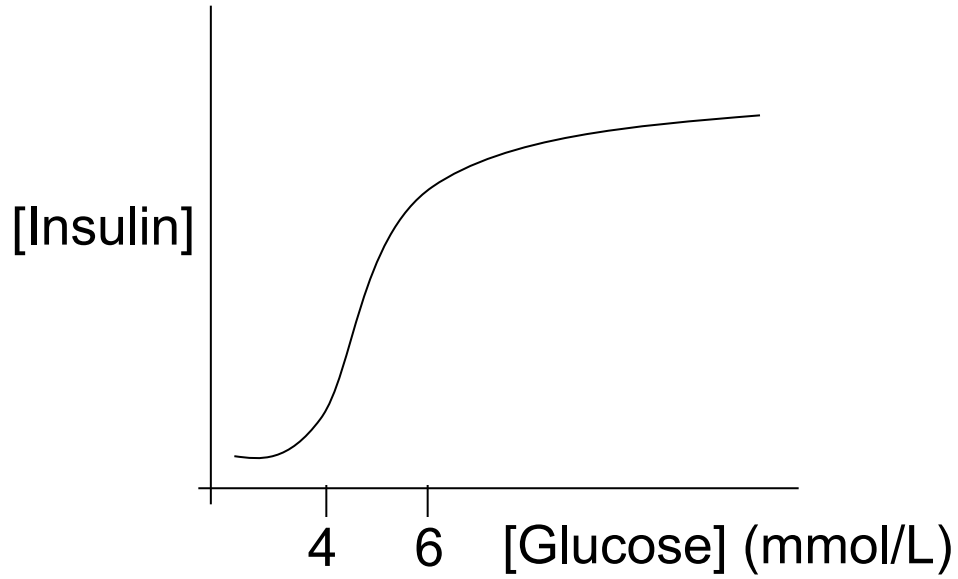
Autonomic innervation  
Islets = 2% of pancreatic  
mass, but receive 15%  
of perfusion

# Pancreas - Embryology

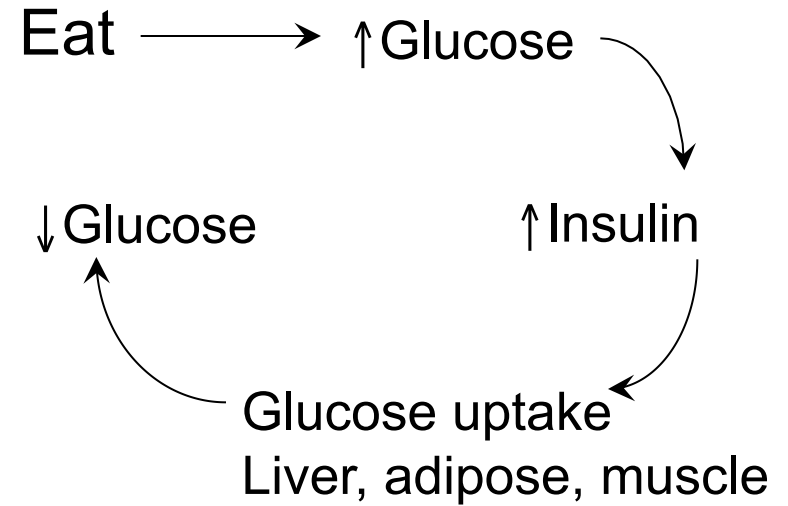
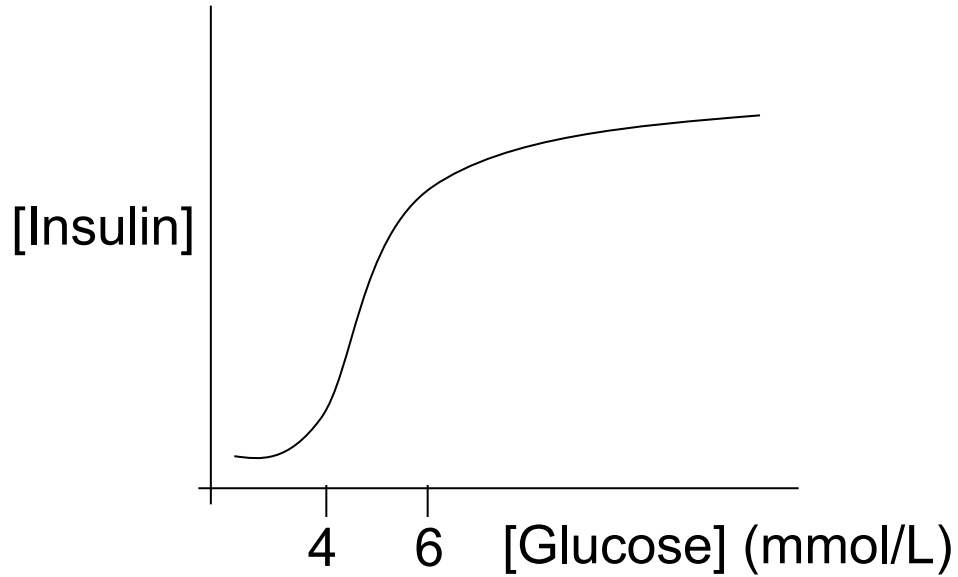
- Develops from two buds from the primitive gut
- Buds grow, branch and fuse
- Islet cells differentiate from cells adjacent to buds
- Endocrine function from 10–15 weeks



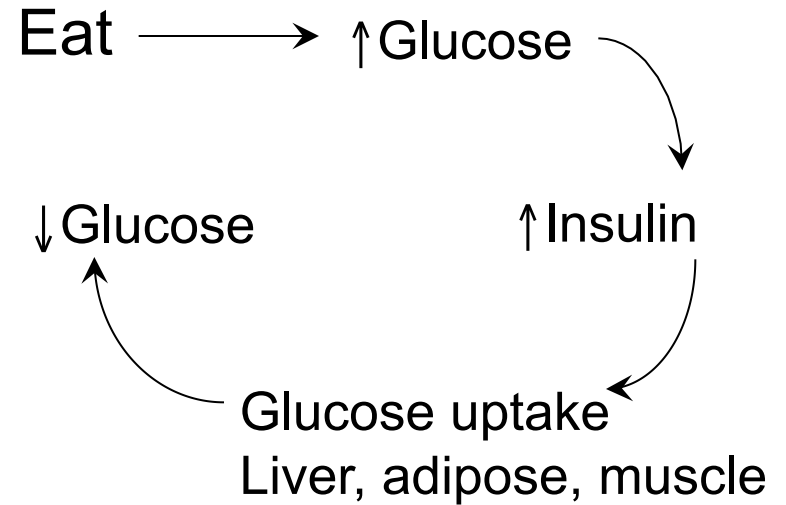
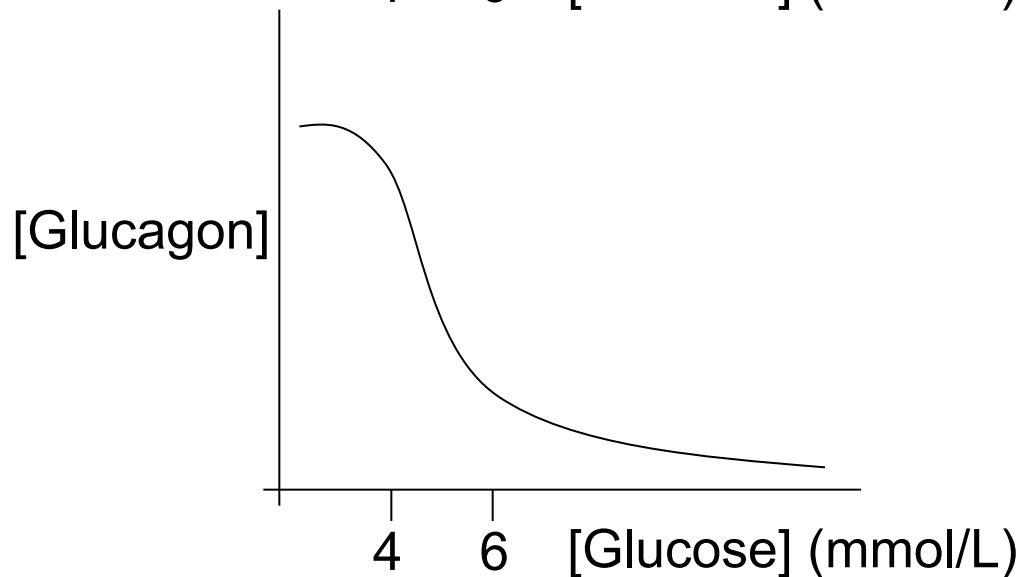
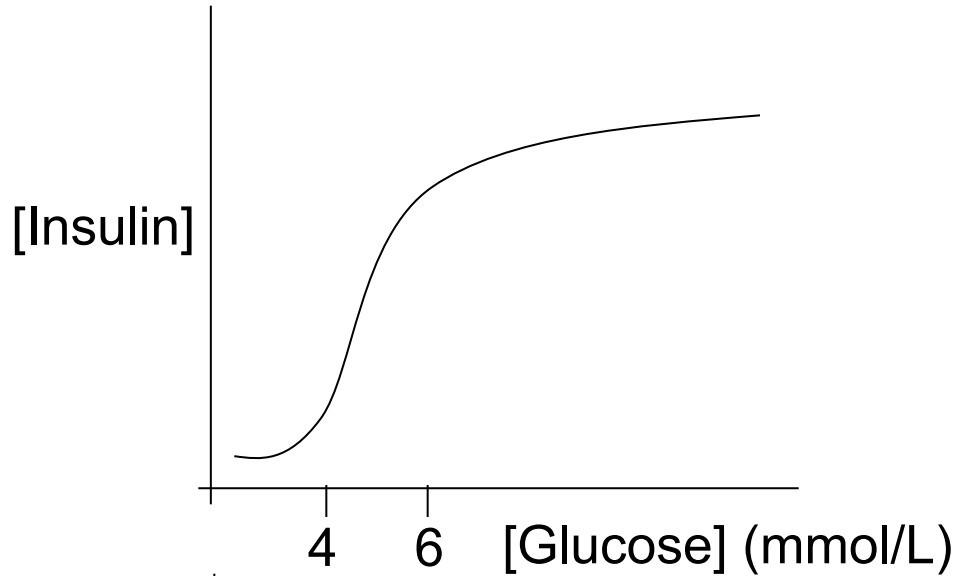
# Pancreas - Physiology



# Pancreas - Physiology

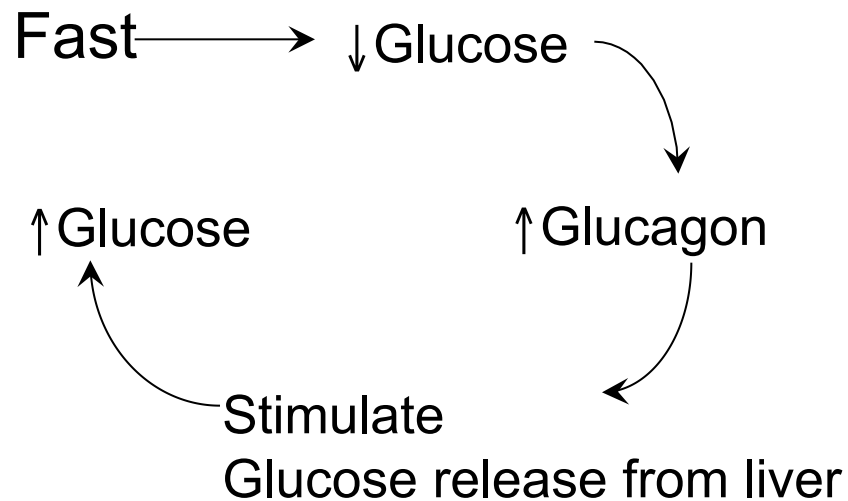
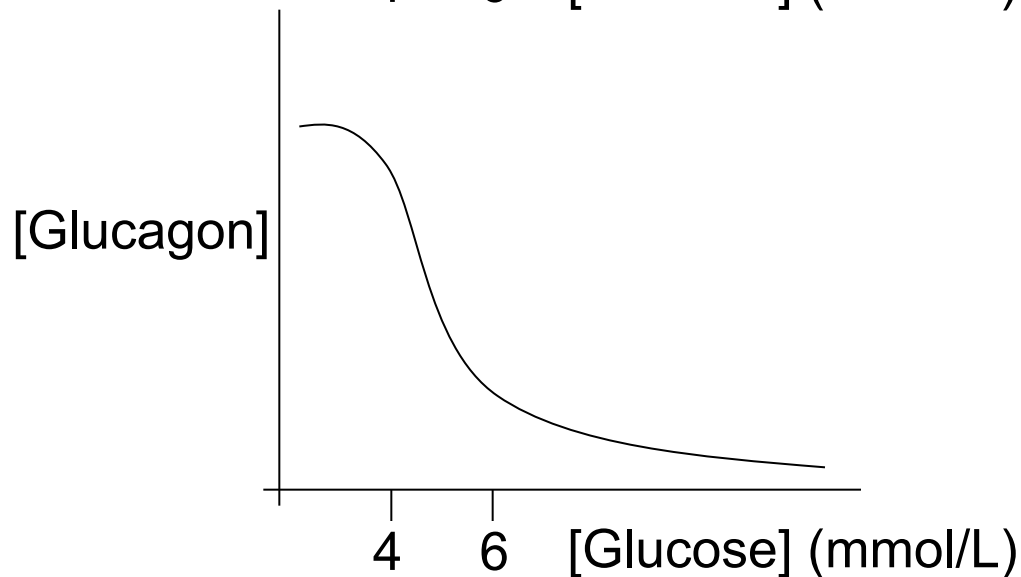
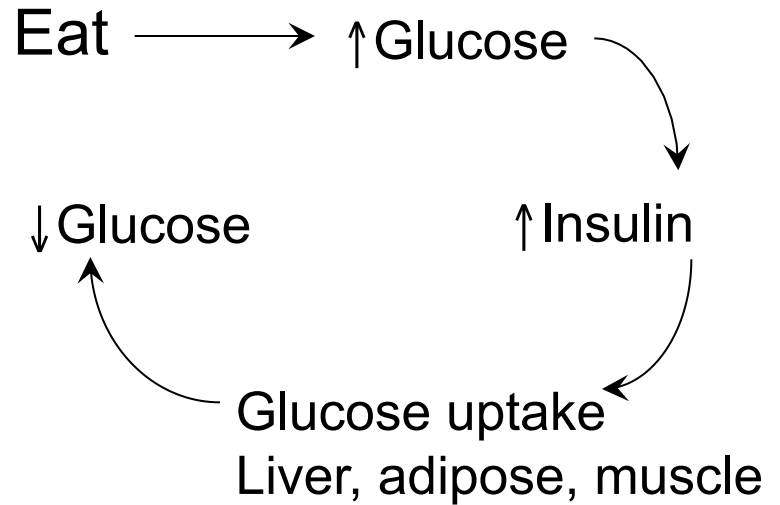
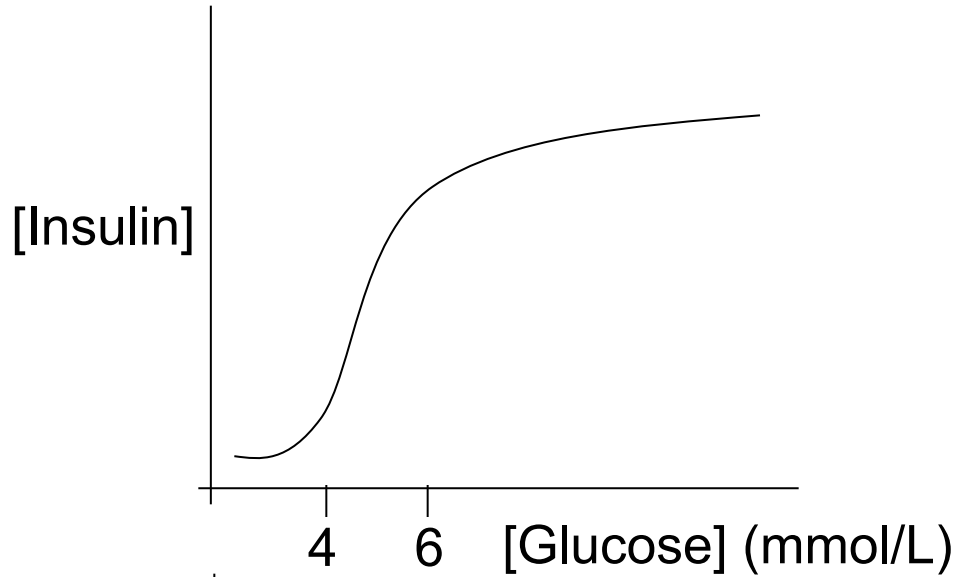


# Pancreas - Physiology

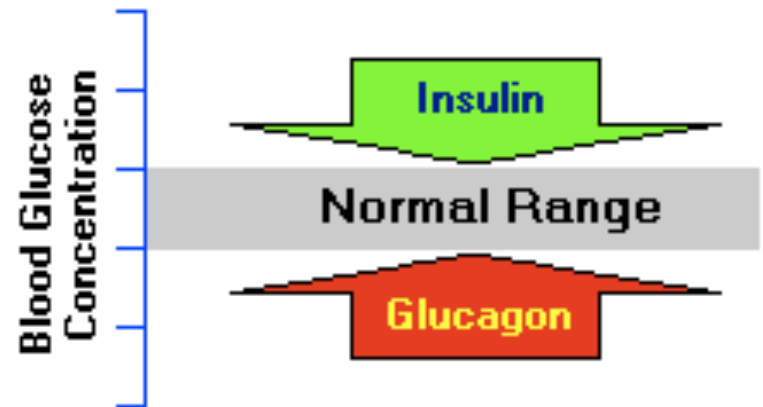
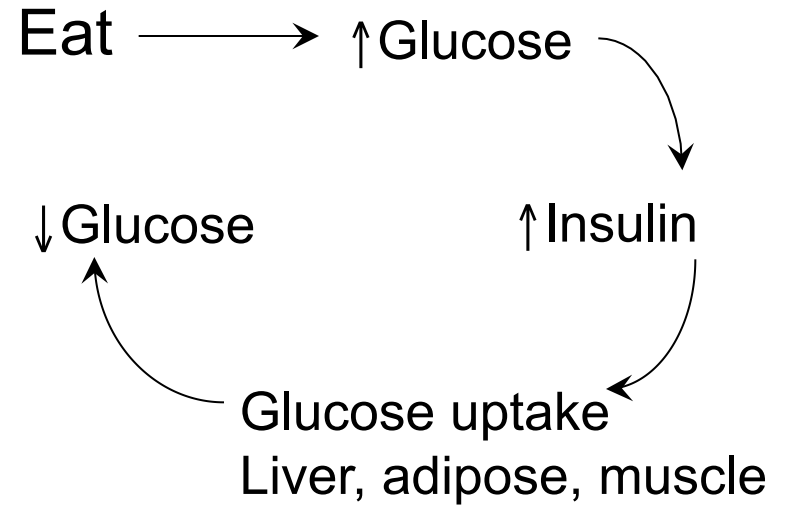
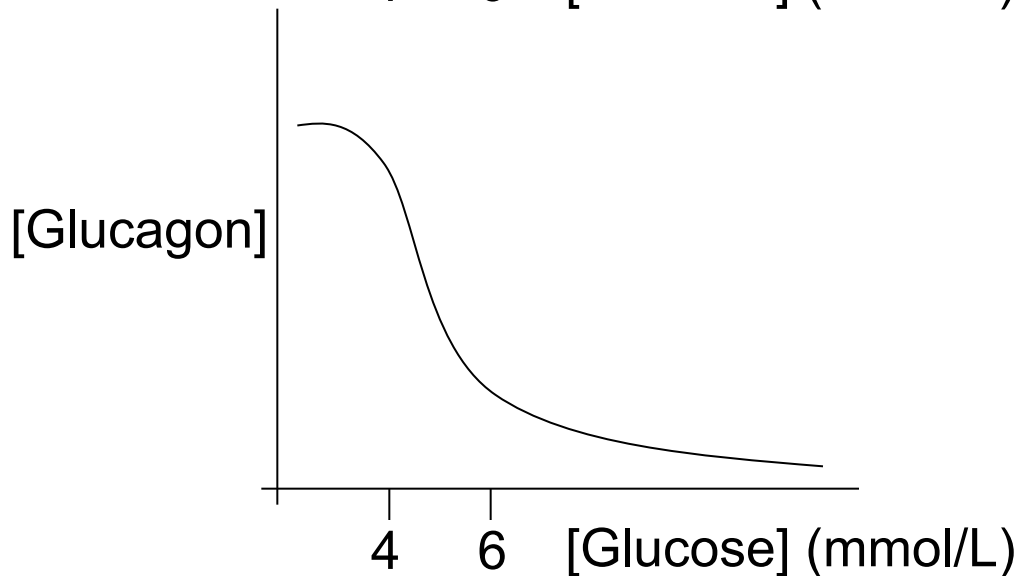
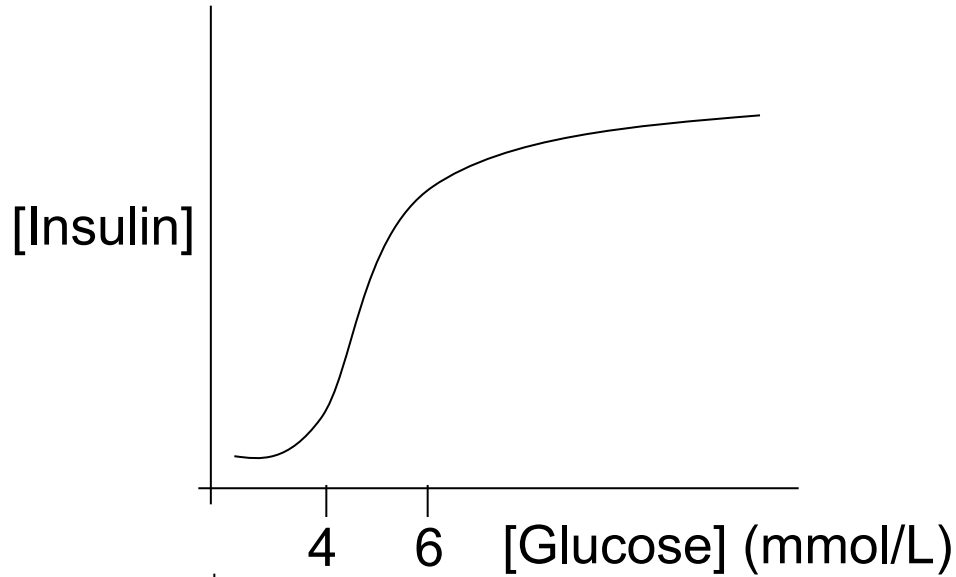




# Pancreas - Physiology



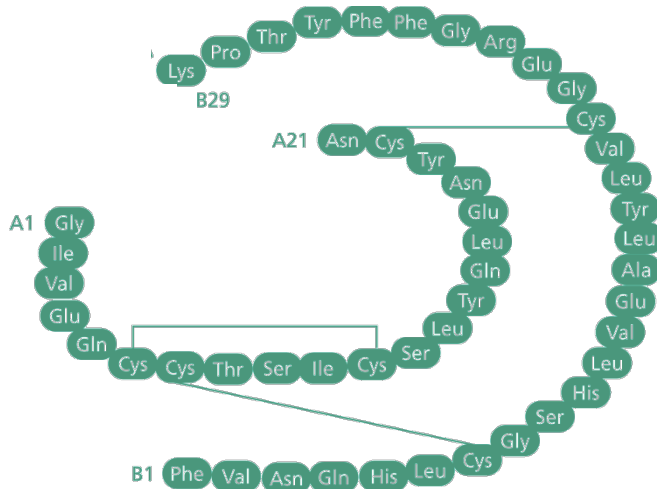
# Pancreas - Physiology



# Banting/Best/Collip Isolate Insulin in 1920

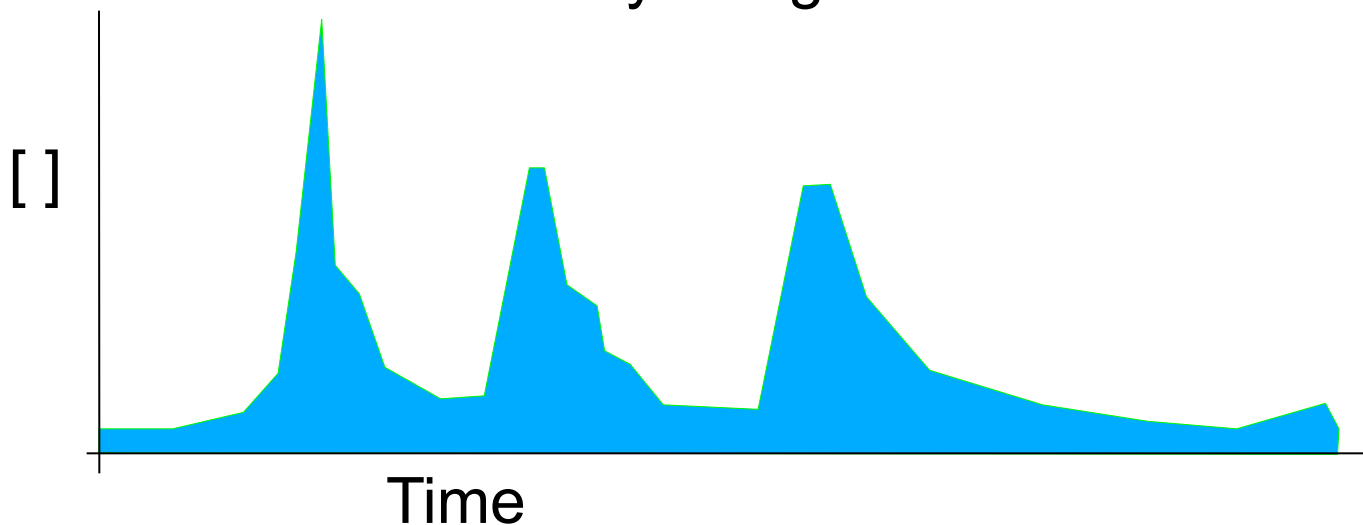


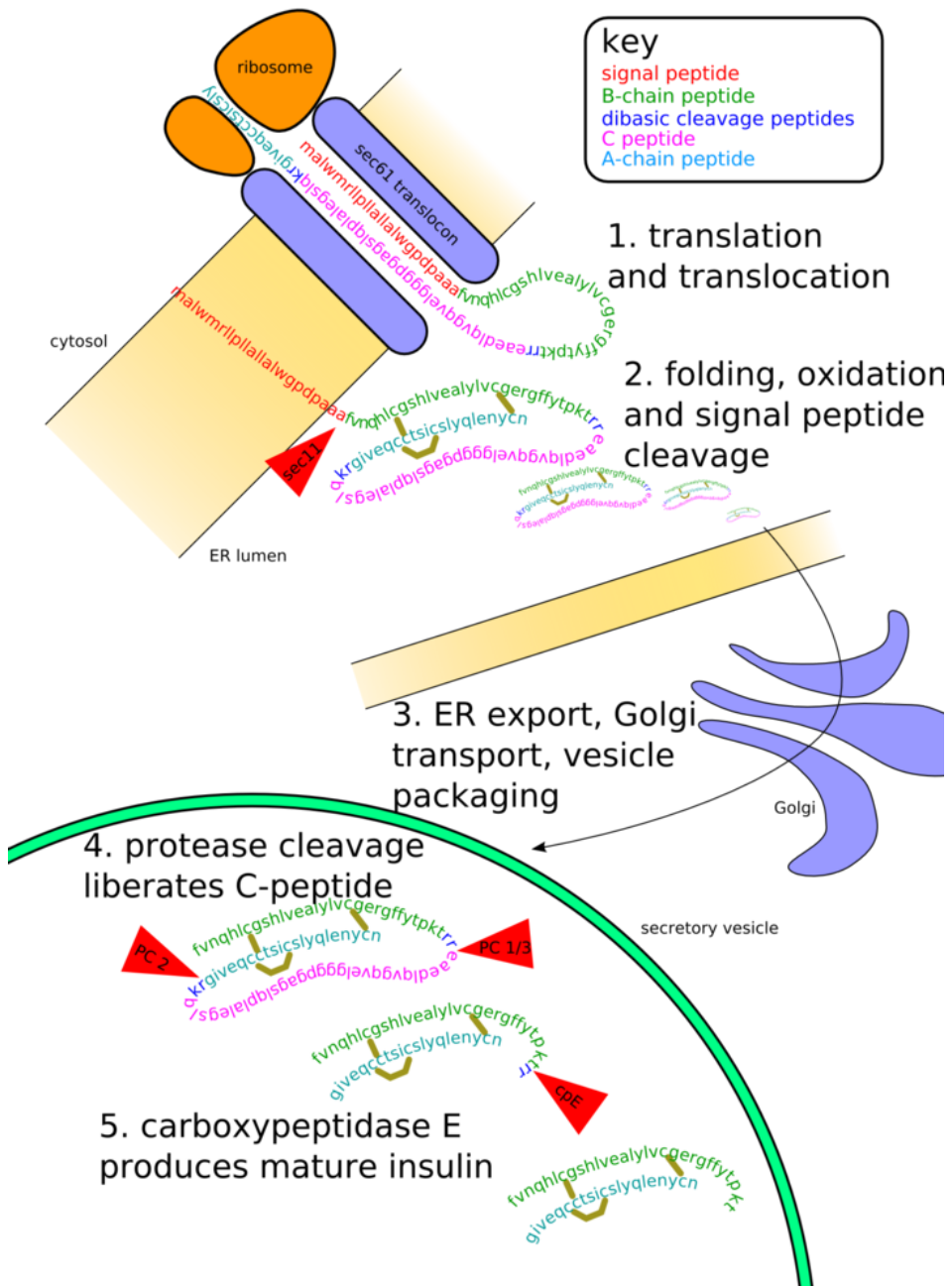
# Insulin Synthesis and Secretion



- 50 AA peptide, 3 intramolecular disulphide bridges, 5808 kDa
- Synthesised as preproinsulin
- Peptidases cleave C-peptide off
- Half life of insulin in the circulation = 6 minutes

## Physiological Insulin Profile:





**key**  
 signal peptide  
 B-chain peptide  
 dibasic cleavage peptides  
 C peptide  
 A-chain peptide

**1. translation and translocation**

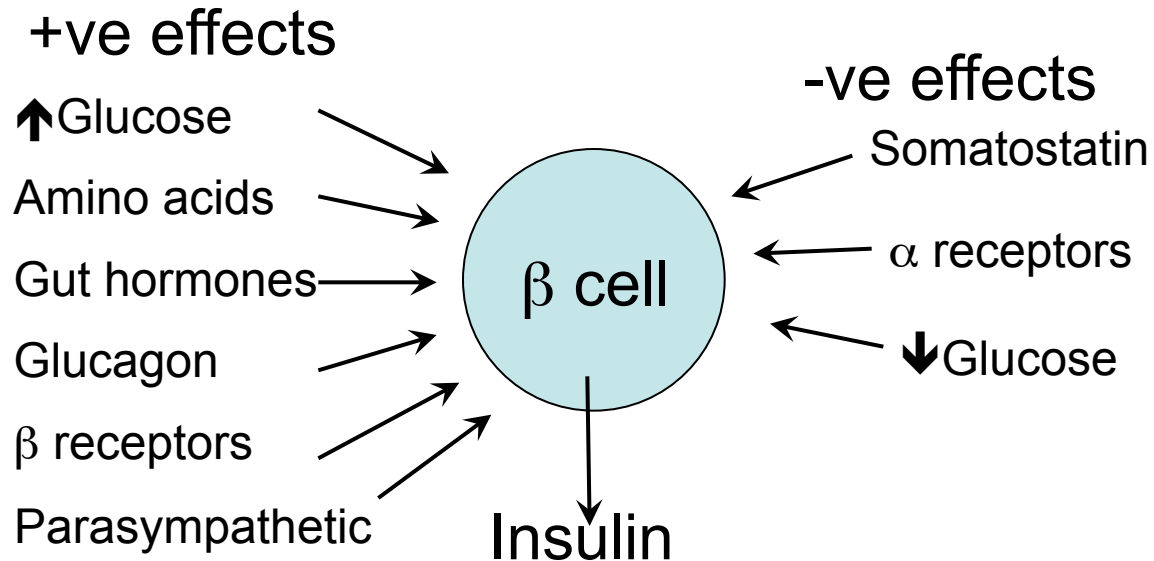
**2. folding, oxidation and signal peptide cleavage**

**3. ER export, Golgi transport, vesicle packaging**

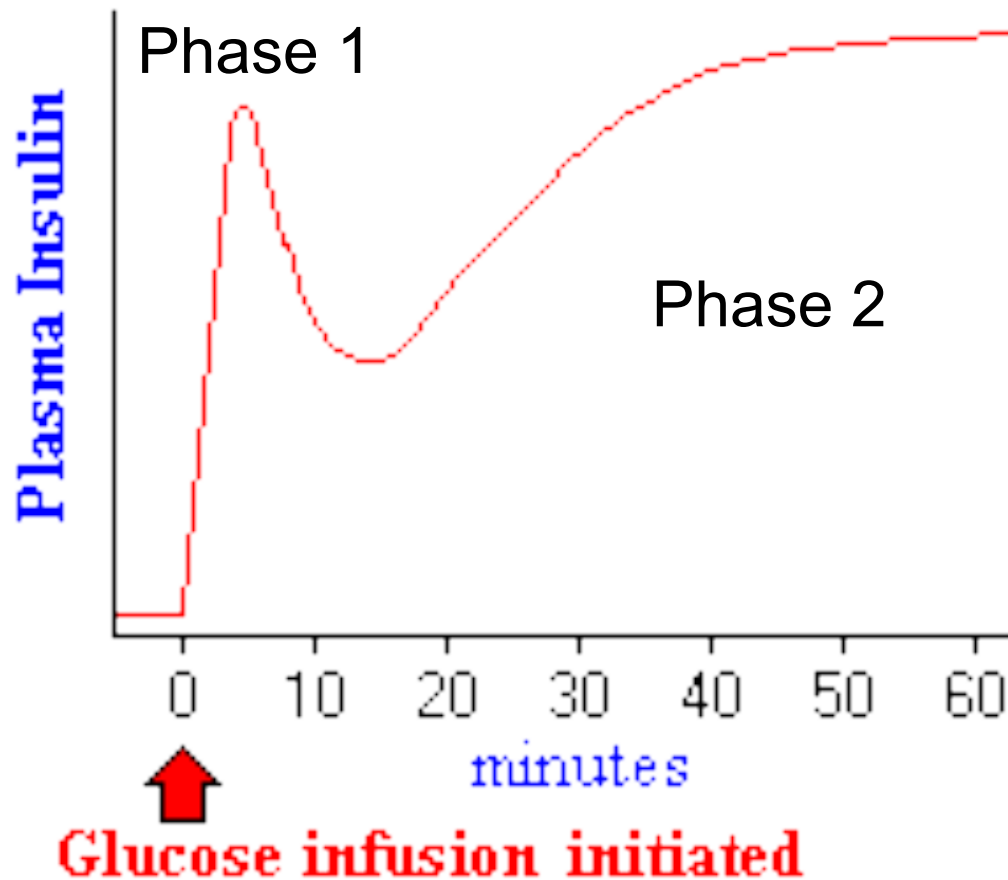
**4. protease cleavage liberates C-peptide**

**5. carboxypeptidase E produces mature insulin**

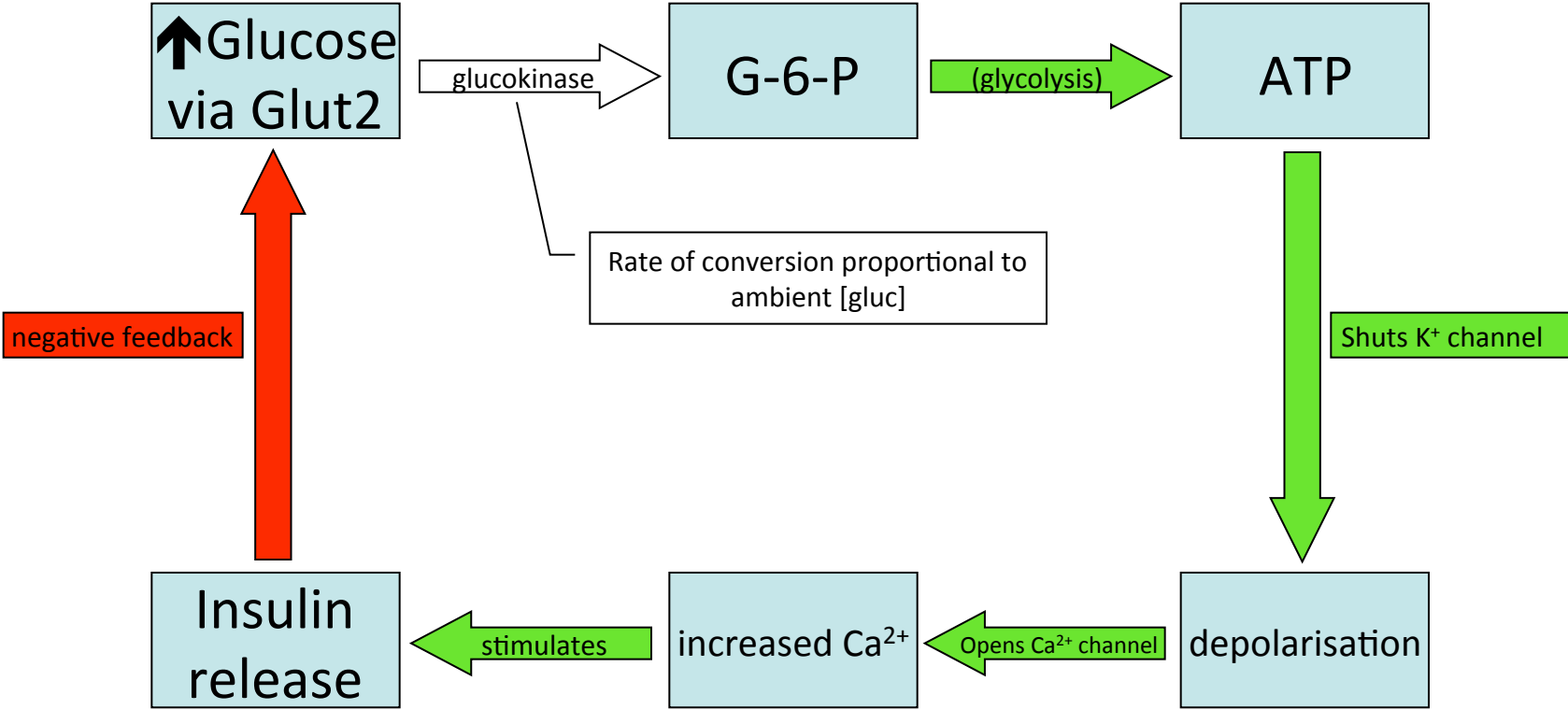
# Insulin Release



# Biphasic insulin release

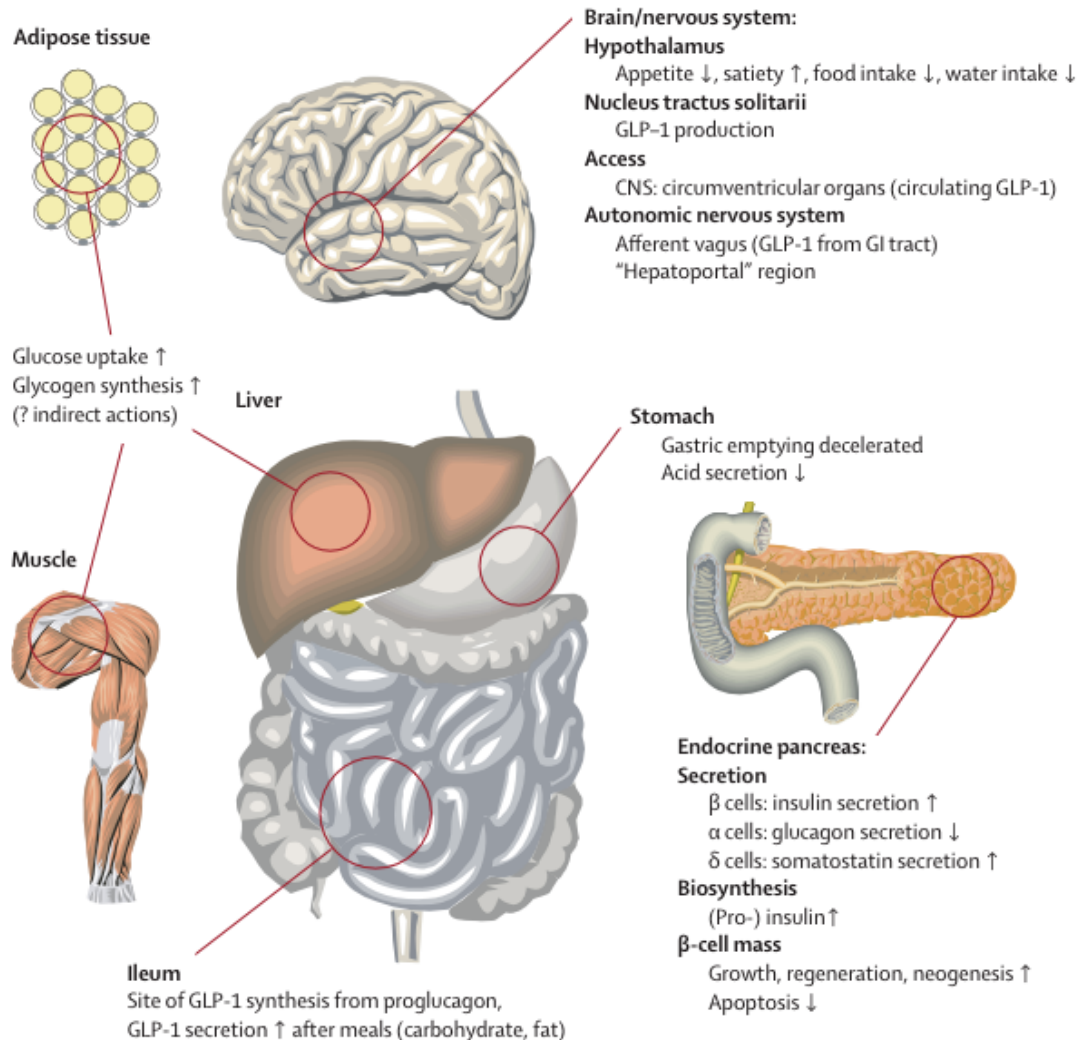


# Glucose sensor in beta cells



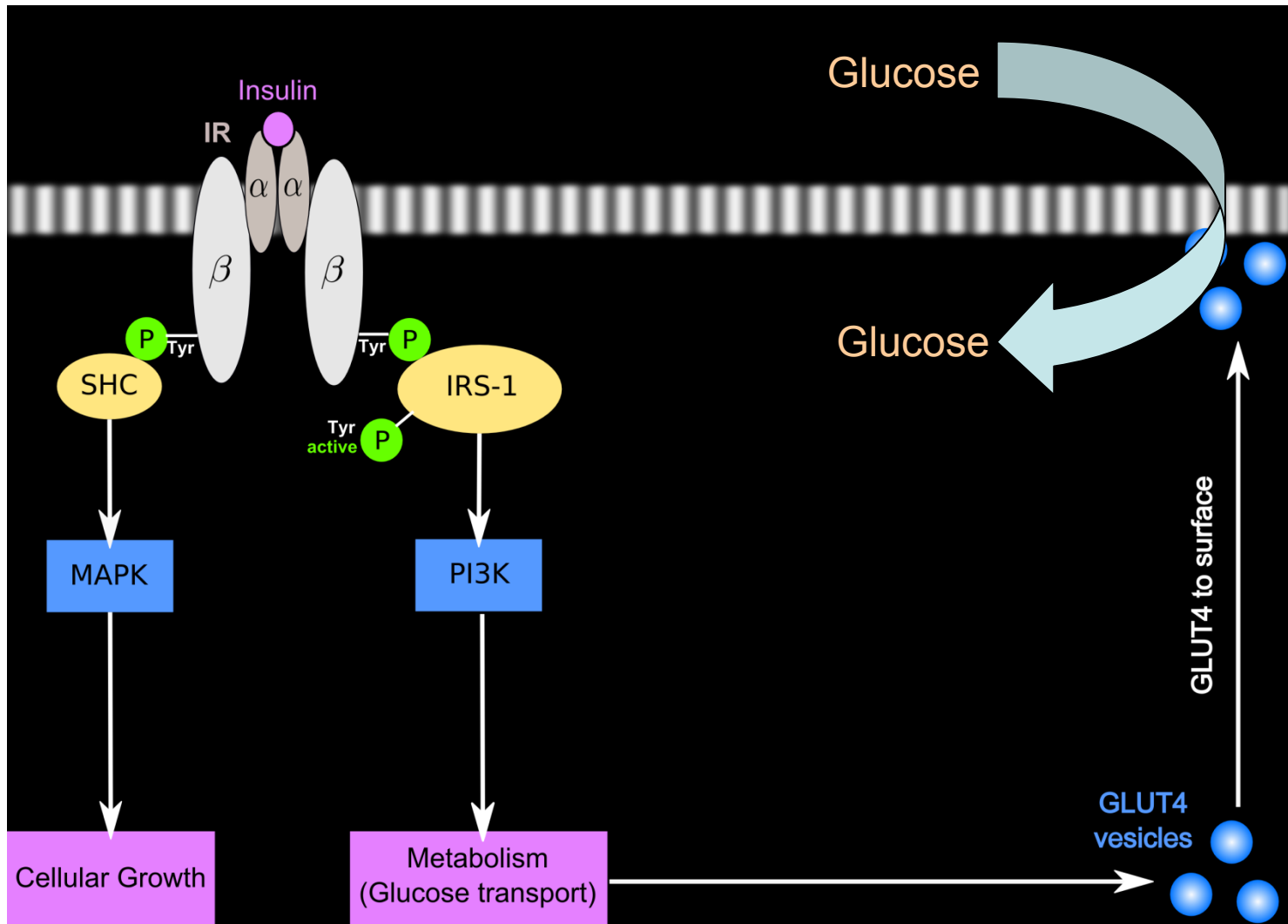


# Glucagon-like peptide 1 (GLP-1) is an incretin



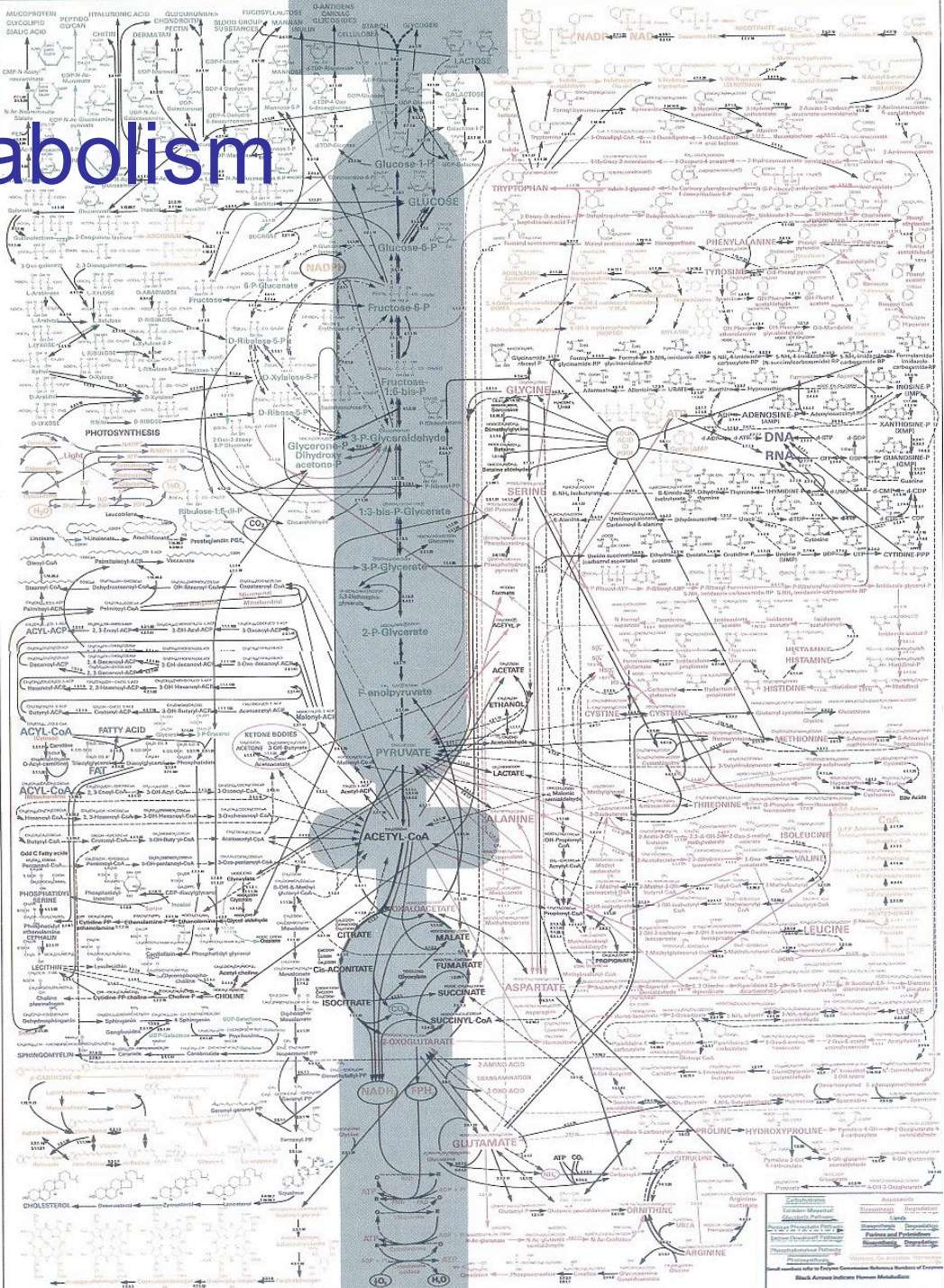
- Stimulates Insulin secretion
- Inhibits Glucagon secretion
- Inhibits Gastric emptying
- Inhibits Appetite
- Stimulates Nausea

# Molecular Basis of Insulin Action

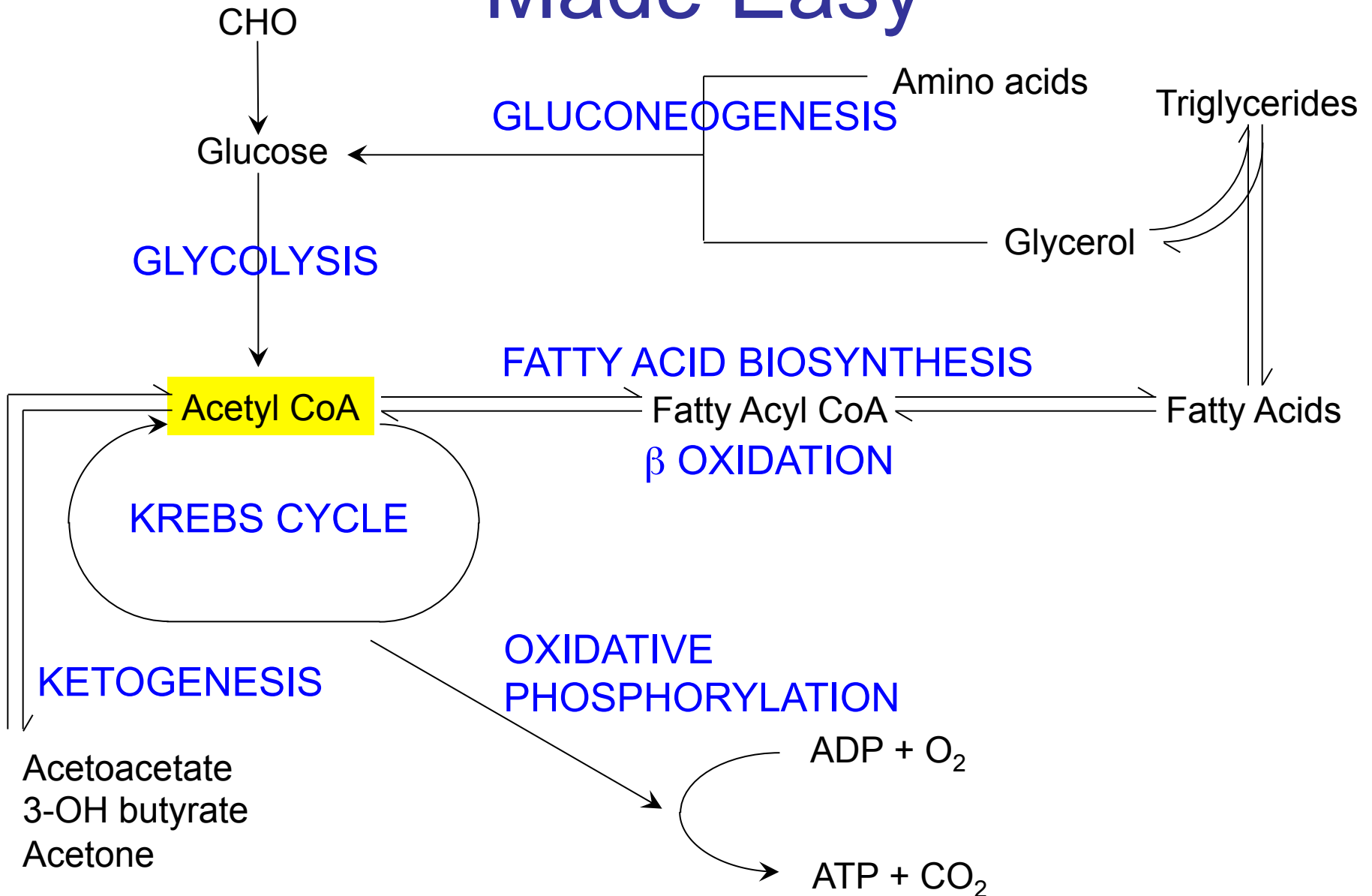


# Intermediary Metabolism

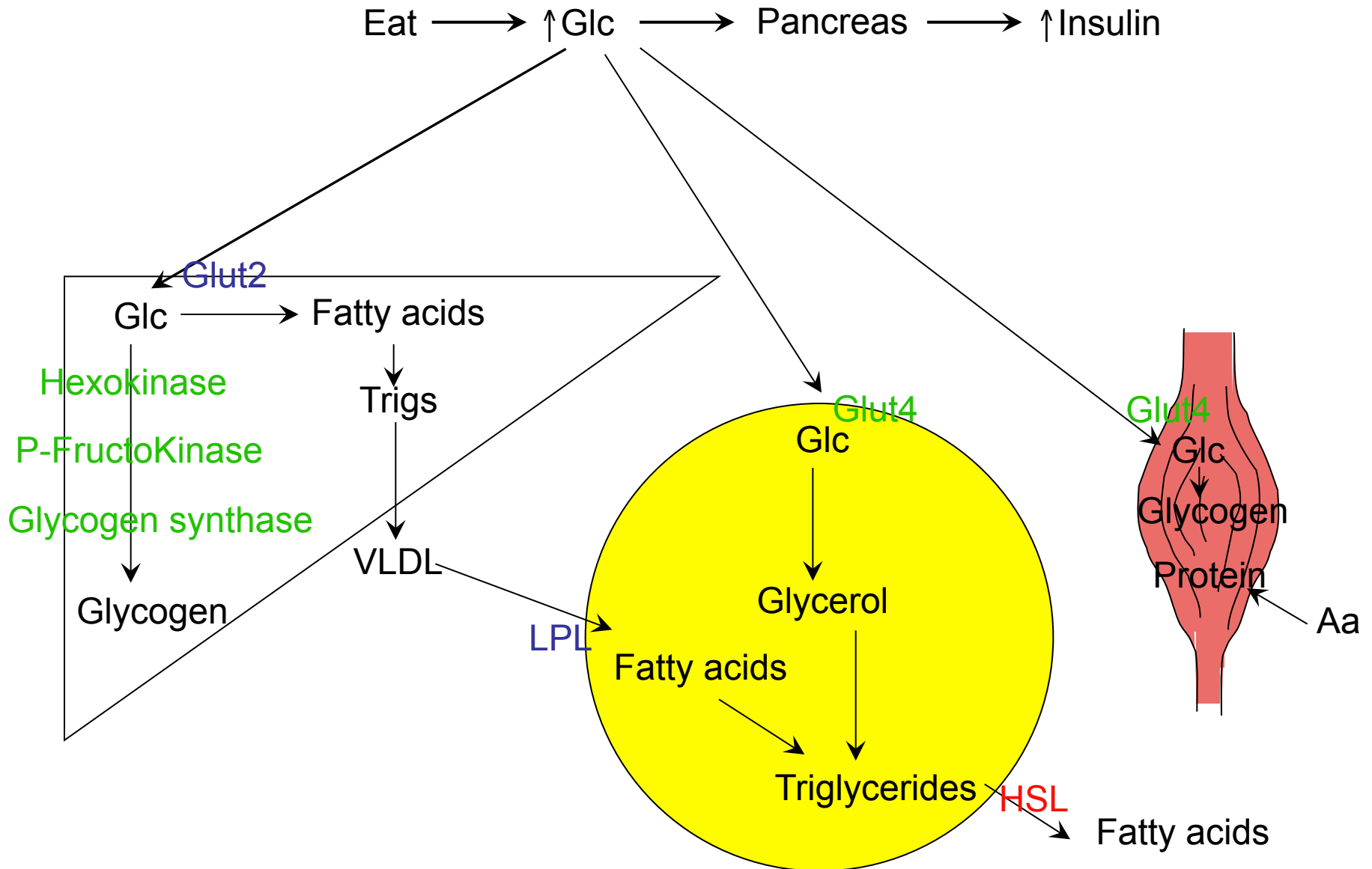
All reactions concerned with storing and generating metabolic energy. Using that energy in cellular processes



# Intermediary Metabolism Made Easy



# Insulin & Intermediary Metabolism

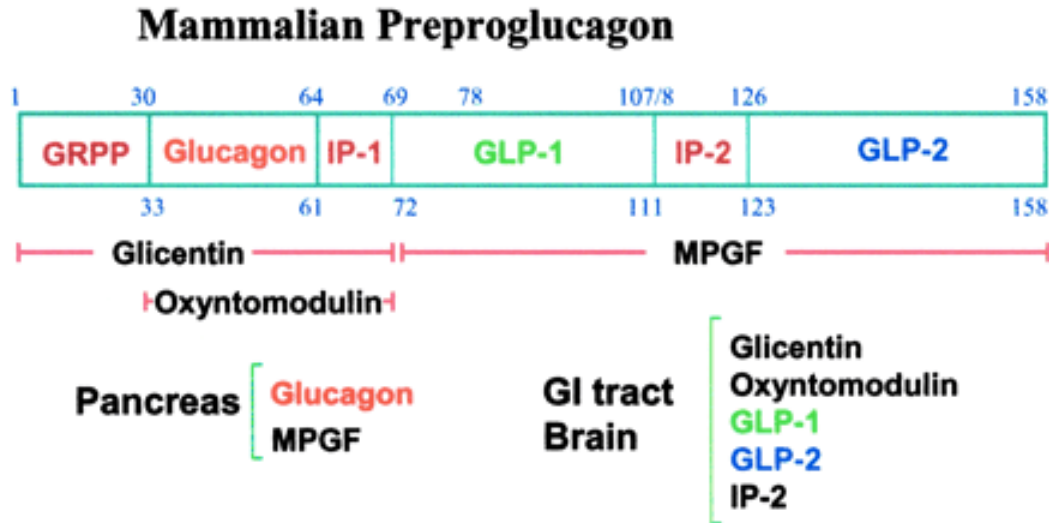


# Actions of Insulin

- Carbohydrate
  - Glucose uptake
  - Glycogenesis
  - Inhibit glycogenolysis
  - Inhibit gluconeogenesis
- Lipid
  - Inhibit HSL
  - Hepatic fatty acid synthesis
  - Suppress ketone body production
- Protein
  - Aa uptake
  - Anabolic
- Others
  - $K^+$  uptake
  - $H_2O$  retention

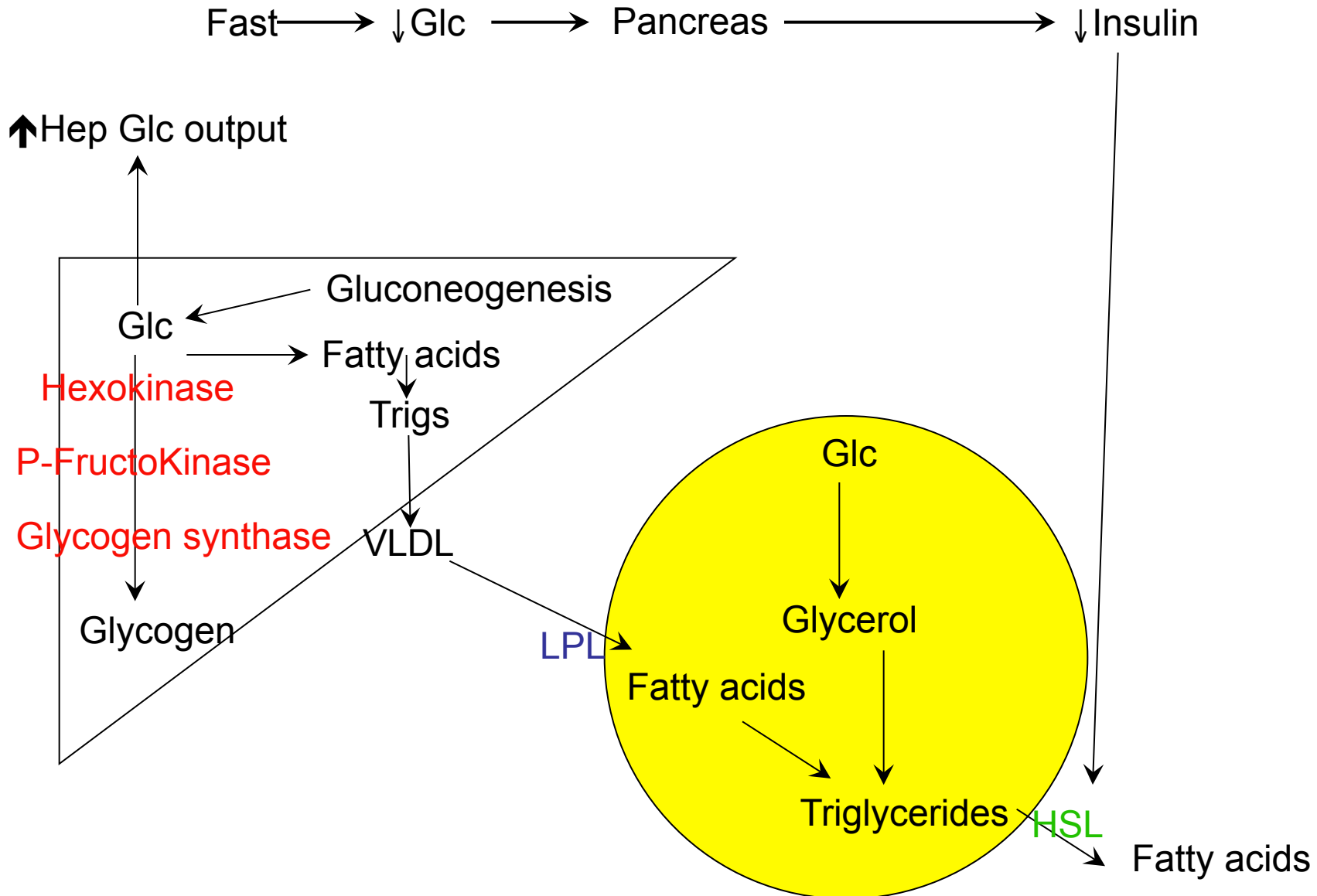
# Glucagon

- 29 Aa peptide hormone from alpha cells
- Synthesised from preproglucagon



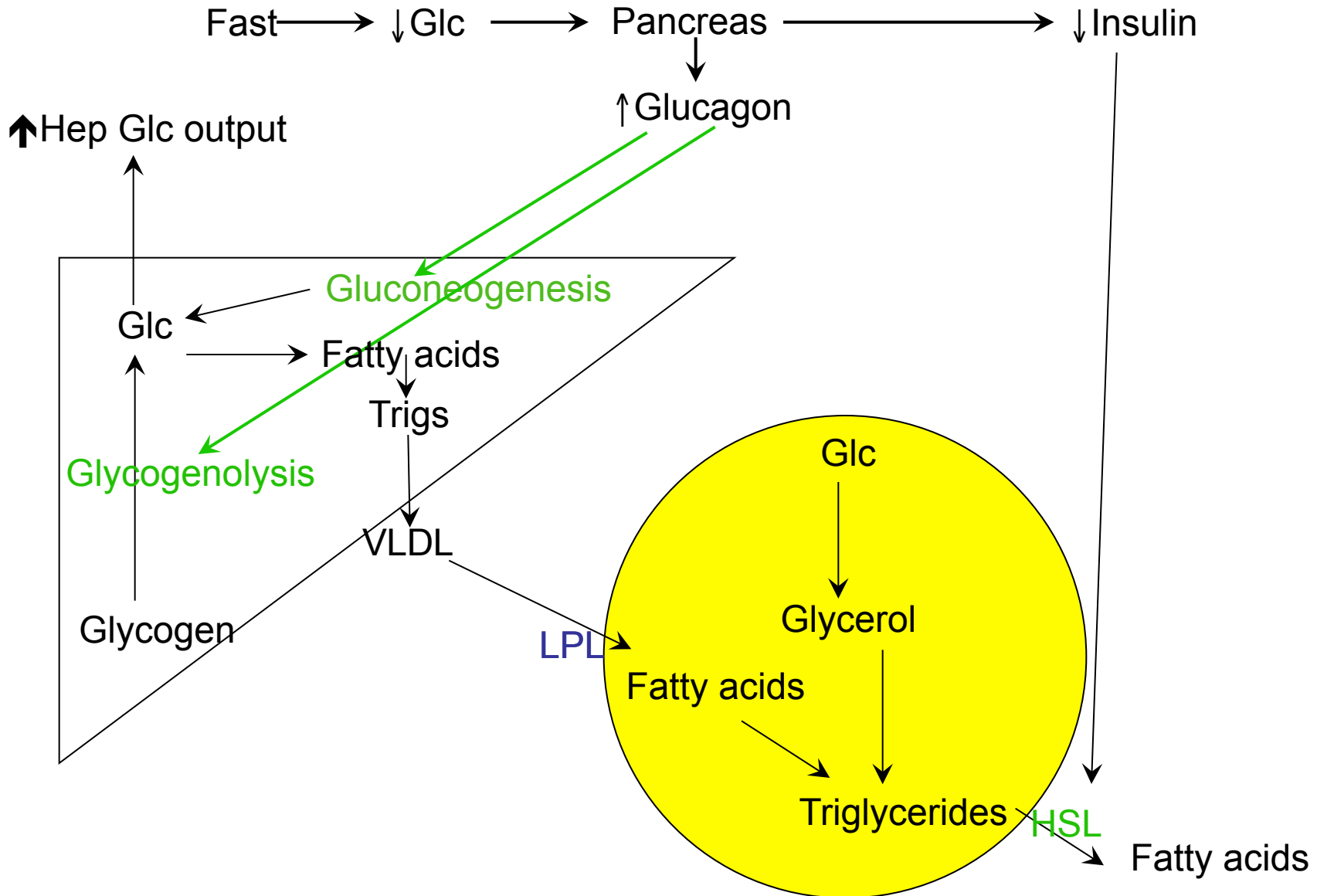
- Released in response to low blood glucose
- Stimulates glycogenolysis and gluconeogenesis
- Disordered secretion also occurs in diabetes mellitus

# Insulin & Intermediary Metabolism

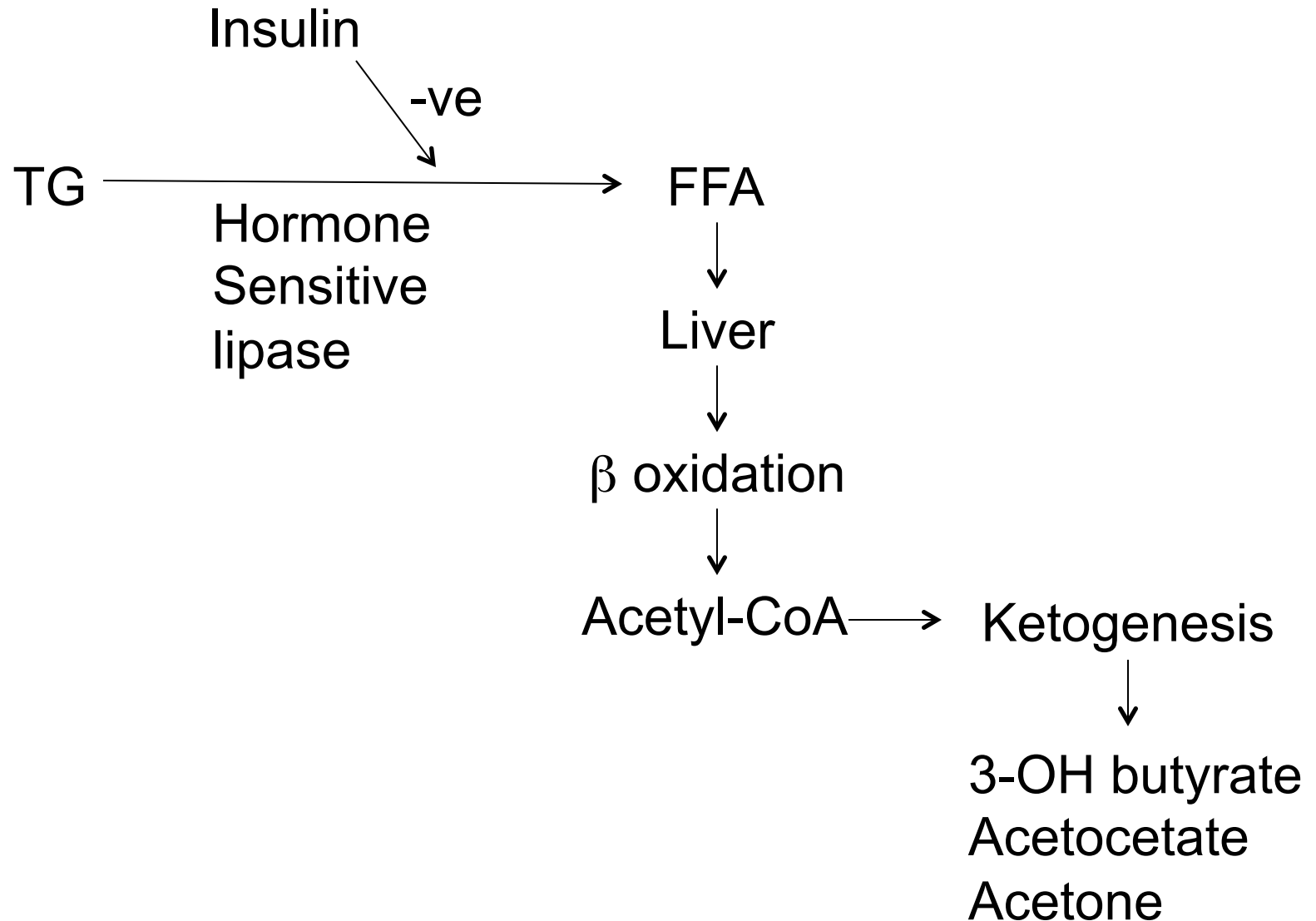




# GCG & Intermediary Metabolism



# Ketogenesis



# N.B.

- Islets do secrete other hormones
  - Pancreatic Polypeptide
  - Vasoactive Intestinal Polypeptide
  - Ghrelin
  - Gastrin
  - Somatostatin
- Rarely functional endocrine tumours of the pancreas release these hormones
- This can occur in genetic diseases such as multiple endocrine neoplasia type 1

# Summary

- The endocrine pancreas mainly secretes insulin ( $\beta$  cells) and glucagon ( $\alpha$  cells)
- They have opposing effects on blood glucose (insulin  $\downarrow$ , glucagon  $\uparrow$ )
- Insulin controls much more than just carbohydrate metabolism (lipids and protein, K)
- The principal insulin-responsive tissues are liver, adipose and muscle
- Diabetes mellitus, the commonest endocrinopathy is caused by a lack of insulin action and excessive glucagon
- Neuroendocrine tumours of the pancreas are rare but important (especially at Hammersmith Hospital!)