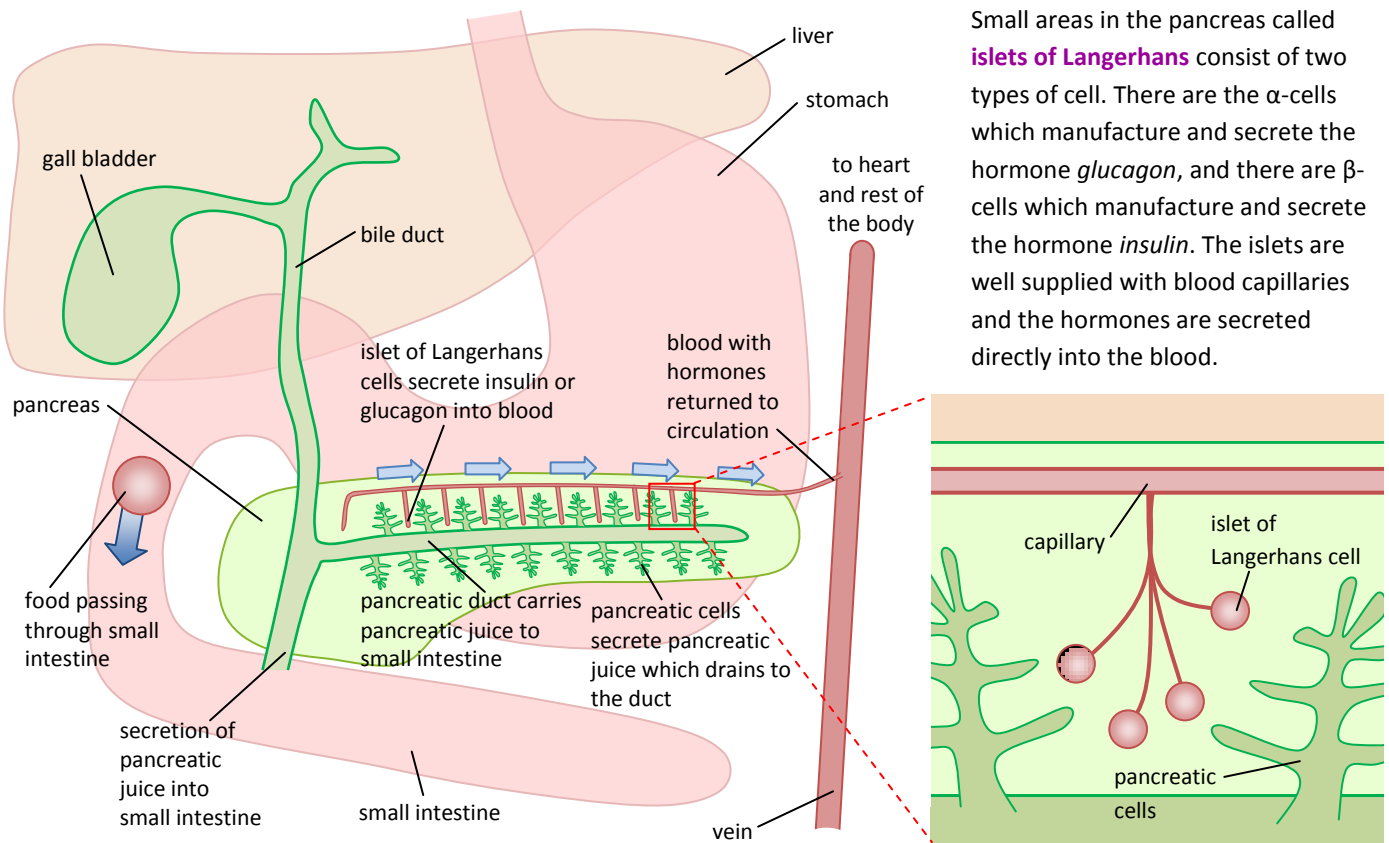# 1.6 Regulation of blood glucose

The pancreas, and control of blood glucose concentration, insulin and glucagon
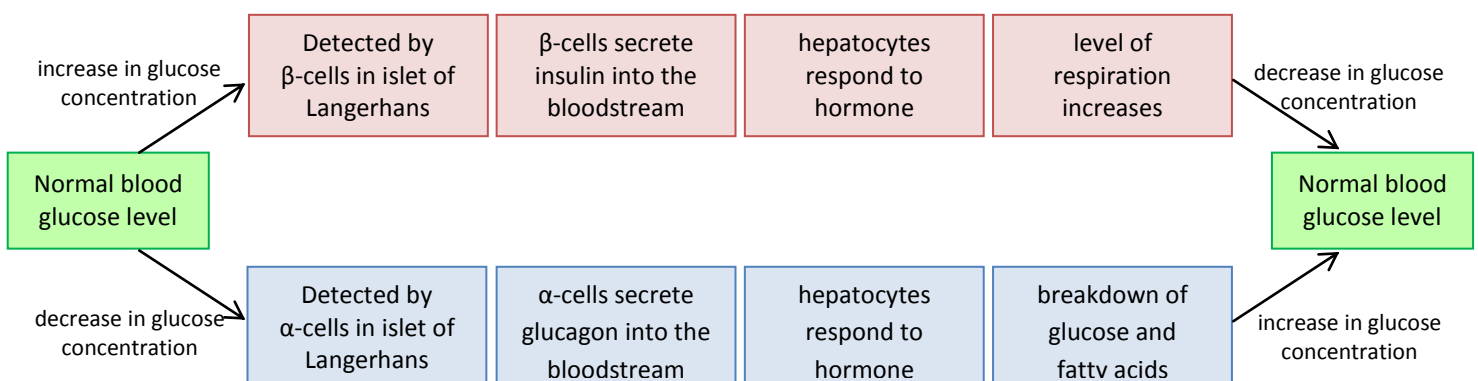
The pancreas

The **pancreas** is an organ which is both an endocrine gland and an exocrine gland, as it has functions of both types. The majority of cells in the pancreas have an exocrine function, in secreting digestive enzymes. Such cells are found surrounding tiny tubules into which they secrete **pancreatic juice**, a liquid containing a number of digestive enzymes, and the tubes will join up at the **pancreatic duct** which carries the pancreatic juice into the first section of the small intestine. The pancreatic juice includes the enzymes amylase, pancreatic lipase, carboxypeptidase, elastase and trypsinogen.

liver

stomach

to heart and rest of the body

gall bladder

bile duct

islet of Langerhans cells secrete insulin or glucagon into blood

blood with hormones returned to circulation

pancreas

food passing through small intestine

pancreatic duct carries pancreatic juice to small intestine

pancreatic cells secrete pancreatic juice which drains to the duct

secretion of pancreatic juice into small intestine

small intestine

vein

Small areas in the pancreas called **islets of Langerhans** consist of two types of cell. There are the α-cells which manufacture and secrete the hormone *glucagon*, and there are β-cells which manufacture and secrete the hormone *insulin*. The islets are well supplied with blood capillaries and the hormones are secreted directly into the blood.

capillary

islet of Langerhans cell
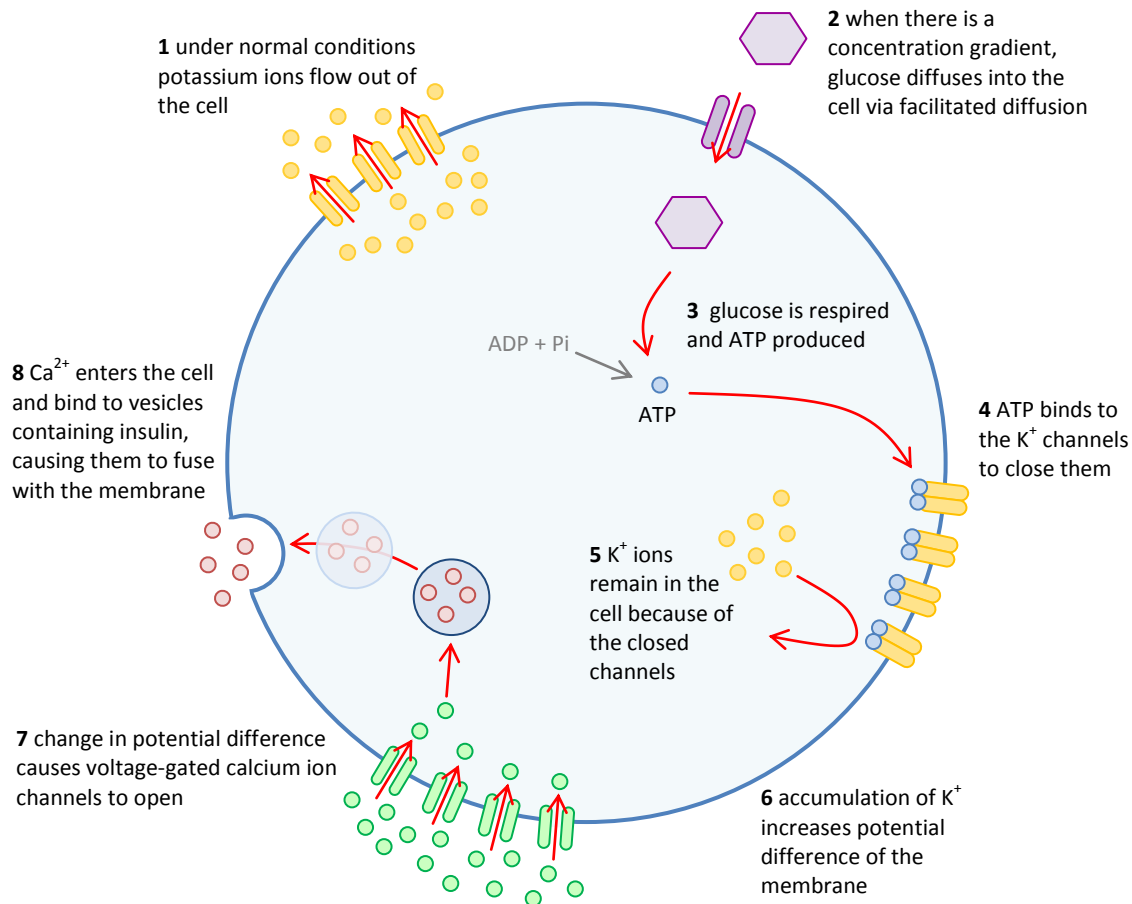
pancreatic cells

Regulating blood glucose levels

It is the role of the cells in the islets of Langerhans to monitor the concentration of blood glucose. If they detect a concentration which lies outside the acceptable range, the appropriate cells (either α-cells or β-cells) are activated to release hormones to respond and return the blood glucose concentration to an acceptable level.

increase in glucose concentration

| Detected by β-cells in islet of Langerhans | β-cells secrete insulin into the bloodstream | hepatocytes respond to hormone | level of respiration increases |

decrease in glucose concentration

Normal blood glucose level

Normal blood glucose level

decrease in glucose concentration

| Detected by α-cells in islet of Langerhans | α-cells secrete glucagon into the bloodstream | hepatocytes respond to hormone | breakdown of glucose and fatty acids |

increase in glucose concentration

The diagram above shows how the cells in the islet of Langerhans help to maintain a regular blood glucose concentration.

A rise in blood glucose concentration

When blood glucose levels increase, possibly just after eating a meal, the change in concentration is detected by **β-cells** in the islets of Langerhans. The cells then secrete the hormone **insulin** directly into the bloodstream. Insulin, like adrenaline, has a number of effects on multiple cell types around the body. The target cells for insulin are the **hepatocytes** (liver cells) as well as muscle cells. The diagram shows insulin secretion:

1 under normal conditions potassium ions flow out of the cell

2 when there is a concentration gradient, glucose diffuses into the cell via facilitated diffusion

3 glucose is respired and ATP produced

ADP + Pi

ATP

8 Ca^{2+} enters the cell and bind to vesicles containing insulin, causing them to fuse with the membrane

4 ATP binds to the K^+ channels to close them

5 K^+ ions remain in the cell because of the closed channels

7 change in potential difference causes voltage-gated calcium ion channels to open

6 accumulation of K^+ increases potential difference of the membrane

In the resting β-cell, potassium ions (K^+) are moving out of the cell down the concentration gradient, via facilitated diffusion. When there is a concentration of glucose from outside the cell to inside the cell, for example, after eating, glucose enters the cell through specialised glucose channels in the membrane (again, by facilitated diffusion). The glucose inside the cell is then respired, producing ATP.

The ATP moves to the potassium ion channels on the cell surface membrane, and binds to the channels, causing them to close. This means that the potassium ions stay inside of the cell. Quickly, the build up of the ions depolarises the membrane (it becomes less negative), causing the voltage-gated calcium ion (Ca^{2+}) channels to open, which results in an influx of calcium ions into the cell. These ions then bind to vesicles within the cell which carry the insulin hormones. The calcium causes the vesicles to move to the cell surface membrane, and undergo exocytosis: the vesicle fuses with the membrane and the insulin is released out of the cell, and into the bloodstream.

When insulin is released into the blood, it is transported all around the body, and when it passes the target tissues (mainly the hepatocytes), the hormone binds to the receptor sites, activating the adenyl cyclase enzyme on the inner cell membrane. This produces cyclic AMP (cAMP) from a molecule of ATP, and the cyclic AMP activates a number of intracellular reactions. The effects of the hormone insulin, or these end intracellular reactions, are:
- more glucose channels are inserted into the cell surface membrane, so that more glucose can enter the cell
- glucose inside the cell is polymerised into **glycogen** by a process known as **glycogenesis**
- more glucose is converted into fats, and more glucose is respired

Needless to say, as these events cause more and more glucose to enter the target cells, the result is a decreased glucose concentration in the bloodstream. The concentration returns to an acceptable level using this process.

A drop in blood glucose concentration

An example of an activity that would cause a fall in blood glucose level is after exercise. The drop in glucose concentration in the bloodstream is detected by **α-cells** in the islets of Langerhans. In response to this, the α-cells will secrete the hormone **glucagon**, which again uses the hepatocytes as target cells.

When glucagon is released, it binds to the receptors on its target cells. This activates the adenyl cyclase, stimulating the production of cAMP, which will be the eventual trigger for the reactions. The effects of glucagon are:

- the polymer glycogen is broken down into the monomer glucose, this process is called **glycogenolysis**
- more fatty acids are used in respiration
- amino acids and lipids are converted into glucose by a process known as **gluconeogenesis**

The effects of glycogenolysis and gluconeogenesis (breakdown of glycogen and conversion of non-sugars into glucose) results in the release of much glucose into the blood, restoring it to an acceptable level.

Diabetes

Diabetes mellitus is a disease where the body is no longer able to maintain an acceptable blood glucose concentration, and is described as a lack of control over blood glucose regulation. It can lead to **hyperglycaemia** (very high levels of blood glucose) after a meal rich in sugars, and also **hypoglycaemia** (very low levels) after exercise.

Type I diabetes

Also known as *insulin dependent* diabetes, **type I diabetes** is early-onset, meaning it occurs from when the sufferer is very young. It is an auto-immune disease, where the body's own cells destroy the insulin-releasing β-cells, and so the effect is that little or no insulin is released, which can lead to hyperglycaemia, for example after eating a meal.

The treatment for type I diabetes is using insulin injections. Precise dosages of insulin to counteract food eaten is injected. The necessary dosage is calculated by measuring blood glucose levels using a pin-prick. Originally, the insulin to be injected was obtained from the pancreas of pigs. This was because it was fairly similar to humans' insulin and easy to rear, although there were some problems, including low extraction efficiency, a risk of the immune system rejecting the pig insulin, and not to mention the moral and ethical issues.

Ergo the more modern treatment which uses injections of insulin produced by genetically-modified bacteria. Larger quantities can be produced in batches more easily and quickly in this method, and the chances of rejection by the immune system are far slimmer, as human DNA coding is used in the genetic modification (restriction enzymes cut out the DNA coding for insulin production, and other enzymes place that coding into the bacteria, which reproduces over time). There are obviously fewer ethical issues concerning artificial insulin production. This insulin is closer to human insulin, also, and so it is more likely to bind to the receptor sites on hepatocytes than pig insulin is.

Type II diabetes

Described as *non-insulin dependent* or late-onset diabetes, **type II diabetes** is not due to problems with β-cells, but the problem lies with the not-functioning receptors in the hepatocytes. People with type II diabetes can still manufacture and release insulin, but certain factors will reduce the responsiveness to the hormone over time. The most common factor is age: as people grow older, they become less reactive to the hormone, and so insulin doesn't bind to the target tissues as readily. But other factors can result in an earlier onset of this type of diabetes, including obesity, diets high in sugars, race (Asian and Afro-Caribbean people are less responsive to insulin) and family history.

The treatment of type II diabetes is simply monitoring lifestyle. Regular exercise and a healthy diet are the best ways to reduce the chance of developing late-onset diabetes.