MOSAIC VARIANTS IN HYPERINSULINISM

This summarises our information sheet on **mosaic variants in congenital hyperinsulinism (shortened to HI)**. For more on different types of genetic changes, check out our information sheets linked here!

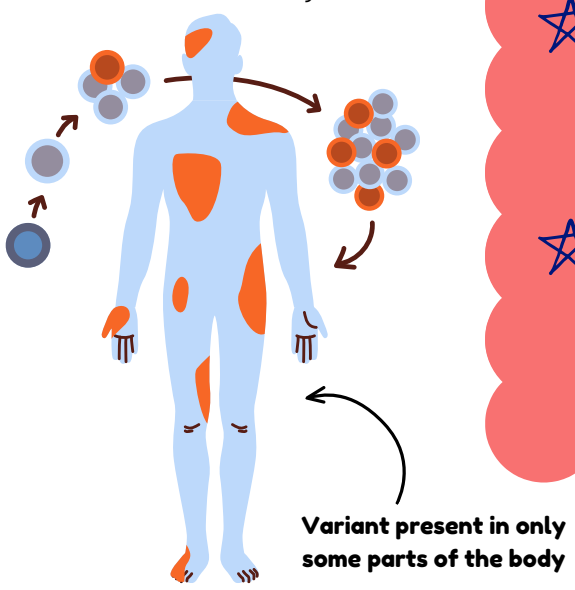
KEY MESSAGES:

- A **mosaic variant** is where the genetic change is in **only some of the cells** in your body
- Having a **mosaic variant** in the **beta cells** of your **pancreas** can **cause congenital HI**
- Mosaic variants are ***de novo*** (which means they happen for the first time in that individual) and are **usually dominant variants**, although **some mosaic recessive variants** have been seen before
- People can have **different levels of mosaicism** in different places in the body, which can mean that they **might have milder symptoms or different additional features**

WHAT IS A MOSAIC VARIANT?

In most people with a genetic change, we know that the genetic change is present in all cells in their body. BUT if a **genetic change is present in only some cells in the body**, it is called a **mosaic variant**.

If there is a mosaic variant in the **cells in the pancreas that release insulin,** it can cause **congenital HI**. We have seen these in genes like ***GCK, HK1,GLUD1, KMT2D, KDM6A,*** **and** ***ABCC8***.



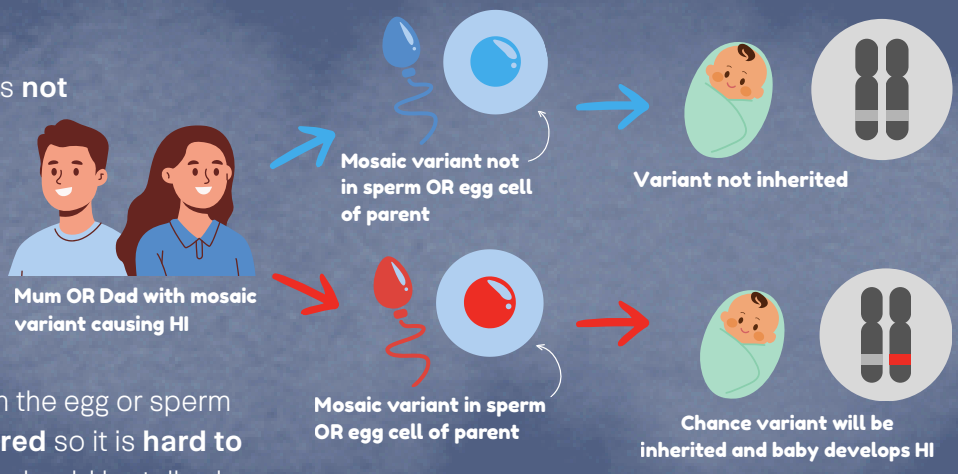
Mosaic variants that cause congenital HI are usually **dominant variants**, although **some mosaic recessive variants have been found before**. To learn more about dominant and recessive variants, check out our other information sheets linked here.

These mosaic variants are also ***de novo*** **variants**. This means the mosaic variant appeared for the **first time** in the **egg or sperm cells** of the parents or in the **baby** as it was **growing in the womb.**

CAN MOSAIC VARIANTS BE PASSED ON TO OTHER FAMILY MEMBERS?

A person with HI caused by a mosaic variant is **not expected to have a sibling with HI.** They could have a **child with HI** if the **mosaic variant** is in their **egg or sperm cells.**

If the mosaic variant is **passed on to their child**, it is **no longer mosaic** because it will be in **every cell of the body** of the child. Knowing if the mosaic variant is in the egg or sperm cells is **not something that is easily measured** so it is **hard to know how likely** it is for this to happen. This should be talked through with a **genetic counsellor or a clinical geneticist.**



HOW DO YOU FIND A MOSAIC VARIANT?

Mosaic variants are often found during **genetic tests of blood samples.** Laboratories can then **estimate the level of the mosaicism,** which shows how many molecules of DNA carry the mosaic variant in the body.

This can change around the body. For example, the level of mosaicism in the blood could be different than in the pancreas, which could be different in the eggs or sperm cells.

DOES THIS CHANGE YOUR SYMPTOMS?

We are still looking to see if someone with a **mosaic variant** will have **milder symptoms** or **may not get common additional features.**

For example, in congenital HI caused by a genetic change in the ***GLUD1*** **gene**, a common feature is **hyperammonaemia** because the genetic change is also **in the kidneys**. As *GLUD1* mosaic variants can be **in the pancreas but not in the kidneys,** some people may **develop HI but not develop hyperammonaemia.**