DE NOVO VARIANTS IN HYPERINSULINISM

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

WHAT IS A *DE NOVO* VARIANT?

De novo is a Latin term meaning "**new**." In genetics, it describes a **genetic change** that is found in a person but is **not found** in the samples tested from their **biological parents**.

De novo variants **happen by chance,** usually as a **random event.**

WHEN DO THEY HAPPEN?

A *de novo* variant can happen when an **egg or sperm cell is being formed** in a parent, or during the development of the baby **in the womb**.

Sometimes, a parent may have the **genetic change in their egg or sperm cells**, even though it is **not found in their blood or saliva sample**. This is called **germline mosaicism**. To find out more about this, have a look at our information sheet on mosaic variants linked here.

KEY MESSAGES:

- A ***de novo* variant** is a **new genetic change** identified in a person that is **not found in their biological parents**
- *De novo* variants can happen in **genes related to HI**
- A *de novo* variant can happen when an **egg or sperm is being formed**, or early in a **baby's development in the womb**
- *De novo* variants can happen because there is **germline mosaicism** in their parents
- The risk of having **another child** with the **same *de novo* variant** is usually **very low**
- A person with HI caused by a *de novo* variant may be able to **pass the genetic change to their children**
- Your **genetics team** can help you understand what this means for **your family and future pregnancies**

HOW COMMON ARE THEY?

Everyone is born with new genetic changes (*de novo* variants) that are not found in their parents. Most of these changes **do not affect a person's health.** Changes and differences in our DNA are a **normal part of genetic variation**, and this is what makes us all unique and different.

Occasionally, a ***de novo* variant affects a gene** that is important for making sure the **body works properly.** Some of these changes can **cause health conditions**, including some forms of **hyperinsulinism (HI)**.

De novo variants that cause HI have been reported in several genes, including ***ABCC8, GCK, GLUD1, HNF4A, HNF1A, HK1, KCNJ11, KDM6A, KMT2D*** **and *SLC16A1*** as well as **large deletions on chromosome 9 and chromosome 20**.

COULD SOMEONE WITH THIS TYPE OF VARIANT PASS IT ON TO THEIR KIDS?

Yes. A person with a *de novo* variant may be able to pass the genetic change on to their children.

There are **two things** to consider: the **chance of passing the genetic change** on to a child, and whether a **child who inherits** the genetic change **will develop HI**. These are **not always the same.**

Your **genetics team** can explain what **your genetic results means for you and your children.**

WHAT DOES THIS MEAN FOR SIBLINGS?

For most families, the chance of having **another child with the same *de novo* variant is very low,** but it is not zero.

One reason for this is **germline (gonadal) mosaicism** which is explained above.

The chance of this happening **varies between families** and **depends on the specific genetic change** involved. Your **genetics team** can discuss what this may mean for **future pregnancies.**