Monogenic diabetes, or Maturity-Onset Diabetes of the Young (MODY)

What is monogenic diabetes?

Monogenic diabetes, also known as maturity-onset diabetes of the young (MODY), is a rare form of diabetes characterized by mutations or alterations in a single gene that disrupts normal insulin production and secretion. Unlike type 1 diabetes and type 2 diabetes, which are multifactorial and involve complex interactions between genetic and environmental factors, monogenic diabetes is primarily caused by genetic mutations inherited in an autosomal dominant pattern.

MODY accounts for a small proportion of all diabetes cases, estimated to be less than 2% of all diagnosed cases of diabetes. It typically presents in younger individuals, often before the age of 25, and is often misdiagnosed as type 1 or type 2 diabetes due to its clinical similarities.

How do you get MODY?

MODY is inherited in an Autosomal Dominant pattern. This means that when a person has it, their child will have a 50% chance of getting the mutation as well. So in most cases, people develop MODY by getting the gene mutation from one of their parents.

You CAN have obesity and have MODY, but you did not develop MODY because of your weight.

What are the subtypes of MODY?

There are several subtypes of MODY, each associated with mutations in specific genes that play key roles in pancreatic beta cell function and insulin secretion. The most common subtypes of MODY include:

1. MODY 2 (GCK-MODY): This subtype is caused by mutations in the glucokinase (GCK) gene, which encodes the enzyme glucokinase involved in glucose sensing and insulin secretion. Individuals with GCK-MODY typically have mildly elevated blood sugar levels from birth but usually do not require treatment unless they develop symptoms of hyperglycemia.

2. MODY 3 (HNF1A-MODY): This subtype is caused by mutations in the hepatocyte nuclear factor 1-alpha (HNF1A) gene, which regulates the expression of genes involved in glucose metabolism and insulin secretion. HNF1A-MODY is characterized by progressive hyperglycemia and typically presents in adolescence or early adulthood.
3. MODY 1 (HNF4A-MODY): This subtype is caused by mutations in the hepatocyte nuclear factor 4-alpha (HNF4A) gene, which also regulates genes involved in glucose metabolism and insulin secretion. HNF4A-MODY is associated with impaired insulin secretion and often presents in adolescence or early adulthood.
4. MODY 4 (PDX1-MODY): This subtype is caused by mutations in the pancreatic and duodenal homeobox 1 (PDX1) gene, which is involved in pancreatic development and beta cell function. PDX1-MODY is associated with impaired insulin secretion and often presents in adolescence or early adulthood.
5. MODY 5 (HNF1B-MODY): This subtype is caused by mutations in the hepatocyte nuclear factor 1-beta (HNF1B) gene, which is involved in pancreatic development and beta cell function. HNF1B-MODY is associated with a wide range of clinical features, including pancreatic abnormalities, renal abnormalities, and genital tract malformations, in addition to diabetes.

How do you test for MODY?

Diagnosis of MODY involves genetic testing to identify specific mutations in the genes associated with the condition. Treatment and management of MODY depend on the specific subtype and may involve lifestyle modifications, oral medications, or insulin therapy to control blood sugar levels and prevent complications.

Genetic testing in the form of Next generation Sequencing is required.

Why is understanding your MODY diagnosis so important?

Because MODY is often misdiagnosed as type 1 or type 2 diabetes, genetic testing is recommended for individuals with a clinical suspicion of MODY, especially those with a strong family history of diabetes or unusual clinical features.

Early diagnosis and appropriate management of MODY are essential for optimizing outcomes and preventing complications associated with diabetes.