

HNF4A- MODY (MODY 1)

Legend: A transcription factor molecule binds to the DNA at its binding site, and thereby regulates the production of a protein from a gene.

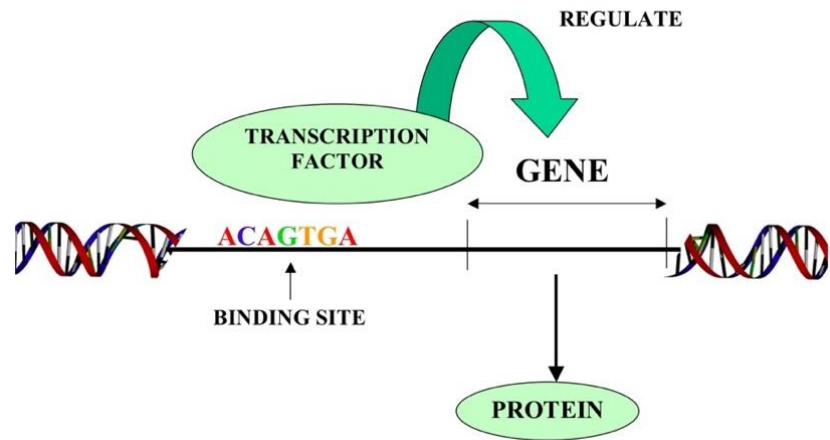


Image: http://www.bio.miami.edu/dana/pix/transcription_factor.jpg

Overview:

Diabetes caused by genetic changes (sometimes called ‘mutations’) in the *HNF4-alpha* gene is a less common type of MODY. We call this HNF4A-MODY. This type of MODY used to be called MODY 1. The HNF4A gene contains instructions for a transcription factor called hepatocyte nuclear factor-4 alpha that is important for the normal development of beta cells. Beta cells are cells in the pancreas that make insulin and help to keep blood sugars in a normal range.

Presentation:

People with HNF4A-MODY are typically diagnosed with high blood sugars before 35 years of age and are often misdiagnosed as having Type 1 diabetes. People with HNF4A-MODY usually have symptoms associated with high blood sugars when they are first diagnosed. These include increased frequency of urination (polyuria), increased thirst (polydipsia), and weight loss.

These genetic changes in HNF4A can occur spontaneously, such as when a person does not inherit the change from their parent, but usually the genetic changes are passed on from a parent to a child. If a parent has HNF4A-MODY, there is a 50% chance that their child will inherit the genetic change and be at risk of developing diabetes at a young age.

Distinguishing HNF4A-MODY from Type 1 diabetes can be difficult. Features that make us suspect HNF4A-MODY include:

- Negative antibody testing. These tests are typically done around the time of diabetes diagnosis and, if positive, indicate an autoimmune type of diabetes such as Type 1 diabetes.
- Persistently detectable C-Peptide. This is a test that tells us if your body is still making any insulin on its own.
- Very sensitive to sulfonylurea medications (often having low blood sugars while taking these medicines)
- No history of diabetic ketoacidosis
- Higher birth weight as a baby
- Low blood sugars shortly after birth
- A strong family history of diabetes - 2 or 3 generations of diabetes diagnosed at a young age (typically under age 35 years old)

Treatment:

Many patients with HNF4A-MODY can be successfully treated for years with low doses of sulfonylurea medications. Diagnosing somebody with HNF4A-MODY can sometimes allow a change in treatment with some patients changing from insulin therapy to pills (sulfonylurea medications).

Inheritance:

Finding out someone has HNF4A-MODY may have implications for other family members as those family members may also have HNF4A-MODY. A child of a person with HNF4A-MODY will have a 50% chance of inheriting the genetic change and developing diabetes.

Research:

If you or a family member have HNF4A-MODY, or think you may have it, then please contact us at monogenicdiabetes@uchicago.edu to learn more about our studies.