# *GBA* GENE INFORMATION

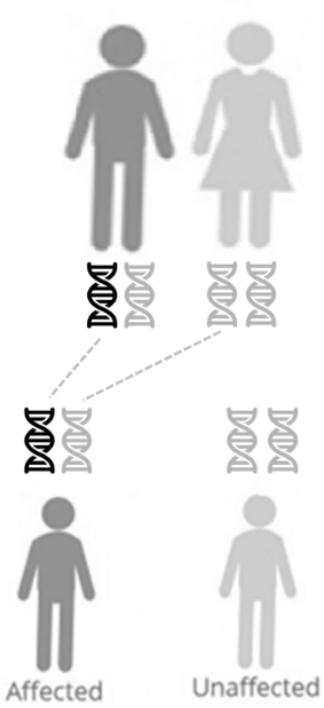
## PARKINSON'S DISEASE FACT SHEET

Parkinson's disease is multifactorial in most families; it is likely caused by an interplay of both genetic and environmental factors. A number of genes have been identified as risk factors for Parkinson's disease, with many others still unknown. This fact sheet outlines basic information about the *GBA* gene as well as risk to individuals and their relatives. If you have a *GBA* variant or are concerned about your risk, speaking with a genetic counselor can be helpful.

### *GBA* Variants

Individuals with one or two *GBA* gene variants have a higher risk of developing Parkinson's disease than the general population. The risk of Parkinson's disease increases with age, and may vary depending on the type of variant and whether one or two variants are present. However, many people with a *GBA* variant do not develop Parkinson's disease; this is called incomplete penetrance. It is likely other risk factors are needed for an individuals to develop Parkinson's disease in addition to a *GBA* gene variant.

For Parkinson's disease, *GBA* variants are inherited in an autosomal dominant fashion (see Figure). This means that a person only needs to inherit one *GBA* gene variant to have an increased risk of Parkinson's disease. This also means that both males and females can pass on and inherit the variant.




Variants in the *GBA* gene are inherited (or passed on) through families, and therefore each child of a person with a *GBA* variant has a 50% (or 1 in 2) chance to inherit the variant. Similarly, this individual has a 50% (or 1 in 2) chance to not inherit the variant from their parent. Only one *GBA* variant is needed to have a risk of Parkinson's disease risk. Having two *GBA* gene variants is associated with a risk of Parkinson's disease, as well as a condition call Gaucher disease (see below).

Variants in the *GBA* gene are the most common genetic factor currently associated with Parkinson's disease. Approximately 20% of Parkinson's disease patients of Ashkenazi Jewish descent will carry a *GBA* variant, while approximately 7% of Parkinson's disease patients of non-Jewish ancestry will carry a *GBA* variant. Over 300 different *GBA* variants have been identified. There is a very common *GBA* variant called N370S that makes up 70% of all reported *GBA* variants in the Ashkenazi Jewish population.

Two unique *GBA* variants, T369M and E326K, have recently been reported. These variants are considered susceptibility factors for Parkinson's disease, and more research is needed to better understand how they impact the risk for Parkinson's disease. Both variants are commonly found in the general population, and do not appear to cause Gaucher disease.

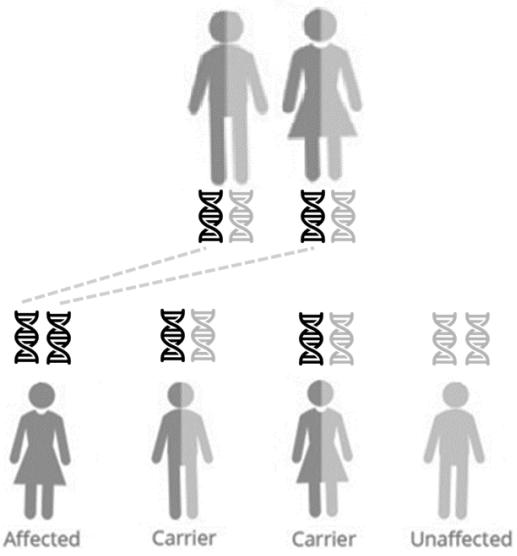
### Gaucher Disease

When an individual has a variant in both *GBA* genes, they will usually have a condition called Gaucher disease. Symptoms of Gaucher disease include enlarged spleen/liver, abnormal blood cell counts, bone pain, fractures and, in some cases, neurologic problems. There are three recognized types of Gaucher disease. Type 1 is the most mild and common type, and can be either childhood or adult onset. There is treatment available for type 1 Gaucher disease called enzyme replacement therapy, which may help reduce many of the symptoms of the condition. Individuals with type 2 or 3 or other types of Gaucher disease may have more severe symptoms.

## Gaucher Disease *(cont.)*

Gaucher disease is usually diagnosed by measuring the amount of the beta-glucocerebrosidase enzyme through a blood test. Genetic testing for *GBA* variants can provide confirmation of a diagnosis of Gaucher disease. However, some types of genetic testing may not identify all variants that cause Gaucher disease.

Gaucher disease is an autosomal recessive disorder (see Figure). This means a person with a variant in both copies of the *GBA* gene will usually have Gaucher disease. A person with a variant in one copy of the *GBA* gene is called a carrier and not affected with Gaucher disease, but is at an increased risk for Parkinson's disease (see above).




A person with Gaucher disease typically inherits one *GBA* variant from their mother and one from their father. Parents and children of a person with Gaucher disease are all carriers of a *GBA* variant, and thus at an increased risk for Parkinson's disease. Other relatives may be carriers, too.

It is estimated that about 1 in 100 individuals in the general population and 1 in 18 individuals with Ashkenazi Jewish ancestry carry a *GBA* gene variant. *GBA* variant carriers often have no family history of Gaucher disease. Carrier screening is a genetic test that some people choose to have as part of the family planning process. A person who has carrier screening is sometimes screened for Gaucher disease and may learn *GBA* carrier status as part of this process.

## Research Opportunities

Many research studies are interested in enrolling people with *GBA* variants. This is true whether or not that person or anyone else in their family has Parkinson's disease. Some studies are trying to understand more about the causes of Parkinson's disease. Other studies are working to develop new treatments. Trials of new medications for people with Parkinson's disease and *GBA* variants are ongoing.

Various research projects at the Indiana University School of Medicine include genetic testing and genetic counseling for Parkinson's disease. These projects enroll volunteers with and without Parkinson's disease. To learn more, please contact our team at wrd@iu.edu or call 888-830-6299.

## References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